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THE FUNCTIONAL ABILITY AND HEALTH RELATED QUALITY OF LIFE OF SURVIVORS OF CRITICAL ILLNESS AFTER HOSPITAL DISCHARGE

Johannes van Aartsen
BSc Physiotherapy (Wits)

Dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Master of Science in Physiotherapy

Johannesburg, 2016

DECLARATION

I, Johannes van Aartsen, declare that this dissertation is my own work. It is being submitted for the degree of Master of Science in Physiotherapy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

_____

29th day of August, 2016

DEDICATION

Dedicated to my Saviour, Fiancé, Family, Colleagues and Patients

ABSTRACT

Background: Critically ill patients face physical, psychological, and health-related quality of life (HRQOL) problems. Factors relating to the intensive care unit (ICU) stay of a critically ill patient may affect a patient's HRQOL after discharge from hospital and may include the development of acute respiratory distress syndrome (ARDS) and sepsis, prolonged length of mechanical ventilation (MV) and prolonged periods of immobility. Organ dysfunction and multiple organ failure (MOF) influence a patient's QOL after hospital discharge. The presence of chronic diseases such as chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and obesity may also contribute to the development of and severity of critical illness. Survivors of critical illness may be confronted with major problems during their recovery from critical illness. Limited South African data is available regarding the QOL of survivors of critical illness and limited research evidence is available to support rehabilitation services for this population after hospital discharge.The population of South Africa is a complex society and therefore has its own unique challenges that patients may face on a daily basis after a period of critical illness. These challenges may result in patients experiencing functional problems and a reduced HRQOL after critical illness. The aim of this study was to determine the functional ability and HRQOL of survivors of critical illness when assessed in the first six months after discharge from hospitals in South Gauteng.

Methods: A prospective, observational, and longitudinal study was conducted using patients, who met the inclusion criteria for the study, in the ICU's of a private hospital in Johannesburg. The acute physiology and chronic health evaluation II (APACHE II) and simplified acute physiology score II (SAPS II) were calculated and recorded for enrolled participants, as well as duration of MV, ICU length of stay (LOS) and hospital LOS. The physical function in ICU test scored (PFIT-s) was performed at the time of discharge from ICU and repeated at discharge from hospital. At one and six months after discharge from hospital, participants' peripheral muscle strength was measured using a handheld dynamometer (HHD), exercise endurance was assessed using the six minute walking test (6MWT), and participants completed the short form 36 (SF-36) questionnaire, EuroQol Group 5 dimension (EQ-5D) questionnaire, patient health questionnaire (PHQ-9) and recent physical activity questionnaire (RPAQ).

Results and Discussion: Twenty-four participants were enrolled into the study. The mean age was 51 (± 13.8) years, the majority were male (n=19, 79.2%), and most participants were employed (n=20, 83.3%) prior to the onset of critical illness. Half of the participants in

this study presented with pre-existing disease prior to critical illness (n=12; 50%). Majority of participants underwent surgical interventions (n=19, 79.2%) which led to ICU admission and half of participants (n=12, 50%) reported having pre-morbid disease. All participants in the current study received physiotherapy treatment for the duration of their hospital stay. A significant change between mean PFIT-s interval scores (p=0.02) at ICU discharge and hospital discharge was found with a 0.4 points (± 0.7) change in interval scores. This change was not clinically significant, suggesting that not all the rehabilitation needs of these participants, who were recovering from critical illness, were met before their discharge from hospital. The increase in median 6MWT distance achieved was 65 meters, this being of clinical significance. There was no significant change in mean 6MWT distance achieved (53 meters ± 74.9).The limited mean distances that participants in this study were able to achieve during the 6MWT suggests that their endurance is impaired, which may impact their ability to perform activities of daily living. A marginally significant relationship was found between 6MWT distance at one month follow-up and SF-36 mental component score (MCS) at six months (p=0.05).

Significant mean changes in peripheral muscle strength over six months after discharge were observed for right-sided (dominant side in all participants) elbow flexion (17.3 ±15.7, p=0.00), elbow extension (32.6 ± 37, p=0.02), hip abduction (53.4 ± 52.3, p=0.01), knee extension (59.9 ± 40.3, p=0.00), knee flexion (42.4 ± 31.3, p=0.00) and ankle dorsiflexion (29.9 ± 36.9, p=0.02), left-sided hip abduction (36.4 ± 45.2, p=0.02), knee flexion (40 ± 43.3, p=0.01), and ankle dorsiflexion (43.3 ± 48.1, p=0.03). The fact that majority of participants in this study lived alone may account for the improvements in muscle strength observed as they would be dependent on themselves for performing daily activities.The median PHQ-9 score showed an improvement of 2 points between one month and six months follow-up. A significant change in mean SF-36 physical component score (PCS) of 8.8 points (± 7.6, p=0.00) was observed over the six months period. This relates to improvements in the physical domain of HRQOL over the first six months after discharge from hospital following critical illness. The significant improvement in HRQOL related to PCS in the current study may be due to the fact that most participants lived alone and were self-dependent for daily activities even though they had some form of support from family and friends, and some of them had also returned to work by six months following discharge. Participants in the current study had several co-morbidities which may also have contributed to the lower observed mean PCS scores at six months. Significant changes in mean SF-36 domain scores were observed over six months for the role physical (RP) (p=0.00), bodily pain (BP) (p=0.05), general health (GH) (p=0.00), vitality (VT) (p=0.01) and the social functional (SF) (p=0.00). A significant mean change of 14.6 points (± 9.7) in EQ-5D visual analogue scale (VAS) scores

was observed over six months after discharge. Participants' abilities to mobilise, care for themselves and participate in usual activities (measured using the EQ-5D) improved over time as they continued to recover from critical illness. Large reduction in level of pain and discomfort experienced at six months as measured with the EQ-5D questionnaire may be due to wound healing that took place as the majority of participants underwent surgery. A significant relationship was found between the SF-36 PCS at one month follow-up and severity of illness (SAPS II) scores.Very weak and weak relationships were found between the SF-36 PCS and APACHE II scores (r=0.036) and SAPS II scores (r= 0.31) and moderate strength relationships were found between SF-36 PCS and PHQ-9 scores (r= -0.49) and 6MWT distance (r= 0.54) at six months follow-up. None of these relationships were statistically significant. Moderate strength negative relationships which were statistically significant, were identified between the SF-36 MCS and ICU LOS (r= -0.56; p=0.04) and hospital LOS (r= -0.56; p=0.04) at six month follow-up. A strong negative relationship was found between the SF-36 MCS at six months follow-up and duration of MV which was statistically significant (r= -0.7; p= 0.01). A strong negative relationship was found between SF-36 MCS scores and PHQ-9 scores at six months after discharge from hospital which was statistically significant (r= -0.72; p= 0.01). The main reasons reported by participants for not returning to work were pensioner status and physical weakness; however, at six months more than half of participants had returned to employment. The presence of depressive disorders did not directly influence return to work. The relatively good return to work rate observed may be attributed to the significant increases in muscle strength and PCS observed as well as the reduction in problems reported in relation to mobility, self-care, pain or discomfort and participation in usual activities over the first six months following discharge. Length of MV, SF-36 MCS and SF-36 PCS scores had no statistically significant relationship with exercise endurance at six months after hospital discharge. Limitations to this study include the small sample size and high drop-out rates.

Conclusion: Survivors of critical illness in Gauteng province suffered from limitations in functional abilities at ICU discharge and improvements observed at hospital discharge were not clinically significant. Even though peripheral muscle strength improved significantly for participants in the six months following discharge, they still presented with limitations in exercise endurance. Significant improvements were observed in QOL related to physical functioning but little improvements were observed for QOL related to mental health. Some participants presented with symptoms of depression. More than half of participants returned to employment by six months following discharge. Findings from this study suggest that survivors of critical illness don't recover fully on their own after an episode of acute illness. These results should be used to motivate for implementation of structured rehabilitation

programmes, including counselling, to aid the physical, emotional and mental recovery of survivors of critical illness in the long term after hospital discharge.

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LIST OF ABBREVIATIONS

6MWT	: 6 Minute Walking Test
APACHE II	: Acute Physiology and Chronic Health Evaluation II
ARDS	: Adult Respiratory Distress Syndrome
ATS	: American Thoracic Society
BP	: Bodily Pain
BMI	: Body Mass Index
COPD	: Chronic Obstructive Pulmonary Disease
CI	: Confidence Intervals
CABG	: Coronary Artery Bypass Graft
CIM	: Critical Illness Myopathy
CIP	: Critical Illness Polyneuropathy
DM	: Diabetes Mellitus
DALY'S	: Disability-Adjusted Life Years
EQ-5D	: EuroQol Group 5 Dimension
GH	: General Health
HHD	: Hand-held Dynamometry
HRQOL	: Health Related Quality of Life
HIV	: Human Immunodeficiency Virus
ICU	: Intensive Care Unit
ICU-AW	: Intensive Care Unit Acquired Weakness
LOS	: Length of Stay
MOS	: March On Spot
MV	: Mechanical Ventilation
MRC	: Medical Research Council
MCS	: Mental Component Score
MH	: Mental Health
MCID	: Minimally Clinically Important Difference
MOF	: Multiple Organ Failure
NIV	: Non-Invasive Ventilation
PHQ-9	: Patient Health Questionnaire
PCS	: Physical Component Score
PF	: Physical Function
PFIT	:Physical Function in ICU Test
PFIT-s	: Physical Function in ICU Test Scored

QOL	: Quality of life
RPAQ	: Recent Physical Activity Questionnaire
RE	: Role Limitations due to Emotional Problems
RP	: Role Physical
SF-36	: Short Form 36
SAPS II	: Simplified Acute Physiology Score II
SF	: Social Functional
SD	: Standard Deviation
SIRS	: Systemic Inflammatory Response Syndrome
VAS	: Visual Analogue Scale
VT	: Vitality
WHO	: World Health Organisation

CHAPTER 1

1. INTRODUCTION

1.1 BACKGROUND

Patients admitted to intensive care units (ICU's) due to critical illness may face reduced quality of life (QOL) after discharge from hospital. There are many definitions of health related QOL (HRQOL) available in the literature; however, there is not one universally accepted definition. A commonly used definition for health is that provided by the World Health Organisation (WHO, 1948). They define health as "A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (WHO, 1948, p.1). One of the basic rights of every human being is to be able to enjoy the highest level of health attainable (WHO, 1948). The WHO QOL Group defines QOL as being the perception of a person of his or her own position in life in the specific context of the value and culture systems in which he or she lives. This is relative the individual's goals, expectations, standards, and concerns (WHO, 1995). Mendlowicz and Stein (2000) describe QOL as being a person's perception of the quality of his or her own life. They further describe QOL to be multi-dimensional as it involves a person's social life, health status, and ability to function well during activities of daily living as well as activities at work (Mendlowicz and Stein, 2000). They concluded in their review of epidemiological and clinical studies investigating QOL that a more thorough understanding of the impact of QOL is needed (Mendlowicz and Stein, 2000).

Critically ill patients admitted to ICU face physical, psychological, and HRQOL problems (Rattray, 2013). Survivors of critical illness may suffer from health problems of a physical and psychological nature for an extended period of time after discharge. These health problems consequently impact negatively on a patient's social life (Ramsay, et al., 2012). According to Rattray (2013), physical difficulties may include muscle wasting, muscle weakness, fatigue, lethargy, ICU-acquired weakness (ICU-AW) covering both critical illness myopathy (CIM) and critical illness polyneuropathy (CIP). Recently there has been a shift in approaches in the assessment of the quality of care in ICU's with more emphasis being placed on a patient's functional abilities and QOL instead of mortality rates (Boots, et al., 2013). Psychological problems may include anxiety, depression, post-traumatic stress, delirium and cognitive dysfunction (Rattray, 2013). All these difficulties may influence HRQOL negatively. This reflects in the HRQOL of survivors of critical illness being consistently poorer than that of the

general population norms when using standardized measures of HRQOL such as the Short Form-36 (SF-36) Health Survey and the EuroQol Group 5 Dimension (EQ-5D) questionnaires (Rattray, 2013). Survivors of critical illness may also be faced with problems when they need to return to their occupation.

Factors relating to the ICU stay of a critically ill patient may affect such a patient's HRQOL after discharge from hospital. Such factors may include development of acute respiratory distress syndrome (ARDS) and sepsis, prolonged duration of mechanical ventilation (MV) and prolonged periods of immobility. Organ dysfunction or failure developed during a patient's ICU stay may have consequences on the HRQOL of such a patient after hospital discharge (Ivaskevicius, et al., 2011). When the abovementioned factors are present during the ICU stay of a patient, a significant reduction in HRQOL is seen (O'Neill, et al., 2014).

Many patients with critical illness in ICU's may be treated with prolonged MV. Prolonged MV and prolonged periods of immobility in bed have a major influence on the body including the disruption of endocrine homeostasis, circulatory shock, respiratory failure, catabolism of muscles with subsequent muscle weakness (Van Aswegen, et al., 2011). Consequently, a reduction in muscle mass may have a negative impact on a patient's HRQOL after critical illness (Van Aswegen, et al., 2011).

Other factors present prior to admission to ICU and not directly related to the ICU stay of a patient such as the presence of chronic diseases may also contribute to the development of and severity of critical illness. Chronic diseases contribute 60 to 75 percent of all deaths worldwide and may result in discrepancies in health outcomes between different social groups (WHO, 2005). An important chronic disease worldwide is chronic obstructive pulmonary disease (COPD).

Chronic obstructive pulmonary disease is fourth of the top 10 leading causes of death worldwide. It resulted in approximately 5.8 percent of all global deaths in 2011 as reported by the WHO. Patients suffering from COPD have been shown to have reduced HRQOL as measured using the EQ-5D (Jo, et al., 2014; Wu, et al, 2015). Coventry and Hind (2007) report that patients with COPD present with increased psychosocial morbidity and this consequently impacts negatively on the HRQOL of these patients.

Patients with COPD present with airflow limitation with irreversible respiratory disease. This has a large impact on their physical abilities, social functioning and their sense of well-being (Wu, et al., 2015). Wu et al. (2015) reported that almost 40 percent of COPD participants in their study had problems with mobility, their usual daily activities, pain and discomfort, as assessed using the EQ-5D questionnaire. Twenty percent of their participants also reported problems with self-care activities. The degree of difficulty experienced by these participants was significantly associated with the severity of COPD (Wu, et al., 2015). Not only patients with COPD suffer from reductions in HRQOL, but patients with other chronic diseases also feel the burden of their disease.

Patients with diabetes mellitus (DM) also show increased psychosocial morbidity and resultant reduction in HRQOL (Coventry and Hind, 2007). They are reported to have a lower HRQOL as compared to the general population as reflected in lower SF-36 scores of the physical functioning (PF), role limitations due to emotional problems (RE), and global HRQOL domains compared to scores for the general population (Ak, et al., 2015). These patients also have a higher incidence of anxiety and depression when compared to the general population, consequently having a detrimental effect on their HRQOL (Bahar, 2006). When DM occurs in combination with other chronic diseases, patients show a further reduction in HRQOL (Johnson, 1996). The HRQOL of patients with DM type two is influenced by low quality sleep, mild depression, and mild anxiety which may ultimately result in a reduced HRQOL for these patients (Ak, et al., 2015).

Patients with cardiac disease may also experience reduced HRQOL. Limited literature is available regarding the HRQOL of patients undergoing coronary artery bypass graft (CABG) surgery pre- and post-operatively (Oberai, 2014). Reductions in HRQOL have been reported by some researchers who have shown that there is an association between the reduction in HRQOL and the severity of cardiac disease and mental distress (Peric, et al., 2006; Stafford, et al., 2007; Faller, et al., 2009; Faller, et al., 2011). There are no available South African studies investigating the HRQOL of patients with cardiac disease following a period of critical illness.

It is therefore clear that in the absence of ICU admission and critical illness, patients with chronic diseases such as COPD, DM and cardiac disease experience reductions in QOL (Lopes, et al., 2005; Mallon, et al., 2005; Alves, et al., 2009; Ringburg, et al.,

2011; Ak, et al., 2015). It is however also important to consider the effects of critical illness on the HRQOL of such patients admitted to the ICU.

After a period of critical illness, a patient returns to his or her daily life and this may require that they return to work. The available literature regarding the effect of return to work on patients' HRQOL is conflicting. Some studies suggest a positive effect of actively working on HRQOL (Cox, et al., 1992; Chan, et al., 1994). Others suggest that there is no association between actively working and HRQOL (Talbot and Nülmen, 2000). There is limited literature regarding the financial impact of a period of critical illness on a patient and his or her immediate family (Griffiths, et al., 2013). Critical illness has been shown to have a negative effect on a patient's socio-economic status (Griffiths, et al., 2013).

As with COPD and DM, those patients admitted to ICU with pneumonia, respiratory failure, organ dysfunction, surgical interventions, penetrating and blunt trauma to the trunk who undergo surgical intervention as a result of the injuries sustained, and patients admitted for elective and non-elective cardiac surgeries (for example mitral valve replacements, aortic valve replacements, and CABG) may also suffer from reduced HRQOL (Dowdy, et al., 2005; Orwelius, et al., 2010; Van Aswegen, et al., 2010; Van Aswegen, et al., 2011; Goixart, et al., 2013; Scheneiderman, et al., 2013; De Jongh, et al., 2014; Di Battista, et al., 2014). This may be related to the detrimental effects of critical illness and its negative influences on the HRQOL of critically ill patients.

As survivors of critical illness may be confronted with major problems during their recovery and rehabilitation from critical illness, the outcomes of intensive care cannot be assessed only by patient's survival rates, but should be expanded to include the return to an acceptable HRQOL (Rattray, 2013). Furthermore, limited literature is available to support rehabilitation services after hospital discharge (O'Neill, et al., 2014). Clarity is needed on where the focus of rehabilitation after hospital discharge should be (O'Neill, et al., 2014).

1.2 STATEMENT OF PROBLEM AND JUSTIFICATION FOR RESEARCH

In view of the information shared in section 1.1 (mostly from international reports) it would be reasonable to assume that patients admitted to ICU in hospitals in South Africa may be faced with similar physical, psychological or social difficulties after discharge from these units and from hospital as reported in the abovementioned studies. Delay in return to occupation may also be a reality for ICU survivors in South

Africa. The survival rate of critically ill patients has improved in recent years and this requires the assessment of the HRQOL of the increased number of survivors of critical illness (Rubenfeld, et al., 1999; Angus and Carlet, 2003). It is important to understand the HRQOL of patients recovering from critical illness as they face increased risk of mortality after discharge. This is required to ultimately assess the effect of specific interventions during a period of critical illness on these patients (Dowdy, et al.,2005).Even with the achievement in intensive care outcomes, survivors of critical illness face an increased risk of mortality for a few years after discharge from hospital (Wright, et al., 2003; Williams, et al., 2005; Williams, et al., 2008).

Limited literature is available regarding the HRQOL of survivors of critical illness within the South African population. A study conducted by Van Aswegen et al. (2011) investigated the HRQOL of survivors of penetrating trunk trauma in Johannesburg. This was the first study of its kind in South Africa. Almost 60 percent of all cases of trauma admitted to South African hospitals are admitted with penetrating trunk injuries(Van Aswegen, et al., 2011). Van Aswegen et al. (2011) reported that participants who survived critical illness showed significant initial reductions in HRQOL; however, this improved in the first six months after discharge. They also reported that those patients requiring MV for prolonged periods of time experienced more impairment in the PF domain of HRQOL compared to the mental health (MH) domain at six months after discharge from hospital (Van Aswegen, et al., 2011). A cross-sectional study conducted in Johannesburg by Schneiderman et al. (2013), investigating the HRQOL of survivors of trauma six months after discharge, showed that these patients experienced reductions in the emotional and physical domains of HRQOL at six months after discharge from hospital.

Another South African study by Karachi et al. (2011), conducted in the Western Cape province, investigated the survival and HRQOL of 46 patients at 12 months following discharge from an adult surgical ICU. They found that severity of illness as measured using Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were correlated to long-term patient survival and the physical functioning domain of HRQOL. Health related quality of life was also found to be slightly lower than that of comparable international ICU populations (Karachi, et al., 2011). As their study focused on the surgical ICU patient population, further research is required to investigate the HRQOL of survivors of critical illness in other ICU subgroups such as

the medical, trauma (blunt trauma to the thorax) and cardiac patient populations in South Africa.

Certain limitations have been reported in these South African studies investigating the HRQOL of survivors of critical illness. Karachi et al. (2011) reported difficulties in generalising their results to the surgical ICU patient population due to a small sample size. Van Aswegen et al. (2010) reported from their prospective observational study a small sample size and a high dropout rate of 46 percent in their short term MV study group. They speculated that a possible reason for the high drop out in this group was that these patients felt well enough to deem follow-up assessment as unnecessary. Two international studies by Cuthbertson et al. (2005) and Michaels et al. (2000) also reported a high dropout rate in the trauma patient population. Small sample sizes and high dropout rates in HRQOL studies are thus well-documented in the literature and needs to be addressed in future studies.

Other reported problems in HRQOL studies are that of missing data and language barriers. Schneiderman et al. (2013) reported missing data during their cross-sectional study(level three evidence) of the HRQOL of survivors of trauma as the APACHE II scores for all participants were not obtained on admission. They also reported that some of their participants struggled to comprehend the English language used in the SF-36 version one questionnaire. The issue of missing data in HRQOL studies was confirmed by a systematic review conducted by Dowdy et al. (2005) investigating HRQOL of adult survivors of critical illness. They reported inconsistencies in baseline data reporting and reporting methods. Future HRQOL research should emphasize the punctual and accurate collection of baseline data as this is lacking in the current literature.

The shortfalls in the current available literature on HRQOL after critical illness are therefore the following; limited South African data; small sample sizes; high dropout rates; missing baseline data; comprehension of the language used in certain HRQOL questionnaires.

Survivors of critical illness in South Africa may have other important factors influencing their recovery from critical illness after discharge from hospital. These factors may include socioeconomic status, poverty, residential environment, work situation, and cultural factors. All of these factors may affect a patient's willingness to and opportunities to obtain rehabilitative services after critical illness. The population of South Africa is a complex society and therefore has its own unique challenges that

patients may face on a daily basis after a period of critical illness. These challenges may result in patients experiencing functional problems and a reduced HRQOL after critical illness. Due to the unique challenges faced by South African survivors of critical illness, results from international studies may not always be applicable to the South African patient population. More information is thus needed to provide insight into the functional abilities and HRQOL of survivors of critical illness in the first six months after hospital discharge in South Africa with attention being paid to the abovementioned shortfalls in the literature. The current study aimed to determine the functional ability and HRQOL of survivors of critical illness when assessed in the first six months after discharge from hospitals in South Gauteng.

1.3 RESEARCH QUESTIONS

1.3.1 What are the functional and physical abilities of survivors of critical illness at ICU discharge and how do these change at hospital discharge and over the first six months after discharge?

1.3.2 What is the HRQOL of survivors of critical illness and how does it change over the first six months after discharge from hospital?

1.3.3 Do survivors of critical illness return to employment within the first six months after hospital discharge?

1.4 RESEARCH AIMS

1.4.1 To determine functional ability of survivors of critical illness at the time of ICU discharge and at hospital discharge.

1.4.2 To determine physical activity and HRQOL of survivors of critical illness over the first six months after hospital discharge.

1.4.3 To determine if survivors of critical illness return to employment within six months after hospital discharge.

1.5 RESEARCH OBJECTIVES

1.5.1 To establish the level of functional ability of survivors of critical illness at discharge from ICU and to determine changes in their level of functional ability at hospital discharge.

1.5.2 To establish the exercise endurance and peripheral muscle strength of survivors of critical illness at one month after hospital discharge and to determine changes in their exercise endurance and peripheral muscle strength at six months.

1.5.3 To establish the level of depression of survivors of critical illness at one and six months after discharge from hospital and to determine changes in level of depression at six months.

1.5.4 To establish baseline levels of physical and mental health domains of HRQOL of survivors of critical illness at one month after hospital discharge and to determine changes in these domains of HRQOL at six months.

1.5.5 To establish the level of physical activity of survivors of critical illness at one and six months after discharge and to determine changes in physical activity at six months.

1.5.6 To determine if survivors of critical illness return to employment in the first six months after hospital discharge.

1.5.7 To determine if a relationship exists between functional ability and severity of illness on ICU admission [APACHE II and Simplified Acute Physiology Score II (SAPS II)], duration of MV, ICU length of stay (LOS) and hospital LOS.

1.5.8 To determine if a relationship exists between exercise endurance and severity of illness on ICU admission (APACHE II and SAPS II), duration of MV, ICU LOS and hospital LOS, HRQOL, level of depression of survivors of critical illness at one and six months after discharge

1.5.9 To determine if a relationship exists between HRQOL and severity of illness, duration of MV, ICU LOS and hospital LOS, level of depression and exercise endurance of survivors of critical illness at one and six months after discharge.

1.5.10 To determine if a relationship exist between level of depression and return to employment in the first six months after hospital discharge.

1.5.11 To determine which factors influence exercise endurance at six months after hospital discharge.

1.5.12 To determine which factors influence HRQOL at six months after hospital discharge.

1.6 TYPE OF STUDY

A prospective, observational, longitudinal study was conducted in order to answer the research questions and objectives.

1.7 HYPOTHESES

1.7.1 Alternate Hypothesis

1.7.1.1 Participants who were admitted to ICU due to critical illness suffer from limitations in physical activity and HRQOL at six months after hospital discharge.

1.7.1.2 Participants who survived critical illness do not return to employment in the first six months after hospital discharge.

1.7.2 Null Hypothesis

1.7.2.1 Participants who were admitted to ICU due to critical illness do not suffer from limitations in physical activity or HRQOL at six months after hospital discharge.

1.7.2.2 Participants who survived critical illness return to employment in the first six months after hospital discharge.

1.8 SIGNIFICANCE OF RESEARCH

The current study contributes to the available limited evidence in South Africa relating to the functional ability and HRQOL of survivors of critical illness at ICU discharge and over the first six months after discharge from hospital. This information, together with data from existing studies, provides an indication of where rehabilitation interventions should be focused by exposing the possible causes of prolonged recovery, reduced functionality and poor HRQOL of patients recovering from critical illness. Based on this information, rehabilitation interventions may be developed and its effectiveness tested in improving functional ability and HRQOL for survivors of critical illness in South Africa in future research.

CHAPTER 2

The following chapter will consist of the review of literature pertaining to worldwide and South African burden of chronic diseases of lifestyle, acute respiratory tract infections, and trauma; the effect of these on ICU admission rates; the complications of and risks associated with diseases of lifestyle; respiratory diseases or infections and the role they play in development of respiratory failure; the effects of hypovolaemic shock on oxygenation levels; severity of illness scoring systems used in ICU; the effects of immobility and critical illness on physical recovery; ICU-AW and post-ICU syndrome; changes observed in muscle power and exercise endurance of survivors of critical illness after discharge from hospital; the functional and physical abilities of survivors of critical illness as reported by other researchers; effects of critical illness on MH; and recovery from critical illness in the South African context. The outcome measures used to assess the functional ability and HRQOL of survivors of critical illness in this study will also be explored. The available literature involves studies with levels of evidence two and three.

2. LITERATURE REVIEW

2.1 INTRODUCTION

Patients are admitted to ICU's for various reasons which may include respiratory failure, dysfunction or disease of one or more organ, multiple injuries or following surgery (Benson, et al., 2011; Du, et al., 2013). Patients admitted to ICU are often critically ill. These patients are faced with many challenges, both during their ICU stay and during recovery after discharge from the ICU. These challenges may include immediate life-threatening conditions, organ failure, ICU-AW, and depression (Rattray, 2013). Survival rates for patients with critical illness have increased (Rubenfeld, et al., 1999; Angus and Carlet, 2003), however, the challenges experienced by these individuals are not only limited to the hospital environment. Patients may face challenges and potential problems after discharge from hospital resulting in difficult and often extended recovery from critical illness (Rattray, 2013). These challenges may be physical, social, emotional or cognitive in nature. The assessment of the success of intensive care provision should thus include the return of a patient to an acceptable level of HRQOL. There has consequently been a shift of research focus to the investigation of HRQOL of survivors of critical illness (Wright, et al., 2003; Dowdy, et al., 2005; Williams, et al., 2005; Williams, et al., 2008).

The following search engines and databases were used to find relevant literature for this review: Elton Brysan Stephens Company Host, Cumulative Index to Nursing and Allied Health Literature, Public Medical Literature Analysis and Retrieval System online, The Cochrane Library, Physiotherapy Evidence Database, and Google Scholar. The following key words and combinations of key words were used to identify relevant information for the study topics: critical illness and QOL; physical function in ICU Test (PFIT); six minute walking test (6MWT); EQ5-D; SF-36; Patient Health Questionnaire (PHQ-9); depression; depression after critical illness; PHQ-9 and critical illness; PHQ-9 and ICU; Pro-inflammatory Cytokine Storm; Systemic Inflammatory Response Syndrome (SIRS); SIRS and QOL; APACHE II and SAPS II; APACHE II; critical illness; PHQ-9 and ICU; EQ-5D and ICU; EQ-5D Afrikaans; SF-36 Afrikaans; validation of the Afrikaans SF-36; validation of the Zulu SF-36; validation of the Sotho SF-36; COPD and QOL; DM and QOL; hand-held dynamometry (HHD); HHD validity and reliability; Recent Physical Activity Questionnaire (RPAQ); WHO and World Bank global burden of disease; cardiac disease and QOL; pneumonia and QOL; organ dysfunction and QOL; trauma and QOL; QOL after ICU in South Africa; incidence DM; DM; DM South Africa; COPD South Africa; COPD incidence; COPD incidence South Africa; COPD prevalence; obesity; obesity prevalence; obesity incidence; obesity incidence South Africa; obesity incidence global; pneumonia incidence; pneumonia incidence South Africa; bronchitis South Africa; hypovolaemic shock and oxygenation; shock and oxygenation; shock; hypovolaemia; respiratory failure; critical illness and respiratory failure; respiratory infections; critical illness and return to work; critical illness and return to work South Africa; ICU admission rates; SAPS II and QOL; APACHE II and QOL; and ICU admission rates South Africa.

Publications from all years up to and including February 2016 were included in the search. English language full text articles and abstracts were selected from the lists generated by the search and were reviewed.

2.2 INCIDENCE AND PREVALENCE OF DISEASE

2.2.1 Diseases of Lifestyle

Diseases associated with lifestyle account for 60 to 75 percent of all deaths worldwide and these diseases are one of the main causes resulting in differences in health between different groups in society (Kenealy, et al., 2015). Many patients are admitted to the ICU with exacerbations of chronic diseases such as COPD and DM.

Chronic obstructive pulmonary disease is defined by Boon, et al. (2006) as the presence of airway obstruction which does not change significantly over several months and is not fully reversible. According to the WHO, COPD is the fourth leading cause of death worldwide and by 2020, it is predicted to be the third (WHO, 2010; Biron, et al., 2014). The WHO and World Bank global burden of disease study published in 1990, reported that the prevalence of COPD worldwide is 9.33 per 100 000 people for males and 7.33 per 100 000 people for females (Murray and Lopez, 1996). In sub-Saharan Africa the prevalence was found to be 4.41 per 100 000 people for males and 2.49 per 100 000 people for females (Murray and Lopez, 1996). The 2010 WHO and World Bank global burden of disease study does not provide updated figures on the abovementioned statistics. The 1990 study noted that the prevalence of COPD may be higher than the figures mentioned due to the fact that COPD is usually only diagnosed when the disease has reached a moderately advanced stage and is mostly diagnosed after the age of 45 (Ait-Khalet, et al., 2001). The 2014 WHO Non-communicable Diseases Country Profile for South Africa reported that chronic respiratory diseases accounted for three percent of all deaths across all ages and both genders(WHO, 2014).The most important etiological factor in COPD is tobacco smoking. Tobacco smoking accounts for more than 75 percent of worldwide cases of COPD (Gross, 1994; Burchfiel, et al., 1995; Kerstjens, et al., 1997). The WHO Non-communicable Diseases Country Profile for South Africa reported that the total percentage of the South African population who smokes was 18 percent in 2011 (WHO, 2014).It has been reported that the prevalence of COPD in Africa is largely related to pollution in the workplace (Ait-Khalet, et al., 2001).

Chronic obstructive pulmonary disease has been reported to be among the top 20 causes of death in South Africa in 2000 accounting for 113 499 deaths (Bradshaw, et al., 2003). The South African Demographic and Health Survey (2003) reported that the highest prevalence of self-reported chronic bronchitis and asthma in the Western Cape was found in female patients (5.7 percent and 8.9 percent respectively), with the second highest found in males (3.4 percent and 5.7 percent respectively) (Ehrlich and Jithoo, 2006; DOH, 2007). The Burden of Obstructive Lung Disease study conducted in 2007 found the prevalence of mild and moderate COPD to be 19.1 percent in Cape Town. This study did not report the prevalence of COPD for Johannesburg (Bradshaw, et al, 2000).

Chronic obstructive pulmonary disease may result in a patient being admitted to an ICU. Patients suffering from acute exacerbations of COPD who are admitted to the

ICU with acute hypercapnic respiratory failure often have poor outcomes. These patients may require intubation and mechanical ventilation. Patients with COPD admitted to ICU have mortality rates as high as six to 24 percent, increasing to 14 to 57 percent in patients requiring ventilator support. The mortality rate of these patients is influenced by factors such as the type of ICU, the presence of co-existing diseases and personal characteristics of the patient (Alatas, et al., 2006).

Biron et al. (2014) found that patients with COPD experienced reductions in HRQOL, with HRQOL being lower in women affected by the condition as compared to men. The progressive deterioration of the respiratory system and the systemic effects of COPD result in disability due to dyspnoea, fatigue and reductions in exercise tolerance. Consequently, these patients present with reductions in HRQOL (Basuthakur, et al., 2015).

One of the most frequently diagnosed chronic metabolic diseases of lifestyle is DM type two. Diabetes mellitus is a characterised by raised levels of blood glucose associated with abnormal fat, protein and carbohydrate metabolism (Abbas, et al., 2015). Some risk factors have been identified for the exacerbation of the disease. These include poor education status, low income, smoking, obesity, and the female gender (Gebel, 2011; Australian Diabetes Council, 2014). Diabetes mellitus type two occurs worldwide with 300 million people expected to have the condition by 2025 (International Diabetes Federation, 2006). There are few epidemiological studies related to the prevalence of DM in South Africa. The South African demographic and health survey conducted in 1998 (MRC, 1998) investigating the demographics and health of the South African population found that the self-reported prevalence of DM was 2.4 percent for males and 3.7 percent for females. The Gauteng province reported a prevalence of 4.3 and 3.3 percent respectively for females and males (MRC, 1998). In the urban areas the prevalence was found to be 4.4 and 2.9 percent for females and males respectively. A much lower prevalence was found in the rural areas of South Africa (2.7 and 1.7 percent for females and males respectively). The study had a large sample size of 13827 adults aged 15 years and older (MRC, 1998).Although valuable, these statistics are however outdated and more up to date statistics are now available. Diabetes mellitus is a major financial burden on healthcare facilities worldwide (Boon, et al., 2006). Diabetes mellitus accounted for 1.1 million deaths worldwide in 2004 (1.9 percent of all worldwide deaths) according to the 2004 update on the 2010 World Bank Global Burden of Diseases Study. This updated report found that DM affects 9.7 million people in Africa in 2004 (WHO,

2008). The 2010 World Bank Global Burden of Disease Study reported that globally, DM is the fourteenth leading cause of disability-adjusted life years (DALY's) and twenty fourth in sub-Saharan Africa. The same study reported that in South Africa, DM is the sixth leading cause of DALY's.The WHO non-communicable Diseases Country Profile for South Africa reported in 2014 that DM accounted for 5.7 percent of all deaths in South Africa in 2012, making it the third leading cause of death in South Africa in 2012 (WHO, 2014). It is clear that DM is a major health concern globally and in South Africa.

Diabetes Mellitus may result in a number of different complications as the chronic hyperglycaemia associated with DM causes damage to many organ systems in the body. Some of these complications include coronary heart disease, myocardial infarctions, cerebrovascular accidents, retinopathy, neuropathies, nephropathy and arterial occlusive disease (Boehme et al., 2015). These complications may be life-threatening and may result in patients being admitted to the ICU and they may suffer from critical illness. This may consequently result in reduced HRQOL and life expectancy.

A major current health concern is the prevalence of obesity worldwide. Obesity is characterised by a body mass index (BMI) of more than 30 kilogram per meter squared associated with alterations in metabolic functions as a result of increased body fat and an accumulation of visceral adipose tissue (Kopelman, et al., 1997). The WHO recognises obesity as a chronic disease. In many countries the prevalence rates tripled in the last 30 years (Walls, et al., 2012). Obesity is a real problem in developed and developing countries (Filozof, et al., 2001; Puoan, et al., 2002; Rivera, et al., 2002). The global incidence of obesity is reported to be 1.3 billion people (WHO, 2005). The South African Medical Research Council (MRC) reported in 2007 that the incidence of obesity or 'being overweight' is as high as 29 percent in adult males and 56 percent in adult females. Another concerning finding by the MRC is that 17 percent of children aged nine years and under in South Africa were found to be overweight (MRC, 2007; Stein, 2007). Daily mortality rates in South Africa due to obesity show that 60 patients die from diseases related to obesity daily (MRC, 2007; Stein, 2007). The WHO Non-communicable Diseases Country Profile for South Africa reported in 2014 that the prevalence of obesity was 31.3 percent of the population in South Africa in 2012 (WHO, 2014).

This disturbing rise in the incidence of obesity in South Africa, more specifically in the women and young children population, may be the result of misconceptions in the

beliefs of these people about the health risk of being overweight or obese (Mvo, et al., 1999; Ndlovo, et al., 1999). A common misconception is that an increased body weight indicates a good health state. Studies reporting on BMI values of different ethnic groups in South Africa have been inconsistent in the reporting of their results and therefore comparisons of results between these studies becomes difficult. The prevalence of obesity was reported by Puoane et al. (2002) to be 31 to 34 percent in black woman, 18 to 24 percent in white women, 20 to 22 percent in Indian women, and 26 to 28 percent in coloured women. Much lower prevalence rates were reported from the same study in some male groups being eight percent in black men, three to nine percent in Indian men, and six to nine percent in coloured men. Fifteen to 20 percent of white men were reported to be obese, representing the highest prevalence rate of all groups (Puoane, et al., 2002).

A major factor which may contribute to the development of obesity is poverty. The inaccessibility of healthy food for a healthy, balanced diet as a result of poverty may lead to obesity as the unhealthy food is consumed on a daily basis because it may be more affordable (Bradshaw, et al., 2000). There are many challenges to the development and implementation of obesity prevention programmes in South Africa. These include poverty as mentioned above, the high incidence of human immunodeficiency virus (HIV) and the ability to access a healthy, balanced food supply (Puoane, et al., 2002).

A method of assessing whether a patient has obesity is the BMI. Cross-sectional studies, however, have shown a relationship between BMI scores and physical activity. They reported that BMI scores increase as physical activity is reduced. Thus, patients with a higher BMI, were reported to have lower levels of physical activity (Cooper, et al., 2000; Ball, et al., 2001; Ewing, et al., 2003; Bernstein, et al., 2004; Thompson, et al., 2004).

Pre-existing obesity is factor that may affect the outcomes of critically ill patients in the ICU. Pepper et al. (2016) reports that a minimum of 25 percent of all adults admitted to the ICU in the United States of America are classified as obese or morbidly obese. Obesity is associated with increased risks of co-morbidities such as DM, cardiovascular disease, musculoskeletal disorders, cerebrovascular accidents, some types of cancer and respiratory and gastrointestinal diseases. These co-morbidities are all linked to premature death and reduced HRQOL (Chittleborough, et

al., 2014). Any of the mentioned co-morbidities to obesity may result in patients being admitted to ICU due to critical illness.

2.2.2 Acute Respiratory Tract Infections

Acute respiratory infections like pneumonia and bronchitis contribute to ICU admission rates. Pneumonia is defined by the Merck manual of medical information as an infection of the alveoli and the tissues around them (Merck, 2003, p. 237). Boon et al. (2006) also describes pneumonia as an acute respiratory illness associated with characteristic changes on lung x-rays. It can be lobar, segmental or multi-lobar in nature. According to Boon et al. (2006), pneumonia can be classified as being community-acquired, occurring in patients with pre-existing lung damage or in those who are immune-compromised or nosocomial. These categories of pneumonia are also described by Merck (2003). Pneumonia is a common condition which can be successfully treated at home. However, 20 to 40 percent of patients diagnosed with pneumonia require admission to hospital (Boon, et al., 2006). Of those patients admitted to hospital, five to 10 percent are critically ill and require admission to an ICU (Boon, et al., 2006). Each of the mentioned categories of pneumonia shows a different presentation in terms of incidence and contribution to mortality rates (Boon, et al., 2006). In sub-Saharan Africa, lower respiratory tract infections were found to be the third leading cause of years of healthy life lost (World Bank, 2010). Community acquired pneumonia is estimated to affect four to five million people annually in the United States of America with 25 percent of patients needing hospital admission (Schmitt, 2010). It usually occurs by droplet spread infection in the community. It contributes five to 12 percent of all lower respiratory tract infections (Boon, et al., 2006). Certain individuals may be more prone to the development of community acquired pneumonia than others. Predisposing factors include smoking, upper respiratory tract infections, alcohol abuse, corticosteroid therapy, advanced age, recent infection with influenza, and the existence of a previous lung disease (Boon, et al., 2006).

Nosocomial pneumonia involves the presence of a new episode of pneumonia which occurs after two days of hospital admission. This type of pneumonia is more often seen in patients with chronic lung conditions admitted to hospital, MV patients, patients with general debilitation, and those patients with aspiration pneumonia. Nosocomial pneumonia affect annually approximately 250 000 people per year in the United States of America and accounts for 15 to 18 percent of all nosocomial infections (Schmitt, 2010). No data related specifically to the ICU admission rates as

a result of pneumonia in South Africa could be identified. Patients who present with a compromised immune system, aspiration of nasopharyngeal or gastric secretions, exposure of the lower respiratory tract to bacteria, or those with bacteraemia are at higher risk of development of nosocomial pneumonia. Nosocomial pneumonia is of particular importance to critically ill patients as the onset of pneumonia in addition to their pre-existing and admission diagnoses may have a major impact on their outcomes (Merck, 2003; Boon, et al., 2006).

Patients with compromised immune systems are more prone to the development of pneumonia, especially *Pneumocystis* pneumonia (Merck, 2003).A laboratory-based surveillance study conducted at 61 South African hospitals reported that 1537 cases of *Pneumocystis Jirovecii* pneumonia occurred between 2006 and 2010 across these hospitals. Eighty-nine percent of these patients were infected with the human immunodeficiency virus (Du Plessis, et al., 2016). These patients may receive drugs which suppress their immune systems or have diseases which impair their immune systems for example HIV. The pathogens resulting in pneumonia in these patients are the same as the pathogens involved in community acquired pneumonia and nosocomial pneumonia (Boon, et al., 2006).

Pneumonia is a major contributor to death rates worldwide. Hospital mortality rates for adult patients are between five and 10 percent (Boon, et al., 2006). Patients who are critically ill in ICU as a result of pneumonia have a mortality rate of as high as 50 percent (Boon, et al., 2006). Those patients treated at home have a mortality rate of less than one percent (Boon, et al., 2006). Pneumonia (together with influenza) was the second leading cause of death in South Africa in 2013 at 5.1 percent accounting for 24 323 deaths (Statistics South Africa, 2014). According to the WHO, the environmental burden of disease of respiratory infections in South Africa is 3.9 DALY's per 100 000 people (WHO, 2009). The WHO Non-communicable Diseases Country Profile for South Africa reported in 2014 that lower respiratory tract infections accounted for 4.2 percent of all deaths in South Africa in 2012, making it the fifth leading cause of death in South Africa in 2012 (WHO, 2014).

Bronchitis is another condition which may result in hospital or ICU admission. Bronchitis is defined as inflammation of the bronchi which is usually causes by infection but may also be as a result of irritation after exposure to gasses or particles (Scanlan, et al., 1990; Merck, 2003, p. 236). Acute bronchitis is characterised by an irritating unproductive cough with tracheitis. When there is involvement of the

bronchi, chest tightness, wheezing and dyspnoea will present. Common complications associated with acute bronchitis are the development of bronchopneumonia, acute exacerbation of bronchial asthma, or acute exacerbation of severe COPD. In patients with severe COPD, acute bronchitis may result in type two respiratory failure (Boon, et al., 2006).

Chronic bronchitis is a disease classified under COPD together with emphysema. Chronic bronchitis is characterised by the enlargement of mucous-secreting glands and an increase in the number of goblet cells in the large airways. This consequently results in excessive secretion of airway mucus and a prolonged productive cough(Scanlan, et al., 1990; Merck, 2003; Boon, et al., 2006). COPD was discussed in section 2.2.1.

2.2.3 **Traumatic Injury**

Patients recovering from traumatic injury also experience reduced HRQOL. According to the WHO global burden of disease update (2004), 10 percent of all deaths worldwide were due to injuries (WHO, 2008). There is a difference between the two genders relating to death due to injuries with one in every eight male deaths being due to injury and one in every 14 female deaths being due to injuries (WHO, 2008). Road accidents are the ninth leading cause of death worldwide which resulted in one point three million deaths in 2004 (WHO, 2008). The worldwide incidence of in injuries sustained in 2004 was 24.3 million from road traffic accidents, 37.3 million from falls, and 17.2 million from violence (including penetrating trauma) (WHO, 2008). These injuries often result in critical illness. The high incidence of violence in South Africa leads to many patients being admitted to South African hospitals with penetrating trunk trauma. Penetrating trunk injury results from injuries caused by firearms or sharp instruments and frequently necessitate surgical intervention (Van Aswegen, et al., 2011). Penetrating trauma accounts for nearly 60 percent of all trauma cases in South African hospitals (Van Aswegen, et al., 2010). A cross-sectional study conducted by Bergen et al. (2014) investigating psychological complaints and HRQOL in severely injured trauma patients concluded that psychological problems are underestimated and plays a major role in the reduced HRQOL experienced by these trauma survivors. It is suggested in the literature that psychological problems may have a greater impact on HRQOL compared to somatic dysfunction or disability (De Jongh, et al., 2014). The WHO Non-communicable Diseases Country Profile for South Africa reported in 2014 that road injuries accounted for two percent of all deaths in South Africa in 2012, making it the tenth

leading cause of death in South Africa in 2012 (WHO, 2014). They also reported that traumatic injuries account for eight percent of all deaths in South Africa across all ages and genders (WHO, 2014).

2.2.4 **Cardiac Disease**

According to the WHO, the environmental burden of disease of cardiovascular disease in South Africa was 3.9 DALY's per 100 000 people (WHO, 2009). In the South African population, hypertension is more prevalent in the black population than in any other race group (Seedat, 1998). One of the important factors in the development of hypertension in black African women is obesity (Seedat, 1998; Van Rooyen, et al., 2000). A major cause of worldwide mortality is coronary artery disease; however, patients' lives can be prolonged due to the developments in CABG surgery (Oberai, 2014). Another important cardiac condition related to coronary artery disease is heart failure. The incidence of heart failure increases with age and is more prevalent in males as compared to females. Two of the most important contributors to the development of heart failure are hypertension and coronary artery disease (Ho, et al., 1993).

In South Africa, 195 people died per day between 1997 and 2004 due to cardiovascular disease-related conditions, 33 from myocardial infarctions and 37 from heart failure (Bradshaw, unpublished). More than half of the cases of cardiovascular disease occur before these patients reach the age of 65 years (Pestana, et al., 1996; Bradshaw, et al., 2003). The highest death rate due to cardiovascular disease in South Africa is found in the Indian population (Norman, et al., 2006).The WHO Non-communicable Diseases Country Profile for South Africa reported in 2014 that ischaemic heart disease and hypertensive heart disease accounted for 4.8 and 2.7 percent of all deaths in South Africa in 2012, making it the fourth and seventh leading causes of death in South Africa respectively in 2012 (WHO, 2014). The cardiac diseases described above are life-threatening and patients are often admitted to ICU for close monitoring. Such patients may contract infections in the ICU setting or develop organ dysfunction due to poor organ perfusion as a result of cardiac disease and therefore present with critical illness.

2.3 COMPLICATIONS AND RISKS ASSOCIATED WITH DISEASES OF LIFESTYLE

The diseases of lifestyle discussed earlier may be associated with particular complications and risks. This section will highlight the prominent complications and risks associated with COPD, DM, and obesity.

2.3.1 Chronic Obstructive Pulmonary Disease

In COPD, the progression of respiratory system deterioration and the systemic effects of COPD result in disability due to dyspnoea, fatigue and reductions in exercise tolerance. The early respiratory system manifestations of COPD include coughing and breathlessness, with the latter being the symptom resulting in a patient seeking medical assistance. In the later stages of the disease, oedema and morning headaches may be present and this is indicative of hypercapnia (Boon, et al., 2006). The musculoskeletal and systemic signs of COPD are mostly seen in the later stages of the disease and include muscular weakness due to cellular changes in skeletal muscles and reduced mobility, an increase in the blood-markers for inflammation, peripheral oedema due to impairment in salt and water excretion by the kidneys, weight loss due to changes in fat metabolism and impaired nutritional status, and an increase in the prevalence of osteoporosis. Patients with poor prognosis include those who develop pulmonary hypertension in the late stage of the disease (Boon, et al., 2006). Consequently, these patients present with a reduction in HRQOL (Basuthakur, et al., 2015). Of particular concern in patients suffering from COPD is the occurrence of acute exacerbations. Acute exacerbation involves a worsening in symptoms with deterioration of lung function and poorer health status. Bacteria, viruses or changes in the quality of the air breathed may result in acute exacerbations of COPD. Exacerbations become more frequent as the disease progresses. Severe acute exacerbations may result in respiratory failure and possible death (Boon, et al., 2006).During these acute exacerbations of COPD, patients may be admitted to the ICU for management of respiratory failure and may become critically ill if their response to therapy received is suboptimal. Respiratory failure is discussed further in section 2.4.

2.3.2 Diabetes Mellitus

The chronic hyperglycaemia associated with DM type two results in damage to many organ systems and consequently affects the patient negatively. The negative influences on the patient stems from the vascular complications both on a

microscopic and macroscopic level, including coronary heart disease, myocardial infarction, cerebrovascular accidents, retinopathy, nephropathy, neuropathy, and arterial occlusive disease. Diabetes mellitus is also associated with the development of other co-morbidities such as hypertension, dyslipidaemia, obesity and depression (Abbas, et al., 2015). Many of these co-morbidities associated with DM type 2 are however treatable. The mentioned vascular complications of and co-morbidities associated with DM may result in a patient being critically ill and admitted to the ICU. Patients suffering from DM are also susceptible to complications like lower extremity infections, urinary tract infections and fungal infections. This is due to the weakened immune system in patients with DM (Mann, 2010; Weintrob and Sexton, 2015). Diabetes mellitus type two may therefore result in a reduced lifespan with functional limitations in activities of daily living. This may ultimately reduce such a patient's QOL (Rendell, et al., 1993; Zimmet, et al., 2001; Liebl, et al., 2002; Narayan, et al., 2003; Sarwar, et al., 2010; Danaei, et al., 2011; Hu, 2011; O'Reilly, et al., 2011; Seshasai, et al., 2011; Chen, et al., 2012; Schunk, et al., 2012; Boehme, et al., 2015). Another significant finding is that by Ak et al. (2015) who found that the majority of patients with DM type two experienced low quality sleep, mild depression, and mild anxiety. Due to the psychological and physical difficulties seen in patients with DM, there is progression of the disease and this result in a reduced HRQOL in these patients. Poor control of blood glucose levels in women suffering from DM type 2 has been found to be correlated with poorer HRQOL (Weintrob and Sexton, 2015).

2.3.3 **Obesity**

Obesity has been correlated with an increased risk of young mortality and also with the development of conditions which affects HRQOL negatively (Lafortune, et al., 2009). Certain diseases may develop as a result of obesity including cardiovascular diseases, cerebrovascular accidents, musculoskeletal disorders, certain neoplasms, gastrointestinal conditions, osteoarthritis and mental disorders (WHO, 2000; WHO, 2003; Guh, et al, 2009), all of which could be life-threatening and result in ICU admission and critical illness.

As reported by the Australian Diabetes, Obesity and Lifestyle Study, a relationship exists between the reduction in physical activity levels and obesity (Cameron, et al., 2003). This was confirmed by Pan et al. (2011) who reported that the incidence of obesity was higher in adults who were inactive. There is very limited literature related to the correlation between physical inactivity and the development of obesity. It is unclear whether the development of obesity is a result of physical inactivity or vice

versa. Peterson et al. (2003) found in a longitudinal study that there was no evidence to show that reduced physical activity may lead to obesity.

2.4 CAUSATIVE FACTORS FOR ADMISSION TO INTENSIVE CARE

2.4.1 Respiratory Failure

Respiratory failure refers to the failure of pulmonary gas exchange to maintain the normal levels of oxygen and carbon dioxide in arterial blood. Two types of respiratory failure are identified: type one and type two (Boon, et al., 2006).

Type one respiratory failure is characterised by hypoxia with normal carbon dioxide levels in the blood (also known as failure of oxygenation). This is seen in diseases where there is local ventilation impairment in the lungs. Arterial blood gas testing in type one respiratory failure will show a partial pressure of oxygen in arterial blood of less than 60 mmHg and a normal partial pressure of carbon dioxide in arterial blood or a partial pressure of carbon dioxide in arterial blood of less than 50 mmHg (Boon, et al., 2006). Type one respiratory failure can be acute or chronic in nature. Acute causes include acute asthma, pulmonary oedema, pneumonia (Carillo, et al., 2012) collapse of a lung lobe, pneumothorax, pulmonary embolus, and ARDS. Chronic type one respiratory failure may be caused by emphysema, lung fibrosis, lymphangitis, carcinomatosa, and brain stem injuries or lesions (Boon, et al., 2006).

In contrast, type two respiratory failure is characterised by hypoxia in combination with hypercapnia (also known as failure of ventilation). Type two respiratory failure is seen in situations where there is a generalised ventilation-perfusion mismatch in the lungs or diseases where total ventilation is reduced. Type two respiratory failure can also be acute or chronic in nature. Acute type two respiratory failure may be caused by acute exacerbations of COPD, acute severe asthma, obstructions of the upper airway, acute neuropathies, acute paralysis, narcotic drugs, primary alveolar hypoventilation, and chest wall injuries through trauma. Chronic causes include COPD, sleep apnoea, kyphoscoliosis, myopathies, muscular dystrophies, and ankylosing spondylitis (Boon, et al., 2006). People who develop acute or acute chronic respiratory failure may require admission to ICU for management which may include endotracheal intubation and MV (Pryor and Prasad, 2008).

People suffering with COPD are at particular risk of developing hypercapnic respiratory failure (Behera and Sidhu, 2000) as they present with a diminished respiratory drive especially in the later stages of the disease. They present with a

loss of elastic tissues in the lungs with inflammation and fibrosis in the airway wall resulting in premature closure of the airways (Pryor and Prasad, 2008). This results in trapping of gas in the airways and dynamic hyperinflation. This in turn results in alterations in the compliance of the lungs and chest wall. When patients with COPD suffer from an acute exacerbation of disease and subsequent respiratory failure, non-invasive ventilation (NIV) is used successfully in most cases to support the patient until the acute exacerbation has been resolved (Lightowler, et al., 2003). As there are many complications of endotracheal intubation (Keith and Pierson, 1996), NIV is preferred. It allows the patient to speak, eat, and mobilize, and also lessens the need for sedation (Pryor and Prasad, 2008). As NIV does not necessarily need to be administered in the ICU but may also be used in the general hospital ward setting, it assists in reducing the rates of ICU admissions. Endotracheal intubation in acute exacerbations of COPD, unfortunately, may not always be prevented, resulting in ICU admission of these patients with a period of MV and immobilisation (Behera and Sidhu, 2000; Pryor and Prasad, 2008).

2.4.2 **Shock**

An important and dangerous condition often associated with patients admitted to the ICU is that of circulatory shock. This condition is often referred to as circulatory failure. In circulatory shock, cardiac output is low and this consequently reduces the delivery of oxygen to the tissues. The reduction in cardiac output could be a result of major haemorrhage, left heart failure, major pulmonary embolus, exacerbation of COPD, or septic shock. In critically ill patients, the state of circulatory failure is seen in association with hypotension. Hypotension, however, is a late sign of circulatory shock and thus shock may be present in the absence of hypotension and the patient may present with a normal blood pressure initially. It is thus important to identify the presence of circulatory shock as early as possible as it may result in inadequate regional tissue perfusion and a consequent lack of cellular oxygenation. This will result in cell death and subsequent multiple organ failure (MOF) (Baskett, 1990; Rivers, et al., 2001; Brealy, et al., 2002; Boon, et al., 2006; Regueira, et al., 2012).

There are six different types of shock namely hypovolaemic, septic, cardiogenic, obstructive, neurogenic, and anaphylactic. Two types of particular importance to the critically ill patient are that of hypovolaemic shock and septic shock (Boon, et al., 2006). Hypovolaemic shock occurs when the perfusion of tissues is relatively inadequate due to the loss of blood or plasma, typically after injury to the vascular

system. This could result from penetrating trauma to the trunk. There are four different classes of hypovolaemic shock. Class one involving blood losses of up to 750 ml, class two up to a loss of 1.5 litres of blood, class three with a blood loss of up to two litres, and grade four with a blood loss of 2.5 to three litres (Baskett, 1990).

Septic shock involves overwhelming inflammation. During the process of sepsis there is an excessive production of pro-inflammatory cytokines with resultant hypotension, hypovolaemia, reduced tissue perfusion and oedema. Damage to vascular endothelium and resultant increase in capillary permeability stem from the uncontrolled activation of neutrophils that cause the release of proteases and oxygen free radicals in blood vessels (Boon, et al., 2006). The consequences of septic shock involve cardiovascular system dysfunction, ARDS, disseminated intravascular coagulation, MOF, and possible death (Boon, et al., 2006). It has been reported that patients who suffered septic shock in ICU had reduced physical activity on the physical component score (PCS) of the SF-36 at one year after septic shock (Poulson, et al., 2009). Systemic inflammatory response syndrome and MOF are discussed in more detail in section 2.7.

2.5 SEVERITY OF ILLNESS SCORING SYSTEMS USED IN ICU

Patients admitted to ICU are assessed for severity of illness and predicted mortality. Two commonly used scoring systems are APACHE II and SAPS II (Le Gall, et al., 2005). When interpreting the scores of these two systems, higher scores predict greater risk of mortality (Du, et al., 2013). The APACHE II scoring system is one of the most widely used scoring system in ICU. It is an overall severity scoring system and is useful in predicting hospital mortality, hospital LOS, and assists in clinical reasoning and decision making (Balreldin, et al., 2011). It also allows for the comparison of ICU outcomes and for monitoring of the quality of care in ICU. The SAPS II was developed in 1994 to provide the probability of hospital mortality for ICU patients over 18 years of age (Balreldin, et al., 2011). The APACHE II and SAPS II scoring systems can aid therapeutic decision making by determining disease severity (Balreldin, et al., 2011).

Cardosa and Chiavoni (2013) evaluated the APACHE II scoring system by assessing its performance in predicting the mortality rate of 355 patients discharged from the ICU. They found that it is useful in identifying those patients who have higher likeliness of dying after discharge from ICU. Karachi et al. (2011) found a strong correlation between APACHE II scores on ICU admission and PF as related to

HRQOL in adult surgical patients at 12 months after hospital discharge. Long term survival after critical illness was also found to be significantly correlated to APACHE II scores (Karachi, et al., 2011). Schneiderman et al. (2013) found a relationship between APACHE II scores on ICU admission and the degree of problems experienced with usual daily activities as measured with the EQ-5D in trauma survivors at six months after hospital discharge. Goixart et al. (2013) however did not find a significant correlation between APACHE II scores on ICU admission and HRQOL (SF-36 and EQ-5D scores) of trauma survivors at six and 12 months after ICU admission. The design of the study by Goixart et al. (2013) was a prospective observational study. Van Aswegen et al. (2010) found no significant correlation between APACHE II scores and muscle strength in a prospective observational study involving adult survivors of penetrating trunk trauma and MV. Both the research of Goixart et al. (2013) and Van Aswegen et al. (2010) are considered level three evidence as it involves observational study designs with controls.

During a long-term mortality and HRQOL follow-up study of patients who suffered septic shock, the group of participants who survived critical illness had lower SAPS II scores and a longer hospital LOS, with a reduction in HRQOL at six months after critical illness (Nesseler, et al., 2013). It has also been reported from a prospective cohort study by Flaatten and Kvale (2003) that there was no significant difference in the SAPS II scores of patients with increased SF-36 scores as compared to those with decreased SF-36 scores at two years after medical and surgical ICU discharge. Higher SAPS II scores in medical patients were also associated with higher ICU mortality after ICU admission (Roch, et al., 2011).

2.6 EFFECTS OF IMMOBILITY AND CRITICAL ILLNESS ON PHYSICAL RECOVERY

One of the main treatments for acute trauma and acute and chronic illnesses is immobilisation and bedrest (Dittmer and Teasell, 1993a). It is a good choice to ensure protection and recovery in the acute phase of injury or illness, but if immobilisation and bedrest is prolonged, it has many negative effects on the human body. The complications of immobilisation can be very severe, complicating the acute injury or illness. These complications can be so severe that they may threaten the life of the patient more than the original injury or disease (Dittmer and Teasell, 1993a). The complications of immobilisation may include muscle weakness, muscle atrophy, contractures, osteoporosis due to disuse, and cardiovascular complications (tachycardia, reduced cardiac reserve, orthostatic hypotension, and venous thromboembolism), respiratory complications (such as decreased ventilation,

atelectasis, pneumonia), endocrine complications, renal complications, gastrointestinal complications, pressure sores, central nervous system complications and problems with balance and coordination(Dittmer and Teasell, 1993a; Dittmer and Teasell, 1993b).Certain patient populations are more likely to develop complications of immobilisation such as chronically ill patients, disabled patients, and older adults (Dittmer and Teasell, 1993a; Dittmer and Teasell, 1993b).Patients in ICU with critical illness are prone to development of the mentioned complications of bedrest as they are also often treated with prolonged bedrest and immobility (due to various reasons related to their clinical presentation, diagnoses and injuries).

The immobility of patients after admission to ICU, results in muscle weakness. Muscle weakness is increasingly recognized in ICU patients who have survived the initial acute phase of critical illness. This can partly be attributed to immobility and bed rest. It has been reported that muscle weakness in patients regaining their normal consciousness after more than seven days of being treated with MV, occurs in 25 to 60 percent of patients (De Jongh, et al., 2009). This muscle weakness may subsequently result in difficulty of weaning such patients from mechanical ventilation. Intensive care acquired weakness is discussed in more detail in section 2.6.2.

As a result of the reduced physical activity during a period of immobilisation, patients may have problems with the function of the musculoskeletal and cardiovascular systems. This will consequently affect such a patient's ability to achieve functional independence in the hospital environment and in the community after discharge from hospital (Topp, et al., 2002).

2.6.1 Sepsis and Systemic Inflammatory Response Syndrome

Systemic inflammatory response syndrome is described as a complex patho-physiologic response, in the form of systemic inflammation to insults like trauma, burns, ketoacidosis or pancreatitis. This definition was adopted by The American College of Chest Physicians and the Society of Critical Care Medicine at their sepsis definitions consensus conference held in Chicago, Illinois, in August 1991 (Balk, 2014).

Sepsis is defined as SIRS with infection, is a common life-threatening complication of critical illness and may lead to the development of MOF (Baba, et al., 2012; Davies, et al., 2014). Patients with sepsis may present with disseminated intravascular coagulation which is characterised by development of intravascular microthrombi

leading to alterations in organ perfusion, ultimately contributing towards the development of multiple organ dysfunction syndrome (Davies, et al., 2014). Sepsis can thus lead to hypotension, MOF and death (Davies, et al., 2014). Sepsis also results in damage to the microcirculation in peripheral nerves and muscles and contributes to the development of CIM and CIP (Apostolakis, et al., 2014). In the clinical setting, it is often difficult to differentiate sepsis from SIRS. This is a barrier to the effective treatment of these patients (Battle, et al., 2014). Sepsis develops in 900 000 people in the United States of America annually with a 33 percent mortality rate (Kellum, et al., 2007). A multicentre study by Orwelius et al. (2013) conducted in medical and surgical ICU's investigated the HRQOL of patients admitted with community-acquired sepsis, severe sepsis, and septic shock at six months after ICU discharge. They concluded that patients admitted to the ICU with sepsis and septic shock did not have significantly different levels of HRQOL as compared to ICU patients admitted for other diagnoses when assessed using the EQ-5D questionnaire at six months after discharge from ICU (Orwelius, et al., 2013).

2.6.2 Post Intensive Care Unit Syndrome and Intensive Care Unit Acquired Weakness

On admission to an ICU, a critically ill patient may present with any number of specific medical or surgical problems, for which treatment and monitoring is needed. Some of these problems may result in a patient being MV for a prolonged period of time and subsequently having a prolonged ICU LOS (Boots, et al., 2013).

Post-intensive care syndrome refers to the combination of poor physical, functional and cognitive outcomes in survivors of critical illness. It negatively affects the availability of ICU beds and length of waiting lists for surgeries and the health, productivity and return to occupation rates of survivors of critical illness. It also results in healthcare services being more expensive (Boots, et al., 2013). A major component of the post-intensive care syndrome is ICU-AW (Boots, et al., 2013).

Intensive care unit acquired weakness is a major physical problem presenting as the onset and progression of severe muscle wasting and subsequent muscle weakness and fatigue (Rattray, 2013). The exact pathology of ICU-AW which results in the muscle weakness and fatigue is still unknown, however, it has been reported that it involves abnormalities in muscles and nerves with the entire neuromuscular junction implicated (Bat and Dos Santos, 2012). As patients with critical illness often experience dysfunction or failure of multiple organs in the body (more often the renal,

respiratory and cardiovascular systems) these patients are treated using MV, vasopressor drugs and haemodialysis, resulting in immobility and reduced PF. With focus being placed on the treatment of the life-threatening MOF, neuromuscular dysfunction may not be identified at first (Benson, et al., 2011). Griffiths and Hall (2010) report that patients may lose two to four percent of their muscle mass per day during a period of critical illness. This was also reported by others (Fan, et al., 2009; Herridge, 2009; Hall, et al., 2010). This together with other factors results in the development of ICU-AW.

Intensive care unit acquired weakness includes two distinctly different conditions namely CIM and CIP. It is suggested by some researchers that CIP and CIM co-exist (Khilnani, et al., 2014).

Apostolakis et al. (2014) reported on the ICU-AW in a brief review of the diagnosis, risk factors, and management of patients with ICU-AW. Critical illness myopathy involves the atrophy, fibrosis and fatty degeneration of muscle fibers (Apostolakis, et al., 2014). Critical illness polyneuropathy on the other hand is characterised by the degeneration of sensory and motor nerve fibres, affecting mostly the nerves of the legs (Apostolakis, et al., 2014). Both CIM and CIP presents as diffuse skeletal muscle weakness (Khilnani et al., 2014). Patients suffering from ICU-AW present with progressive generalised muscle weakness and muscle atrophy due to functional and structural abnormalities in the muscles and nerves as a result of the surge in systemic inflammation associated with critical illness. Often the muscle weakness is to such an extent that it presents the same as flaccid areflexic quadriparesis (Khilnani, et al., 2014). The pathogenesis of ICU-AW seems to involve the entire neuromuscular junction as distal axonal neuropathy which affects muscles of the limbs and respiratory system is observed (Batt and Dos Santos, 2012). The facial nerves are not affected by ICU-AW (Batt and Dos Santos, 2012).

Intensive care unit acquired weakness is more commonly seen in patients with a prolonged ICU stay, especially those who reside in ICU for longer than seven days (Herridge, 2007; Dryer, et al., 2009). Mechanically ventilated patients in ICU have a greater risk of developing ICU-AW, with patients presenting with sepsis, prolonged ICU stay, and advanced age also being at higher risk (Denehy, et al., 2014). Severely critically ill patients such as those with ARDS and those with sepsis, SIRS, or MOF, and longer ICU stay with more than one organ dysfunction, are more at risk to develop ICU-AW (Khan, et al., 2004; Hall and Schweickert, 2007; Linos, et al.,

2007; Dryer, et al., 2009; Herridge, 2009; Truong, et al., 2009). It is reported that the combination of immobilisation of a patient during long periods of bed rest, critical illness, the body's inflammatory response, and the circulation of toxins in the blood, results in ICU-AW (Fan, et al., 2009; Herridge, 2009; Hall, et al., 2010). The extent of disability a patient presents with as a result of ICU-AW is related to pre-morbid functional status, the effects of co-morbidities, and the nature and duration of critical illness (Batt and Dos Santos, 2012).

As a result of ICU-AW, patients treated with MV may have difficulties in weaning from ventilation or may even fail to wean. This is due to the respiratory muscle weakness associated with ICU-AW, especially weakness of the diaphragm, intercostal muscles and the accessory muscles of respiration (Hall, et al., 2007; Khilnani, et al., 2014). Intensive care unit acquired weakness is often identified when weaning from sedation and MV is commenced (Hall, et al., 2007) and may be present in 25 to 60 percent of MV patients (Chambers, et al., 2009; Griffiths and Hall, 2010). This results in a longer ICU and hospital stay for these critically ill patients (Dryer, et al., 2009).

2.7 ASSESSMENT OF FUNCTIONAL ABILITY IN THE INTENSIVE CARE UNIT

Assessment of the functional ability of ICU survivors, while in hospital and at discharge from hospital, would be important in order to observe whether improvement occurred. The PF status of a patient during his/her ICU stay can be measured using a variety of tests. Recently three tests have been developed specifically for use in the ICU patient population for the assessment of physical function. These tests are: the Functional Status Score for the ICU(Thrush, et al., 2012)), the Chelsea Critical Care Physical Assessment Tool (Corner, et al., 2012), and the PFIT (Denehy, et al., 2013; Denehy, et al., 2014). All three of these outcome measures have been reported through pilot studies to be safe, feasible, and responsive measures to assess the functional abilities of a patient. Only one of these three tests has undergone further psychometric validation testing and scale analysis: the PFIT (Berney, et al., 2009: Zanni, et al., 2010; Corner, et al., 2013; Denehy, et al., 2013; Denehy, et al., 2014).

The PFIT was developed by physiotherapy researchers in Australia to assess the PF of ICU survivors during their hospital stay in order to comment objectively on the improvements observed (Berney, et al., 2009). In response to many patients in ICU not having the ability to perform the 6MWT, the development of the PFIT test was commenced. As more evidence suggests the effectiveness of early mobilisation in

ICU's for critically ill patients to counter ICU-AW (Bailey, et al., 2007; Morris, et al., 2008; Schweickert, et al., 2009; Denehy, et al., 2013), an objective measure was needed to measure a patient's functional status during their ICU stay. An objective measure is also important to assist with determining the effect on rehabilitation on these patients' abilities. Many tests assessing the functional ability in ICU fail to measure the endurance of patients. The PFIT however assesses patient endurance for task performance as well as strength and function (Denehy, et al., 2014). The PFIT includes five components namely amount of assistance needed to stand up, shoulder flexion and knee extension strength, marching on the spot (MOS), and upper limb endurance using arm elevation above 90 degrees of shoulder flexion range of movement. The upper limb endurance component of the PFIT was removed from the scoring by Denehy et al. (2013) after they refined the testing components using principle component analysis, resulting in an ordinal score for PFIT scoring.

The PFIT is useful to assess and subsequently prescribe an appropriate exercise programme for ICU patients. Safety of the test in ICU is achieved through the assessment of a patient's heart rate, blood pressure, respiratory rate, and blood oxygen saturation during the testing procedure (Denehy, et al., 2014). The assessment of these vital signs during the test allows for the assessment of a patient's exercise endurance in ICU and therefore an appropriate rehabilitation programme can be devised. This serves as an alternative to the sub maximal exercise tests commonly used in the acute care setting such as the 6MWT. Another advantage of the PFIT is that it can be used very early on during a patient's stay in ICU to identify strength and functional problems. The PFIT is also beneficial as it can be used again at discharge from the ICU and therefore allows for the assessment of change in a patient's functional abilities during their ICU stay. Appropriate rehabilitation can then be prescribed at the time of discharge by using data obtained from the PFIT (Denehy, et al., 2014).

Unfortunately, the PFIT cannot be used if a patient is unable to follow commands. The PFIT is the best choice of assessment for physical abilities early on during a critically ill patient's ICU stay (Denehy, et al., 2014).

It has been observed during a study of 116 participants that those participants with high PFIT scores were more likely to be discharged directly home from hospital and have higher scores during assessment of HRQOL at three-, six-, and 12-months after discharge from hospital (Denehy, et al., 2013). It was also found in the same study

that participants with low PFIT scores were more likely to have a longer hospital LOS in the acute care setting and be discharged to a rehabilitation centre rather than home (Denehy, et al., 2013).This nested cohort study aimed to further develop the PFIT to derive the interval score (PFIT-s) and also to determine the validity, responsiveness, and predictive utility of the PFIT-s. This study has a level of evidence of two. Denehy et al. (2013) suggested that the PFIT test be adopted to assess a patient's PF in the ICU and those being discharged from the ICU. The PFIT should however be used in combination with other outcome measures (Denehy, et al., 2013). Skinner et al. (2009) reported that the participants in their study showed an increase in muscle strength with an increase in the MOS cadence component of the PFIT. Denehy et al. (2014) reported on the use of the PFIT in ICU patients. They found that PFIT scores at ICU discharge was strongly correlated with hand grip strength measured with a HHD at ICU discharge (r=0.76) (Denehy, et al., 2014). The study by Denehy et al. (2014) constitutes level two evidence as it is a high quality randomized, controlled trial with narrow confidence intervals (95 percent). This study had a large sample size of 51 participants recruited from four different ICU's in Denver. The author could not identify other studies assessing participants with the PFIT in the ICU.

2.8 CHANGES IN MUSCLE POWER, EXERCISE ENDURANCE AND FUNCTIONAL ABILITY AFTER DISCHARGE FROM ICU

The presence of CIM and CIP during a period of critical illness results in negative effects on skeletal muscle power and may lead to reduction in muscle mass and functional difficulties. Intensive care unit acquired weakness places a huge burden on critically ill patients as they suffer from distal muscle weakness and sensory weakness for some time after discharge from ICU due to the axonopathy evident in ICU-AW. Recovery from ICU-AW is variable, with some patients experiencing spontaneous recovery in a few weeks (mild cases of ICU-AW) and some experience recovery within months (moderate to severe cases of ICU-AW) and some presenting with no recovery at all (Khilnani, et al., 2014). Recovery from neuromuscular problems like ICU-AW may still be present for up to five years after hospital discharge, where the possibility exists for incomplete recovery (Benson, et al., 2011). This consequently has a negative effect on a patient's health status after critical illness. Patients with CIP have a worse prognosis than those with CIM (Khilnani, et al., 2014).

Van Aswegen et al. (2011) found in the retrospective and observational, prospective study with level of evidence three of survivors of penetrating trunk trauma that those patients who underwent prolonged MV had reduced HRQOL for up to six months after hospital discharge. This reduction in HRQOL was especially seen in the PF (Van Aswegen, et al., 2011). Schneiderman et al. (2013) also reported a reduction in PF at six months after hospital discharge in survivors of trauma in Johannesburg when they had prolonged ICU and hospital LOS. Van Aswegen et al. (2010) reported that patients with penetrating trunk trauma treated with MV for five or more days presented with significant limitations in muscle strength, exercise capacity, and the PF domain of SF-36 for up to six months after discharge from hospital. A significant relation was found between the length of immobility and muscle weakness suffered by patients at one and three months after discharge (van Aswegen, et al., 2010).

Internationally, a landmark study by McHugh et al. (1994) reported that 52 patients who were followed -up for one year after surviving critical illness experienced severe impairments in HRQOL. These subjects' HRQOL at one year after discharge from hospital was persistently lower than that of healthy population norms. Similar findings were reported by Herridge et al. (2003) who showed that their participants reported problems mainly in functional abilities and HRQOL as a result of the loss of muscle mass, muscle fatigue and muscle weakness following recovery from ARDS. The patient sample for this study who presented with ARDS during a period of critical illness, were healthy and young prior to critical illness (median age 45) with minimal co-morbidities and full employment prior to hospital admission (Herridge, et al., 2003). Despite this, the patients still presented with poor outcomes following discharge from hospital.

After discharge from hospital, exercise capacity and peripheral muscle strength can be assessed by utilising the 6MWT as described by the American Thoracic Society (ATS) (2002)(Holland, et al., 2014; Singh, et al., 2014) and HHD respectively (Van Aswegen, et al., 2010). The 6MWT is an appropriate test to use for patients after discharge from ICU. If a patient recovers to such an extent that they are able to perform the 6MWT, it is a good measure to use in an outpatient setting (Denehy, et al., 2014). Herridge et al. (2011) reported lower 6MWT distances achieved by 64 ARDS survivors at one year after onset of ARDS compared to predicted distances for 6MWT. Eighty percent of predicted 6MWT distance was achieved by only 39 percent of patients in their study (Herridge, et al., 2011). Very limited literature is available on

the use of the 6MWT in survivors of critical illness (Aitken, et al., 2012). Aitken et al. (2012) reported increases in mean 6MWT distances in survivors of critical illness at one week (15 metres), eight weeks (13 metres), and at 26 weeks (9 metres) hospital discharge. They also reported a relationship between 6MWT distance and SF-36 PF score at one (r=0.62), eight (r=0.55) and 26 (r=0.47) weeks after hospital discharge (Aitken, et al., 2012). This study by Aitken et al. (2012) was performed as a secondary analysis on data of a previous randomized, controlled trial that included 173 participants. This constitutes level two evidence as the original study was a randomized, controlled trial.

Herridge et al. (2003) reported an increase of median 6MWT distance from 281 metres at three months after ARDS to 396 metres at six months. Van Aswegen et al. (2010) showed better results in their short-term MV group that had an improved median 6MWT distance from 633 metres at three months after discharge to 680 metres at six months, and their long-term MV group had an improved median 6MWT distance of 586.5 metres at three months to 626 metres at six months. Secombe et al. (2013) however reported no significant increase in 6MWT distance from their investigation of survivors of critical illness at high risk of future morbidity between ICU discharge and six months follow-up.

An essential part of a patient's physical assessment is that of mobility assessment. Muscle strength and joint range of movement form part of a patient's mobility (Jannsen and Le-Ngoc, 2012). An outcome measure to assess a patient's PF is muscle strength assessment. It is important to obtain objective and discrete measurements of muscle strength during assessment. This may be obtained using a HHD.

Some studies have reported on the use of HHD in survivors of critical illness at ICU discharge. Burtin et al. (2009) reported a significant correlation between changes in lower limb muscle strength and ambulatory ability in the ICU. Ali et al. (2008) examined handgrip strength in critically ill patients using a HHD to diagnose muscle weakness in the ICU. Schweickert et al. (2009) and Chiang et al. (2006) reported from their randomised controlled trials that there was no significant change in handgrip strength in response to physical therapy interventions in ICU when measured using a HHD. Other studies have also reported using the HHD in the ICU (Hough, et al., 2011: Hermans, et al., 2012; Baldwin, et al., 2013). Baldwin et al. (2013) reported from their investigation of HHD the minimally detectable differences

in measurements. These were 71 Newton on the left side of the body and 57 Newton on the right.

Van Aswegen et al. (2010) used HHD to measure the peripheral muscle strength of survivors of critical illness due to penetrating trunk trauma in Johannesburg. They found that patients who were MV for short periods of time had significantly greater muscle strength in most peripheral muscle groups at one month follow-up after discharge when compared to participants who had been MV for longer periods of time. They found that the weaknesses recorded between the groups were specific to the biceps, triceps, quadriceps and hamstrings muscles, and were persistent at six months after discharge. The short term ventilation group had significant weakness of the right deltoid and triceps muscles at one month after discharge which resolved at three months after discharge. The group who received MV for longer periods of time, however, had muscle weakness in all upper limb muscle groups from one to six months after discharge (Van Aswegen, et al., 2010). Significant relationships were reported by Van Aswegen et al. (2010) between ICU LOS of participants MV for longer periods of time and right deltoid, right triceps, and right hamstrings muscle strength at one month after discharge and left triceps muscle strength at six months. In the same study, hospital LOS of participants mechanically ventilated for longer periods of time was significantly correlated with left deltoid, right triceps, left hamstrings, and right hamstrings muscle strength at one month follow-up and left deltoid, left triceps, right triceps and right hamstrings muscle strength at three months after discharge (Van Aswegen, et al., 2010). On the contrary, in their participant group receiving short-term MV, no statistically significant relationship wad found between peripheral muscle strength and ICU LOS (Van Aswegen, et al., 2010). Van Aswegen et al. (2010) also reported no statistically significant relationships between peripheral muscle strength and APACHE II scores.
Baldwin and Bersten (2014) reported that septic patients with critical illness who were MV showed reduced muscle strength (measured during their ICU stay) in all peripheral muscle groups as measured using a HHD.

This reduction in functional abilities together with certain psychological problems may consequently affect a patient's HRQOL negatively after discharge from hospital.

2.9 EFFECTS OF CRITICAL ILLNESS ON MENTAL HEALTH

2.9.1 Anxiety and Depression

Psychological problems such as anxiety and depression are experienced by survivors of critical illness after discharge from hospital (Rattray, 2013). As is the case with physical problems such as ICU-AW, these psychological problems may negatively influence a patient's HRQOL. The gold standard to diagnose psychological problems is with a clinically structured diagnostic interview. However, self-report measures such as the PHQ-9 which has been standardised with established validity and reliability may be helpful in identifying specific symptoms of these conditions. It may therefore serve as a screening tool for psychological problems (Rattray, 2013).

The PHQ-9 is an example of a standardised screening tool for depression. A reduction in HRQOL after critical illness may be the result of patient depression. Depression is the third leading cause of disease burden in the world (WHO, 2008). Depression is a mental illness and requires identification and appropriate treatment as it greatly impacts on a person's HRQOL. Depression is a common illness and may lead to suicide (Chan, et al., 2013). The detection of major depressive disorders may lead to early treatment and thus better outcomes, such as HRQOL. By this, the risk of a patient committing suicide may be reduced and the patient may function better at work and in society in general.

Davydow et al. (2009) reported from their systematic review of depression of ICU survivors, a 28 percent point prevalence of depression symptoms in these patients in the first year after discharge from hospital. As rehabilitation takes place, patients may realize that they may not achieve the same level of function as they had before ICU admission. This together with a prolonged recovery period from critical illness may make these patients more prone to developing symptoms of depression (Rattray, 2013). The HRQOL of patients with coronary artery disease and heart failure has been correlated with the severity of disease in these patients, the social support available to the patient, and patient psychological factors (Brozaitiene, et al., 2015). Patients with a longer ICU and hospital LOS and those with a higher severity of disease on admission may also be more prone to developing symptoms of depression (Rattray, 2013). It is suggested in the literature that psychological problems may have a greater impact on HRQOL compared to somatic dysfunction or disability (De Jongh, et al., 2014).

Severely injured patients also experience reduced HRQOL after such a traumatic event. A cross-sectional study conducted by De Jongh et al. (2014) investigating psychological complaints and HRQOL in severely injured trauma patients concluded that psychological problems are underestimated and play a major role in the reduced HRQOL experienced by these trauma survivors (De Jongh, et al., 2014). The author could not identify other studies using the PHQ-9 in the ICU patient population.

2.10 THE EFFECT OF CRITICAL ILLNESS ON QUALITY OF LIFE

Different aspects of HRQOL namely the physical and mental components need consideration when investigating HRQOL after critical illness. Various measures of HRQOL of survivors of critical illness have been described, but the SF-36 and EQ-5D questionnaires have been used and reported on by most researchers (Dowdy, et al., 2005; Oeyen, et al., 2012; Goixart, et al., 2013; Nesseler, et al., 2013).

The PCS of the SF-36 questionnaire was found to be consistently impaired in survivors of ARDS at five years after admission to hospital (Herridge, et al., 2011). Herridge et al. (2011) also found that the PF score of the SF-36 was strongly correlated with 6MWT distance achieved by their participants. These results were reproduced by Aitken et al. (2012). They reported the PF score of the SF-36 questionnaire to be a strong indicator of 6MWT distance achieved during the early recovery stage from critical illness (Aitken, et al., 2012). They reported a relationship between PF scores and 6MWT distance at one, eight, and 26 weeks after discharge from hospital (Aitken, et al., 2012). Ivaskevivius et al. (2011) found a reduction in PF and RP domain scores of the SF-36 in survivors of critical illness (as a result of medical conditions) at six months after discharge.

In their investigation of the HRQOL of survivors of trauma, Schneiderman et al. (2013) reported that participants scored the lowest scores in the role physical (RP) and RE scores of the SF-36 at six months after discharge from hospital. They reported that mean PCS scores were higher than mean mental component score (MCS) scores at six months after discharge from hospital (Scheniederman, et al., 2013). An inverse relationship was also found between SF-36 PF scores and ICU and hospital LOS at six months after hospital discharge (Schneiderman, et al., 2013). They concluded that survivors of trauma in Johannesburg experienced limitations in the emotional and physical domains of HRQOL at six months after discharge from hospital (Schneiderman, et al., 2013). At six months after penetrating trunk trauma, Van Aswegen et al. (2010) found a statistically significant difference between short-

term MV and long-term MV groups in SF-36 PF, bodily pain (BP), general health (GH), and PCS scores, but not in MCS scores.

Van Aswegen et al. (2011) investigated the HRQOL of survivors of penetrating trunk trauma in Johannesburg. They found the PCS scores of the SF-36 to be significantly reduced at one and three months in the group of participants who were MV for a short period of time. The MCS scores of the SF-36 for the same group were also significantly reduced at one, three and six months after discharge from hospital. For the group of participants receiving long-term MV, the SF-36 PCS and MCS scores were also significantly reduced at one, three and six months after discharge from hospital (Van Aswegen, et al., 2011). The same study reported that at one month after discharge from hospital, the short-term MV group showed significant differences compared to healthy controls in the PF, RP, BP, social functional (SF) and vitality (VT) domains and PCS scores of the SF-36. This however changed to no statistically significant differences in these domains or summary scores between the short-term MV group and healthy controls at six months after discharge (Van Aswegen, et al., 2011). At one month after discharge from hospital, the long-term MV group showed significant differences compared to healthy controls in the PF, RP, BP, GH, SF, RE and MH domains and PCS scores of the SF-36 (Van Aswegen, et al., 2011). At six months the long-term MV group still scored significantly lower in the PF, RP, BP, GH, SF domains and PCS scores of the SF-36 compared to the healthy group (Van Aswegen, et al., 2011).Granja et al. (2004) and Herridge et al. (2003) reported reduced HRQOL in survivors of sepsis at six months after discharge from hospital.

A systematic review of the HRQOL of adult survivors of critical illness by Dowdy et al. (2005) reported that survivors of critical illness have lower HRQOL in all domains of the SF-36 questionnaire, except for BP, from six months to 14 years after discharge from hospital. They reported that an increase in severity of illness may be associated with poorer PF and GH perceptions and that the survivors of critical illness in their review did not experience significant improvements in HRQOL at six months after discharge. They also added that small improvements in HRQOL are seen up to 36 months after discharge (Dowdy, et al., 2005).These findings by Dowdy et al. (2005) are very valuable as the study involved level one evidence. Niskanen, et al., (1999) reported from their cohort study with level of evidence two b that QOL at six months after prolonged ICU LOS was found to be the highest for cardiac surgery patients and lowest for patients admitted to ICU for trauma and respiratory conditions. The results of the study by Niskanen et al. (1999) was obtained from a large sample of

ICU patients (n=718), allowing for easier generalization of the results to a general ICU population.

Other studies have reported reductions in HRQOL after critical illness as compared to pre-admission HRQOL when measured using the SF-36 questionnaire. Pettila et al. (2000), Vedio et al. (2000), Flaatten and Kvali (2001), Kaarlola et al. (2003), Graf et al. (2003), and Wehler et al. (2003) reported statistically significant reductions in HRQOL which were clinically significant (more than five points reduction on the SF-36).

The EQ-5D is used widely in clinical studies. It is the most used preference-based outcome measure, being used in half of studies published (Chen, et al., 2014b). Schneiderman et al. (2013) reported from their retrospective cross-sectional study of an adult cohort (level three evidence)that the majority of participants in their study reported some problems with their usual activities and with pain or discomfort at six months after hospital discharge as measured using the EQ-5D questionnaire. They reported a relationship between EQ-5D VAS scores and age at six months after discharge from hospital (Schneiderman, et al., 2013).The relatively small sample size of the study limits the degree to which the results can be generalized to the ICU population. Badia et al. (2001),from their prospective cohort study (level three evidence), reported a significant increase in mobility and significant decreases in self-care and usual activities from baseline to 12 months after ICU discharge in survivors of critical illness as measured by the EQ-5D questionnaire. They also reported no statistically significant changes in pain or discomfort, anxiety or depression or in the EQ-5D VAS over the first 12 months after discharge from ICU (Badia, et al., 2001). This study involved 334 ICU patients and assessed the HRQOL of ICU patients before and after admission to ICU. The study was published in 2001, however the data is slightly outdated as it was collected from1994 to1995 (Badia, et al., 2001). This may limit the ability to generalize the results to today's ICU patient populations. Significant relationships have been reported by Granja et al. (2002) and Garcia et al. (2003) between APACHE II scores and EQ-5D VAS and EQ-5D usual activities at six and 18 months after discharge from hospital respectively. Orwelius et al. (2010) reported no increase in EQ-5D scores in survivors of critical illness up to 36 months after discharge.

As discussed, certain physical and psychological problems, may affect a patient's HRQOL negatively. Patients admitted to ICU due to critical illness may face reduced

HRQOL after discharge from hospital (Ivaskevicius, et al., 2011; Fan, et al., 2012). It was reported by Oeyen et al. (2012) that the PF domain of HRQOL is worst in the first three months after discharge from hospital and that it will slowly improve thereafter. On the contrary, mental function may not improve and patients may struggle with these problems for a prolonged period of time (Oeyen, et al., 2012). It is thus important to assess and measure the health perception of patients after critical illness. Reduction in HRQOL can be considered a consequence of ICU admission and thus these patients can't be seen as fully recovered from their illness while their HRQOL is still reduced. Backman et al. (2010) reported that few studies on HRQOL in ICU survivors accounted for and adjusted results for the existence of pre-morbid conditions. They found that the major factor contributing to the reduced HRQOL found at 36 months after critical illness was the existence of pre-morbid conditions and diseases. Their study hada large sample size of 262 ICU participants, but the design of their prospective trial did not include randomization (Backman, et al., 2010). The study reported improved HRQOL during the three year follow-up period in those participants who received their study intervention (ICU-diary), however, the effect of their intervention needs to be duplicated in a randomized study as the level of evidence for their study is a level three (Backman, et al., 2010).

Certain factors relating to the ICU stay of a critically ill patient may affect his or her HRQOL after discharge from hospital (Elliot and Rattray, 2012). Such factors include the effects of the disease or illness on admission, organ dysfunction prior to admission, pre-morbidities, complications that develop during ICU stay and prolonged length of ICU stay (Ivaskevicius, et al., 2011). Patients who suffered from ARDS, severe sepsis, severe trauma or prolonged length of MV show more reductions in HRQOL after discharge from hospital (Kapfhammer, et al., 2004; Hopkins, et al., 2005; Oeyen, et al., 2012).

2.11 RETURN TO WORK FOLLOWING CRITICAL ILLNESS

Van Aswegen et al. (2010) reported from their prospective, observational study (level three evidence) that there was no difference between their short-term MV and long-term MV groups in the rate of return to work over the first six months after hospital discharge.This study had a good sample size of 42 participants, allowing for easier generalizability of the results to other patients suffering from penetrating trunk trauma being treated with MV.A multicenter questionnaire-based study conducted by Griffiths et al. (2013) showed that patients in the United Kingdom have difficulties with employment following a period of critical illness in a general ICU. The main reported

reason for the difficulties is the physical disabilities experienced by these patients. Many of their participants required additional care after discharge from hospital and this care was mostly provided by family members of the patient. This negative impact of critical illness on return to employment was seen at six months after discharge from hospital (33 percent of participants) and did not show significant improvement at 12 months post discharge (28 percent of participants) (Griffiths, et al., 2013). Similar results were reported by Myhren et al. (2010) in a 12 months follow-up study of general ICU patients. Only 50 percent of their study participants had returned to work or school at 12 months after discharge from hospital (Myhren, et al., 2010).

2.12 RECOVERY FROM CRITICAL ILLNESS IN THE SOUTH AFRICAN CONTEXT

In contrast to the wealth of available international literature on recovery of survivors of critical illness, limited information is available regarding recovery of survivors of critical illness in the South African context. The purpose of this section is to specifically highlight the findings of South African studies; however, the international literature (as reviewed throughout the other sections of this literature review) may also be applicable to the South African context.

As mentioned previously, Karachi et al. (2011) investigated the survival and HRQOL of patients at 12 months following discharge from an adult surgical ICU in the Western Cape Province. They concluded that the HRQOL scores of their study population were lower than that reported for ICU populations internationally. Participants presented with limitations in HRQOL mainly in the domains of PF, RP and RE domains of the SF-36 questionnaire.

Results from other South African studies namely Schneiderman et al. (2013), Van Aswegen et al. (2010) and Van Aswegen et al. (2011) have already been discussed above. The current study was conducted in order to add information to the existing limited body of evidence on recovery of South African survivors of critical illness but it also describes outcomes related to patients' PF in ICU and their level of depression as this has not previously been described in the South African context.

2.13 **CONCLUSION**

From the literature presented in this reading it is evident that there are many challenges facing critically ill patients admitted to the ICU, both during their ICU stay and during recovery from critical illness. Furthermore, limited literature is available to support rehabilitation services after hospital discharge (O'Neill, et al., 2014). More research and subsequent evidence is needed to identify those factors in the South African patient population that affect patients' functional abilities and QOL after a period of critical illness and to identify relationships between these factors to motivate for the establishment of structured rehabilitation services for this patient population.

Chapter three describes the methods used to answer the research questions posed in chapter one.

CHAPTER 3

3. METHODS

The methodology discussed in this chapter is based on the findings of the literature review discussed in chapter two. The ethical considerations that were taken into account during the study are given. The study design, sample population, inclusion and exclusion criteria as well as instrumentation and data collection procedure used during the study are discussed in detail. An explanation of the pilot study, its aims, methodology and its implications on the main study procedure is given. The methods for data analysis are also discussed.

3.1 ETHICAL CONSIDERATIONS

Ethical clearance to perform this study was obtained from the University of the Witwatersrand Human Research Ethics (Medical) Committee (Certificate number: M130404) (appendix A). Permission to perform the study in hospitals belonging to the Netcare group was obtained from the Netcare Research Ethics Committee (Certificate number: UNIV-2014-005) (appendix B). Permission was also obtained from the hospital management of Netcare Union (appendix C) and Netcare Mulbarton (appendix D) hospitals to access patient's ICU charts and files and to recruit patients for this study. For the purpose of patient follow up after discharge from the acute care setting, permission was obtained from the hospital management of the following rehabilitation facilities: Netcare Rosebank Rehabilitation centre (appendix E), Life Kensington clinic (appendices F and G), Netcare Rehabilitation hospital (appendix H) and Life Riverfield lodge (appendices F and G). This study was registered on the South African National Clinical Trials Registry and received trial number DOH-27-0614-4751.

3.1.1 Anonymity of Data

Each participant was assigned a participant code at the time of recruitment to ensure anonymity of data. On all data sheets and appointment cards, only the participant code appeared. Each participant's code could be corresponded to his or her name on the list of participant's only. The participants' list was kept in a safe location (hard copy) by the researcher for the duration of the study. By doing this, confidentiality and safe-keeping of participant details were ensured. The participants' list was destroyed by the researcher at the end of the study.

3.1.2 Informed Consent

All participants were provided with an information document about the study and questions they had about the study were answered by the researcher in the presence of a healthcare practitioner known to the participant prior to requesting written informed consent from them for participation. All participants had the right to withdraw from the study at any given time without prejudice or any penalty. Such participants did not have to provide any reasons for withdrawal from the study. All participants had the right to access their own study results if they wished to see it. The results of this study will be made publicly available and the researcher will attempt to publish the results in peer-reviewed journals.

3.1.3 Participant Referral to Specialised Services

If it was found that any given participant was suffering from depression after completion of the PHQ-9 questionnaire, the participant was referred to a psychiatrist for appropriate treatment at the end of the six months follow-up period for this study. The need for assessment by a psychiatrist was discussed with the participant prior to referral and the participant could choose to either attend the assessment or to refuse it.

3.2 STUDY DESIGN

A prospective, observational and longitudinal study was conducted.

3.3 STUDY SETTING

3.3.1 Study Locations

The study sites included the Netcare Union hospital in Alberton and Netcare Mulbarton hospital in Mulbarton. Both of these hospitals are in the South Gauteng province of South Africa.

Alberton is a town situated in the Ekurhuleni Metropolitan Municipality in Gauteng, South Africa. This municipality covers an area of 1975 kilometres squared. This is mainly an urbanised municipality, with 99.4 percent of the population living in urban settlements (Statistics South Africa, 2011). These settlements range from informal to residential suburbs. Ekurhuleni has a population size of 3 178 470. The general population of Ekurhuleni consists of 24.3 percent young people (aged zero to 14) and 71.7 percent working age individuals (age 15 to 64). At the time of the survey, the elderly population represented four percent of the total population of Ekurhuleni. The unemployment rate was 28.8 percent. Three point six percent of persons aged 20

and above had no schooling, 14.6 percent received higher education, and 35.4 percent completed grade 12. The municipality contained 1 015 465 households of which 85 percent had flush toilets with a sewage connection, 57.3 percent had piped water inside the dwelling, and 82.2 percent had electricity for lighting (Statistics South Africa, 2011).

Mulbarton is a town situated in the City of Johannesburg Local Municipality in Gauteng, South Africa. This municipality covers an area of 1645 kilometres squared. This is mainly an urbanised municipality. Johannesburg is the largest city in Africa. It is also the provincial capital of Gauteng. Gauteng is known to be the wealthiest province in South Africa. At the time of the survey, the City of Johannesburg had a population size of 4 434 827 (Statistics South Africa, 2011). The general population of the City of Johannesburg consisted of 23.2 percent young people (aged zero to14) and 72.7 percent working age individuals (age 15 to 64). The elderly population represented 4.1 percent of the total population. The unemployment rate was at 25 percent. Two point nine percent of persons aged 20 and above had no schooling, 19.2 percent received higher education, and 34.7 percent completed grade 12. The municipality contained 1 434 856 households of which 87.1 percent had flush toilets with a sewage connection, 64.7 percent had piped water inside the dwelling, and 90.8 percent had electricity for lighting (Statistics South Africa, 2011).

3.3.2 **Duration of Study**

Participant recruitment took place from 1 March 2014 to 31 March 2015 (13 month period). All final follow-up assessments were completed by August 2015.

3.4 **PARTICIPANTS**

3.4.1 **Eligibility Criteria**

3.4.1.1 **Inclusion criteria**

Patients 18 years or older of both genders who were admitted to the ICU due to respiratory failure (pneumonia, exacerbation of COPD or penetrating or blunt trauma to the chest wall), organ dysfunction or postoperatively (exploratory surgery following trunk trauma; elective cardiac surgery e.g. CABG surgery or valve replacement) and were MV for more than 24 hours were eligible for recruitment.

3.4.1.2 **Exclusion criteria**

Patients with the following conditions were not considered for participation in this study. Those with:

- Terminal illness
- Cognitive impairments or history of mental disorders
- Multiple orthopaedic injuries
- Unstable cardiac conditions e.g. myocardial infarction if they did not undergo CABG surgery, uncontrolled cardiac arrhythmias, aortic stenosis, pulmonary infarction, myocarditis, pericarditis, and dissecting aneurysm.

3.4.2 **Sample Size Estimation**

For this study, the power calculations normally used by statisticians to calculate the estimated sample size for randomized, controlled trials, was not applicable as this was a longitudinal study without randomization and without specific study groups.

Proposed sample size for this study was therefore calculated as follows:

The number of patients admitted to the Union hospital general ICU and cardiac ICU per month was on average 163 patients (estimated from data available over a four month period). Of these patients, on average, 13 fitted the inclusion criteria for the study per month. Approximately 156 patients were therefore potentially available for inclusion in the study over a 12 month recruitment period, depending on their rate of survival as a result of critical illness and their willingness to participate in the study. Each participant that gave consent for inclusion in the study was followed up for six months after discharge. By convention, it was decided to include ten participants for each of the three main outcome measures for this study namely PFIT score, 6MWT distance, and HRQOL (PCS and MCS of SF-36 and EQ-VAS) (Nunally, et al., 1978).To allow for withdrawals and participants being lost to follow-up, ten participants were added to the estimated sample size, thus making allowance for withdrawals or loss to follow of up of 20 percent of the estimated sample size. Therefore the estimated sample size was 50 participants.

3.4.3 **Sample Selection**

Consecutive patient sampling was done from all patients admitted to the ICU (Mulbarton and Union Hospitals) and cardiac ICU (Union Hospital) at the two study sites from 1 March 2014 to 31 March 2015 (13 months period). The initial participant

recruitment period was 12 months, but was prolonged to 13 months due to low recruitment numbers at 12 months. Each patient admitted to the ICU and CICU (Union Hospital) during this period was screened to determine whether they met the eligibility criteria for this study. Those who met the criteria were available for potential recruitment in the study. Recruitment in the study depended on the rate of survival of potential participants as a result of critical illness and their willingness to participate in the study.

3.5 DATA COLLECTION PROCEDURE

3.5.1 Pilot Studies (Inter- and Intra-Rater Reliability Studies)

3.5.1.1 Pilot study one

3.5.1.1.1 Objectives

To familiarise the researcher and research assistant with the PFIT; to establish the inter-rater reliability of the PFIT, used at ICU discharge and hospital discharge to assess participants' functional ability, between the researcher and the research assistant.

3.5.1.1.2 Procedure

The researcher and one research assistant (senior physiotherapist) across the two study sites were involved in PFIT-s assessment of study participants. The number of participants recruited for this pilot study was eight, representing 20 percent of the .estimated sample size of 40 participants. The study site was the Netcare Mulbarton hospital. The participants were patients discharged from the ICU. The researcher and the research assistant each performed the PFIT-s once on the eight participants on separate occasions in the hospital ward by the participant's bedside. The PFIT-s procedure was explained to each participant prior to assessment and consent was obtained from each participant. Each participant was given a rest period of 30 minutes between testing sessions. To calculate the inter-rater reliability, the Pearson correlation was determined between the data sets or scores (from each assessor) collected for each participant using Microsoft Excel 2010.

The Pearson correlation was calculated as r=1 (p=00) for this pilot study. Inter-rater reliability is accepted as sufficient if the Pearson correlations are > 0.80 (indicating an excellent correlation). The inter-rater reliability was therefore excellent for the PFIT-s. These eight participants were not enrolled in the main study. Appendix I shows the PFIT-s pilot study results and

Pearson correlation data. No changes regarding PFIT-s assessment needed to be made for the main study.

3.5.1.2 **Pilot study two**

3.5.1.2.1 Objectives

To familiarise the researcher with study outcome measures and to establish the intra-rater reliability for the 6MWT and HHD measurements that would be performed by the researcher on ICU survivors at one and six months after hospital discharge.

3.5.1.2.2 Procedure

Five participants (healthy volunteers at Union hospital) were involved in pilot study two. The researcher performed the 6MWT and HHD measurements three times on each participant allowing a 30 minutes rest period between test sessions. The 6MWT was administered as per guidelines published by the ATS (ATS, 2002). Three measurements were taken to determine the correlation between three data sets. Handheld dynamometry was applied using the MicroFet2® HHD to measure the strength of the following peripheral muscle groups: Triceps Brachii (elbow extension) and Hamstrings (knee flexion). The procedure for the measurement of peripheral muscle strength using a HHD was adhered to as discussed under 'main study procedure' in section 3.5.2 below.

Measurements were taken three times on the left and right side of each participant. The average muscle strength from the three measurements was then calculated for each muscle tested. This process was repeated 30 minutes later.

To determine the intra-rater reliability, the Pearson correlation was calculated between the data sets or scores collected of the five participants using Microsoft Excel 2010.

The Pearson correlation for right-sided knee flexion HHD was calculated as r=0.88 (p=0.02). The Pearson correlation for right-sided elbow extension HHD and the distance covered during the 6MWT assessment was r=0.99 (p=0.00) for all other data sets. Intra-rater reliability is accepted as sufficient if the Pearson correlations are > 0.80 (indicating an excellent correlation). The intra-rater reliability for right-sided knee flexion and elbow extension HHD and

the 6MWT distance was therefore excellent. Appendices J to L summarises the 6MWT and HHD pilot studies results and Pearson correlations.

From the results of this pilot study, it was concluded that the intra-rater reliability was excellent for the HHD and 6MWT measurements. No changes were made to the testing procedure laid out for the main study.

Each participant was also asked to complete the SF-36, EQ-5D, PHQ-9 and RPAQ questionnaires in order to establish the amount of time that would be needed for the administration of the questionnaires during the main study. It took approximately 20 minutes in total for participants to complete the four questionnaires.

3.5.2 **Main Study**

3.5.2.1 **Initial contact**

Patients admitted to the ICU's of the two mentioned research sites were screened daily by the researcher (Union hospital) or research assistant (Mulbarton hospital) for eligibility for the study. The researcher or assistant approached patients who fit the inclusion criteria and explained the nature of the study on the day prior to discharge from the ICU to the ward. Only patients with a Glasgow Coma Scale score of 15 with the ability to understand and respond appropriately to simple questions were approached. If a patient was unable to do this or had a GCS score of fewer than 15, the researcher or research assistant would approach the patient again on the following day to see if the status of the patient had changed. If a patient's level of awareness was not sufficient to be able to provide signed, informed consent for the study, such a patient was excluded from the study.

A participant information sheet (see appendix M) was given to the participant fitting the eligibility criteria. The contact details (telephone number, mobile number, e-mail address) of the researcher, research supervisor, and ethics committee were also provided. The researcher or assistant approached the participant the following day to answer any questions that the person might have and to obtain written, informed consent (see appendix N) for inclusion in the study. On receipt of written consent the researcher or assistant captured information required for the demographic questionnaire (see appendix O) during a short interview. The ICU charts of each participant were reviewed and the necessary data needed to calculate APACHE II and SAPS II scores were collected from the charts. The length of MV and ICU LOS

were also recorded. Thereafter, the PFIT-s was performed in the hospital ward by the patient's bedside. The PFIT-s was performed in accordance with the prescribed guidelines.

Prior to discharge from the hospital, the researcher or assistant performed the second PFIT-s on each participant. The length of hospital stay was also recorded at this point. The researcher provided each participant with an appointment date for the one month post discharge assessment specifying the date, time, and venue as well as the contact details of the researcher. The participants were informed that they would be reimbursed for their travel costs at a fixed rate, if requested, and that they had to wear comfortable clothing and shoes (due to the nature of the outcome measures assessed) when they arrived for the follow-up assessment.

Each participant was sent a mobile text message (one week before the appointment) and was phoned (two days before appointment) as a reminder and confirmation of their attendance at the follow-up appointment.

3.5.2.2 **One month follow-up assessment**

The researcher assessed one participant at the Netcare Rehabilitation hospital in the physiotherapy department. The researcher met with all the remaining participants at the treatment rooms of Sklaar, Laidler and Associates Physiotherapists in Alberton where the researcher is employed.

On arrival, each participant was asked to sit and relax in a chair for 10 minutes prior to testing. During this time demographic information were verified with the participant (including details on returning to employment). After the 10 minutes rest period, the researcher explained the 6MWT to the subject. The subject then performed the 6MWT according to the ATS procedure and all measurements (blood pressure, heart rate, and oxygen saturation) were recorded. The 6MWT was performed a second time after a 30 minute rest period with all measurements recorded to account for a 'learning effect' and the best of the two tests was captured for data analysis.

After the 6MWT the participant was asked to complete the SF-36, EQ-5D, PHQ-9 and RPAQ questionnaires in a self-administered fashion. The researcher inquired about the participant's preferred language for completing the SF-36, EQ-5D, and PHQ-9 questionnaires, and provided the questionnaire in that language. The researcher seated the patient on a comfortable chair at a desk in an office with

sufficient ventilation and lighting. The researcher explained the purpose of each questionnaire to the participant and provided instructions on how to complete it according to the prescribed guidelines. No attempts were made by the researcher to influence the responses of the participant to any of the questions in the questionnaires.

After completion of the questionnaires, peripheral muscle strength testing was performed by the researcher. The specific muscle groups tested, starting positions and dynamometer placements are summarised in appendix P. All muscle testing was performed on both sides of the body and muscle strength values were recorded in Newton using the HHD. A practice trial was performed with each participant prior to measurements being recorded to ensure they understood the testing procedure and experienced the feel of pushing against the dynamometer. The researcher explained each movement/muscle group tested to the participant prior to testing. During the tests, isometric force was measured using “make” tests. The participant was asked to build his/her force gradually over two seconds and then maintain a maximal contraction for five seconds. During this seven second procedure, the researcher held the dynamometer stationary against the limb segment involved (Andrews, et al., 1996).Each muscle was tested three times and the measurements recorded. The mean of the three values for each muscle was used for data capturing. No rest periods were given between measurements of different joint or limb movements (Andrews, et al., 1996).

At the end of the appointment, refreshments were provided to the participant in the form of bottled water and a small maize snack. The participants were provided with an appointment card for the six months follow-up assessment. Data was transferred from the data collection sheets and questionnaires onto Microsoft Excel spreadsheets in preparation for data analysis.

Each participant was sent a mobile text message (one week before the appointment) and was phoned (two days before appointment) as a reminder and confirmation of their attendance at the six months follow-up appointment.

3.5.2.3 **Six months follow-up assessment**

The procedures followed during this assessment session were exactly the same as discussed for one month follow up above. The researcher met with all the remaining

participants at the treatment rooms of Sklaar, Laidler and Associates Physiotherapists in Alberton.

Throughout all assessment sessions, emergency medical equipment was available for use. The researcher and assistant were trained in basic life support and in the use of an automated external defibrillator. Sklaar, Laidler and Associates Physiotherapists had an agreement with the casualty department of the Netcare Union hospital to contact them if an emergency arose. This agreement also applied to the study assessments. No emergency situations related to the study participants arose during the data collection period.

At the end of the six month assessment each participant was thanked for his/her participation in the study. The participant was given informal feedback as to observed changes in their condition and ensured that the final results of the study would be made available to them at the end of the data analysis and interpretation phase of the study if they requested this. Those participants who showed the possibility of having depression, after screening using the PHQ-9 questionnaire, were given the name and contact details of a psychiatrist in Alberton, which they could consult if they wished to do so.

For this observational, longitudinal study, all participants were followed-up at discharge from hospital, at one month and six months after discharge. At discharge from hospital, 30 minutes were spent with each of the 22 participants to complete the PFIT and to arrange the details of the follow-up appointments. At one month after discharge from hospital, one hour was spent with each of the 15 participants for follow-up purposes. At six months after discharge from hospital, one hour was spent with each of the 11 participants for follow-up purposes. The total time spend by the researcher on follow-up was 37 hours.

3.6 VARIABLES

3.6.1 Dependent Variables

Physical activity (6MWT distance) at six months; HRQOL (PCS and MCS of SF-36 and EQ-VAS) at six months; peripheral muscle power; PFIT-s scores; level of depression; return to work.

3.6.2 Independent Variables

Severity of illness (APACHE II and SAPS II scores); ICU and hospital LOS

3.6.3 Confounding Variables

Smoking status, alcohol consumption, substance abuse, diet and previous physical disability.

3.7 OUTCOME MEASURES AND INSTRUMENTATION

3.7.1 Severity of Injury Scoring Systems

The APACHE II was calculated for each participant using the QxMD Calculator (2010) using each participant's data on admission to ICU. This is a free smart phone/ tablet application developed by QxMD Software. The QxMD is recognized as a leading developer of free medical software for mobiles devices. Their software content is developed in cooperation with expert physicians from their respective fields. The software is available from http://www.QxMD.com. The APACHE II is a general mortality prediction model widely used in the ICU (Badreldin, et al., 2011). It was released in 1985 and developed to predict the mortality of ICU patients (Knaus, et al., 1985; Desai and Lakhani, 2013) It is useful in predicting mortality outcomes, LOS, assisting clinical decision making and in monitoring of the services provided in the ICU (Bouch and Thompson, 2008) The validity and reliability of the APACHE II scoring system is well established (Grmec and Gasparovic, 2001; Chou, et al., 2010; Tsai, et al., 2012; Raj, et al., 2014). Cardosa and Chiavona (2013) reported that the APACHE II scoring system is useful to stratify patients who are at greater risk of mortality after discharge from ICU. Some limitations in the APACHE II scoring system have also been reported in the literature. Girbes et al. (2001) conducted a study assessing the reliability and accuracy of the APACHE II scoring system in two ICU's. They reported that APACHE II scoring may be flawed as too high scores are entered by physicians when scoring the APACHE II. Scores were reported to be too high resulting in the over-estimation of mortality risk. They concluded that assessment using the APACHE II scoring system can show variable scores and that these scores can be unreliable to a certain extent (Girbes, et al., 2001).

The SAPS II freely available on-line calculator was used to calculate SAPS II scores for each participant. The SAPS II calculator by Clinical Calculator was used. This is a free online version available on http://clincalc.com/IcuMortality/SAPSII.aspx. The SAPS II is used to calculate the probability of hospital mortality for ICU patients over the age of 18 years (Badreldin, et al., 2011). This calculator is based on the SAPS II tool developed from a large sample of 12997 medical and surgical patients in North America and Europe as reported by Le Gall et al. (1993). The SAPS II includes 17 variables including 12 physiological variables, age, admission type, and three

underlying disease variables (Le Gall, et al., 1993). During the initial development and validation of the SAPS II it showed good validity for the large international patient sample (Le Gall, et al., 1993). Capuzzo et al. (2000) reported the SAPS II to be valid in the surgical ICU population. In a study evaluating different models to predict 30-day mortality in primary pontine haemorrhage, the SAPS II was found to be fit to approximately predict 30-day mortality with very good calibration(p=0.89). A study by Kim et al. (2005) investigating the performance of the SAPS II, concluded that the SAPS II is an excellent predictor of mortality with excellent calibration. One limitation of the SAPS II is that the score is complicated to calculate. The discrimination of the SAPS II was reported to be moderate with an aROC (area under receiver operating characteristic curve) of 0.76 by Sakr, et al. (2012).Capuzzo et al. (2000) also reported that the predictive ability of the SAPS II is affected by the type of ICU admission as well as the location of the patient in the hospital prior to ICU admission.

3.7.2 **Peripheral Muscle Strength**

Peripheral muscle strength was assessed using a MicroFet2® HHD (Hoggan Health Industries, Inc., Draper, Utah). The reliability and validity of using HHD for patients who are older, weak or physically impaired has been well established in the literature (Kwoh, et al., 1997; Roebroeck, et al., 1998; Wang, et al., 2002 Dunn and Iversen, 2003; Roy and Doherty 2004; Taylor, et al., 2004). During a reliability study by Gontkof et al. (2008), HHD was found to have very high intra-rater reliability with the experience of the tester having very little or no significant effect on the intra-rater reliability. Arnold et al. (2010) reported from a study, using repeated HHD measures of 18 older adult (age 65 to 92 years) male and female participants, that HHD showed good inter-rater and intra-rater reliability and validity for the assessment of muscle strength at the hip and knee, but not at the ankle. They concluded that a HHD can be used effectively in the older adult population (Arnold, et al., 2010).The inter-rater reliability for the MicroFet HHD was reported to be excellent by Bellew, et al. (2003) who investigated the reliability of the MicroFet HHD in measuring hip abduction muscle strength (r=0.94). They also found the intra-rater reliability to be excellent (r=0.88 – r=94) (Bellew, et al., 2003).

The use of a HHD also has certain limitations. Handheld dynamometry would not be an appropriate measurement tool if the assessor has insufficient strength to overcome that of the patient being assessed. The dynamometer surface does not conform to the body surface being tested as an assessor’s hand would, resulting in patients reporting tenderness over the place where the HHD is applied to. Gontkof

etal. (2008) reported that problems of stabilising of the HHD were experienced when difficult movements were assessed in strong patients. Advantages of using a HHD are that it is inexpensive, portable, and requires minimal training for proper use (Gontkof, et al., 2008). A HHD provides more objective testing results as compared to manual muscle testing (Arnold, et al., 2010; Jannsen, et al., 2012). The HHD provides an objective measure of isometric muscle strength at a fixed static joint position in kilograms, pounds or Newton (Arnold, et al., 2010; Jannsen, et al., 2012). During manual muscle testing, the assessor will rate muscle strength subjectively on a zero to five scale. The accuracy of this rating is subject to the education and experience of the assessor. Due to the accuracy and reliability of manual muscle testing being poor, HHD may be a better option for objective muscle strength assessment (Jannsen, et al., 2012). Other researchers have used HHD in the assessment of critically ill patients (Van Aswegen, et al., 2010). Appendix P shows the testing positions and HHD placement followed in this study.

3.7.3 Exercise Endurance

Exercise endurance was assessed using the 6MWT. The 6MWT has excellent short term reproducibility when administered by the same assessor (ATS, 2002). Equipment needed for the 6MWT as per ATS guidelines are: a stopwatch, two small cones to mark turnaround points, standard chair, worksheets on a clipboard to record measurements, supplemental medical oxygen, sphygmomanometer, telephone and automated external defibrillator to be used in the case of emergencies (ATS, 2002). A tape measure to measure out a 30 meter walking distance is also needed. The 6MWT has been used in several studies on the outcomes of survivors of critical illness (Herridge, et al., 2003; Van Aswegen, et al., 2010; Aitken, et al., 2012).Test-retest reliability for the 6MWT has been established in patients with Alzheimer's diseases (r=0.95) (Ries, et al., 2009), the geriatric population (r=0.95) (Steffen, et al., 2002), patients with osteoarthritis (r=0.94) (Kennedy, et al., 2005), patients who had stroke (r=0.99) (Fulk, et al., 2008) and patients who had traumatic brain injuries (Van Loo, et al., 2004). The construct validity of the 6MWT has been reported to be excellent in patients with COPD mobilizing independently (r=0.65) (Szekely, et al., 1997).Jones and Rikli (1998) reported that the 6MWT had moderate convergent validity from their investigation of the reliability and validity of the 6MWT in older adults.

3.7.4 Health-Related Quality of Life

Health related quality of life was assessed using the SF-36 and EQ-5D questionnaires. The following translations of the SF-36 questionnaire were used

(depending on patient preference) in this study: English (South African) (appendix Q), Afrikaans, Sesotho and Zulu. Appendices R to T contain the translation certificates of the questionnaires. Scores of the SF-36 were calculated using the QualityMetrics Health Outcome Scoring Software 4.5. This was provided by Quality Metrics through OptumInsight Life Sciences Inc. together with the license to administer the SF-36. License number: QM023025 (appendix U). The SF-36 questionnaire has been comprehensively validated in the critically ill patient population (Dowdy, et al., 2005; Khoudri, et al., 2012) and is reported to be an acceptable, reliable and valid outcome measure to assess HRQOL in survivors of critical illness (O'Neill, et al., 2014) and in many other disease populations (Németh, 2006; Cox, et al, 2015).

The SF-36 questionnaire is a generic health profile measure of general health status which is relevant across age, disease, and treatment groups. It is valuable as it can be used across a range of conditions and in different settings (Nemeth, 2006).The SF-36 questionnaire utilises 36 items to obtain two summary scores of physical and mental health and eight domain scores of HRQOL (Dowdy, et al., 2005). The eight domains are: PF, BP, GH, VT, SF, RE and MH. The eight domain scores make up the summary scores for SF-36 namely PCS and MCS (Dowdy, et al., 2005; Williams, et al., 2015). The SF-36 summary scores (PCS and MCS) allow for ease of interpretation of results (Dowdy, et al., 2005). Due to the fact that participant responses to the questions posed in the SF-36 are completed using a point scale instead of 'yes' or 'no' answers, it allows for positive and negative health states to be identified (Brazier, et al., 1992).

The EQ5D questionnaire is a simple preference-based health profile measure of HRQOL of which the reliability and validity has been well established in the ICU environment (Flaatten, et al., 2008; Khoundri, et al., 2012).The EQ-5D can be used in population health surveys and it can also be used in combination with other condition-specific measures. The EQ-5D is a self-administered questionnaire (Nemeth, 2006). The EQ5D was available to participants in the following language translations (depending on patient preference) during the current study: English (South African) (appendix V), Afrikaans, Zulu, Sesotho, Setswana, and Xhosa. Permission to use the EQ-5D free of charge was provided by the EuroQol Group Foundation (appendix W). The EQ-5D consists of two sections: the first section consists of five questions (each with three possible responses) that evaluate various dimensions (mobility, self-care, usual activities, pain or discomfort, and depression or anxiety) of QOL; the second section consists of a visual analogue scale (VAS) in the

form of a vertical line that depicts worst to best possible health state (Chen, et al., 2014b). Results from the EQ-5D could provide 243 possible health profiles (Flaatten, et al., 2008). Some researchers have used and reported on the EQ-5D in the critical care population (Dowdy, et al., 2005; Sacanella, et al., 2011; Parson, et al., 2012; Goixart, et al., 2013; Schneiderman, et al., 2013). Sacanella et al. (2011) investigated the HRQOL and functional status of the elderly medical ICU population after discharge from hospital in a prospective study, and reported that the survival of these patients was low and their HRQOL did not improve significantly.

Many studies have compared the EQ-5D and the SF-36 questionnaires in different patient populations. The two measures differ and the validity and responsiveness differ depending on the specific patient population studied (Chen, et al., 2014a).It is beneficial to assess a specific study population using both the SF-36 and EQ-5D questionnaires as they contain different domains of HRQOL, all of which are important to assess. The SF-36 is useful as it provides continuous data sets for each domain of HRQOL as well as providing information on the mental and physical domains of HRQOL. The EQ-5D questionnaire is useful as it provides categorical data for the different domains of HRQOL. The EQ-5D questionnaire VAS section provides a self-reported measure of health status. The SF-36 and EQ-5D questionnaires differ in the domains under investigation, scoring procedures, and type of data obtained. It would therefore be important to include both these questionnaires in a study investigating HRQOL as it will ensure that all domains of HRQOL are thoroughly investigated. It is important to investigate all domains of HRQOL in a mixed ICU population as these patients may differ with regards to the domains of HRQOL they find problematic after discharge from hospital.

3.7.5 **Presence and Severity of Depression**

The presence and severity of depression symptoms among study participants was screened for using the PHQ-9. The PHQ-9 is an easy to use and reliable screening tool commonly used for detecting depression. It is a self-administered version of the Primary Care Evaluation of Mental Disorders diagnostic instrument for common mental disorders (Wu, 2014). It consists of nine self-report questions about symptoms of depression. A score of eight to 11 on the PHQ-9 is recommended as the cut-off score for depression (Kumei, et al., 2015). The PHQ-9 score indicates the presence of mild, moderate, moderately severe, and severe depression. These descriptions are represented by PHQ-9 scores of five, ten, 15 and 20 respectively. It

is free for usage to online users and is available in more than 35 languages, including English.

A study by Wu (2014) investigated the PHQ-9 questionnaire to determine its validity and reliability in patients with chronic disease and found it to be a valid and reliable tool. It is easy to administer as it takes approximately ten minutes to complete (Wu, 2014). The PHQ-9 was also found to be a valid and reliable screening tool for depression in the primary care setting (Chan, et al., 2013). No studies were found that had assessed the validity and reliability of the PHQ-9 in critically ill patients or in those recovering from critical illness after discharge from hospital.

There are no South African translations of the PHQ-9 questionnaire. The PHQ-9 was available to participants in English in the current study (appendix X). Appendix X also shows the usage and scoring instructions for the PHQ-9. The PHQ-9 has specificity and sensitivity of 88 percent for major depressive disorders at a cut-off score of more or equal to ten. It has a good internal consistency, indicated by a Cronbach's α being 0.89 (Chan, et al., 2013).

3.7.6 **Functional Ability**

Functional ability of participants in ICU was assessed using the PFIT-s. The PFIT-s is a reliable and responsive measure used in the ICU patient population (Skinner, et al., 2009). Appendix Y shows the scoring sheet of the PFIT-s. Denehy et al. (2013) reported on the validity, responsiveness, and predictive utility of the PFIT-s's interval scores in the ICU. They concluded that the PFIT-s's intervals scores are valid, responsive, and predictive of key outcomes. The PFIT-s was found to be a safe and inexpensive outcome measure to use in the ICU and its use is recommended in the ICU patient population (Denehy, et al., 2013). Skinner et al. (2009) examined the reliability and responsiveness of the PFIT-s in mechanically ventilated patients with tracheotomies in the ICU and found that it was good. They reported no adverse effects during testing in the ICU. The conclusion was that the PFIT-s is an outcome measure with good reliability and responsiveness and that it can be used to prescribe and assess exercise and mobilisation in the ICU (Skinner, et al., 2009). Denehy et al. (2014) reported on the use of the PFIT-s in survivors of critical illness. They concluded that the PFIT-s is valid to measure the functional status of critically ill patients mechanically ventilated in ICU for more than 96 hours if they are alert and

awake, able to follow commands and have enough muscle strength to participate in the testing process (Denehy, et al., 2014).

3.7.7 Physical Activity

Physical activity level of participants after discharge from hospital was assessed using the RPAQ. The RPAQ has been found to be a valid questionnaire to use to rank patients on the basis of time spent on activities of vigorous intensity and also total energy expenditure (Besson, et al., 2010). This questionnaire was only available in English (appendix Z) and its use is free of charge.

3.8 BIAS

The only possible bias involved in this study may be that some of the participants were known to the researcher as he was one of the treating physiotherapists during their time in ICU. These participants were not treated any different during study assessments and received their regular physiotherapy treatment. All physiotherapy treatment sessions and study assessment sessions were kept completely separate with no coaching of any participant.

3.9 FUNDING

The study was funded by the South African Society of Physiotherapy Research Foundation and the University of the Witwatersrand Medical Faculty Research Endowment Fund.

Neither the researcher nor research assistant gained financial or other benefits from the results of the study.

3.10 STATISTICAL METHODS

Data were captured and entered on Excel spreadsheets. The Statistical Programming for the Social Sciences Statistics Version 23 software package was used for data analysis. Descriptive statistics were used to present the data. Continuous data such as PFIT-s interval scores, 6MWT distance, peripheral muscle strength, APACHE II and SAPS II scores and LOS were summarised as means and standard deviations (SD). Categorical data such as gender were summarised as numbers and percentages. Paired samples t-tests were used to assess changes in continuous data over time. Chi-square tests were used to compare categorical data.

Due to the small sample size (n=24), the Spearman's rho was used to measure the degree of association between variables. A linear regression model was used to assess relationships between multiple variables.

Relationships were considered to be very strong if the value of r was -1.0 to -0.8 or 0.8 to 1.0, strong if the value of r was -0.79 to -0.6 or 0.6 to 0.79, moderate if the value of r was -0.59to -0.4 or 0.4 to 0.59, weak if the value of r was -0.39 to -0.2 or 0.2 to 0.39, or none or very weak if the value of r was -0.19 to 0.0 or 0.0 to 0.19.

During statistical analysis, testing was done at the 0.05 level of significance ($p \leq 0.05$) and confidence intervals (CI) were set at 95%.

Assistance was sought from a statistician at the Faculty of Health Sciences of the University of the Witwatersrand and a statistician external to the University. Guidance was sought from the study supervisor. The results of the study are discussed in detail in chapter four.

CHAPTER 4

4. RESULTS

Intensive care unit patients who survived critical illness in the private health care sector of South Gauteng province were included in this study. Results in this chapter are reported in the format of the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines for reporting a cohort study. A total of 166 potential study participants were identified over a 13 month period. After recruitment, 24 patients from the two hospitals were enrolled in this study (see Figure 4.1).

4.1 PARTICIPANTS

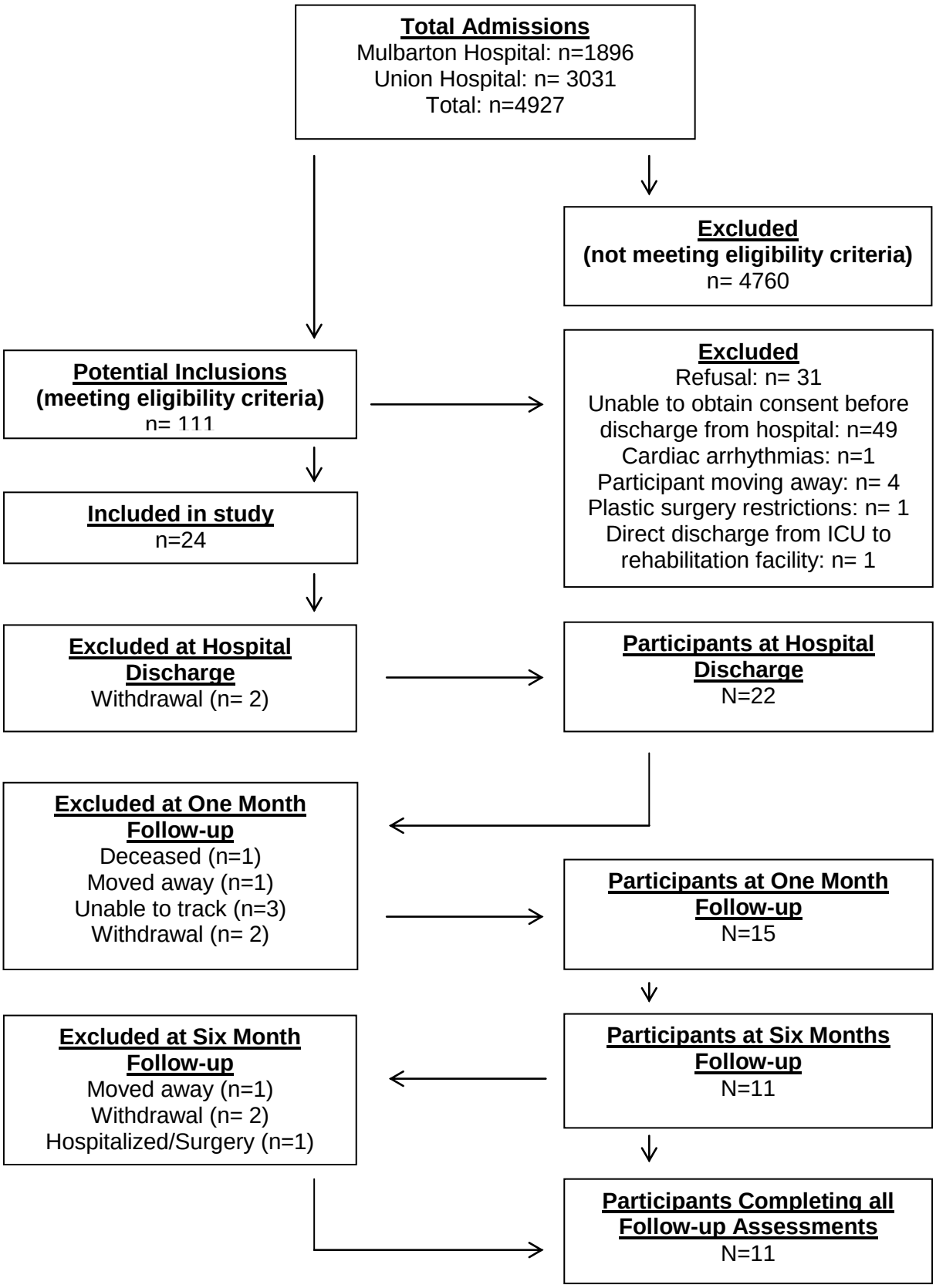


Figure 4.1: Flow of Participations throughout the Study

Forty nine patients were excluded from the potential study participant's list due to the inability to trace these patients. The reason for this is that patients who were transferred from the ICU to the normal hospital ward were often discharged home within one or two days after ICU discharge. Participants required time to read the information document for the study and often requested to first discuss their participation with their family members before consenting to participate. This process delayed the recruitment of participants and these patients were then discharged before a decision regarding participation in the study was made; hence they were lost to follow-up. The researcher made an effort to visit these participants twice a day to inquire whether they had made a decision regarding participation in the study. Some participants also reported that they were not feeling well at the time they were approached with the information document and requested that the researcher return the next day to explain details regarding the study, only to find that the patient had in fact been discharged home. A number of participants were discharged home directly from the ICU and were not able to perform the PFIT-s at the specific time points in the study design. The researcher viewed these participants as "unable to obtain consent before discharge from hospital" due to the fact that they were discharged from hospital before the researcher could recruit them.

At the time of discharge from hospital, two participants withdrew. The reason provided by both was that they felt they had a long hospital stay and did not want any further tests done on them. At one month follow-up, two participants withdrew from the study. One stated a lack of time to participate further in the study and one reported return to work and resultant time constraints to attend sessions for reassessment as the reason for withdrawal. At six months after discharge from hospital, a further two participants withdrew from the study. Both provided the reason of being very busy at work as the reason for withdrawal.

Data sets for 24 participants were in included in analyses at the time of study enrolment. At time of discharge from hospital, data sets for 24 participants were included in analysis. At one month follow-up assessment, data sets for 15 participants were included in analysis. At six months follow-up assessment, data sets for 11 participants were included in analysis.Not all participants completed all assessments of all outcome measures. The recorded drop-out rate for the study was 37.5% (n=9) at one month follow-up and 54.2% (n=13) at six months.During data analysis, per protocol analysis was performed.

At the time of discharge from ICU to the ward, three participants were unable to complete the march on spot (MOS) component of the PFIT-s due to weakness. At hospital discharge 21(87.5%) participants performed the PFIT-s. One participant chose not to perform the test due to weakness, but agreed to continue participation in the study. One participant could not complete the MOS component of the PFIT-s due to pain. There were three missing data sets.

4.2 BASELINE CHARACTERISTICS AND DEMOGRAPHICS OF STUDY PARTICIPANTS

Demographic and admission details, mortality and morbidity estimation scores, surgical details, length of MV and length of ICU stay were collected for 24 (100%) participants at baseline.Table 4.1 summarises the baseline characteristics and demographics of the study participants.

Table 4.1: Baseline Characteristics and Demographics of Study Participants

Characteristic	Median (n=24)	Percentiles 25 (n=24)	Percentiles 50 (n=24)	Percentiles 75 (n=24)
Age (years)	51.5	41.3	51.5	60.8
	N		**Percentage (%) (n=24)**	
Gender				
▪ Males	19		79.2	
▪ Females	5		20.8	
Handedness				
▪ Right	24		100	
▪ Left	0		0	
Living arrangements				
▪ Living alone	3		12.5	
▪ Living with others	21		87.5	
▪ Support available at home	24		100	
Level of education				
▪ Grade 9	1		4.2	
▪ Grade 11	1		4.2	
▪ Grade 12	9		37.5	
▪ Diploma	7		29.2	
▪ Basic degree qualification	2		8.3	
▪ Honours degree qualification	2		8.3	
▪ Masters degree qualification	2		8.3	
Type of occupation				
▪ Unemployed	1		4.2	
▪ Physical labourer	5		20.8	
▪ Office worker	15		62.5	
▪ Pensioner	3		12.5	
Previous disabilities and pre-morbid diseases:	12		50	
▪ Dyslipidaemia	3		25	
▪ Hypertension	1		8.3	
▪ Cardiac stenting surgery	1		8.3	
▪ Cardiac valve replacement surgery	1		8.3	
	1		8.3	
▪ Diabetes mellitus	1		8.3	
▪ Chronic renal failure	1		8.3	
▪ Laparotomy	1		8.3	
▪ Visual difficulties	1		8.3	

▪ Cancer ▪ Low back pain	1	8.3

A variety of pre-morbid diseases and disabilities were reported by study participants, with the most common pre-morbid disease being dyslipidemia (n=3). No participants reported a smoking history, history of alcohol or substance abuse or a history of dietary abnormalities.

Figure 4.2 shows the age distribution and frequencies of study participants.

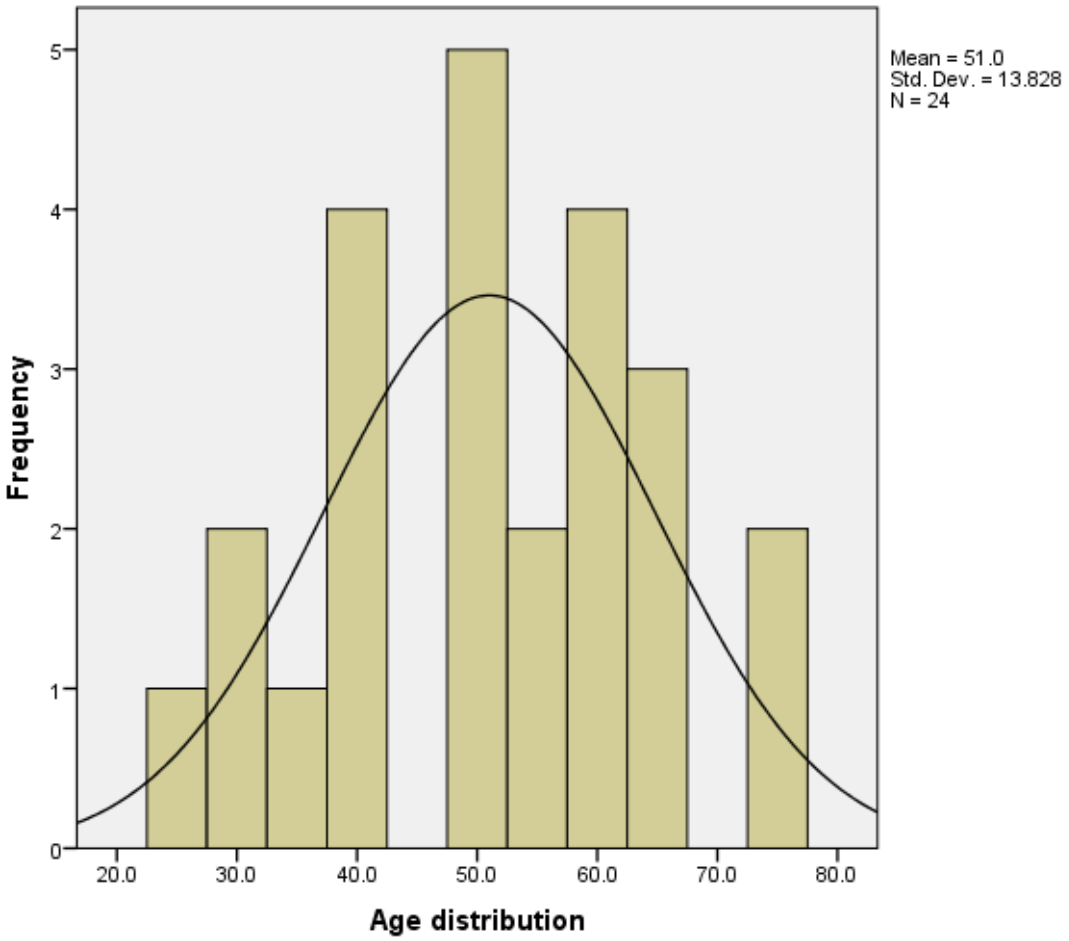


Figure 4.2: Age Distribution and Frequency of Study Participants

Table 4.2 summarises the reasons for admission and types of surgery that study participants underwent.

Table 4.2: Reasons for Admission and Types of Surgery Recorded for Study Participants

Admission type	N	Percentage (%) (n=24)
Medical admissions	8	33.3
▪ Pneumonia	2	25
▪ Pulmonary Tuberculosis	1	12.5
▪ Pleural effusion	1	12.5
▪ Pulmonary oedema	1	12.5
▪ COPD	1	12.5
▪ Septicaemia	1	12.5
▪ Chronic renal failure	1	12.5
Trauma admissions	7	29.2
▪ Penetrating thorax trauma	1	14.3
▪ Blunt trauma to the thorax and abdomen	6	85.7
Cardiac admissions	7	29.2
▪ Congestive cardiac failure	1	14.3
▪ Coronary artery bypass graft	4	57.1
▪ Mitral valve replacement	1	14.3
▪ Aortic valve replacement, mitral valve replacement and coronary artery bypass graft	1	14.3
Surgical interventions	19	70.8
▪ Elective surgical intervention	6	31.5
▪ Non-elective surgical intervention	11	57.8

The number of medical (n=8), trauma (n=7) and cardiac (n=7) admissions were almost equally distributed in the study sample, with the majority of participants (n=19) undergoing surgical interventions.

All participants received physiotherapy treatment during their ICU and hospital ward stay. These treatment sessions would generally consist of chest physiotherapy treatment, assistance with mobilization and strengthening exercises.

Those participants admitted with medical conditions were unlikely to continue with physiotherapy treatment after discharge from hospital unless they still had problems with retained pulmonary secretions or physical weakness. If required, treatment would generally involve chest physiotherapy treatment and rehabilitation to improve muscle strength and exercise endurance. Those participants who were admitted with trauma were likely to continue with physiotherapy treatment after discharge from hospital and would generally include physical rehabilitation to improve muscle strength and exercise tolerance. Those participants who underwent CABG surgery would generally also continue with physiotherapy after discharge from hospital. The first six weeks after discharge would consist if an unsupervised home exercise

programme, after which the participant would continue with a supervised cardiac rehabilitation in the physiotherapy outpatient department.

Table 4.3: Mechanical Ventilation Duration, ICU LOS, ward LOS, APACHE II Scores, SAPS II Scores, and predicted mortality rates for all 24 participants.

Characteristic	Mean (±SD) (n=24)	Median (n=24)	Percentiles 25 (n=24)	Percentiles 50 (n=24)	Percentiles 75 (n=24)
MV duration (days)	9.1 (8.4)	7	2.3	7	15.3
ICU LOS (days)	18.3 (10)	15.5	10.3	15.5	28
Hospital LOS after ICU discharge (days)	7.8 (11.1)	4.5	2	4.5	8.5
APACHE II scores	15.3 (8)	12.5	9.3	12.5	21.8
Predicted mortality rate percentage (APACHE II)	23.5 (16.6)	15.6	10.3	15.6	38.9
SAPS II scores	44 (20.9)	41.5	27	41.5	64.8
Predicted mortality rate percentage (SAPS II)	36.3 (33.5)	27.6	7.9	27.6	73.5

A higher APACHE II or SAPS II score indicates a higher chance of mortality. The relatively high risk of mortality of this group of participants resulted in prolonged duration of MV and ICU and hospital stay.

4.3 PARTICIPANTS' LEVEL OF FUNCTIONAL ABILITY AT DISCHARGE FROM ICU AND CHANGES IN THE LEVEL OF FUNCTIONAL ABILITY AT HOSPITAL DISCHARGE

Participants' level of functional ability at discharge from ICU and at hospital discharge was measured using the PFIT-s. Table 4.4 summarises the findings.

Table 4.4: PFIT-s scores at ICU Discharge and Discharge from Hospital

PFIT Variable	ICU discharge (n=24)	Hospital Discharge (n=21)	95% CI	p-Value	IQR		
					Percentiles 25 (n=24) ICU Discharge/Hospital Discharge	Percentiles 50 (n=24) ICU Discharge/Hospital Discharge	Percentiles 75 (n=24) ICU Discharge/Hospital Discharge
PFIT-s Interval Score (score out of 10)							
▪ Mean (±SD)	6.7 (1)	7.1 (1.2)	-0.7, -0.06	0.02*	6/ 6.4	6.8/ 7.1	7.7/ 7.9
▪ Median	6.8	7.1					
▪ Minimum	4.9	4.4					
▪ Maximum	7.9	8.8					
Marching on Spot (steps/minute)							
▪ Mean (±SD)	37.9 (11.5)	43.8 (16.4)	-12.4, 0.5	0.07	30.5/ 37.2	38.5/ 45.2	43.6/ 51.8
▪ Median	27.6	38.5					
▪ Minimum	0	0					
▪ Maximum	58.6	83.5					
Shoulder Flexion Endurance (repetitions/minute)							
▪ Mean (±SD)	27.9 (8.1)	29.1 (10.5)	-3.3, 1.3	0.38	20/ 20	27.6/ 25.3	33.8/ 40
▪ Median	25.3	45.2					
▪ Minimum	12.9	15.1					
▪ Maximum	42.2	47.8					

*Indicates significance at level p<0.05.

The changes in PFIT-s variables were determined by a paired samples t-test. The change in mean PFIT-s interval score between ICU discharge and hospital discharge was 0.4 points (± 0.7) which was statistically significant (p=0.02). The change in mean cadence for MOS component of PFIT-s between ICU discharge and hospital discharge was 6 steps per minute (± 14.2). This change was not statistically significant (p=0.07). The change in mean cadence for shoulder flexion component of PFIT-s between ICU discharge and hospital discharge was one repetition/minute (± 4.9) but again this change was not statistically significant (p=0.38). For the MOS component and shoulder flexion endurance component of PFIT-s p>0.05, thus the null hypothesis is not rejected. The null hypothesis is rejected for the PFIT-s interval score as p<0.05.

4.4 EXERCISE ENDURANCE OF SURVIVORS OF CRITICAL ILLNESS AT ONE MONTH AFTER HOSPITAL DISCHARGE AND CHANGES IN EXERCISE ENDURANCE AT SIX MONTHS

Exercise endurance was measured using the 6MWT over the first six months after discharge from hospital. Each participant's percentage of age-predicted distance achieved with the 6MWT was calculated using the following equation: expected 6MWT distance= 868.8 – (2.99 x age) – [74.7 x gender (male= 0; female=1)] (Gibbons et al., 2001). Table 4.5 summarises the findings of the 6MWT.

Table 4.5: Results for 6MWT as Assessed at One and Six Months following Discharge

Variable	1-month (n=14)	6-months (n=11)	95% CI	p-Value	IQR		
					Percentiles 25 (n=24) 1 Month/6 Months	Percentiles 50 (n=24) 1 Month/6 Months	Percentiles 75 (n=24) 1 Month/6 Months
6MWT distance (m)							
▪ Mean (±SD)	421.5 (134.5)	474.5(110)	-104.5, 2.6	0.60			
▪ Median	425	490			332.5/ 400	425/ 490	517.5/ 570
▪ Minimum	110	300					
▪ Maximum	628	630					
Percentage of predicted distance achieved (%)							
▪ Mean (±SD)	60.45 (19.1)	68.8 (16.2)	-15.4, 0.1	0.53	48.6/ 58	61.5/ 73.3	76/ 83.4
▪ Median	61.5	73.3					
▪ Minimum	16	43.7					
▪ Maximum	88.4	88.8					

*m = meters.

Non-statistically significant improvements were observed in 6MWT distance achieved (p=0.6) and percentage of predicted distance achieved (p=0.53).

4.5. PERIPHERAL MUSCLE STRENGTH AT ONE MONTH AFTER HOSPITAL DISCHARGE AND CHANGES IN PERIPHERAL MUSCLE STRENGTH AT SIX MONTHS

Peripheral muscle strength was assessed using a HHD at one and six months following discharge. Table 4.6 shows the mean changes in peripheral muscle strength for participants at the one and six months assessments.

Table 4.6: Peripheral Muscle Strength Results at One Month and Six Months after Discharge from Hospital

	Peripheral Muscle Strength (Newton) (n=11)						
Muscle group (Right)	**Mean at one month (±SD)**	**Median at one month**	**Mean at six months (±SD)**	**Median at six months**	**Mean difference (±SD)**	**95% CI**	**Significance (p)**
Shoulder flexors (Anterior Deltoid)							
▪ **Right**	91.7(24.5)	92	98 (25.1)	94	6.3 (15.4)	-16.6, 4	0.20
▪ **Left**	91.7(24.4)	91.7	97.9 (28.6)	92	6.2 (19.7)	-19.4, 7.1	0.33
Elbow flexors (Biceps Brachii)							
▪ **Right**	141.5 (20.4)	141.3	158.8 (13)	164	17.3 (15.7)	-27.8, -6.8	0.00*
▪ **Left**	136.4 (25.9)	145.3	141.4 (17)	141.3	5 (25.7)	-22.2, 12.3	0.54
Elbow extensors (Triceps Brachii)							
▪ **Right**	122.5 (30.8)	142	155.1 (33.8)	144	32.6 (37)	-57.5, -7.7	0.02*
▪ **Left**	118.4 (33.7)	126	141.3 (31.8)	142	22.9 (34.8)	-46.3, 0.4	0.05**
Hip abductors (Gluteus Medius)							
▪ **Right**	143.4 (43.7)	206.8	196.7 (31.8)	193	53.4 (52.3)	-88.5, -18.2	0.01*
▪ **Left**	157.3 (38.5)	153.3	193.6 (32.3)	206.8	36.4 (45.2)	-66.7, -6	0.02*
Ankle dorsiflexors (Tibialis Anterior)							
▪ **Right**	123.9(29.7)	157	153.7 (40.7)	168.1	29.9 (36.9)	-54.7, -5.1	0.02*
▪ **Left**	131.3 (35.4)	125	174.7 (42.8)	157	43.3 (48.1)	-75.7, -11	0.01*
Knee extensors (Quadriceps Femoris)							
▪ **Right**	149.7(48.9)	187	209.6	220	59.9 (40.3)	-87, -32.8	0.00*
▪ **Left**	155 (45.7)	181	(46.4) 183.7 (43.3)	187	28.8 (48.7)	-61.5, 3.9	0.08
Knee flexors (Hamstrings)							
▪ **Right**	128.5 (28.2)	166.2	170.9 (21.4)	171.7	42.4 (31.3)	-63.4, -21.4	0.00*
▪ **Left**	125.8 (36.4)	119.7	165.8(39.5)	166.2	40 (43.3)	-69, -10.9	0.01*

*Indicates significance at level p<0.05; **Indicates significance at level p=0.05

Statistically significant improvements were observed in right sided elbow flexors (p=0.00), elbow extensors (p=0.02), hip abductors (p=0.01), knee extensors (0.00), knee flexors (p=0.00) and ankle dorsiflexors (p=0.02) muscle strength.
Statistically significant improvements were also observed in left sided elbow extensors (p=0.05), hip abductors (p=0.02), knee flexors (p=0.01) and ankle dorsiflexors (p=0.01) muscle strength.

4.6 LEVEL OF DEPRESSION AT ONE AND SIX MONTHS AFTER DISCHARGE FROM HOSPITAL

Level of depression was assessed using the PHQ-9 questionnaire. Table 4.7 summarises the difficulties reported by participants and the severity of depressive disorders at follow-up.

Table 4.7: Reported Difficulties and Severity of Depressive Disorders as Measured with the PHQ-9 at One and Six Months following Discharge

PHQ-9: Reported Difficulties and Severity of Depressive Disorders		
	At one month follow-up(n=15)	**At six months follow-up(n=11)**
Number of participants who reported that they experience difficulties n (%)	11 (73.3)	11 (100)
Difficulty if problems present ▪ **Not difficult at all** ▪ **Somewhat Difficult** ▪ **Very Difficult** ▪ **Extremely Difficult** **n (%)**	 8 (53.3) 2 (13.3) 1 (6.7) 0 (0)	 4 (36.4) 2 (18.2) 0 (0) 0 (0)
Depression Severity ▪ **None** ▪ **Mild** ▪ **Moderate** ▪ **Moderately severe** ▪ **Severe** **n (%)**	 6 (40) 4 (26.7) 1 (6.7) 0 (0) 1 (6.7)	 4 (0) 2 (18.2) 0 (0) 0 (0) 0 (0)
▪ **Major Depressive disorder** ▪ **Other Depressive disorder** **n (%)**	1 (6.7) 1 (6.7)	0 (0) 0 (0)

The mean PHQ-9 scores was 3.3 (± 2.6) at one month follow-up and 1.8 (± 2.6) at six months. The median PHQ-9 score was 3 at one month follow-up and 1 at six months. The mean PHQ-9 score showed a positive change of 1.5 points (± 3.7) but was not statistically significant (p= 0.22). The null hypothesis was not rejected for these measurements as p>0.05.

4.7 HEALTH-RELATED QUALITY OF LIFE REPORTED AT ONE MONTH AFTER HOSPITAL DISCHARGE AND CHANGES IN HRQOL AT SIX MONTHS

In this study HRQOL was assessed using the SF-36 and EQ-5D questionnaires. Results obtained from each questionnaire are reported in the sections below.

4.7.1 Quality of Life of Participants as Reported using the SF-36 Questionnaire in the First Six Months after Discharge from Hospital

On average it took participants ten minutes to complete the SF-36 questionnaire. Participants choose either the English (South African), Afrikaans or isiZulu translated versions of the SF-36 questionnaire to complete. Table 4.8 summarises results obtained for the domain scores and summary scores of the SF-36 for participants at one and six months following discharge.

Table 4.8: Mean SF-36 Domain and Summary Scores for Participants Obtained at One and Six Months after Discharge

	SF-36 Scores				
	Mean at one month (±SD) (n=15)	**Mean at six months (±SD) (n=11)**	**Mean difference (±SD)**	**95% CI**	**Significance (p)**
PCS	42.9 (8.8)	51.7 (10.5)	8.8 (7.6)	-13.9, -3.7	0.00*
MCS	49.2 (10.5)	53.3 (7.7)	4 (7.7)	-9.2, 1.1	0.11
PF	63.2 (16.7)	77.3 (20.8)	14.1 (17)	-25.5, -2.7	0.21
RP	46 (26.3)	80.1 (27.1)	33.5 (24.6)	-50, -17	0.00*
BP	59 (22.5)	72.2 (28.1)	13.2 (19.4)	-26.2, -0.1	0.05*
GH	70.1 (18.9)	82 (16.3)	11.9 (10.8)	-19.2, -4.6	0.00*
VT	57.4 (15.5)	77.3 (17.7)	19.9 (21.8)	-34.5, -5.2	0.01*
SF	58 (28.7)	84.1 (19.4)	26.1 (27.6)	-44.7, -7.6	0.01*
RE	72 (29.6)	84.1 (19.5)	12.1 (25.4)	-29.2, 4.9	0.14
MH	76.3 (18.7)	76.8 (17.1)	0.5 (18.6)	-13, 12.1	0.94

*Indicates significance at level p<0.05; *indicates significance at level p=0.05.

4.7.2 Quality of Life of Participants as Reported using the EQ-5D Questionnaire in the First Six Months after Hospital Discharge

On average it took participants five minutes to complete the EQ-5D questionnaire. Participants choose either the English (South African), Afrikaans or isiZulu translated versions of the EQ-5D questionnaire.

The mean EQ-5D VAS score was 72.5 (± 15.9) at one month follow-up and 87.2 (± 11.1) at six months. A change in mean EQ-5D VAS scores of 14.6 (± 9.7) was observed between one month and six months following discharge. This change in mean EQ-5D VAS score was statistically significant (p=0.00) with 95% CI of -21.2 and -8.1. The null hypothesis was therefore rejected as p< 0.05.

The EQ-5D domains evaluate five different aspects of HRQOL. These are the ability to mobilise, to perform self-care and to perform usual activities of daily living including work and leisure activities, establishes the presence of pain and anxiety or depression. The response frequencies to the categorical questions of the EQ-5D health survey is summarised in table 4.9.

Table 4.9: Response Frequencies for Categorical Data Obtained for the Various Domains of the EQ-5D

EQ-5D Domains	At one month follow-up (n=15) n (%)	At six months follow-up (n=11) n (%)
Mobility		
▪ No Problem	9 (60%)	10 (90.9%)
▪ Problem	6 (40%)	1 (9.1%)
Self-Care		
▪ No Problem	11 (73.3%)	10 (90.9%)
▪ Problem	4 (26.7%)	1 (9.1%)
Usual Activities		
▪ No Problem	6 (40%)	9 (81.8%)
▪ Problem	9 (60%)	2 (18.2%)
Pain/Discomfort		
▪ No Problem	3 (20%)	9 (81.8%)
▪ Problem	12 (80%)	2 (18.2%)
Anxiety/Depression		
▪ No Problem	10 (66.7%)	8 (72.7%)
▪ Problem	5 (33.3%)	3 (27.3%)

4.9 PHYSICAL ACTIVITY AT ONE AND SIX MONTHS AFTER DISCHARGE AND CHANGES OBSERVED OVER THE SIX MONTH PERIOD

Participants' level of physical activity at one and six months after hospital discharge was assessed using the RPAQ. Results were obtained for 15 (62.5%) of 24 participants at one month after discharge and for eleven (45.8%) of 24 participants at six months after discharge. The participants' means of transport at one month follow-up included motor vehicles (n=11; 73.3%) and walking (n=4; 26.7%). At one month follow-up 12 participants (80%) had paid employment and three participants (20%) reported no paid employment. Employment varied between sedentary employment (n=2; 16.7%), manual work (n=1; 8.3%) or standing occupation (n=9; 75%). At the six months follow-up assessment six participants (54.4%) had no paid employment and only five (45.5%) reported that they had paid employment. Employment varied between sedentary employment (n=2; 40%), manual work (n=1; 20%) or standing occupation (n=2; 40%).

Time spent working was measured using the RPAQ questionnaire over the first six months after discharge from hospital. Table 4.10 summarises the findings from the RPAQ results.

Table 4.10: Changes in Time Spent Working as Reported by Study Participants on the RPAQ at One and Six Months after Discharge

	RPAQ time spent working				
	Mean at one month (±SD) (n=15)	**Mean at six months (±SD) (n=11)**	**Mean difference (±SD)**	**95% CI**	**Significance (p)**
Time spent at work: (hours)					
▪ Four weeks ago	30 (0)	40 (0)	10 (0)	-20.8, 48.8	0.22
▪ Three weeks ago	30 (0)	40 (0)	10 (0)	-120.8, 158.	0.33
▪ Two weeks ago	19.5 (21.9)	42.5 (3.5)	23 (25.5)	-251.7, 205.7	0.42
▪ One week ago	22 (25.5)	42.5 (3.5)	20.5 (29)	-281, 240	0.5

*h = hours.

There was no statistically significant differences in the mean time spent working at one week (p=0.5) and two weeks (p=0.42) prior to assessment.

4.9 RETURN TO EMPLOYMENT IN THE FIRST SIX MONTHS AFTER HOSPITAL DISCHARGE

Return to employment was assessed at one and six months after discharge from hospital using the demographic information sheet and interview. Information gathered from each participant included return to work status, time to return to work, and reasons for not returning to work (if applicable). Table 4.11 shows the mean time to return to work and participants' return to work status at one and six months respectively. Results are presented for 15 participants at one month follow-up and eleven at six months follow-up due to participant drop-out.

Table 4.11: Mean Time to Return to Work and Return to Work Status at One and Six Months Follow-Up

	Mean (±SD)	Minimum	Maximum	Median
Time to return to work at one month (days) (n=3)	35.3 (11.6)	23	46	37
Time to return to work at six months (days) (n=6)	78.8 (64.3)	30	180	43
	N (n=15)		**Percentage (%) (n=15)**	
Returned to work at one month	3		20	
Returned to same work at one month	3		20	
Not returned to work at one month	12		80	
	N (n=11)		**Percentage (%) (n= 11)**	
Returned to work at six months	6		54.5	
Returned to same work at six months	5		83.3	
Not returned to work at six months	5		45.5	

One participant with a job requiring manual labour decided to retire and did not return to work. One participant with a job requiring manual labour did not return for follow-up and the researcher was unable to track this participant. Other reported reasons for not returning to employment at one and six months follow-up are summarised in table 4.12.

During data analysis it was noted that there is conflict between the data presented in tables 4.10 and 4.11. The researcher concluded that the reason for this was that the participants did not fully understand the question posed by the RPAQ questionnaire section on occupation and this led to the conflicting data.

Table 4.12: Reasons for not Returning to Work at One and Six Months

	One month		Six months	
	N	**Percentage (%) (n=12)**	**N**	**Percentage (%) (n=5)**
Physical weakness	2	16.7	0	0
Re-admission to hospital	1	8.3	0	0
Family pressure	1	8.3	0	0
Personal preference	2	16.7	0	0

*Family pressure: The family of the participant recommended to the participant not to return to work.

4.10 THE RELATIONSHIP BETWEEN FUNCTIONAL ABILITY AND SEVERITY OF ILLNESS AND LENGTH OF STAY

To determine if a relationship existed between functional ability (PFIT-s) and severity of illness (APACHE II and SAPS II), ICU LOS, duration of MV, and hospital LOS, a univariate analysis of variance using general linear model was calculated. No statistically significant relationships were shown to exist between the variables. The null hypothesis was not rejected as $p > 0.05$. The adjusted R squared value was 0.13 ($p=0.22$).

4.11 THE RELATIONSHIP BETWEEN EXERCISE ENDURANCE AND SEVERITY OF ILLNESS, LENGTH OF STAY, HRQOL, AND LEVEL OF DEPRESSION

To determine if a relationship existed between exercise endurance (measured as 6MWT distance) and severity of illness (APACHE II and SAPS II), ICU and hospital LOS, duration of MV, HRQOL (PCS and MCS and EQ-5D VAS), level of depression of survivors of critical illness, a linear regression analysis was calculated.

Table 4.13: The Relationship Between Exercise Endurance And Severity Of Illness, Length Of Stay, HRQOL, And Level Of Depression

6MWT at six months follow-up.		
Variables	**p-value**	**r-value (95 % CI)**
APACHE II	0.62	0.17 (-8.8 - 13.9)
SAPS II	0.66	0.15 (-3.7- 5.6)
ICU LOS	0.37	0.3 (-5.6- 13.8
Hospital LOS	0.65	0.16 (-4.2- 6.4)
Duration of MV	0.09	0.53 (-1.4- 15.9)
SF-36 PCS score at six months follow-up	0.09	0.54 (-0.98- 12.23)
SF-36 MCS score at six months follow-up	0.31	-0.34 (-15 – 5.3)
EQ-5D VAS score at six months follow up	0.37	0.3 (-4.2 – 10.1)
PHQ-9 score at six months follow-up	0.7	0.13 (-26.4- 37.7)

*indicates significance at level p=0.05.

A moderate strength, positive relationship (r= 0.53) was found between duration of MV and 6MWT distance at six months after discharge from hospital. A moderate strength, positive relationship (r= 0.54) was found between SF-36 PCS score at six months after discharge from hospital and 6MWT distance at six months after discharge from hospital. A weak strength, negative relationship (r= -0.34) was found between SF-36 MCS score at six months after discharge from hospital and 6MWT distance at six months after discharge from hospital. All these relationships were not statistically significant.

4.12 THE RELATIONSHIP BETWEEN HRQOL AND SEVERITY OF ILLNESS, LENGTH OF STAY, LEVEL OF DEPRESSION AND EXERCISE ENDURANCE

A linear regression analysis was used to determine if a relationship existed between the abovementioned variables. These relationships are shown in table 4.14.

Table 4.14: The Relationship Between HRQOL (SF-36 PCS) And Severity Of Illness, Length Of Stay, Level Of Depression And Exercise Endurance

HRQOL (SF-36 PCS) at six months follow-up.		
Variables	**p-value**	**r-value (95 % CI)**
APACHE II	0.3	0.36 (-0.5 – 1.6)
SAPS II	0.35	0.31(-0.24- 0.61)
ICU LOS	0.89	-0.04 (-1.03- 0.92)
Hospital LOS	0.23	-0.4 (-0.75- 0.2)
Duration of MV	0.41	0.28 (-0.58- 1.3)
PHQ-9 score at six months follow-up	0.13	-0.49 (-4.7- 0.7)
6MWT Distance at six months follow-up	0.09	0.54 (-0.01-0.11)

*indicates significance at level p=0.05.

A weak strength, positive relationship (r= 0.36) was found between SF-36 PCS at six months after hospital discharge and APACHE II scores. A weakstrength, positive relationship (r= 0.31) was found between SF-36 PCS score at six months after discharge from hospital and SAPS II scores. A moderate strength, negative relationship(r= -0.49) was found between SF-36 PCS score at six months after discharge from hospital and PHQ-9 scores at six months after discharge from hospital. A moderate strength, positive relationship (r= 0.54) was found between SF-36 PCS score at six months after discharge from hospital and 6MWT distance at six months after discharge from hospital. All these relationships were not statistically significant.

Table 4.15: The Relationship Between HRQOL (SF-36 MCS) And Severity Of Illness, Length Of Stay, Level Of Depression And Exercise Endurance

HRQOL (SF-36 MCS) at six months follow-up.		
Variables	**p-value**	**r-value (95 % CI)**
APACHE II	0.96	-0.02 (-0.8 - 0.8)
SAPS II	0.94	-0.03(-0.34- 0.32)
ICU LOS	0.07	-0.56 (-1.1- 0.6)
Hospital LOS	0.07	-0.56 (-0.59- 0.03)
Duration of MV	0.02*	-0.69 (-1.2- -0.14)
PHQ-9 score at six months follow-up	0.01*	-0.72 (-3.73- -0.6)
6MWT Distance at six months follow-up	0.31	-0.34 (-0.07- 0.03)

*indicates significance at level p=0.05.

A strong negative relationship (r= -0.69) with statistical significance (p=0.02) was found between SF-36 MCS score at six months after discharge from hospital and duration of MV. A strong, negative relationship (r= -0.72) with statistical significance (p= 0.01) was found between SF-36 MCS score at six months after discharge from hospital and PHQ-9 scores at six months after discharge from hospital.

Table 4.16: The Relationship Between HRQOL (EQ-5D VAS) And Severity Of Illness, Length Of Stay, Level Of Depression And Exercise Endurance

HRQOL (EQ-5D VAS) at six months follow-up.		
Variables	**p-value**	**r-value (95 % CI)**
APACHE II	0.44	0.26 (-0.73 - 1.53)
SAPS II	0.11	0.5(-0.09- 0.73)
ICU LOS	0.53	-0.22 (-1.3- 0.71)
Hospital LOS	0.68	-0.14 (-0.64- 0.44)
Duration of MV	0.93	-0.03 (-0.99- 1.08)
PHQ-9 score at six months follow-up	0.7	0.13 (-26.4- 37.7)
6MWT Distance at six months follow-up	0.78	-0.09 (-3.66 – 2.85)

*indicates significance at level p=0.05.

Only weak correlations were identified, without statistical significance.

4.13 THE RELATIONSHIP BETWEEN LEVEL OF DEPRESSION AND RETURN TO EMPLOYMENT IN THE FIRST SIX MONTHS AFTER HOSPITAL DISCHARGE

To calculate the relationship between participants' level of depression as measured using the PHQ-9 questionnaire and return to work frequencies at one and six months follow-up, a univariate analysis of variance using general linear model was calculated. No statistically significant relationships were identified between PHQ-9 scores and return to work frequencies, neither at one month follow-up nor at six months follow-up. The adjusted R squared value was -0.04 (p=0.49) at one month follow-up and 0.12 (p=0.25) at six months. The null hypothesis was not rejected for these measurements as p> 0.05.

4.14 FACTORS INFLUENCING EXERCISE ENDURANCE AT SIX MONTHS AFTER HOSPITAL DISCHARGE

To determine which factors had an influence on exercise endurance (6MWT distance) at six months after hospital discharge, Spearman's rho was calculated to measure the degree of association between variables (APACHE II, SAPS II, duration of MV, ICU LOS, and hospital LOS). No statistically significant associations were identified.

To determine the relationship between factors that might influence exercise endurance (6MWT distance) at six months after hospital discharge, linear regression analyses were conducted. The results are presented in table 4.13.

4.15 FACTORS THAT INFLUENCE HRQOL AT SIX MONTHS AFTER HOSPITAL DISCHARGE

To determine which factors had an influence on HRQOL (PCS, MCS and EQ-5D VAS) at six months after hospital discharge, Spearman's rho was calculated. A strong negative association was found between SF-36 PCS scores at six months follow-up and length of hospital stay (r=-0.69; p=0.02). A strong negative association was found between SF-36 MCS scores at six months follow-up and the duration of MV (r=-0.69; p=0.02). A moderate positive association was found between SF-36 MCS scores and PFIT interval scores at ICU discharge (r=0.59; p=0.06).

To determine the relationship between factors that might influence HRQOL (PCS, MCS and EQ-5D VAS) at six months after hospital discharge, linear regression analyses were calculated. The results are presented in tables 4.14 to 4.16.

CHAPTER 5

5. DISCUSSION

To the best of the researcher's knowledge, this is one of the few studies in South Africa investigating the functional ability and HRQOL of survivors of critical illness. The study results showed various statistically significant changes in and relationships between variables.

5.1 Physical Function in ICU

5.1.1 Changes in PFIT Scores

A statistically significant change in mean PFIT-s interval scores was found for participants in this study when assessed at ICU discharge and hospital discharge. There were changes in the medians of all the domains of PFIT-s in the current study's participants. The median interval score increased from 6.8 and 7.1. The median MOS component however reduced from 38.5 to 27.6 steps per minute. The median shoulder flexion endurance component also reduced from 45.2 to 25.3 repetitions per minute. This shows that the participants actually had reduced functional ability between discharge from ICU and discharge home. This could indicate that not all the rehabilitation needs of these participants were met before they were discharged home. There is also the possibility that the participants were not feeling well on the day of assessment with resulting lower scores with the PFIT-s. Denehy et al. (2013) reported that the minimum change that needs to occur in the PFIT interval score to reflect a clinically meaningful change, the minimal clinically important difference (MCID), is 1.5 points in a mixed ICU population. The change in mean PFIT scores observed in the mixed ICU population in the current study was 0.4 points and the change in the median score was 0.3 points; therefore much less than the MCID, indicating that the change in PFIT-s scores observed for participants between ICU discharge and hospital discharge was not clinically significant even though it was statistically significant. All participants received daily physiotherapy treatment (consisting generally of chest physiotherapy treatment, exercise and rehabilitation) while they were in the hospital ward and if this was continued for a longer period of time (as opposed to them receiving physiotherapy for median time of 4.5 days between ICU discharge and home discharge), a larger increase in PFIT-s scores may have been observed. As the participants in this study had relatively high

severity of illness levels on admission to ICU, this may have resulted in these patients requiring a longer period of recovery from critical illness in order to have MCID in PFIT-s scores. This may result from severe physical weakness after a prolonged period of critical illness. The current study however, found that there was not a statistically significant relationship between severity of illness and PFIT-s scores. Another explanation could be thatas patients recover from critical illness, they become more motivated to be discharged home and they may be discharged prior to reaching a MCID in their PFIT-s score.

5.1.2 Relationships between PFIT results and other variables

No statistically significant relationships were shown to exist between PFIT-s results and severity of illness (APACHE II and SAPS II), ICU LOS, duration of MV, and hospital LOS. In contrast, Denehy et al. (2013) reported that their participants with low PFIT-s scores were more likely to have a longer hospital LOS versus those with high PFIT-s scores. All participants in the current study received physiotherapy treatment for the duration of their hospital stay. The less than clinically significant improvement in PFIT-s interval scores could therefore suggest that not all the rehabilitation needs of these participants, who were recovering from critical illness, were met before their discharge from hospital. The PFIT-s is not regularly used in clinical practice as an outcome measurement by physiotherapists in Gauteng province to assess patients' responses to rehabilitation while in hospital. Raising awareness among physiotherapists about this tool and exploring its usefulness as an outcome measure in the South African critical care setting, should be the focus of future clinical trials.

5.2 Physical Function after Hospital Discharge

5.2.1 Changes in 6MWT results

The participants in this study showed some improvement in exercise endurance as the distance that they walked on the 6MWT improved from one to six months after discharge; however this change in distance walked was not statistically significant. The mean distance achieved improved from 421.5 (±134.5) to 474.5 (±110) meters between one and six months after discharge from hospital. The median distance also improved from 425 to 490 meters between one and six months follow-up. The mean and median percentage of predicted distance achieved thus also improved from

60.45 to 68.8 and from 61.5 to 73.3 percent respectively. The MCID reported for 6MWT distance is 54 meters in patients with COPD (Rasekaba, et al., 2009).

Only one participant in the current study was admitted to ICU due to exacerbation of COPD; the majority of participants underwent surgery. There is no MCID data available for 6MWT distance in the surgical or critical care populations. Aitken et al. (2012) reported increases in mean 6MWT distances in survivors of critical illness at one week (15 metres), eight weeks (13 metres), and at 26 weeks (9 metres) after hospital discharge. The current study showed much larger increases in mean 6MWT distances, although the follow-up time points were different than that of Aitken et al. (2012). Other researchers reported on the increase in median 6MWT distance in survivors of critical illness. Van Aswegen et al. (2010) reported an improved median 6MWT distance of 47 metres in their short-term MV group and 39.5 metres in their long-term MV group from three months to six months after hospital discharge. This differs from the current study's results as these changes took place over a three month period and the changes observed in our participants took place over a five month period (from one to six months after discharge from hospital). Herridge et al. (2003) reported an increase of 115 metres in median 6MWT distance at six months after discharge. This is a much larger increase in 6MWT distance as reported in our participants.The increase in 6MWT distance observed in the current study may possibly be a result of patients staying at home by themselves and therefore they needed to perform tasks at home independently; thus they experienced an increase in their exercise tolerance. Some participants also returned to work and this may have contributed to the improvement seen in their exercise tolerance.

Study participants achieved between 60.5 percent and 68.8 percent of their mean percentage of age predicted 6MWT distance at one month and six months respectively. Herridge et al. (2011) reported that only 39 percent of their participants achieved 80 percent of age predicted 6MWT distance at one year following ARDS. Herridge et al. (2011) also reported a strong relationship between 6MWT distances achieved and the PF score of the SF-36 questionnaire.

5.2.2 **Relationships between 6MWT results and other variables**

No statistically significant relationships were shown to exist between 6MWT distance at six months follow-up and APACHE II or SAPS II scores, ICU or hospital LOS, EQ-5D VAS or level of depression in the current study. A moderate strength, negative correlation (r= -0.34) was found between SF-36 MCS score and 6MWT distance at

six months after discharge from hospital. This was however statistically insignificant (p=0.31). No other studies reported similar findings.

A moderate strength, positive correlation (r= 0.54) was found between SF-36 PCS score and 6MWT distance at six months after discharge from hospital, but this was also not statistically significant (p=0.09). The limited distances that participants in this study were able to achieve during the 6MWT therefore suggests that their endurance is impaired which may impact their ability to perform activities of daily living. The small increase in 6MWT distance observed in the current study could be due to the fact that almost half (45.5%) of the participants did not return to work at six months after discharge from hospital and thus did less physical work-related activities with less subsequent improvement in exercise tolerance. Exercise training is associated with numerous physical and mental health benefits (Dahn and Penedo, 2005) and seems to be indicated for this mixed ICU population to enhance their recovery from critical illness (Denehy and Berney, 2006; Morris, 2007; Schweickert, et al., 2009).

A moderate strength, positive correlation (r= 0.53) was found between duration of MV and 6MWT distance at six months after discharge from hospital, but this was not statistically significant (p=0.09). This has not been reported by other researchers.

5.3 **Peripheral Muscle Strength**

Statistically significant changes in mean peripheral muscle strength were observed in the upper and lower limbs of participants over the six months following discharge from hospital. Large improvements in median peripheral muscle strength was observed for the right-sided elbow flexors (22.7 Newton), left-sided elbow extensors (16 Newton), left-sided hip abductors (53.5 Newton), left-sided ankle dorsiflexors (32 Newton), right-sided knee extensors (33 Newton), and left-sided knee flexors (46.5 Newton).

According to Lang et al. (2008) who studied the use of the HHD in acute stroke survivors who were critically ill, the MCID for HHD measurements in patients following stroke is 50 Newton for the affected dominant side of the body and 62 Newton for the non-dominant side. All participants in the current study reported to have right-handed dominance. Baldwin et al. (2013) reported from their investigation of HHD in alert critically ill patients, the minimally detectable differences in measurements. These were 71 Newton on the left side of the body and 57 Newton on the right. No MCID data could be found in the literature for HHD measurements in

the critical care population. The increase in peripheral muscle strength observed in the current study is much less than that reported by Baldwin et al. (2013) and therefore not of clinical significance. The median age of the participants in their study was 78 years, thus much older than the median age of the current study's participants (51.5 years). Fifty-nine percent of their participants were male whereas the current study had a 79.2 percent male representation. The difference in the results could be attributed to the difference in admission diagnoses between the current study and Baldwin et al. (2013). Although Baldwin et al. (2013) also had a mixed ICU patient sample in their study, the current study had more patients with trauma (n=7) and cardiac conditions (n=7) as compared to the four cardiac admissions and the one trauma admission of Baldwin et al. (2013). No other studies reported on the change in peripheral muscle strength at six months after hospital discharge following critical illness, but rather on the relationships between peripheral muscle strength and factors like ICU and hospital LOS and severity of illness.

Van Aswegen et al. (2010) reported on ICU LOS of participants mechanically ventilated for longer periods of time and right deltoid, right triceps, and right hamstrings muscle strength at one month after discharge and left triceps muscle strength at six months. In the same study, hospital LOS of participants mechanically ventilated for longer periods of time was significantly correlated with left deltoid, right triceps, left hamstrings, and right hamstrings muscle strength at one month follow-up and left deltoid, left triceps, right triceps and right hamstrings muscle strength at three months after discharge (Van Aswegen, et al., 2010). Van Aswegen et al. (2010) did not find a significant relationship between peripheral muscle strength and ICU LOS in their participants receiving short-term MV (Van Aswegen, et al., 2010). They reported no statistically significant relationships between peripheral muscle strength and APACHE II scores (Van Aswegen, et al., 2010).

From these results it seems that there may be an association between longer duration of MV, severity of illness, and peripheral muscle strength at three and six months follow-up. The results from the current study cannot accurately be compared with these findings as the study did not aim to identify relationships between ICU LOS, severity of illness and peripheral muscle strength.

The fact that majority of participants in this study lived alone may account for the improvements in muscle strength observed as they would be dependent on themselves for performing daily activities.

5.4 Health Related Quality of Life

5.4.1 Changes in HRQOL (SF-36) Scores

Significant changes in mean RP, BP, GH, VT and SF domain scores of the SF-36 as well as PCS scores were observed for participants at six months following discharge; however MCS scores did not change significantly. Mean MCS scores were slightly higher than mean PCS scores at six months. Schneiderman et al. (2013) reported higher mean PCS scores compared to mean MCS scores at six months after discharge for survivors of trauma. When comparing the current study's results, the opposite was found. Even though their subjects had a slightly longer ICU LOS than that reported for the current study, their mean severity of illness scores (APACHE II) were significantly lower (12.7 ±10.3) than the APACHE II scores observed in the current study. This may explain why the mean PCS scores for Schneiderman et al.'s (2013) participants were higher at six months (62.1 ±27.8) compared to the current study participants' scores as they were less severely ill. Participants in the current study had several co-morbidities which may also have contributed to the lower observed mean PCS scores at six months. Van Aswegen et al. (2011) reported lower mean PCS scores than MCS scores at six months after discharge for the survivors of penetrating trauma that underwent prolonged MV in their study. Findings from the current study are similar to these. Participants in the current study had a prolonged duration of MV and ICU stay and are thus comparable to the long-MV group in Van Aswegen et al.'s (2011) study.

A large increase from one to six months follow-up was observed in SF-36 PCS scores (more than five points), but not for MCS scores (less than five points). This relates to improvements in the physical domain of HRQOL over the first six months after discharge from hospital following critical illness. In contrast to this, Dowdy et al. (2010) concluded that survivors of critical illness did not experience statistically significant improvements in HRQOL at six months after discharge. They added that small improvement in HRQOL is seen up to 36 months after discharge (Dowdy, et al., 2010). The statistically significant improvement in HRQOL related to PCS in the current study may be due to the fact that most participants lived alone and were self-dependent for daily activities even though they had some form of support from family and friends. Some of them had also returned to work by six months following discharge.

5.4.2 **Relationships between HRQOL (SF-36) and other variables**

A positive relationship was found between the PCS of the SF-36 questionnaire at six months follow-up and severity of illness (measured with APACHE II and SAPS II) on ICU admission. No other studies except for Orwelius et al. (2010) reported such findings. Orwelius et al. (2010) found no association between HRQOL up to 36 months after discharge and severity of illness (measured with APACHE II). A positive relationship was also found between SF-36 PCS scores at six months follow-up and 6MWT distance achieved at six months after discharge from hospital. Participants in this study had impaired exercise endurance at six months following discharge as they were only able to achieve 68.8% of their predicted distance walked on the 6MWT.

They also had a prolonged duration of MV and hospital LOS. It is a well-known fact that the inflammatory processes associated with critical illness lead to muscle protein breakdown and muscle weakness (Batt and Dos Santos, 2012; Apostolakis, et al., 2014). These effects are compounded by prolonged immobility in ICU (Dittmer and Teasell, 1993a; Dittmer and Teasell, 1993b). Muscle weakness and impaired exercise endurance will impact negatively on HRQOL. These factors may explain the association found between PCS, severity of illness and 6MWT distance achieved at the six months assessment. These relationships must however be interpreted with caution as they were not statistically significant.

Furthermore, the current study found no relationship between the PCS of the SF-36 questionnaire at six months follow-up and length of MV. There was however a moderate strength negative correlation ($r= -0.69$) of statistical significance ($p= 0.02$) between SF-36 MCS scores at six months after discharge from hospital and length of MV. This suggests that participants with longer length of MV had poorer mental health scores at six months after discharge from hospital. Van Aswegen et al. (2010) found different results with regards to the relationship between SF-36 scores and duration of MV. At six months after penetrating trunk trauma, they found a statistically significant difference between short-term MV and long-term MV groups in SF-36 PF, BP, GH, and PCS scores, but not in MCS scores. They also found an improvement in the exercise capacity, muscle strength and QOL at six months after discharge in patients treated with long-term MV, but they were still weaker than those treated with short-term MV. They concluded that the short-term MV group (also with shorter ICU LOS) showed faster improvement in exercise capacity compared to the long-term

ventilated group (Van Aswegen, et al., 2010). Ivaskevivius et al. (2011) reported a reduction in SF-36 PF and RP domain scores at six months after discharge in the survivors of critical illness. Kapfhammer et al. (2004), Hopkins et al. (2005) and Oeyen et al. (2012) also reported that patients with prolonged duration of MV showed more reductions in HRQOL after discharge from hospital.

A strong statistically significant negative relationship (r= -0.72; p= 0.01) was identified between SF-36 MCS scores and PHQ-9 scores at six months after discharge from hospital. This suggests that participants with lower levels of depression as measured using the PHQ-9, scored higher on the SF-36 MCS, indicating better mental HRQOL.

From the results of the current study it seems that longer hospital stay may have an influence on a patient's HRQOL at six months after discharge from hospital as indicated by the relationship (however statistically insignificant; p= 0.07) identified between hospital LOS and SF-36 MCS scores at six months after hospital discharge (r=-0.56). A possible explanation for this is that patients who stay longer in hospital may become more physically weak and de-motivated and this may influence their HRQOL after discharge from hospital.

Results from other researchers suggest that duration of MV may have an influence on exercise capacity and muscle strength at six months after discharge. These relationships were not observed in the current study. Possible explanations for the results obtained could be the small sample size of the current study, possible differences in baseline characteristics and ICU admission diagnoses of participants in this study, the inclusion of cardiac surgery patients with a short length of MV, as well as differences in eligibility criteria.

5.4.3 **Changes in HRQOL (EQ-5D) Scores**

Significant improvement in EQ-5D VAS scores (14.6 points ± 9.7) were observed for participants in the current study between one and six months after discharge. A higher score on the VAS indicates a better health state. Pickard et al. (2007) reported that the MCID in EQ-5D VAS scores was seven points. This study involved participants with cancer. No other data relating to the MCID for the EQ-5D VAS in other patient populations could be found. A clinically significant improvement was thus observed in the EQ-5D VAS scores for participants in this study over six months after discharge from hospital. The current study found a reduction in problems experienced with mobility from 40 percent at one month follow-up to 9.1 percent at

six months. Reductions were also found in problems with self-care (from 26.7 to 9.1 percent) and usual activities (60 to 18.2 percent) from one to six months after discharge from hospital. This suggests that participants' abilities to mobilise, care for themselves and participate in usual activities improved over time as they continued to recover from critical illness. Badia et al. (2001) reported a significant increase in mobility from baseline to 12 months after ICU discharge in survivors of critical illness. They did however find significant increases in reported problems with self-care and usual activities. They reported no statistically significant changes in pain or discomfort, anxiety or depression or in the EQ-5D VAS over the first 12 months after discharge from ICU (Badia, et al., 2001). The current study found a large reduction in reported problems with pain/discomfort from 80 percent at one month to 18.2 percent at six months after discharge. The majority of participants underwent surgery and may have experienced less pain over time as wound healing took place which could account for the large reduction in level of pain and discomfort experienced at six months. Participants reported little improvement in problems experienced in the anxiety/depression domain of the EQ-5D which showed a reduction from 33.3 percent at one month to 27.3 percent at six months after discharge. A possible explanation for this finding is that participants may experience more anxiety/depression as a result of physical weakness, the inability to perform the activities they did before the period of critical illness, and the inability to return to work with resultant financial strain on the participant and his or her family.

5.4.4 **Relationships between HRQOL (EQ-5D) and other variables**

Significant relationships were reported by Granja et al. (2002) and Garcia et al. (2003) between APACHE II scores and EQ-5D VAS and EQ-5D usual activities at six and 18 months after discharge from hospital respectively. The current study did not identify statistically significant relationships between EQ-5D VAS scores and APACHE II or SAPS II scores at one or six months follow-up.A possible explanation for these results from the current study is that the participants continued with their normal physiotherapy treatment during their hospital stay and possibly after discharge from hospital. This could subsequently impact the degree that the participants have improved after discharge from hospital resulting in a lack of relationship between HRQOL and APACHE II and SAPS II scores. A participant who received more physiotherapy treatment after hospital discharge may have improved more in terms of HRQOL as would a participant not receiving the same intervention.

The current study however did not include data on the therapeutic interventions a participant received after discharge from hospital.

The current study also did not identify statistically significant relationships between EQ-5D VAS scores at six months follow-up and ICU and hospital LOS, duration of MV, level of depression at six months follow-up, and 6MWT distance at six months follow-up.

5.5 Level of depression

A significant association was found in the current study between mean MCS scores of the SF-36 questionnaire and level of depression (measured with PHQ-9) at one and six months after discharge. A clinically significant change in PHQ-9 scores would involve a reduction in PHQ-9 score of five points or more (Smarr and Keefer, 2011). As the current study observed an increase in PHQ-9 scores over six months after hospital discharge, the participants seemingly suffered from more symptoms of depression. Although there was a reduction in the mean and median PHQ-9 scores of 1.5 and 2 points respectively, there was a reduction in the number of participants presenting with depressive disorders; however the drop-out rate for the study was high and therefore it is not known whether those who didn't come back for follow up suffered with depressive disorders. The increase in mean PHQ-9 scores corresponds with the small reduction in problems experienced with depression/anxiety as measured using the EQ-5D questionnaire. A possible explanation for this finding is that patients may realise that they may not achieve the same level of function as they had before ICU admission. This together with a prolonged recovery period from critical illness may make these patients more prone to developing symptoms of depression (Rattray, 2013). Patients with a longer ICU and hospital stay and those with a higher severity of disease on admission may also be more prone to developing symptoms of depression (Rattray, 2013). Many participants in this study reported co-morbidities which may have a chronic influence on HRQOL related to mental health.

5.6 Return to Work

The presence of depressive disorders did not directly influence return to work for participants in this study. The median time to return to work at one month after discharge from hospital was 37 days and 43 days at six months after discharge from hospital. No data relating to the MCID for the RPAQ could be found by the author. In

South Africa, Van Aswegen et al. (2010) reported no statistically significant difference in return to work rate between their short-term MV and long-term MV groups over the first six months after hospital discharge. In the United Kingdom, Griffiths et al. (2013) found that patients had difficulties with employment after a period of critical illness; mainly due to physical disabilities experienced. In the current study the main reason reported by participants for not returning to work was pensioner status. Only 16.7 percent of participants had not returned to work by one month follow-up as a result of physical weakness. This could be explained by the demographics of the participants. The mean age of the participants was 51 (± 13.82) years with the maximum age being 76 years. The mean age of participants therefore approached early retirement age in South Africa (55 years). Griffiths et al. (2013) reported that employment was affected by critical illness at six months after discharge from hospital and that it was still affected at 12 months post discharge. Similar results were reported by Myhren et al. (2010) where only 50 percent of their study participants returned to work or school at 12 months after discharge from hospital (Myhren, et al., 2010). Physical, psychological and social problems may affect a patient's behavior of returning to work and consequently have an influence on readiness to return to work (Franche and Krause, 2002). The relatively good return to work rate observed in the current study may be attributed to the significant increases in muscle strength and PCS observed as well as the reduction in problems reported in relation to mobility, self-care, pain or discomfort and participation in usual activities over the first six months following discharge.

5.7 Factors influencing exercise endurance and HRQOL after hospital discharge

The current study found that severity of illness, ICU LOS, and hospital LOS did not have an influence on exercise endurance (6MWT distance) at six months after hospital discharge. Length of MV, and SF-36 MCS and PCS scores had no statistically significant influences on exercise endurance at six months after hospital discharge from hospital. Van Aswegen et al. (2010) reported that morbidity (measured using the Sequential Organ Failure Assessment) in ICU was significantly correlated with distance walked on the 6MWT at three and six months after discharge for those subjects who underwent prolonged MV. As morbidity was not assessed in the current study it is not known whether this might have contributed to participants' performance on the 6MWT. The relationships between exercise endurance at six months after discharge from hospital and severity of illness, hospital and ICU LOS, length of MV, HRQOL and level of depression were discussed under section 5.2.2.

The current study found that SAPS II score on admission to ICU had an influence on EQ-5D VAS scores at six months after discharge from hospital (r=0.5), however this was not statistically significant (p=0.11). Length of MV was found to have an influence on the MCS of the SF-36 questionnaire at six months after hospital discharge as previously discussed.

The negative association found between duration of MV and SF-36 MCS scores at six months confirms that participants' QOL related to mental function was lower when MV duration was prolonged.

Many participants in this study presented with pre-existing disease prior to critical illness (n=12; 50%). The reductions in HRQOL observed may partly be due to the influence of these pre-existing conditions. The relationship between the study variables and pre-existing diseases and the influence of these pre-existing diseases, however, was beyond the scope of this study. The existence of pre-existing diseases may have been a potential confounding variable in this study and therefore may have influenced the outcomes.

5.8 LIMITATIONS OF CURRENT STUDY

- Small sample size. The study failed to meet the projected sample size. As many patients were discharged to rehabilitation or step-down centres from the ICU and did not spend time in the hospital wards prior to discharge home, these patients could not be enrolled in the study. The researcher had to allow time for participants to decide whether they wished to participate in the study and many patients went home during this time before a decision was made. Some participants were confused and could not be included in the study as they could not provide written, informed consent. The researcher was unable to include many possible participants due to various reasons out of his control. After realising the challenge of attaining the required number of participants, the number of recruitment sites could not be increased due to funding limitations. The small sample size limits the degree to which the results can be extrapolated to a larger ICU population. The results obtained from this study were often different to the available literature base and could partly be a consequence of the small sample size. The objectives of the study which relate to the relationships between different variables may therefore not been accurately achieved due to the small

number of participants which limits the accuracy of the results. The results obtained should therefore be interpreted with caution.

- A significant limitation to the study is that a large number (n=49) of potential participants were not included due to the inability to obtain consent prior to hospital discharge. Participants who were discharged directly from the ICU to rehabilitation facilities or discharged to these facilities from the hospital ward prior to the researcher obtaining consent for participation in the study were not followed up for inclusion in the study. This can be seen as a limitation as recruitment of these participants would have assisted in increasing the sample size. Only one participant who had his baseline PFIT-s assessment at Netcare Union Hospital was seen for his PFIT-s follow-up assessment at Netcare Rehabilitation hospital after he was discharged from Netcare Union hospital. He was already enrolled in the study before he was discharged from Netcare Union Hospital. There were however no participants who consented to participation in the study that were not followed-up as a result of their transfer to a rehabilitation facility.

- High drop-out rate of 37.5 percent at one month follow-up and 54.2 percent at six months. Van Aswegen et al. (2010) reported high drop-out rates for participants in their observational study. Methods employed by the researcher to limit drop-out rate included collection of participants' contact details at the time of study enrolment which included telephone numbers, mobile phone numbers, email addresses and physical addresses. A possibility exists that those participants who could not be tracked down after discharge changed their contact details. A limitation is that the researcher did not visit a participant's place of living in the case where he could not reach the participant by phone or email. The researcher did however attempt numerous times to contact all participants who did not arrive for follow-up appointments to re-schedule their appointments.

- Assessment of pre-morbid HRQOL at the time of discharge from ICU by participant recall could have provided insight into the change in a participant's HRQOL prior to critical illness and to six months after discharge from hospital.

- Assessment for and diagnosis of ICU-AW was not within the scope of this study. This information could however have been valuable in the interpretation of study findings.

- Use of the RPAQ tool was a limitation to this study as it was not possible to obtain a total score for the items in the questionnaire which made interpretation and comparison of data problematic.

- Recording of therapeutic interventions received by participants after discharge from hospital was not included in the current study. This information could however have been valuable in the interpretation of study findings.

- Only articleswritten in the English language were included in the literature review for this study and not articles writtenin other South African languages.

- The inclusion of elective cardiac surgery patients in the study may not have been appropriate as these patients do not neccesarily suffer from critically ill or have prolonged length of ICU stay, even if mechanically ventilated after surgery for up to 48 hours.

- Overly strict eligibility criteria added to the failure of the study to reach the desired sample size.

5.9 RECOMMENDATIONS FOR FUTURE RESEARCH

- Future studies must have strict controls in place to ensure retention of recruited participants. Home follow-up of participants and collection of family members' contact details would assist in follow-up of participants and possibly a lower drop-out rate. Other strategies to improve participant recruitment could be the following:
  - Maintaining weekly or biweekly telephonic contact with participants between follow-up assessments.
  - Having a larger number of research assistants to assist in the recruitment process and follow-up of participants.
  - Having more study sites initially or increasing these if it is noted that participant recruitment numbers are low.
  - Particular attention needs to be paid to study recruitment processes and early detection of pitfalls to participant recruitment.
  - Very detailed study planning, particularly dealing with procedures to follow in order to track patients for follow-up may also assist to maintain recruited

participants in future studies. Therefore more rigorous processes to ensure follow-up of discharged participants are recommended.

- Future studies may include the assessment and diagnosis of ICU-AW in order to further investigate the differences in HRQOL of survivors of critical illness who had ICU-AW and those who did not have ICU-AW.

- Researchers intending to use the RPAQ questionnaire may consider using additional questionnaires focusing on physical activities which will provide the researcher with continuous data and a total questionnaire score for ease of data analysis and presentation of results.

- Future studies would benefit from recording the frequency, duration and type of therapeutic interventions a participant receives after discharge from hospital in order to assist interpretation of data.

- Future studies with larger sample sizes should further investigate the influence of variables like pre-morbid conditions and physiotherapy treatment on exercise tolerance and HRQOL in survivors of critical illness after discharge from hospital.

- Future studies should also investigate the outcomes of survivors of critical illness who had different recovery pathways after discharge from hospital eg. rehabilitation centres, step-down facilities, home recovery, or home recovery with outpatient-based therapeutic interventions to see if there are any differences in HRQOL and functional ability of such participants.

5.10 **CLINICAL RECOMMENDATIONS**

- Raising awareness among physiotherapists regarding the PFIT-s tool and exploring its usefulness as an outcome measure in the South African critical care setting, where staff shortages and large patient numbers are real problems faced by clinicians, should be the focus of future clinical trials.
- Patients who suffered critical illness should be followed up by physiotherapists after discharge from hospital to assess the amount of change in their physical function and HRQOL. Based on these findings, individualized rehabilitation programmes should be developed for such patients and its effectiveness tested regarding improvement in outcome measures in future trials.

- Patients who suffered critical illness and experienced prolonged duration of MV and demonstrate a significant reduction in mental aspects of HRQOL and signs of depression should be referred for counseling.

CHAPTER 6

6. CONCLUSION

The findings from this observational, longitudinal study is based on data from a small patient sample (n=24 to n=11). The researcher recommends that the results from this study be interpreted with caution.

The results from the current study rejects the null hypothesis stating that participants who were admitted to ICU due to critical illness do not suffer from limitations in physical activity or HRQOL at six months after hospital discharge. The null hypothesis that stated that participants who survived critical illness returned to employment in the first six months after hospital discharge is accepted as more than half of remaining participants had returned to employment at the six months assessment. Survivors of critical illness in this mixed ICU population showed reductions in physical abilities at ICU discharge and these did not change significantly at the time of hospital discharge. They also showed reductions in exercise endurance as improvements in mean distance walked on the 6MWT over six months after discharge from hospital were not statistically or clinically significant. There was however a clinically significant increase in the median 6MWT distance achieved (65 meters) between one and six months after discharge from hospital. At six months they were only able to achieve 68 percent of their age predicted percentage of 6MWT distance. Clinically and statistically significant changes were observed in participants' peripheral muscle strength over the first six months after discharge. Survivors of critical illness had more limitations in HRQOL related to aspects of physical health than aspects of MH at six months after discharge but statistically and clinically significant improvements in mean SF-36 PCS scores were observed during this six month period. Participants showed a statistically and clinically significant improvement in mean EQ-5D VAS scores over the first six months after discharge form hospital but still experienced problems related to anxiety and depression.

Factors identified from the results that influence HRQOL related to mental health after discharge from hospital are duration of MV and level of depression at six months after discharge from hospital.

Findings from this study suggest that some survivors of critical illness may not recover fully on their own after an episode of acute illness. These results, together with results published by other South African researchers, should be used to motivate for implementation of structured rehabilitation programmes, including counselling, to aid the physical, emotional and mental recovery of survivors of critical illness in the long term after hospital discharge.

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APPENDIX A

- **ETHICAL CLEARANCE**

M130404M130404

R14/49 Mr Johannes van Aartsen

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M130404

NAME: (Principal Investigator)	Mr Johannes van Aartsen
DEPARTMENT:	Department of Physiotherapy Medical School
PROJECT TITLE:	The Functional ability and Health Related Quality of life of Survivors of Critical Illness after Hospital Discharge
DATE CONSIDERED:	26/04/2013
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr H van Aswegen
APPROVED BY:	Professor PE Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 13/08/2013

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature M130404Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX B

- **NETCARE: LETTER OF FINAL APPROVAL OF RESEARCH**

Netcare Management (Pty) Limited

Tel: + 27 (0)11 301 0000
Fax: Corporate +27 (0)11 301 0499
76 Maude Street, Corner West Street, Sandton, South Africa
Private Bag X34, Benmore, 2010, South Africa

RESEARCH OPERATIONAL COMMITTEE FINAL APPROVAL OF RESEARCH

Approval number: UNIV-2014-0005

Mr H van Aartsen

E mail: hannespt@gmail.com

Dear Mr van Aartsen

RE: THE FUNCTIONAL ABILITY AND HEALTH RELATED QUALITY OF LIFE OF SURVIVORS OF CRITICAL ILLNESS AFTER HOSPITAL DISCHARGE

The above-mentioned research was reviewed by the Research Operational Committee's delegated members and it is with pleasure that we inform you that your application to conduct this research at Netcare Union, Mulbarton, Rosebank and Rehabilitation Hospital, has been approved, subject to the following:

i) Research may now commence with this FINAL APPROVAL from the Sustainability Committee of Netcare (Research Operational Committee).

ii) All information with regards to Netcare will be treated as confidential.

iii) Netcare's name will not be mentioned without written consent from the Sustainability Committee of Netcare (Research Operational Committee).

iv) All legal requirements with regards to patient rights and confidentiality will be complied with.

v) Insurance will be provided and maintained for the duration of the research. This cover provided to the researcher must also protect both the staff and the hospital facility from potential liability

vi) In accordance with MCC approval, that medicine will be administered by or under direction of the authorised Trialist

vii) The research will be conducted in compliance with the GUIDELINES FOR GOOD PRACTICE IN THE CONDUCT OF CLINICAL TRIALS IN HUMAN PARTICIPANTS IN SOUTH AFRICA (2000)

viii) Netcare must be furnished with a STATUS REPORT on the progress of the study at least annually on 30th September irrespective of the date of approval from Sustainability Committee of Netcare (Research Operational Committee) as well as a

Directors: M S F da Costa, J du Plessis, K N Gibson R H Friedland, K Naiker, M B Nkosi, C Pallman, N Phillipson, P Warriner, D van den Bergh

Company Secretary: L Bagwandeen Reg. No. 1995/012717/07

FINAL REPORT with reference to intention to publish and probable journals for publication, on completion of the study.

ix) A copy of the research report will be provided to Netcare (Research Operational Committee) once it is finally approved by the tertiary institution, or once complete.

x) Netcare has the right to implement any Best Practice recommendations from the research.

xi) Netcare reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects/Netcare or should the researcher not comply with the conditions of approval.

xii) APPROVAL IS VALID FOR A PERIOD OF 36 MONTHS FROM DATE OF THIS LETTER.

We wish you success in your research.

Yours faithfully

Prof Dion du Plessis
Full member: Research Operational Committee & Medical Practitioner evaluating research applications as per Management and Governance Policy

Shannon Nell
Chairperson: Research Operational Committee
Network Healthcare Holdings Limited (Netcare)
Date: 31/1/2014

APPENDIX C

- **NETCARE: LETTER OF ACKNOWLEDGEMENT**

Netcare Union Hospital

Tel: +27 (0) 11 724 2000
Fax: +27 (0) 11 724 2002
47 Clinton Road, New Redruth, Alberton, South Africa
PO Box 1002, Alberton, 1450, South Africa
www.netcare.co.za

2 October 2013

Dear **Johannes van Aartsen**

Re: **The functional ability and health related quality of life of survivors of critical illness after hospital discharge**

We hereby confirm knowledge of the above named research application to be made to the Netcare Research Operational Committee and in principle agree to the research application for Netcare **Union** Hospital/site/division, subject to the following:

1. That the data collection may not commence prior to receipt of FINAL APPROVAL from the Sustainability Committee of Netcare (Research Operational Committee).
2. A copy of the research report will be provided to Netcare Research Operational Committee once it is finally approved by the tertiary institution, or once complete.
3. Netcare has the right to implement any Best Practice recommendations from the research.
4. That the Hospital/Site/Division Management reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects / Netcare or should the researcher not comply with the conditions of approval.

We wish you success in your research.

Yours faithfully

9-10-2013

Signed by Hospital/Site/Division Management **Date**

Hospital General Manager

(Specify designation)

Netcare Hospitals (Pty) Ltd T/A Netcare Union Hospital
Directors:
J Du Plessis, R H Friedland, K N Gibson
Company Secretary: L Bagwandeen **Reg. No.** 1996/006591/07

APPENDIX D

- **MULBARTON HOSPITAL: LETTER OF ACKNOWLEDGEMENT**

LETTER CONFIRMING KNOWLEDGE OF NON-TRIAL RESEARCH TO BE CONDUCTED IN THIS NETCARE FACILITY

Dear **Johannes van Aartsen**

Re:

The functional ability and health related quality of life of survivors of critical illness after hospital discharge

We hereby confirm knowledge of the above named research application to be made to the Netcare Research Operational Committee and in principle agree to the research application for Netcare **Mulbarton** Hospital/site/division, subject to the following:

1. That the data collection may not commence prior to receipt of FINAL APPROVAL from the Sustainability Committee of Netcare (Research Operational Committee).
2. A copy of the research report will be provided to Netcare Research Operational Committee once it is finally approved by the tertiary institution, or once complete.
3. Netcare has the right to implement any Best Practice recommendations from the research.
4. That the Hospital/Site/Division Management reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects / Netcare or should the researcher not comply with the conditions of approval.

We wish you success in your research.

Yours faithfully

21-08-2013

Signed by Hospital/Site/Division Management **Date**

GHM Netcare Mulbarton Hospital.

(Specify designation)

APPENDIX E

- **ROSEBANK HOSPITAL: LETTER OF ACKNOWLEDGEMENT**

Netcare Rosebank Hospital

Tel: +27 (0) 11 328 0500
Fax: +27 (0) 11 328 0509
14 Sturdee Avenue, Rosebank, South Africa
PO Box 52230, Saxonwold, 2132, South Africa
www.netcare.co.za

LETTER CONFIRMING KNOWLEDGE OF NON-TRIAL RESEARCH TO BE CONDUCTED IN THIS NETCARE FACILITY

Dear **Johannes van Aartsen**

Re:

The functional ability and health related quality of life of survivors of critical illness after hospital discharge

We hereby confirm knowledge of the above named research application to be made to the Netcare Research Operational Committee and in principle agree to the research application for Netcare **Rosebank Rehabilitation** Hospital/site/division, subject to the following:

1. That the data collection may not commence prior to receipt of FINAL APPROVAL from the Sustainability Committee of Netcare (Research Operational Committee).
2. A copy of the research report will be provided to Netcare Research Operational Committee once it is finally approved by the tertiary institution, or once complete.
3. Netcare has the right to implement any Best Practice recommendations from the research.
4. That the Hospital/Site/Division Management reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects / Netcare or should the researcher not comply with the conditions of approval.

We wish you success in your research.

Yours faithfully

15/01/2014

Signed by Hospital/Site/Division Management **Date**

Hospital manager.

(Specify designation)

Netcare Hospitals (Pty) Ltd T/A Netcare Rosebank Hospital
Directors:
J Du Plessis, R H Friedland, K N Gibson
Company Secretary: L Bagwandeen Reg. No. 1998/008591/07

Instruction on completion and signing of:

LETTER CONFIRMING KNOWLEDGE OF NON-TRIAL RESEARCH TO BE CONDUCTED IN THIS NETCARE FACILITY

The Applicant

1. Please fill in the relevant particulars as indicated on the document – please note that each hospital/division/site must receive its own letter
2. Once completed copy onto new document and send to the Netcare hospital/site/division for signature with your proposal and data collection instruments
3. On receipt of letter(s) send, with full application to the Project Manager: Research at research@netcare.co.za it is NOT the responsibility of the hospital/site/division to send these documents to the Project Manager

Dear Netcare Colleagues

The Netcare Research Operational Committee is required to review for possible APPROVAL or not of all research conducted in a Netcare facility. The Research Operational Committee, however, is not prepared to enforce you as management to accept research that the researcher plans to conduct in your hospital/site/division. It could be that you are not prepared to accept either the researcher or the research and therefore the Research Operational Committee affords you the opportunity to decline such application.

1. Should you have no reservations the Research Operational Committee requires that the relevant letter be copied onto your letter head and be signed by the management of your hospital/site/division.

2. Should you have any reservation would you please communicate it to the Project Manager: Research at research@netcare.co.za

APPENDIX F

- **LIFE REHABILITATION: LETTER OF ACKNOWLEDGEMENT**

Life Rehabilitation

National Rehabilitation office
Oxford Manor, 21 Chaplin Road, Illovo, 2196
Private Bag X13, Northlands, 2116, South Africa
Telephone +27 11 219 9620
Facsimile +27 86 686 0441
www.rehab.co.za

9 September 2013

Johannes van Aartsen
Department of Physiotherapy
University of Witwatersrand

Request for permission to conduct research

Dear Johannes

Many thanks for the request for permission to conduct research at our Life Rehabilitation Units at Life Riverfield Lodge, Fourways and Life New Kensington Clinic, Johannesburg on the topic: *The functional ability and health related quality of life of survivors of critical illness after hospital discharge.*

Life Rehabilitation supports the development of the field of rehabilitation through evidence-based research and we have a number of ongoing research projects in our units.

I hereby grant permission to you to access our two Life Rehabilitation units in order to conduct your research under the following conditions:

- As we value patient confidentiality and patients' right to choose, no patient may be identified, either by name or by the unit where the patient received his/her rehabilitation;
- No comparison is to be made between patients receiving rehabilitation at various rehabilitation units;
- Access to patient documentation must be controlled and supervised;
- Patient participation in the study is voluntary, and they may choose not to participate;
- The data gathered may only be used for the purpose of the research no information obtained in our units may be used by third parties

Access to the unit is dependent upon permission by the relevant managers to limit disruption to the unit routine and patients' rehabilitation programmes. Please liaise with Ms Kerusha Govender, Rehabilitation Clinical Specialist, or Ms Ida Geldenhuys, Therapy Manager at Life Riverfield Lodge, and Ms Danny Joelson, Therapy Unit Manager at Life New Kensington Clinic.

I wish you success with your research, and look forward to the results. We would appreciate a copy of your research upon completion.

Sincerely,

Nina Strydom
Support Specialist
Clinical Products
Life Healthcare
Tel: + 27 31 313 7912
Fax: + 27 866781450
Mobile: + 27 84 566 1281
Email: nina.strydom@lifehealthcare.co.za
Website: www.lifehealthcare.co.za

APPENDIX G

- **LIFE REHABILITATION: LETTER OF APPROVAL**

Life Healthcare Head Office
Oxford Manor, 21 Chaplin Road, Illovo 2196
Private Bag X13, Northlands 2116, South Africa
Telephone: +27 11 219 9000
Telefax: +27 11 219 9001
www.lifehealthcare.co.za

Life Healthcare group (Pty) LTD is registered as a
Private Higher Education College with the DHET
Registration number: 2008/HEO7/003

02 October 2013

ATTENTION: J van Aartsen

APPROVAL FOR RESEARCH STUDY
TITLE: The functional ability and health related quality of life of survivors of critical illness after hospital discharge.

Our previous correspondence refers.

The Research Committee of Life Healthcare has granted permission for your study.

We look forward to seeing the results of your research once it is completed.

Yours sincerely

Roodt

Anne Roodt
Nursing Education Specialist

Life College of Learning

Life Healthcare Group (Proprietary) Limited
Reg. no. 2003/024387/07 Registered address Oxford Manor, 21 Chaplin Road, Illovo 2196, Private Bag X13, Northlands 2116
Directors: Prof GJ Gerwel (Chairman), CMD Flemming (Managing Director), RJ Hogarth (Financial Director),
MA Brey, Dr MP Ngatane, GC Solomon

APPENDIX H

- **NETCARE REHABILITATION GROUP: LETTER OF APPROVAL**

Netcare Rehabilitation Hospital

Tel: +27 (0) 11 489 1111
Fax: +27 (0) 11 489 1190
2 Bunting Road, Auckland Park, Johannesburg, South Africa
PO Box 150, Auckland Park, 2006, South Africa
www.netcare.co.za

LETTER CONFIRMING KNOWLEDGE OF CLINICAL MEDICATION RELATED TRIAL OR CLINICAL NON-MEDICATION RELATED TRIAL RESEARCH TO BE CONDUCTED IN THIS NETCARE FACILITY

Dear Hannes van Aartsen

Re ***The functional ability and health related quality of life of survivors of critical illness after hospital discharge.***

We hereby confirm knowledge of the above named research application to be made to the Netcare Research Committee and in principle agree to the research application for Netcare Rehabilitation Hospital, subject to the following:

i) That the research may not commence prior to receipt of FINAL APPROVAL from the Academic Board of Netcare (Research Committee).

ii) That the researcher will notify the Academic Board of Netcare (Research Committee) of the proposed date of commencement of the project, in writing.

iii) That insurance stating the necessary indemnity cover (where applicable) will be provided by the researcher and maintained for the duration of the research, protecting both the staff and the hospital facility from potential liability

iv) That, in accordance with MCC approval, that medicine will be administered by or under direction of the authorised Trialist

v) That Netcare will be furnished with a STATUS REPORT on the progress of the study at least annually on 30th September irrespective of the date of approval from Academic Board of Netcare (Research Committee) as well as a FINAL REPORT with reference to intention to publish and probable journals for publication, on completion of the study.

vi) That the Hospital Management reserves the right to withdraw the approval for research at any time during the process, should the research prove to be detrimental to the subjects / Netcare or should the researcher not comply with the conditions of approval.

We wish you success in your research.

Yours faithfully

Marietha van Vuuren
Hospital General Manager

22-10-13
Date

APPENDIX I

- **INTER-RATER RELIABILITY FOR THE PHYSICAL FUNCTION IN ICU TEST (PFIT)**

	Inter-rater Reliability for The Physical Function in ICU Test (PFIT)															
Participant	1		2		3		4		5		6		7		8	
Assessor	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Outcome																
Sit to stand ability	3	3	3	3	3	3	2	2	3	3	3	3	3	3	3	3
MOS steps	65	65	73	74	10	10	33	34	25	25	3	3	68	68	54	52
MOS time	64	64	79	79	30	30	54	54	40	40	10	10	82	82	116	116
Cadence	60.93	60.93	55.44	56.2	20	20	36.67	37.78	37.5	37.5	18	18	49.76	49.76	27.93	26.89
Shoulder flexion strength right	5	5	5	5	5	5	4	4	5	5	5	5	5	5	5	5
Shoulder flexion strength left	5	5	5	5	5	5	4	4	5	5	5	5	5	5	5	5
Knee extension strength right	5	5	5	5	4	4	5	5	5	5	5	5	5	5	5	5
Knee extension left	5	5	5	5	4	4	5	5	5	5	5	5	5	5	5	5
Shoulder flexion reps	33	33	34	35	7	7	30	30	12	12	11	11	27	27	35	35
Shoulder flexion time	60	60	59	59	24	24	50	50	19	19	22	22	48	48	130	130
Shoulder cadence	33	33	34.57	35.59	17.5	17.5	36	36	37.89	37.89	30	30	33.75	33.75	16.15	16.15
PFIT Ordinal Score	11	11	11	11	9	9	8	8	10	10	10	10	10	10	10	10
PFIT Interval Score	8.8	8.8	8.8	8.8	7.1	7.1	6.4	6.4	7.9	7.9	7.9	7.9	7.9	7.9	7.9	7.9
Pearson Coefficient	**r=1; p=0.00**															

APPENDIX J

- **INTER AND INTRA RATER RELIABILITY TESTING FOR THE SIX MINUTE WALK TEST (6MWT)**

Inter and Intra Rater Reliability Testing For the six minute walk test (6MWT)						
	6MWT Result (meter)					
Assessor	Participant testing session	1	2	3	4	5
A	1	635	450	380	380	580
A	2	644	470	400	370	585
A	3	640	460	410	370	590

	Pearson Coefficient
Assessor A	
Session 1 with 2	r=0.99; p=0.00
Session 2 with 3	r=0.99; p=0.00
Session 1 with 3	r=0.99; p=0.00

APPENDIX K

- **HANDHELD DYNAMOMETRY INTER RATER AND INTRA RATER RELIABILITY TESTING**

Handheld Dynamometry Inter Rater and Intra Rater Reliability Testing											
HHD Reading – Elbow Extension (kilogram)											
Assessor	**Testing session**	**1 Right**	**2 Right**	**3 Right**	**4 Right**	**5 Right**	**1 Left**	**2 Left**	**3 Left**	**4 Left**	**5 Left**
A	1	99	94	148.1	71.6	93	100	71.7	161	76.5	158
	1	92	91	151.7	76.9	92	98	70.2	163.7	72.5	152
	1	91	91	152.1	74.5	94	105	69.8	161.9	67.6	156
	Mean	94	92	150.6	74.3	93	101	70.6	162.2	72.2	155.3
	2	92	90	148.1	73	93	96	73	161.7	74.5	154
	2	91	88	149.1	74.4	91	100	72	162.8	72	155
	2	94	87	150.1	73.6	95	104	70	163.7	70.2	156
	Mean	92.3	88.3	149.1	73.7	93	100	71.7	162.7	72.2	155
Pearson Coefficient		r=0.99; p=0.00					r=0.99; p=0.00				

Handheld Dynamometry Inter Rater and Intra Rater Reliability Testing											
HHD Reading – Knee flexion (kilogram)											
Assessor	**Testing session**	**1 Right**	**2 Right**	**3 Right**	**4 Right**	**5 Right**	**1 Left**	**2 Left**	**3 Left**	**4 Left**	**5 Left**
A	1	119	144	161	122.3	161	122	106.7	173	137	158
	1	120	157	165	132.1	135	154	118.1	181.5	120.1	145
	1	122	147	163	134.3	146	125	109.8	177.5	145.4	156
	Mean	120.3	149.3	163	129.6	147.3	133.7	111.5	177.3	134.1	153
	2	125.4	145	155	131	144.5	116.1	105.8	183	137.4	154
	2	116.1	166.8	158	128	125	133.9	112.5	168	130.8	137
	2	124.5	160.1	158	132	132.5	129.4	108.5	169	132.1	147
	Mean	122	157.3	157	130.3	134	126.5	108.9	173.3	133.4	146
Pearson Coefficient		r=0.88; p=0.02					r=0.99; p=0.00				

APPENDIX L

- **HANDHELD DYNAMOMETRY INTER RATER AND INTRA RATER RELIABILITY TESTING**

Handheld Dynamometry Inter Rater and Intra Rater Reliability Testing											
HHD Reading – Knee flexion(kilogram)											
Assessor	**Testing session**	**1 Right**	**2 Right**	**3 Right**	**4 Right**	**5 Right**	**1 Left**	**2 Left**	**3 Left**	**4 Left**	**5 Left**
A	1	119	144	161	122.3	161	122	106.7	173	137	158
	1	120	157	165	132.1	135	154	118.1	181.5	120.1	145
	1	122	147	163	134.3	146	125	109.8	177.5	145.4	156
	Mean	120.3	149.3	163	129.6	147.3	113.7	111.5	177.3	134.2	153
	2	125.4	145	155	131	144.5	116.1	105.8	183	137.4	154
	2	116.1	166.8	158	128	125	133.9	112.5	168	130.8	137
	2	124.5	160.1	158	132	132.5	129.4	108.5	169	132.1	147
	Mean	122	157.3	157	130.3	134	126.5	108.9	173.3	133.4	146
Pearson Coefficient		p=0.88					p=0.99				

APPENDIX M

- **INFORMATION DOCUMENT**

INFORMATION DOCUMENT

The functional ability and health related quality of life of survivors of critical illness after hospital discharge

Dear patient

I, Johannes van Aartsen, am doing research on the functional ability and health related quality of life of survivors of critical illness after hospital discharge. Research is only the process to learn the answer to a question. In this study I want to learn the functional ability of survivors of critical illness at the time of ICU discharge and hospital discharge, and the physical ability and health related quality of life of survivors of critical illness over the first 12 months after hospital discharge.

I am inviting you to take part in this research study. The study will be an observational study.

Your participation in the study would involve you performing the following tests/assessments:

- The physical function ICU test (PFIT) to assess your level of physical function when you are discharged from the ICU and before you are discharged from the hospital. This test will be done twice at your bed in the hospital ward.

- One month after discharge from the hospital you will be asked to come back to see me for assessment of your recovery. Exercise tolerance will then be assessed using the 6 minute walking test. During this test you will be asked to walk for 6 minutes at your own comfortable pace and the distance you walked will be measured. Before and after this test, your blood pressure and heart rate will be measured.

- Your muscle strength will be assessed with a handheld dynamometer which will give you resistance against your muscle contractions.

- Your physical activity level will be determined as you fill in the RPAQ questionnaire.

- Your health related quality of life will be determined as you fill in the EQ-5D and SF-36 questionnaires.

- To determine if you may suffer from depression you will be asked to fill in the PHQ-9 questionnaire.

You will be asked to return to see me at six and twelve months after hospital discharge. All of the abovementioned tests will again be performed on you.
All tests except for the PFIT will be done at the following venue, depending on the hospital you were at:

- Netcare Union Hospital: Section 5
- Netcare Mulbarton Hospital: ICU
- Chris Hani Baragwanath Hospital: Physiotherapy Department

To determine the severity of your illness and the estimation of morbidity when you were admitted to the ICU, I will use the information in your hospital file and/or ICU charts to calculate your APACHE II and SAPS II scores.

There will be 87 participants in this study, all from South Gauteng.

The entire testing session will take approximately 1 hour to complete.

The only risks involved in participating in this study would be possible tiredness and shortness of breath while doing the 6 minute walking test. I will ensure that emergency equipment is at hand in the case of a medical emergency. You will also be allowed to rest if need be. You will also be screened to determine if it would be safe for you to complete the 6 minute walking test.

The possible benefit of your participation in this study is that you can track your own progress after hospital discharge by having standardised tests administered. You will also contribute to the data available in South Africa and this may help health care services to improve.

You will still be allowed to continue with the treatments of your choice as prescribed by your doctor, physiotherapist and/or other health care professional.

You will be given pertinent information on the study while you are involved in it and after the results of the study are available.

Your participation in this study is voluntary. If you refuse to participate it will not involve any penalty or loss of benefits which you are otherwise entitled to. You may discontinue your participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled to. You do not need to provide any reasons if you want to terminate your participation.

You will be reimbursed for your travel expenses to attend assessment sessions.

All efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information will be disclosed if required by law.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Human Research Ethics Committee of the University of the Witwatersrand.

If results of the study are published, it may lead to individual or cohort identification.

For further information or reporting of study related adverse events, please contact me:

Johannes van Aartsen
Mobile: 079 388 2432
Tel: (011) 976-1754
E-mail: hannespt@gmail.com
Post: PO. BOX 8523
Edleen
1625

To report any complaints or problems, please contact the Human Research Ethics Committee administrator or chair:

Prof Cleyton-Jones
Tel: (011) 717- 2301

APPENDIX N

- **CONSENT FORM**

CONSENT FORM

I have read and understood the information details of the study titled "*The functional ability and health related quality of life of survivors of critical illness after hospital discharge."*

The nature, demands, risks, and benefits of the project have been explained to me. I knowingly participate in the study and understand that I may withdraw my consent and discontinue participation at any time without penalty or loss of benefit to myself.

If circumstances develop during the course of the study that will deem the study continuation to be unsafe for me, my participation will be terminated by the investigator without regards to the participant's consent.

The only additional costs I will encounter during the course of the study will be travel costs.
If significant new findings are developed during the course of the research which may relate to my willingness to continue participation in the study, these findings will be provided to me.
I had the opportunity to ask questions regarding the research study and my participation in it.
My questions were answered fully and appropriately by the researchers.

The consent is given on the basis that my name will not be publicly divulged.

Subject's signature: _____ Date: _____

I certify that I have explained to the above individual the nature and purpose, the potential benefits, and possible risks associated with participation in this research study, have answered any questions that have been raised, and have witnessed the above signature.

Signature of investigator: _____ Date: _____

APPENDIX O

- **DEMOGRAPHIC INFORMATION**

DEMOGRAPHIC INFORMATION

Participant name: _____

Participant code: _____

Age: _____

Gender: _____

Diagnosis: _____

_____

Previous disability or pre-morbid conditions: _____

Do you live alone or with others? _____

If with others, will the people you live with provide you with support after hospital discharge?

_____

If you live on your own, would you have any friends or family to provide you with support at home? _____

Physical address: _____

Telephone number: _____

Mobile number: _____

E-mail address: _____

Highest level of education achieved: _____

Pre-morbid occupational situation: _____

At 1, 6, and 12 months after discharge:

Are you back to work yet?: yes/no _____

If yes, what date did you return to work? _____

Are you doing the same job at work you did before? Yes/no. _____

If no, what type of work are you doing now? _____

If you have not returned to work, what are the reasons for this? _____

_____

APPENDIX P

- **MUSCLE GROUPS AND TESTING POSITIONS FOR HHD**

Muscle action tested	***Patient position *Joint position**	**Dynamometer placement**	**Stabilization region**
Shoulder Flexion	*Supine *Shoulder flexed to 90° and elbow extended	Slightly proximal to Humeral epicondyles	Axillary region
Elbow Flexion	*Supine *Elbow flexed to 90° with the forearm supinated.	Slightly proximal to styloid process of the radius.	Superior surface of the arm or shoulder.
Elbow Extension	*Supine *Elbow flexed to 90° with the forearm in neutral.	Slightly proximal to the ulnar styloid process.	Anterior surface of the arm or shoulder
Hip Abduction	*Supine *Both legs in neutral.	At the point of the lateral femoral condyles.	Stabilization of the opposite leg in a neutral position.
Knee flexion	*Sitting at the edge of the bed *Knees and hips flexed to 90°. Participant's hands resting on hi/her lap.	Slightly proximal to the malleoli on the posterior aspect of the lower leg.	An assistant stabilizes at the shoulders.
Knee extension	*Sitting at the edge of the bed *Knees and hips flexed to 90°. Participant's hands resting on hi/her lap.	Slightly proximal to the malleoli on the anterior aspect of the lower leg.	An assistant stabilizes at the shoulders.
Ankle dorsiflexion	*Supine *The hip, knee and ankle at 0°.	Slightly proximal to the metatarsophalangeal joints of the foot.	Knee to be kept in full extension. The leg is supported on the bed while the foot is off the bed.

APPENDIX Q

- **HEALTH AND WELL-BEING QUESTIONNAIRE**

Your Health and Well-Being

This questionnaire asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

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

Excellent	Very good	Good	Fair	Poor
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now 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
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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3 The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	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	☐ 1	☐ 2	☐ 3
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking more than a kilometre	☐ 1	☐ 2	☐ 3
h. Walking several hundred metres	☐ 1	☐ 2	☐ 3
i. Walking one hundred metres	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

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4. **During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?**

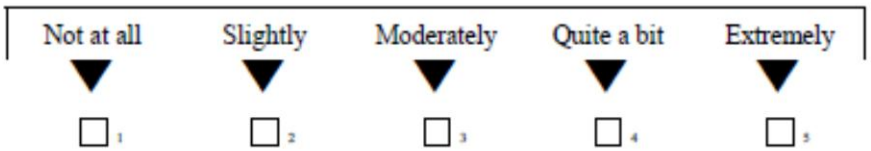
	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. **During the past 4 weeks, how much of the time 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)?**

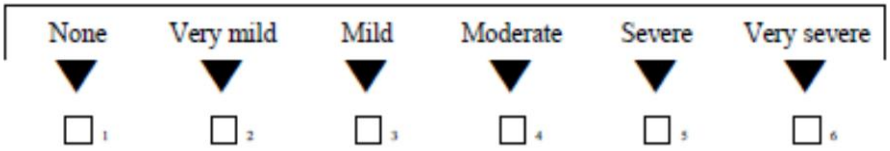
	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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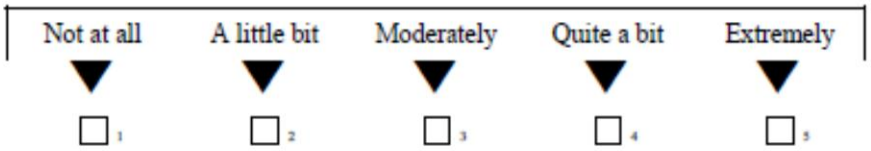
6. **During the <u>past 4 weeks</u>, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?**



7. **How much <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?**



8. **During the <u>past 4 weeks</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?**



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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	Some of the time	A little of the time	None of the time
a. Have you felt full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e. Have you had a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g. Have you felt worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h. Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i. Have you felt tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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 friends, relatives, etc.)?**

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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11. How TRUE or FALSE is <u>each</u> 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	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Thank you for completing these questions!

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APPENDIX R

- **DOCUMENT OF CERTIFICATION FOR THE REVISION OF TEXT STRINGS FOR THE AFRIKAANS (SOUTH AFRICA) SF-12V2 AND SF36v2 SELF ADMINISTERED FORM (STANDARD & ACUTE) PAPER-PENCIL**



February 22nd, 2012

RE: Document of Certification for the revision of text strings for the Afrikaans (South Africa) SF-12v2 and SF36v2 Self-Administered Form (Standard & Acute) Paper-Pencil

To whom it may concern:

HRA is providing this document of attestation to certify that the Afrikaans (South Africa) SF-12v2 and SF36v2 Self-Administered Form (Standard & Acute) Paper-Pencil are appropriately reflective and matches the content in the English versions of the questionnaire. The revised text strings for the Self-Administered Form Paper-Pencil versions of the SF-36v2 and SF-12v2 (Standard & Acute) were adapted from previously accepted changes from the existing Afrikaans (South Africa) Modified Hip Fracture versions for the SA and IS. The remaining items were retained without alteration from the fully linguistically validated existing paper-pencil versions. The corrections that were identified and approved were categorized for this project into 4 different codes and differentiated the types of changes and determined whether a developer review was necessary.

HRA recruited appropriate translation consultants experienced in the preparation of cross-cultural adaptation of outcomes research measures. HRA organized, coordinated and supervised the activities of the translation consultants during all phases of the adaptation. This included performing the evaluation of the suggestions for appropriate content matching and monitoring the paste-up check of the revised Afrikaans (South Africa) versions and producing the final documentation.

HRA further certifies that the appropriate standards of cross-cultural adaptation techniques were used to develop this version of the measure. These include:

- Identification and review of corrections accepted in the existing Afrikaans (South Africa) Modified Hip Fracture versions for the SA and IS
- Evaluation of the suggestions for the revised text strings for content equivalence
- Developer review of the suggestions for the revised text strings if necessary
- Incorporation of accepted changes, final formatting of translation
- Paste-up check of all the measures

A comprehensive report and documentation on the cross-cultural adaptation process will follow delivery of this certification letter.

Sincerely,

Valeska Kantzer

Valeska Kantzer
Language Department Manager

APPENDIX S

- **DOCUMENT OF CERTIFICATION FOR THE REVISION OF TEXT STRINGS FOR THE ENGLISH (SOUTH AFRICA) SF-12v2 AND SF36v2 SELF ADMINISTERED FORM (STANDARD & ACUTE) PAPER PENCIL**



February 22nd, 2012

RE: Document of Certification for the revision of text strings for the English (South Africa) SF-12v2 and SF36v2 Self-Administered Form (Standard & Acute) Paper-Pencil

To whom it may concern:

HRA is providing this document of attestation to certify that the English (South Africa) SF-12v2 and SF36v2 Self-Administered Form (Standard & Acute) Paper-Pencil are appropriately reflective and matches the content in the English versions of the questionnaire. The revised text strings for the Self-Administered Form Paper-Pencil versions of the SF-36v2 and SF-12v2 (Standard & Acute) were adapted from previously accepted changes from the existing English (South Africa) Modified Hip Fracture versions for the SA and IS. The remaining items were retained without alteration from the fully linguistically validated existing paper-pencil versions. The corrections that were identified and approved were categorized for this project into 4 different codes and differentiated the types of changes and determined whether a developer review was necessary.

HRA recruited appropriate translation consultants experienced in the preparation of cross-cultural adaptation of outcomes research measures. HRA organized, coordinated and supervised the activities of the translation consultants during all phases of the adaptation. This included performing the evaluation of the suggestions for appropriate content matching and monitoring the paste-up check of the revised English (South Africa) versions and producing the final documentation.

HRA further certifies that the appropriate standards of cross-cultural adaptation techniques were used to develop this version of the measure. These include:

- Identification and review of corrections accepted in the existing English (South Africa) Modified Hip Fracture versions for the SA and IS
- Evaluation of the suggestions for the revised text strings for content equivalence
- Developer review of the suggestions for the revised text strings if necessary
- Incorporation of accepted changes, final formatting of translation
- Paste-up check of all the measures

A comprehensive report and documentation on the cross-cultural adaptation process will follow delivery of this certification letter.

Sincerely,

Valeska Kantzer

Valeska Kantzer
Language Department Manager

APPENDIX T

- **CONFIRMATION OF TRANSLATION OF THE SF-36v2 HEALTH SURVEY INTO ISIZULU**

QualityMetric

MEDICAL OUTCOMES TRUST

Health Assessment Lab

This is to certify that IQOLA Project researchers have prepared a true translation from English (for United States) into isiZulu (for South Africa) of the SF-36v2™ Health Survey. This translation was developed using the standard IQOLA translation methodology, which involves multiple independent forward translations by native speakers; reconciliation of the translations into one form; backward translation of this translation into English to check for conceptual equivalence; and qualitative debriefing tests with a small number of native isiZulu speakers in South Africa. Further details of the IQOLA translation process can be found in the following peer-reviewed article:

Bullinger M, Alonso J, Apolone G, Leplège A, Sullivan M, Wood-Dauphinee S, et al. Translating health status questionnaires and evaluating their quality: The International Quality of Life Assessment Project approach. J Clin Epidemiol 1998; 51:913-923.

Sincerely,

Barbara Gandek

Barbara Gandek, M.S.
Director, IQOLA Project

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APPENDIX U

- **NON-COMMERCIAL LICENSE AGREEMENT**

OPTUM

NON-COMMERCIAL LICENSE AGREEMENT
Office of Grants and Scholarly Research (OGSR)

License Number: QM023025

Licensee Name: Hannes van Aartsen c/o University of Witwatersrand

Licensee Address: PO Box 8523, , Edleen, Gauteng 1625

Approved Purpose: Non-commercial academic research and/or thesis – Unfunded Student.

Study Name: The functional ability and health related quality of life of survivors of critical illness after hospital discharge.

Study Type: student

Data Collection Method: Paper

Therapeutic Area: Wellness & Lifestyle

Royalty Fee: None, because this License is granted in support of the non-commercial Approved Purpose

Other Definitions: As indicated on Appendix B "License Agreement – Details", including without limitation: Licensed Surveys, Modes of Administration, Fees, Administrations, Services, Approved Languages and (if applicable) Study Term

Licensee accepts and agrees to the terms of this Non-Commercial License Agreement (the "Agreement") from the Office of Grants and Scholarly Research (OGSR) of OptumInsight Life Sciences, Inc. (f/k/a QualityMetric Incorporated) ("OptumInsight") as of the date of last signature below (the "Effective Date").

Subject to the terms of this Agreement, including the OptumInsight Non-Commercial License Terms and Conditions attached as Appendix A: OptumInsight grants to Licensee, and Licensee accepts, a non-exclusive, non-transferable, non-assignable, non-sublicensable worldwide license to use, solely for the Approved Purpose and during the License Term, the Licensed Surveys in the authorized Data Collection Methods, Modes of Administration, and Approved Languages indicated on Appendix B and to administer the Licensed Surveys only up to the approved number of Administrations (and to make up to such number of exact reproductions of the Licensed Surveys necessary to support such Administrations) in any combination of the specific Licensed Surveys and Approved Languages, Data Collection Methods, and Modes of Administration and to use any related software provided by OptumInsight.

Capitalized terms used in this Agreement shall have the meanings assigned to them above, or in Appendices A and B attached hereto. Appendices A and B attached hereto are incorporated into and made a part of this Agreement for all purposes.

EXECUTED, as of the Effective Date, by the duly authorized representatives as set forth below.

OptumInsight Life Sciences, Inc. [OptumInsight]	**Hannes van Aartsen c/o University of Witwatersrand** [Licensee]
Signature: Michelle White	Signature:
Name: Michelle White	Name: J. VAN AARTSEN
Title: Director of Consulting Science	Title: Mr.
Date: 20 FEB 2014	Date: 17/02/2014

APPENDIX A

OPTUMINSIGHT NON-COMMERCIAL LICENSE TERMS AND CONDITIONS

Attached to and Incorporated into License No. QM023025

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Upon OptumInsight's completion of the Initial Review, OptumInsight will provide Licensee with a detailed list of revisions that will need to be made before OptumInsight can approve the electronic format. Licensee is required to submit subsequent screenshots or a link to the Licensed Surveys for each Approved Language incorporating any changes required by OptumInsight until OptumInsight provides its final approval of the electronic format. The parties acknowledge and agree that multiple rounds of review and revisions may be necessary prior to OptumInsight being able to provide final approve of the electronic format. Licensee is solely responsible for the electronic creation of the Licensed Surveys. Licensee does not obtain any rights in the Licensed Surveys not otherwise granted in this Agreement due to the administration and/or use of the Licensed Surveys. Nothing in this Agreement prohibits OptumInsight from creating its own electronic forms of Licensed Survey administration. The Licensed Surveys cannot be used in electronic format except as allowed pursuant to the terms and conditions of this Agreement. Licensee acknowledges that there may be response differences due to effects from use of electronic format compared to a static Mode of Administration such as paper/pencil. Licensee assumes any and all risk of differential effects resulting from the use of electronic format.

14. Miscellaneous –

a. This Agreement constitutes the entire and exclusive agreement between the parties and supersedes all previous communications or agreements, either oral or written, with respect to the subject matter hereof. This Agreement may not be modified or amended except by an instrument in writing signed by both parties. The Appendices attached hereto are incorporated into and made a part of this Agreement for all purposes.

b. Notices, copies of notices or other communications shall be sent to a party at the address set forth on the first page of this Agreement. All notices shall be effective upon delivery of the notice at such address.

c. Any waiver of any breach or default under this Agreement must be in writing and shall not be deemed a waiver of any other or subsequent breach or waiver. Failure to delay by either party to enforce compliance with any term or condition of this Agreement shall not constitute a waiver of such term or condition.

d. If any provision in this Agreement is determined to be invalid or unenforceable, the remaining provisions of this Agreement shall not be affected thereby and shall be binding upon the parties hereto, and shall be enforceable, as though the invalid or unenforceable provision were not contained herein.

e. In the event a Licensed Survey or associated OptumInsight intellectual property is exported by Licensee outside of the country in which Licensee is located, both parties agree that Licensee is obligated and solely responsible for ensuring compliance with all applicable import and export laws and regulations of the United States of America and/or any applicable foreign jurisdictions. Licensee shall indemnify, defend and hold harmless

OptumInsight (including payment of all reasonable costs, fees, settlements and damages) with respect to any suits or proceedings brought against OptumInsight arising from Licensee's export of a Licensed Survey.

f. This Agreement and performance hereunder shall be governed in accordance with the laws of the State of New York, but excluding New York choice of law principles. With respect to any dispute arising in connection with this Agreement, Licensee consents to the exclusive jurisdiction and venue in the state and federal courts located in New York City, New York.

g. This Agreement may be executed in multiple counterparts, each of which shall be deemed an original and all of which shall be deemed the same agreement

h. Licensee, in order to activate Software, may need to click on an "I Agree" radial button included in the End User License Agreement screen in the Software. The parties acknowledge and agree that notwithstanding Section 12 of the End User License Agreement in the Scoring Software, the terms and conditions of this Agreement shall control. For avoidance of doubt, the parties further acknowledge and agree that the terms and conditions of the End User License Agreement are not applicable to Software despite this radial button requirement.

OPTUM

Very Important - Please Read

NO formatting or editing changes to the survey

In order to obtain licensing from Licensor no changes can be made to the survey forms. Any format and/or language changes have the potential to affect the survey data received. Therefore, to maintain the validation and integrity of the SF Health Surveys, **no language or formatting changes** are allowed. The format of the survey is scientifically engineered to facilitate accurate and unbiased data, as well as keeping the SF Health Survey in a visual format that is comprehensible to the patient/participant, including those who may be impaired and/or elderly. **You should administer the survey in the exact format you will receive it in. The only item Licensee may add is a header with patient identification and / or administration information. If you do wish to add a header please ask for a sample copy of the survey to edit and then submit this to your Account Representative for review prior to signing this License Agreement.** Once the licensing process is completed, you will receive a clean set of Survey Forms in a word and .pdf file. These are the forms you will administer. **Please do not use any forms you may already have access to as the ones we send you are the most current versions.**

* * *

APPENDIX B

OPTUM

LICENSE AGREEMENT - DETAILS

Licensee: University of Witwatersrand
Hannes van Aartsen
PO Box 8523
Edleen
Edleen, Gauteng 1625

License Number: QM023025
Amendment to: N/A
Study Term: 03/01/14 to 12/31/15

Approved Purpose
The functional ability and health related quality of life of survivors of critical illness after hospital discharge.

Licensed Surveys (Modes) and Services:

Item	Description	Mode of Admin	Quantity
PROJ01	License Fee	Paper	
ES0220	SF-36v2, Standard Recall	Paper	1

Approved Languages:
South Africa (Afrikaans)
South Africa (English)
South Africa (Sesotho)
South Africa (Zulu)

ADM012	Patients Enrolled		87
ADMINS	Administrations		261
SS075	Scoring Software v4.5		1
SS080	SS v4.5 Key: SF-36v2		261
EM020	SF-36v2 Clinical Trial Guide		1

Approved Languages:
United States (English)

TOTAL FEES: 0.00 USD



APPENDIX V

- **EQ-5D-3L HEALTH QUESTIONNAIRE**



Health Questionnaire

English version for South Africa

By placing a tick in one box in each group below, please indicate which statements best describe your own state of health TODAY.

Mobility

I have no problems in walking about ❑
I have some problems in walking about ❑
I am confined to bed ❑

Self-Care

I have no problems with self-care ❑
I have some problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑
I have some problems with performing my usual activities ❑
I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑
I have moderate pain or discomfort ❑
I have extreme pain or discomfort ❑

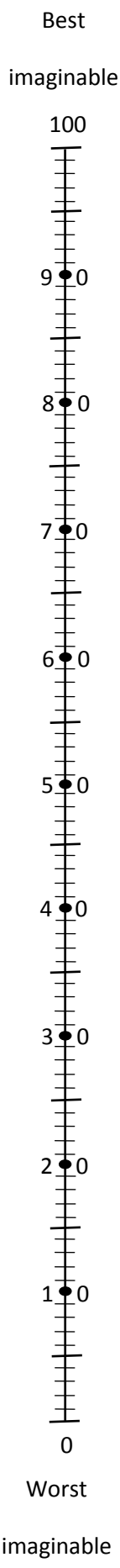
Anxiety/Depression

I am not anxious or depressed ❑
I am moderately anxious or depressed ❑
I am extremely anxious or depressed ❑

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale, in your opinion, how good or bad your own health is today. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

Your own state of health



APPENDIX W

- **EQ-5D REGISTRATION**

EQ-5D registration

Inbox

Tue, May 13, 2014 at 11:42 AM

Mandy Oemar

<oemar@euroqol.org>
To: "hannespt@gmail.com" <hannespt@gmail.com>
Reply | Reply to all | Forward | Print | Delete | Show original

Dear Ms/Mr. Johannes van Aartsen,

Thank you for registering your research at the EuroQol Group Foundation's website.

As the study you registered involves low patient numbers (87) you may use the EQ-5D-3L instrument (Paper version) free of charge. Please note that separate permission is required if any of the following is applicable:

- Funded by a pharmaceutical company, medical device manufacturer or other profit-making stakeholder;
- Number of respondents over 5000
- Routine Outcome Measurement;
- Developing or maintaining a Registry;
- Digital representations (e.g. PDA, Tablet or Web)

Please find attached the Afrikaans (South Africa), English (South Africa), Sesotho (South Africa), Setswana (South Africa), Xhosa (South Africa) and Zulu (South Africa) EQ-5D-3L version (word format). A brief user guide is downloadable from the EuroQol website (www.euroqol.org)

Kind regards,

Mandy Oemar
Communications Officer
T: +31 88 4400190
E: oemar@euroqol.org
W: www.euroqol.org

APPENDIX X

- **PATIENT HEALTH QUESTIONNAIRE (PHQ-9)**

PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME:_____ DATE:_____

Over the last 2 *weeks*, how often have you been bothered by any of the following problems? *(use "✓" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so figety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
	add columns		+	+
(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card).		TOTAL:		

10. If you checked off *any problems*, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all _____ Somewhat difficult _____ Very difficult _____ Extremely difficult _____

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A2663B 10-04-2005

PHQ-9 Patient Depression Questionnaire

For initial diagnosis:

1. Patient completes PHQ-9 Quick Depression Assessment.
2. If there are at least 4 ✓s in the shaded section (including Questions #1 and #2), consider a depressive disorder. Add score to determine severity.

Consider Major Depressive Disorder
- if there are at least 5 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Consider Other Depressive Disorder
- if there are 2-4 ✓s in the shaded section (one of which corresponds to Question #1 or #2)

Note: Since the questionnaire relies on patient self-report, all responses should be verified by the clinician, and a definitive diagnosis is made on clinical grounds taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.
Diagnoses of Major Depressive Disorder or Other Depressive Disorder also require impairment of social, occupational, or other important areas of functioning (Question #10) and ruling out normal bereavement, a history of a Manic Episode (Bipolar Disorder), and a physical disorder, medication, or other drug as the biological cause of the depressive symptoms.

To monitor severity over time for newly diagnosed patients or patients in current treatment for depression:

1. Patients may complete questionnaires at baseline and at regular intervals (eg, every 2 weeks) at home and bring them in at their next appointment for scoring or they may complete the questionnaire during each scheduled appointment.
2. Add up ✓s by column. For every ✓: Several days = 1 More than half the days = 2 Nearly every day = 3
3. Add together column scores to get a TOTAL score.
4. Refer to the accompanying **PHQ-9 Scoring Box** to interpret the TOTAL score.
5. Results may be included in patient files to assist you in setting up a treatment goal, determining degree of response, as well as guiding treatment intervention.

Scoring: add up all checked boxes on PHQ-9

For every ✓ Not at all = 0; Several days = 1;
More than half the days = 2; Nearly every day = 3

Interpretation of Total Score

Total Score	Depression Severity
1-4	Minimal depression
5-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

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A2662B 10-04-2005

APPENDIX Y

- **PFIT RECORDING SHEET**

Subject No: _____
Date:____/_____/20___
Time Point (please circle): Recruitment Other (specify)

ICU Discharge

PFIT RECORDING SHEET		
1. Heart rate (beats per minute)	Pre:_____	Post: _____
2. SpO_2 (%)	Pre:_____	Post: _____
3. Sit to stand Assistance (circle)	0 1 2	
4. MOS 4.1 RPE (pre)	_____	
4.2 Able? (circle)	Yes No	
4.3 Steps (number)	_____	
4.4 Time (seconds)	_____	
4.5. RPE (post)	_____	
5. Strength	**Left**	**Right**
5.1 Shoulder flexion	_____	_____
5.2 Knee extension	_____	_____
6. Shoulder flexion 6.1 RPE (pre)	_____	_____
6.2 Reps (number)	_____	_____
6.3 Seconds	_____	_____
6.4 RPE (post)	_____	_____

Reason for test non-completion:
Patient deceased ☐ Patient lost to follow-up ☐
Patient refused ☐ Patient confusion ☐
Other: _____

APPENDIX Z

- **RECENT PHYSICAL ACTIVITY QUESTIONNAIRE**

MRC | Epidemiology Unit

Participant study No.

Available at http://www.mrc-epid.cam.ac.uk/Research/PA/Downloads.html

RPAQ

Recent Physical Activity Questionnaire

This questionnaire is designed to find out about your physical activity in your everyday life in the last 4 weeks

This questionnaire is divided into 3 sections
Please try to answer every question.

- **Section A** asks about your physical activity patterns in and around the house.
- **Section B** is about travel to work and your activity at work.
- **Section C** asks about recreations that you may have engaged in during the last 4 weeks.

Your answers will be treated as strictly confidential and will be used only for medical research

Section A Home Activities

Getting about

Which form of transport have you used **most often** in the last 4 weeks apart from your journey to and from work? (Please tick (✓) one box only)

Usual mode of travel			
Car / motor vehicle	Walk	Public transport	Cycle

TV, DVD or Video Viewing (Please put a tick (✓) on every line)

Hours of TV, DVD or video watched per day	Average over the last 4 weeks					
	None	Less than 1 hour a day	1 to 2 hours a day	2 to 3 hours a day	3 to 4 hours a day	More than 4 hours a day
On a weekday before 6 pm						
On a weekday after 6 pm						
On a weekend day before 6 pm						
On a weekend day after 6 pm						

Computer use at home *but not at work* (e.g. internet, email, Playstation, Xbox, Gameboy etc) (Please put a tick (✓) on every line)

Hours of home computer use per day	Average over the last 4 weeks					
	None	Less than 1 hour a day	1 to 2 hours a day	2 to 3 hours a day	3 to 4 hours a day	More than 4 hours a day
On a weekday before 6 pm						
On a weekday after 6 pm						
On a weekend day before 6 pm						
On a weekend day after 6 pm						

Stair climbing at home (please put a tick (✓) on every line)

Number of times you climbed up a flight of stairs (approx 10 steps) each day at home	Average over the last 4 weeks					
	None	1 to 5 times a day	6 to 10 times a day	11 to 15 times a day	16 to 20 times a day	More than 20 times a day
On a weekday						
On a weekend day						

Section B Activity at work

Please answer this section to describe if you have been in paid employment at any time **during the last 4 weeks** or you have done regular, organised voluntary work.

Have you been in employment during the last 4 weeks? *Yes* ☐ *No* ☐

During the last 4 weeks how many hours work did you do per week?

	4 weeks ago	3 weeks ago	2 weeks ago	1 week ago
Work hours (excluding travel)				

Type of work

We would like to know the type and amount of physical activity involved in your work. **Please tick** (✓) the option that **best** corresponds with your occupation(s) in the last 4 weeks from the following four possibilities:

Please tick only one of the following

1. Sedentary occupation
You spend most of your time sitting (such as in an office) ☐

2. Standing occupation
You spend most of your time standing or walking. However, your work does not require intense physical effort (e.g. shop assistant, hairdresser, guard) ☐

3. Manual work
This involves some physical effort including handling of heavy objects and use of tools (e.g. plumber, electrician, carpenter) ☐

4. Heavy manual work
This implies very vigorous physical activity including handling of very heavy objects (e.g. dock worker, miner, bricklayer, construction worker) ☐

Section B Activity at work

Travel to and from work in the last 4 weeks

What is the approximate distance from your home to your work?

☐☐☐ Miles *or* ☐☐☐ Kilometers

How many times a week did you travel from home to your main work? ☐☐
Count outward journeys only

Please tick (✓) one box **only** per line

How did you normally travel to work?	Always	Usually	Occasionally	Never or rarely
By car/motor vehicle				
By works or public transport				
By bicycle				
Walking				

What is the postcode for your main place of work during the last 4 weeks?

Postcode ☐☐☐☐☐☐☐

If not known please give your work address
Work address - _____
_____
_____

What is the postcode for your home address?

Postcode ☐☐☐☐☐☐☐

Section C Recreation

The following questions ask about how you spent your leisure time.

Please indicate how often you did each activity on average over the last 4 weeks

Please indicate the average length of time that you spent doing the activity on each occasion.

Example

If you went walking for pleasure for 40 minutes once a week.
If you had done weeding or pruning every fortnight and took 1 hour and 10 minutes on each occasion.
You would complete the table below as follows:

Please give an answer for the NUMBER OF TIMES you did the following activities in the past 4 weeks and the AVERAGE TIME you spent on each activity.

Please complete EACH line

	Number of times you did the activity in the last 4 weeks							Average time per episode	
	None	Once in the last 4 weeks	2 to 3 times in the last 4 weeks	Once a week	2 to 3 times a week	4 to 5 times a week	Every day	Hours	Minutes
Weeding and pruning			✓					*1*	*10*
Walking for pleasure				✓					*40*

Example

Now complete the table on pages 6 and 7

Please give an answer for the average time you spent on each activity and the number of times you did that activity in the past 4 weeks

Please complete each line

	Number of times you did the activity in the last 4 weeks							Average time per episode	
	None	Once in the last 4 weeks	2 to 3 times in the last 4 weeks	Once a week	2 to 3 times a week	4 to 5 times a week	Every day	Hours	Minutes
Swimming - competitive									
Swimming leisurely									
Backpacking or mountain climbing									
Walking for pleasure *(not as a means of transport)*									
Racing or rough terrain cycling									
Cycling for pleasure *(not as a means of transport)*									
Mowing the lawn									
Watering the lawn or garden									
Digging, shovelling or chopping wood									
Weeding or pruning									
DIY e.g. carpentry, home or car maintenance									
High impact aerobics or step aerobics									
Other types of aerobics									
Exercise with weights									
Conditioning exercises e.g. using a bike or rowing machine									

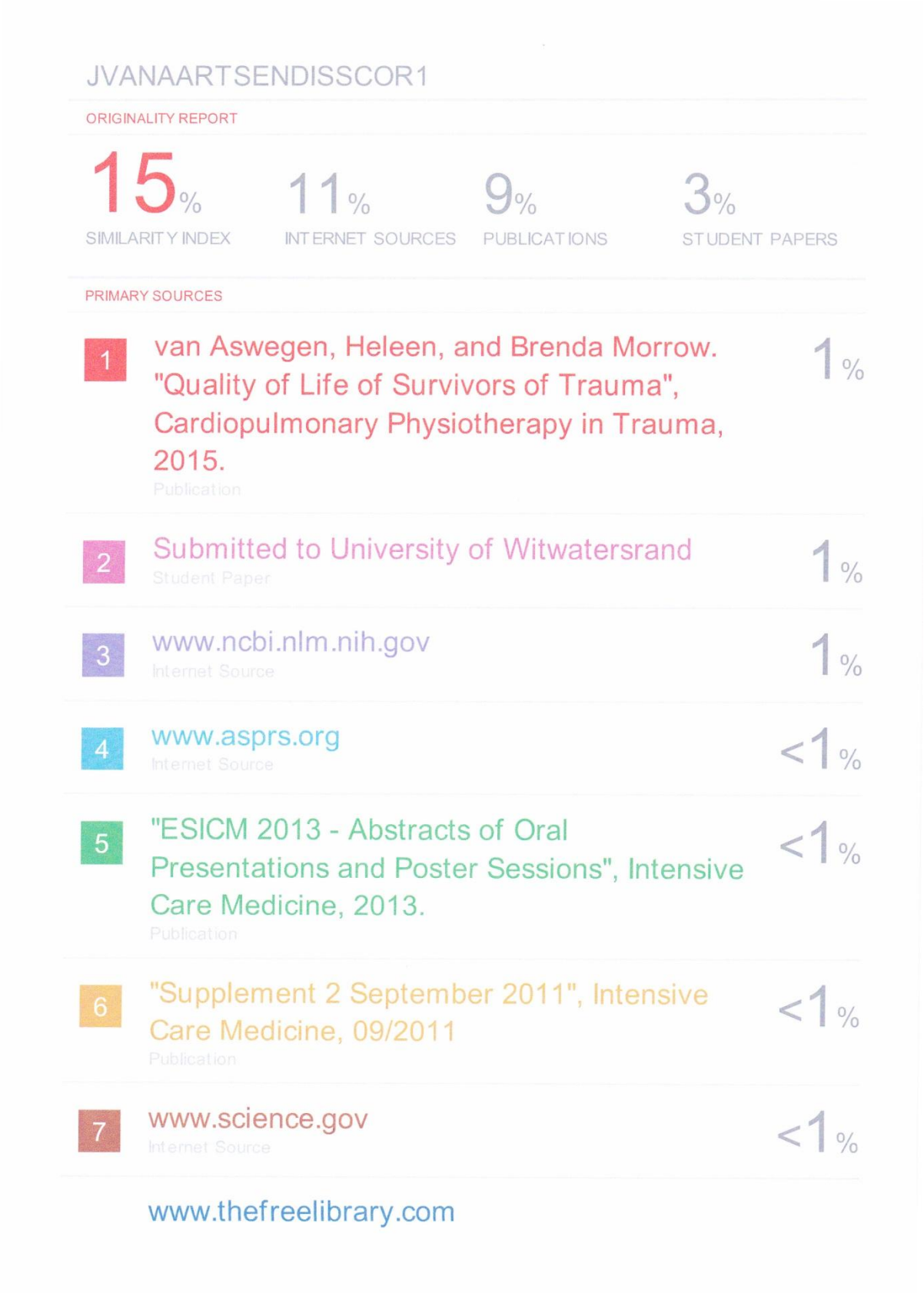
Please complete each line

	Number of times you did the activity in the last 4 weeks							Average time per episode	
	None	Once in the last 4 weeks	2 to 3 times in the last 4 weeks	Once a week	2 to 3 times a week	4 to 5 times a week	Every day	Hours	Minutes
Floor exercises e.g. stretching, bending, keep fit or yoga									
Dancing e.g. ballroom or disco									
Competitive running									
Jogging									
Bowling- indoor, lawn or 10 pin									
Tennis or badminton									
Squash									
Table tennis									
Golf									
Football, rugby or hockey									
Cricket									
Rowing									
Netball, volleyball or basketball									
Fishing									
Horse-riding									
Snooker, billiards or darts									
Musical instrument playing or singing									
Ice skating									
Sailing, wind-surfing or boating									
Martial arts, boxing or wrestling									

Thank you.

APPENDIX AA

- **TURN-IT-IN REPORT**



JVANAARTSENDISSCOR1

ORIGINALITY REPORT

15%	11%	9%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	van Aswegen, Heleen, and Brenda Morrow. "Quality of Life of Survivors of Trauma", Cardiopulmonary Physiotherapy in Trauma, 2015. Publication	1%
2	Submitted to University of Witwatersrand Student Paper	1%
3	www.ncbi.nlm.nih.gov Internet Source	1%
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