Shoulder dysfunction in intensive care survivors
an investigation into prevalence, risk factors and impact on upper limb function

Gustafson, Owen D.

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Shoulder dysfunction in intensive care survivors: an investigation into prevalence, risk factors and impact on upper limb function

Owen D. Gustafson

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Abstract

Background: Limitations in function and quality of life have been reported in intensive care unit survivors for many years after hospital discharge. Shoulder dysfunction is a cause of functional limitation in other patient populations, and has been suggested as a potential cause in intensive care unit survivors. Despite this, the prevalence of shoulder dysfunction, its impact on upper limb function and risk factors for its development are unknown in intensive care unit survivors.

Methods: A cohort study of intensive care unit survivors from a single general intensive care unit was undertaken using prospective and retrospective data. Participants underwent a series of shoulder assessments up to 6 months after hospital discharge to identify shoulder dysfunction and upper limb impairment. Multivariable analysis was used to investigate the risk factors for developing shoulder dysfunction.

Results: Shoulder dysfunction was present in 76% of participants, with 42% presenting with ongoing shoulder dysfunction at 6 months after hospital discharge. Functional impairment of the upper limb was present in 48% of participants and severe impairment in 18%. None of the risk factors analysed were independently associated with shoulder dysfunction.

Conclusions: Shoulder dysfunction is a common problem in intensive care unit survivors, and is a source of functional impairment. Further investigation addressing risk factors for its development, and therapeutic interventions to address this problem is required.

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List of Abbreviations

ICU	Intensive care unit
APACHE	Acute Physiology and Chronic Health Evaluation
SOFA	Sequential Organ Failure Assessment
6MWT	6 Minute Walk Test
SCI	Spinal cord injury
CVA	Cerebrovascular accident
ROM	Range of movement
COPD	Chronic obstructive pulmonary disease
IHD	Ischaemic heart disease
DM	Diabetes myelitis
HTN	Hypertension
CRF	Chronic Renal Failure
ICUAW	Intensive care unit acquired weakness
GHJ	Glenohumeral joint
HSP	Hemiplegic Shoulder Pain
HRQOL	Health related quality of life
LOS	Length of stay
HO	Heteropic ossification
CIP	Critical illness polyneuropathy
CIM	Critical illness myopathy
CINMA	Critical illness neuromuscular abnormalities
VAS	Visual analogue scale
CMS	Constant-Murley score

QD	QuickDash
RRT	Renal replacement therapy

Chapter 1: Introduction

The number of patients admitted to an intensive care unit (ICU), and the number surviving this period of critical illness, is increasing, with over 130,000 admissions and seventy-five percent surviving to hospital discharge in England and Wales each year (HSCIC 2015, ICNARC 2015). Research has shown that ICU survivors present with neuromuscular disorders which contributes to functional impairment and pain; this can last for a significant period of time post discharge and, importantly, affects post ICU quality of life (Nordon-Craft et al 2012, Cuthbertson et al 2010). A recorded, but under reported, musculoskeletal disorder in ICU survivors is shoulder dysfunction. In other populations that frequently find themselves in ICU, for example spinal cord injury (SCI) and cerebral vascular accident (CVA), there is a high incidence and prevalence of shoulder dysfunction (Subbaro et al 1995, Lindgren et al 2006). Therefore, shoulder dysfunction in other patient groups may also present within an ICU setting. This research will establish the nature and frequency of shoulder dysfunction in ICU as well as establishing potential risk factors that may contribute to this disorder.

Shoulder dysfunction is a set of common disorders that can be found in numerous patient populations with similar numerous aeitiologies (Chard et al 1991). There is no consensus in the literature regarding a definition of shoulder dysfunction. Therefore, for the purposes of this thesis, the term shoulder dysfunction will encompass any disorder or pathology of the shoulder complex, impairment as described by a shoulder specific outcome measure, or pain or loss of range of movement (ROM) at the shoulder.

Shoulder pain and dysfunction are common conditions with frozen shoulder affecting approximately 2% of the general population (Robinson et al 2012), however there is disagreement regarding the diagnostic criteria for frozen shoulder (Zuckerman and Rokito 2011). Criteria for diagnosing frozen shoulder according to Robinson et al (2012) include shoulder pain, a pattern of stiffness, prominent loss of external rotation with normal radiographs. There are several conditions associated with frozen shoulder including chronic obstructive pulmonary disease (COPD), ischaemic heart disease (IHD), diabetes mellitus (DM) and trauma (Robinson et al 2012). These are common systemic conditions that exist in ICU patients prior to admission to ICU, and issues that occur during a period of critical illness, and would put these patients at an increased risk of developing frozen shoulder. Specifically, patients in ICU often have abnormal blood glucose levels related to acute illness (Van den Berghe 2004), and when considered with the high incidence of frozen shoulder in the DM population (Anton 1993), could predispose ICU patients to shoulder dysfunction.

Immobility is inevitably seen in patients admitted to ICU (Brewer 2009) and is also associated with frozen shoulder (Robinson et al 2012). In addition to structural changes at the joint that leads to loss of ROM (van der Laar and van der Zwaal 2014), immobility is a contributing factor to the development of intensive care unit acquired weakness (ICUAW) (Stevens et al 2009). Functional impairment of ICU patients following discharge from hospital is often attributed to ICUAW which is associated with periods of prolonged immobility, and presents clinically with severe symmetrical weakness, predominantly

affecting proximal muscle groups (de Jonghe et al 2009, Nordon-Craft et al 2012). As a result of the complex nature of the shoulder, the stability of the glenohumeral joint (GHJ) is severely compromised by muscle weakness (Labrinola et al 2005). Shoulder dysfunction following a CVA is often termed hemiplegic shoulder pain (HSP) and has been attributed to GHJ subluxation secondary to the muscle paresis (Murie-Fernandez et al 2012). Shoulder dysfunction similar to hemiplegic shoulder pain (HSP) could develop in patients experiencing ICUAW. In addition to ICUAW, there are multiple procedures and positions that patients undergo in ICU that result in shoulder joint immobility and therefore may result in shoulder dysfunction. It is unclear what impact these procedures and ICUAW have on shoulder dysfunction, and how this contributes to overall functional impairment after discharge from ICU.

Persistent functional limitation due to muscle wasting and weakness can occur up to 12 months after discharge, with patients reporting moderate or severe difficulties with their mobility, self-care and functional activity (Dowdy et al 2005). These patients are reported to have severely decreased health related quality of life (HRQOL), which is associated with a high socioeconomic burden and can persist up to 5 years after ICU discharge (Herridge et al 2011, Cuthbertson et al 2010, Griffiths et al 2013). The number of studies investigating long term outcomes in ICU survivors is increasing, however only a small number have discussed shoulder dysfunction. The rate of shoulder dysfunction seen in ICU survivors in these studies varies from 5 to 80% (Herridge et al 2011, Clavet et al 2008, Clavet et al 2011, Battle et al 2013, Gustafson 2012). The focus of these studies also varies between HRQOL,

chronic pain and contractures, with only one study specifically investigating shoulder dysfunction (Gustafson 2012). Only two of the studies identify any risk factors for the development of shoulder dysfunction (Battle et al 2013, Clavet et al 2008) which included ICU and hospital length of stay (LOS), and sepsis. However, the number of risk factors investigated were limited and no detailed theories were proposed for the rationale behind developing shoulder dysfunction.

It is apparent that there is a lack of clarity regarding the prevalence, risk factors and functional impact of shoulder dysfunction in ICU survivors. Therefore, the purpose of this study aims to investigate shoulder dysfunction in ICU survivors in more detail. This study intends to answer the following three research questions:

1. What is the prevalence of shoulder dysfunction in adult ICU survivors after discharge from hospital?
2. What are the risk factors associated with the development of shoulder dysfunction in adult ICU survivors?
3. Does shoulder dysfunction in adult ICU survivors result in functional impairment of the upper limb?

This study will be the first study specifically investigating shoulder dysfunction in ICU survivors, and will add to the increasing body of evidence investigating the long term effects of critical illness by identifying a potential specific source of functional impairment. This study will achieve this through an observational research approach in the empirical-analytical paradigm, as it aims to identify

links within data. The design used to undertake the research is a cohort study, with ICU survivors the population and shoulder dysfunction the 'disease' under investigation. Patients with ongoing shoulder dysfunction or whose admitting condition to ICU would independently predispose them to develop shoulder dysfunction are not included in the study. Both prospective and retrospective data collection methods are used to collect information surrounding the patients' ICU stay, before undertaking a series of shoulder assessments over the six months following discharge from hospital.

This thesis will contain the following chapters in order: literature review, research methods, results, discussion. The literature review chapter will critically appraise in detail the previous studies investigating and highlighting shoulder dysfunction in ICU survivors. The theories surrounding immobility and ICUAW, inflammation, systemic conditions and procedures undertaken on the ICU and their association with shoulder dysfunction will be reviewed and the relevant literature critically appraised. The research methods chapter will discuss in detail the positivist framework in which the research is based, cohort study design and the consecutive sampling approach. The inclusion and exclusion criteria and variables chosen for data collection will be discussed, and the outcome measures used will be critically appraised and justified. The research process will be described in detail including data analysis and any ethical considerations. The results chapter will present the data collected and the results of the data analysis, followed by discussion of the results in relation to the research questions in the discussion chapter. The discussion chapter will also discuss the results in relation to the theories identified in the literature

review, prior to discussing the limitations of the study. Finally, the recommendations for the direction of further research regarding shoulder dysfunction in ICU survivors will be made.

Chapter 2: Literature Review

Shoulder dysfunction is an already recognised complication of many specific patient populations including: cerebrovascular accident (CVA), spinal cord injury (SCI) and diabetes (Robinson et al 2012). In the general population, pain and sensory disturbances in the upper limb are common symptoms, with reported point prevalence rates in the UK ranging from 4 to 35% (Walker-Bone et al 2004). The presence of functional impairment in ICU survivors is often attributed to intensive care unit acquired weakness (ICUAW), which is associated with periods of prolonged immobility (de Jonghe et al 2009). Joint contractures and chronic pain have also been identified as contributing factors (Clavet et al 2008, Battle et al 2013). As shoulder dysfunction is associated with many systemic conditions, trauma and immobility, all of which can be present in patients admitted to ICU, it is reasonable to suggest that ICU survivors may go on to develop shoulder dysfunction.

The potential prevalence and impact of shoulder dysfunction in ICU survivors is great as the number of patients admitted to ICU is increasing with approximately 130,000 admissions in England between 2013 and 2014 (ICNARC 2015). The number of patients surviving this period of critical illness is also increasing, with over 90% surviving to discharge from ICU and 75% surviving to hospital discharge (HSCIC 2015). This increase in the number of ICU survivors has been mirrored by high levels of morbidity and poor health related quality of life (HRQOL) following discharge (Nordon-Craft et al 2012).

Shoulder dysfunction is a generic term encompassing multiple specific pathologies such as frozen shoulder and rotator cuff impairment, and symptoms including pain and decreased range of movement (ROM) (Chard et al 1991). There is no consensus on a definition of shoulder dysfunction in the literature. Therefore, for the purpose of this literature review, shoulder dysfunction will encompass any disorder or pathology of the shoulder complex, impairment as described by a shoulder specific outcome measure, or pain or loss of ROM at the shoulder.

The literature review will discuss and explore shoulder dysfunction and its relationship with ICU survivors. All longitudinal follow-up studies of ICU survivors that identify or discuss shoulder dysfunction will be critically reviewed. The relationship between shoulder dysfunction and ICUAW, systemic inflammation, systemic conditions and ICU interventions will be explored, before its impact on function discussed. Following this review, research questions investigating the prevalence, risk factors and impact on function of shoulder dysfunction in ICU survivors will be proposed.

2.1 Prevalence of Shoulder Dysfunction in ICU Survivors

Shoulder dysfunction that was not present prior to admission to hospital has been reported in up to 80% of ICU survivors (Clavet et al 2008, Clavet et al 2011, Herridge et al 2011, Gustafson 2012, Battle et al 2013). Only one study to date has specifically investigated shoulder dysfunction in ICU survivors. In a small study of 20 ICU survivors attending a post-ICU rehabilitation programme, Gustafson (2012) reported that 80% (16) of patients had shoulder pain or loss

of ROM that was not present prior to their admission to ICU. This small study that was published only as an abstract, has multiple methodological problems. There was no description of the methods of measuring and identifying pain or loss of ROM, or justification of what constituted loss of ROM, leaving the study open to observation bias (Grimes and Schulz 2002). The participants were not described, nor the method by which they were invited to the rehabilitation programme, decreasing the external validity of the results (Sedgwick 2013). It is also difficult to rule out the impact of chance in such a small sample size, thereby increasing the potential for type 2 error (Sabari et al 1998). There was also no formal evaluation of the impact of shoulder pain and loss of ROM on patient function, therefore it is difficult to evaluate the clinical significance of the impairment.

Several other studies have reported aspects of shoulder dysfunction as part of an investigation into long term outcomes or musculoskeletal impairment in ICU survivors. One focus of these studies is the loss of ROM at skeletal joints, presenting as contractures. Joint contractures are defined as a fixed limitation in passive range of movement (ROM) of a joint, as a result of changes to peri-articular structures, including bone, muscle, soft tissues and skin (Orford et al 2011). Clavet et al (2008) conducted a retrospective review of medical notes, collecting data on the presence of and risk factors for joint contractures in patients admitted to a regional ICU. They reviewed the medical notes of 155 patients with an ICU length of stay of 14 days or more, extracting numerical data on ROM for 5 large joints: shoulder, elbow, hip, knee and ankle. Data on ROM was collected at ICU discharge and at hospital discharge, while data

collected on risk factors included: demographic characteristics, comorbidities, admission diagnosis, Acute Physiology And Chronic Health Evaluation (APACHE II score), ICU length of stay (LOS), duration of mechanical ventilation, use of steroids and neuromuscular blocking agents (NMBA) and hospital length of stay.

They reported that on discharge from hospital 34% of patients had at least one joint contracture with 23% deemed as functionally significant. They reported 24 shoulder contractures, 13 of which were functionally significant on discharge from the ICU. There is no discussion of how many of these shoulder contractures persisted to discharge from hospital. The significance of shoulder contractures cannot be determined from the statistical analysis as joints were not individually analysed. The authors define a shoulder contracture as "a recorded range of motion that is short of full range", specifically flexion and abduction less than 180^{o} (Clavet et al 2008 p692). This definition is flawed as the authors have not identified previous shoulder dysfunction or taken into account the age related decrease in shoulder ROM (Barnes et al 2001, Roy et al 2009). Therefore, they are unable to identify if a reduction in shoulder ROM was a result of critical illness or if it was pre-existing. This decreases the validity of the definition as an outcome measure for assessing ICU acquired shoulder contractures.

The authors have also not discussed the method by which shoulder ROM was measured. It is reasonable to assume that the healthcare professionals measuring the ROM used a goniometer as it is the most common method of measuring shoulder ROM (Mullaney et al 2010). There is no discussion around

how many different healthcare professionals assessed ROM, and while there is good intrarater reliability in measuring shoulder ROM, the interrater reliability is variable (Boone et al 1978, Riddle et al 1987). The position of the patient during shoulder ROM assessment is also not identified. There is a reduction in intrarater reliability between measurements taken in different positions, and therefore the test position should be routinely recorded, and repeated clinical measures of individual patients should be taken in a consistent position (Sabari et al 1998). The lack of clarity around the assessment of shoulder ROM in this study decreases its reliability. Therefore, it is unclear if the decreased ROM at the shoulder is entirely due to contracture, or if inconsistent measurement contributed to the reduction in ROM.

Clavet et al (2011) used their pre-existing database to complete another retrospective study investigating the link between ICU acquired joint contractures, the provision of physiotherapy in hospital and the presence of contractures and resource utilisation after discharge home. The authors concluded that there was no statistical significance in resource utilisation between those with and without contractures. However, the authors do not distinguish between the location of joint contracture, and as previously discussed, the lack of validity of the outcome measure used to define joint contracture, and lack of reliability in the method of joint assessment makes comparison between the two groups difficult.

Another aspect of shoulder dysfunction investigated in ICU survivors is chronic pain, which has been highlighted in several health related quality of life (HRQOL) studies (Cuthbertson et al 2005, Herridge et al 2011, Eddleston et al

2000). Battle et al (2013) investigated the incidence and site of chronic pain in ICU survivors, and the risk factors for developing this pain. The authors used a questionnaire and telephone follow up at six months post hospitalisation to identify patients' pain, and then undertook a retrospective analysis of the hospital database to identify risk factors for chronic pain. The data collected included: APACHE II score, admission diagnosis, severe sepsis, ventilator days, ICU length of stay and hospital length of stay. The authors included 196 patients that were admitted to a single ICU over a six month period, and found that 44% of patients were experiencing pain with the shoulder being the most common site affected (22%).

The questionnaire used by Battle et al (2013) was designed by them for the study. It had not been previously used or validated in the ICU survivor population, which therefore decreases its external validity (Boynton and Greehalgh 2004). The authors did identify that there were no other validated outcome measures for the use in this study, and attempted to increase the questionnaires reliability and validity by piloting it on a group of ICU survivors attending a follow-up clinic. However, this does not mean that the questionnaire was valid or reliable (Boynton and Greehalgh 2004). To decrease the non-response bias the authors undertook a non-responder analysis to compare the characteristics of the responders. Even though there was a low response rate of 61% which could potentially add a source of bias, there was no significant difference in the characteristics of responders and non-responders (Sheikh and Mattingly 1981). The authors also highlighted that the study was not intended to identify the severity of pain, or its impact on function. Therefore, it is impossible

to quantify the clinical significance of shoulder pain identified in the study. Despite these shortfalls, the study does identify the shoulder as the primary source of chronic pain in ICU survivors.

There have been a number of studies identifying specific shoulder pathologies in their long term follow-up of ICU survivors. In their follow up of patients with Acute Respiratory Distress Syndrome (ARDS), Herridge et al (2011) reported a number of neuromuscular complications at 5 years after ICU discharge including entrapment neuropathies, enlargement and immobility of large joints as a result of heterotopic ossification (HO), finger contractures and frozen shoulders. They reported a prevalence of frozen shoulder in ICU survivors of 3% at 5 years after ICU discharge. Despite the strong methodological rigor of this large longitudinal ICU follow-up study, there was no discussion of how the diagnosis of shoulder dysfunction was made. The authors did not discuss the process of shoulder assessment or if the participants had any shoulder dysfunction prior to ICU admission, which decreases the reliability of the results. It is reasonable to infer from the study that 3% of participants presented with shoulder dysfunction, however there is nothing to suggest that a diagnosis of frozen shoulder could be made.

In addition to Herridge et al (2011), there have been a small number of case reports identifying HO in ICU survivors, specifically of the glenohumeral joint (GHJ). Heteropic ossification is defined as the formation of calcified lamellar bone inside soft-tissue where bone does not exist (Bossche and Vanderstraeten 2005). Heteropic Ossification may develop in multiple different patient populations, including the critical care population in the absence of neurologic

or traumatic lesion, where patients have been immobilised and mechanically ventilated (Clements and Camilli 1993 and Jacobs et al 1999). In a series of case reports, Clements and Camilli (1993) identify HO of the GHJ in patients admitted to ICU for the management of respiratory failure. In a series of case studies, Dellestable et al (1996) radiologically identified HO of the GHJ (among other joints) in patients who were mechanically ventilated for a mean of 32 days. The limited number of case studies identifying this complication of the GHJ, suggests that it is probably a rare occurrence in the ICU population.

2.2 Risk Factors for Shoulder Dysfunction in ICU Survivors

Risk factors for the development of shoulder dysfunction in ICU survivors were only identified in two of the studies highlighting shoulder dysfunction. The risk factors that were independently associated with shoulder pain following logistic regression analysis by Battle et al (2013) were hospital length of stay (p = .026) and sepsis (p = .001). Clavet et al (2008) reported that ICU length of stay was independently associated with developing a contracture (p = .02). However, Clavet et al (2008) did not differentiate between the location of contractures therefore it is not clear if ICU length of stay is independently associated specifically with shoulder contractures.

There was minimal discussion in either of the studies regarding the potential pathophysiology surrounding the development of pain or contractures. Both studies highlighted immobility as a result of prolonged ICU or hospital length of stay as contributing, but neither discussed the pathophysiology behind this. Battle et al (2013) also highlighted mechanical ventilation, dialysis and the

presence of a central venous catheter as limiting joint movement, therefore resulting in pain, however they did not expand on this. Finally, Battle et al (2013) briefly discussed the impact of decreased muscle tone in patients in ICU, resulting in instability of the GHJ. Battle et al (2013) proposed that poor handling of the unstable GHJ by healthcare professionals during an ICU admission could result in chronic shoulder pain, but did not expand this point any further. The other studies identifying shoulder shoulder dysfunction did not propose any theories for the reasons for its development. The theories proposed by Battle et al (2013) and Clavet et al (2008) will be evaluated, and further potential causes for shoulder dysfunction discussed.

2.2.1 Immobility and Weakness

Loss of ROM at a joint occurs when the joints are not subjected to normal mobility and stress (Brower 2009), as seen during the periods of immobilisation that patients are subjected to in ICU. Immobility inevitably occurs with all critically ill patients, with periods of bed rest increasing to days and weeks dependent on the severity of illness (Brower 2009). This period of immobility results in a loss of contractile proteins in anti-gravity muscle, such as the dynamic muscle stabilisers of the shoulder (Robinson et al 2012), and a relative increase in collagen and other non-contractile tissues (Topp et al 2002). This in turn, results in joint contractures as seen in the study by Clavet et al (2008). Battle et al (2013) and Clavet et al (2008) both inferred that the longer the ICU length of stay then the greater the period of immobility, and therefore the greater the risk of shoulder contracture and pain. This is a reasonable inference, however not a guarantee, and a more accurate method of recording

the period of immobility would be to measure the length of time on ICU prior to mobilisation.

Immobility of the GHJ, as seen in ICU patients, can also result in frozen shoulder (Robinson et al 2012). Frozen shoulder is one of the most common shoulder disorders encountered, characterised by the spontaneous onset of pain with significant restriction of both passive and active ROM of the shoulder (Robinson et al 2012). As the shoulder stiffens there is a progressive loss of GHJ motion, with the most significant loss of external rotation followed by abduction and internal rotation (Chambler and Carr 2003). The selective restriction of external rotation that is characteristic of frozen shoulder syndrome is produced by anteriorsuperior capsular tightening, which particularly affects external rotation of the adducted arm, and anteriorinferior tightening, which reduces external rotation in abduction. Posterior capsular tightening limits internal rotation, and may be present in more severe forms (Robinson et al 2012). The deltoid and supraspinatus muscle may be atrophic due to disease followed by the infraspinatus, subscapularis and teres minor muscles (van de Laar and van der Zwaal 2014). As a result of disuse and atrophy of these muscles, the ligaments of the joint will thicken leading to decreased functionality (van de Laar and van der Zwaal 2014). Trivial trauma has been postulated to be an important factor, particularly when it is followed by a prolonged period of immobilisation (Hand et al 2007), as seen in ICU. However, most patients who sustain minimal trauma, even when combined with a period of immobilisation, do not develop frozen shoulder, therefore, it could be concluded that some

patients are more predisposed to frozen shoulder than others (Chambler and Carr 2003).

The impact of immobility in the older population is more pronounced. Kortbein et al (2007) found in their small study (n = 12) of healthy adults with a mean age of 67, that the rate of lean tissue loss after 10 days was greater than at 28 days for a younger population. However, the younger population that the authors compared their results against were from a completely separate study, decreasing the reliability of the results. There is also an age related reduction shoulder ROM, which can be associated with loss of upper limb function, with a reported reduction in mean external rotation to 66^{o} and flexion to 153^{o} for those over the age of 60 (Hussain et al 2016, Roy et al 2009). Some of the reasons suggested for this loss of flexibility include an age specific increase in the stiffness of collagen, damage to the articulating surfaces and a reduction in the use of the full range of movement of the joint (Bassey et al 1989). Battle et al (2013) did not find that increasing age was associated with shoulder pain in ICU survivors, however they did find that it was associated with chronic pain in general terms in ICU survivors. Therefore, age is important to consider when identifying potential risk factors for shoulder dysfunction in ICU survivors.

Immobility is a powerful contributor to reduced muscle mass and strength in healthy individuals, and in critical illness this reduction can reach half of the total muscle mass (Kortbein et al 2007, Lightfoot et al 2009). Immobility potentiates the activation of specific biochemical pathways that lead to enhanced proteolysis and decreased protein synthesis, resulting in structural and metabolic changes in the muscle (Fan et al 2009, Jackman and Kandarian

2009, Lightfoot et al 2009). In healthy individuals on bed rest, muscle mass has been shown to decrease by 1.5% to 2% per day during the first 2- 3 weeks of enforced rest (Adams et al 2003), resulting in a reduction of strength of 15-22% after 14 days (Bamman et al 1998, Hespel et al 2001) and 53% after 28 days (Veldhuizen et al 1993). Correlation between the extent and degree of organ failure and severity of muscle mass loss shown by Puthucheary et al (2013) strongly suggests that atrophy is something more than just the result of inactivity. Puthucheary et al (2013) undertook a prospective characterisation of skeletal muscle wasting in 63 critically ill patients within the first 10 days of their admission to ICU. They found that significant muscle mass was lost during the first 10 days of ICU admission which they concluded was not only due to decreased synthesis but also due to increased proteolysis, however there was no discussion if this indicated a comparative reduction in muscle strength.

Muscle weakness is a common observation among critically ill patients, and has been the subject of an increasing number of studies over a twenty-year period. Several studies have demonstrated diffuse weakness of the peripheral and central musculature leading to prolonged mechanical ventilation, increased hospital length of stay and hospital mortality (Stevens et al 2007). The term intensive care unit acquired weakness (ICUAW) is a clinical diagnosis referring to the presence of muscle weakness in critically ill patients in whom there is no plausible aetiology other than critical illness (Stevens et al 2009). The diagnosis of ICUAW requires the clinical context of an acute process of high illness severity requiring prolonged organ support and is usually associated with a period of protracted immobilisation (Saxena and Hodgson 2012). The

increasing prevalence of reported ICUAW can be ascribed both to growing awareness of peripheral neuromuscular involvement in critical illness among intensivists, and to improved survival of patients with prolonged organ failure who benefit from the considerable advances made in organ support techniques (de Jonghe et al 2009). The incidence of ICUAW has been reported at 25%-60% in patients who are mechanically ventilated for more than seven days (de Jonghe et al 2009) with sepsis, multi-organ failure (MOF) and prolonged mechanical ventilation consistently highlighted as risk factors (Stevens et al 2009, Bednarik at al 2005).

A reduction in muscle mass and associated weakness is particularly relevant in the development of shoulder dysfunction as the motion of the shoulder complex is probably greater than any other joint in the body (Rockwood et al 2009), and as a result is prone to dysfunction. The balance between instability and stiffness is therefore largely maintained by the static and dynamic soft tissue stabilisers (Robinson et al 2012). Dynamic stabilisers include the musculature of the shoulder, namely the rotator cuff unit. The static stabilisers include the glenoid labrum, glenohumeral ligaments and joint capsule. However, due to its wide range of motion and osseous anatomy, there is a relatively high risk of instability in the shoulder compared to other joints (Robinson et al 2012). Instability being a pathological condition in which the laxity of the joint increases abnormally, preventing the ability to maintain the humeral head centred in the glenoid fossa (Itoi et al 1996).

In addition to immobilisation and inflammation related muscle atrophy, neuromuscular disorders are the major causes of ICUAW (Latronico and Bolton

2011), with structural or functional changes in skeletal muscle, including membrane in-excitability, occurring either in isolation or with axonal involvement (de Jonghe et al 2009). These neuromuscular disorders are collectively known as critical illness neuromuscular abnormalities (CINMA), and are separated into critical illness polyneuropathy (CIP), myopathy (CIM) and neuromyopathy (CINM). Critical illness polyneuropathy is a distal axonal polyneuropathy, affecting both sensory and motor nerves, that represents the response of the peripheral nervous system to critical illness and effects between 33-50% of the most severely critically ill patients (Hermans et al 2008). Critical illness polyneuropathy presents with limb weakness, affecting the limbs in a symmetrical pattern. Weakness is most notable in proximal neuromuscular areas (e.g. shoulder and hip) (Latronico and Bolton 2011). In addition, involvement of the respiratory muscles occurs and impedes weaning from mechanical ventilation resulting in a prolonged ICU length of stay (Kress and Hall 2014), which was identified by Clavet et al (2008) as a risk factor for developing joint contractures. Critical illness myopathy is a primary myopathy (distinct from secondary myopathies as a result of denervation), with similar clinical features to CIP but occurring more frequently with a higher rate of recovery (Kress and Hall 2014). It is difficult to distinguish between a neuropathy and myopathy at the bed side as both conditions are manifested by limb weakness, with the combination of CIP and CIM (known as CINM) likely the most common manifestation of neuromuscular weakness in the ICU (Kress and Hall 2014 and Latronico and Bolton 2011). Critical illness polyneuropathy and CIM can cause prolonged severe disability after critical illness, with limb

weakness that persists for months or years after resolution of critical illness. CIP is the main contributor to persistent disability, whereas CIM can be associated with complete recovery (Latronico and Bolton 2011). In a small prospective cohort study of 26 mechanically ventilated patients on a single ICU, Koch at al (2014) found that there was a significant difference in functional outcome at 1 year between patients with CIP and those with CIM. They reported that 88% of CIM patients recovered within 1 year compared to 55% of those with CIP or CINM, indicating that differentiating the conditions can add to prognostication of function. However, the results must be interpreted cautiously, due to the low number of patients recruited and the lack of a validated outcome measure to assess function at 1 year.

There is no direct evidence linking shoulder dysfunction with ICUAW, however there are other conditions where severe weakness results in shoulder dysfunction. Shoulder dysfunction as a result of weakness has been extensively reported in patients presenting with hemiplegia following cerebrovascular accident (CVA). The GHJ is an unstable joint when there is a reduction in muscular tone around the joint (Labriola et al 2005). This instability secondary to profound weakness post CVA results in partial separation of the humeral head from the glenoid fossa and is termed subluxation (Murie-Fernandez at al 2012). Shoulder pain and stiffness is present in 30% of patients with hemiplegia, with the incidence increasing in those patients who require assistance with mobility (Wanklyn et al 1996), and is referred to as hemiplegic shoulder pain (HSP). Patients with ICUAW can exhibit profound weakness and muscle atrophy which, in the shoulder, can mimic that of the paresis seen in

hemiplegia. The musculature of the shoulder girdle effected by CVA can also be effected by ICUAW, and therefore result in similar shoulder instability, subluxation and ultimately, pain and stiffness. Battle et al (2013) highlighted a lack of awareness and handling of the shoulder by healthcare staff on ICU as a potential cause of shoulder pain in ICU survivors. In hemiplegia, HSP occurs during arm movement when the humeral head is not aligned correctly in the glenoid fossa or when shoulder movements take place without normal scapulohumeral rhythm (Murie-Fernandez et al 2012). There is little focus on the care of the upper limb when handling the ICU patients, unlike in the CVA patient population where maintaining the upper limb in the correct position to prevent excessive GHJ subluxation is seen as fundamental in managing HSP (McKenna 2001).

The rising incidence and societal burden of critical illnesses such as sepsis and the ARDS, coupled with declining fatality rates and an aging population, suggest that the number of patients with critical illness neuromuscular abnormalities (CINMA) and its associated problems may be substantial and likely to grow (Stevens et al 2007). In a systematic review in 2007, Stevens et al reviewed neuromuscular dysfunction acquired in the ICU. They found that evidence of neuromuscular dysfunction is present in approximately 50% of adult ICU patients who receive prolonged mechanical ventilation, have sepsis or multi-organ failure. There was a consistent and significant increase in duration of mechanical ventilation and hospitalisation associated with CINMA. However, they also concluded that there is considerable heterogeneity in the way CINMA is diagnosed in the literature. If shoulder dysfunction in ICU survivors is

associated with immobility and ICUAW, then its prevalence is also likely to increase.

2.2.2 Inflammation

As previously identified, immobility can lead to a pro-inflammatory state through increased pro-inflammatory cytokines (de Jonghe et al 2009, Brower 2009). This cytokine shift may potentiate the systemic inflammatory milieu commonly observed during critical illness leading to further damage and loss of muscle (Fan et al 2009). The interaction between bed rest and critical illness also appears to result in more significant muscle loss than bed rest alone (Fan et al 2009). The inevitable nature of muscle injury in critical illness through local and systemic inflammation acts synergistically with bed rest and immobility to produce alterations in metabolic and structural function of muscle, resulting in muscle atrophy and contractile dysfunction (Berney et al 2011, Batt et al 2013). Systemic inflammation as seen in immobility and critical illness is a key concept in the pathophysiology underpinning primary frozen shoulder.

The largest single group of patients with a painful, stiff shoulder are those with the absence of a traumatic event and no detectable underlying cause. This is the primary idiopathic frozen shoulder which is a severely debilitating condition with a prevalence of between two and five percent (Hand et al 2007, Robinson et al 2012). The aetiology remains unknown, although some aspects of the pathophysiology have been discussed (Chambler and Carr 2003). It has been suggested that frozen shoulder is a chronic fibrosing condition in which the cellular element consists of fibroblasts and myofibroblasts, leading to a

contracture of the rotator interval and the coracohumeral ligament, which restricts movement (Bunker et al 2000). Pain characteristically precedes stiffness, which suggests an evolution from inflammation to fibrosis (Robinson et al 2012). Histological changes present within the joint are consistent with chronic inflammation, perivascular infiltration and fibrosis of the subsynovial layer (Leow et al 2005). A proposed mechanism by Bunker (2000) highlights the role of cytokines and growth factors, leading to the accumulation and propagation of fibroblasts, which produce excess type III collagen. The cytokine response may also initiate angiogenesis within the capsule, producing the typical arthroscopic appearances of new blood vessels on the capsular surface.

The chronic inflammatory response with fibroblastic proliferation seen in frozen shoulder, may also be immunomodulated (Hand et al 2007). A similar situation is seen in ICU patients where the cumulative effect of critical illness and underlying comorbidities lead to impaired host defense (Hotchkiss and Opal 2010). A pro-inflammatory state is exaggerated in patients in ICU with sepsis, which is a complex process that encompasses pro-inflammatory and ant-inflammatory involvement resulting from dysregulation of the immune response to infection (Mossie 2013). Approximately 28% of patients admitted to ICU in the UK develop sepsis within the first 24 hours of admission (Harrison et al 2006). Due to exaggerated immune response to the invading pathogen, widespread inflammatory cytokines, as seen in frozen shoulder, are released (Mossie 2013). Sepsis is not only a recognised risk factor for the development of ICUAW (Stevens et al 2009, Bednarik at al 2005), it was also identified by

Battle et al (2013) as being independently associated with shoulder pain in ICU survivors.

2.2.3 Systemic Conditions and ICU Interventions

Shoulder dysfunction has been linked to multiple systemic conditions, many of which are present in patients admitted to ICU. There is a suggestion of a link between atherosclerotic coronary vascular disease and shoulder stiffness, with Bunker and Esler (1995) reporting raised serum lipid levels in a group of patients with primary frozen shoulder when compared to and age and sex matched control. Other conditions reported to have been associated with shoulder dysfunction include: degenerative disease of the cervical spine, thyroid disease, chronic obstructive pulmonary disease, HIV, psychological conditions and Parkinson's Disease (Wright and Haq, 1976, Summers et al 1989, Saha 1966, Riley et al 1989 and Robinson et al 2012). However, these are suggested associations only, and do not have a significant evidence base confirming the association.

Diabetes mellitus (DM) could be a potential factor that predisposes patients to shoulder dysfunction and potentially could develop the clinical presentation of frozen shoulder. Patients with DM have a 10-20% lifetime risk of developing a frozen shoulder, which is a 2-4 times greater risk than the general population (Anton 1993, Bridgman 1972). Moren-Hybbinette et al (1987) report a correlation with the duration of a patient receiving insulin therapy and the incidence of frozen shoulder. They also highlighted a correlation between a diagnosis of DM for greater than 10 years and frozen shoulder persisting for

greater than two years. However, this may also include age related changes as the authors do not comment on the age of the patients included in the study. Tighe and Oakley (2008) carried out tests for DM on 88 patients presenting with frozen shoulder, reporting a combined prevalence rate for diabetes and pre-diabetes as 71.5% (n = 63). Approximately half of these patients had been diagnosed with type 1 or 2 diabetes, and the remainder had pre-diabetes with an abnormal fasting blood glucose tolerance test. The suggested pathophysiology underpinning these studies is that in patients with diabetes, microvascular disease may cause abnormal collagen repair, which could then predispose to frozen shoulder (Robinson et al 2012). Tighe and Oakley (2008) report a very high prevalence of diabetes (38.6%), and with a relatively small sample, the effect of chance cannot be ruled out. However, unlike other studies reporting on diabetes in frozen shoulder, they do investigate pre-diabetes which may be relevant to patients on ICU. Acute illness or injury induces insulin resistance and hyperglycaemia, labelled stress hyperglycaemia or “diabetes of injury” (Van den Berghe 2004).

Patients admitted to ICU undergo multiple investigations and interventions, which can persist for extended periods of time. Despite the numerous acute complications of centrally and peripherally inserted venous catheters, there are no reported long term musculoskeletal complications (Kornbau et al 2015). However, frozen shoulder has been associated with prolonged intravenous infusion (Wadsworth 1986) and Mueller et al (2000) report increased shoulder pain associated with chest drain insertion in patients following cardiac surgery. There have also been reports of frozen shoulder following cardiothoracic

interventions including; cardiac catheterisation via the axilla, coronary artery bypass grafts and thoracotomy (Pineda et al 1990). Battle et al (2013) suggest that immobility as a result of central venous catheters (CVC), dialysis and ventilation may have contributed to shoulder pain in ICU survivors. Neuromuscular blocking agents (NMBA) and sedatives are commonly administered to critically ill patients to induce muscular paresis and allow tolerance of mechanical ventilation respectively (Puthucheary et al 2012). This can result in prolonged periods of immobility, which puts the shoulder at risk of becoming stiff (Haggart et al 1956, Johnson 1959). It is reasonable to suggest that any line, drain or sustained intervention in ICU patients that inhibit upper limb movement for a prolonged period of time are a possible risk factor for the development of shoulder dysfunction.

As previously discussed, shoulder subluxation in hemiplegic patients is exacerbated by the weight of the affected arm, which is also the case in patients with ICUAW. This is exaggerated further by upright positioning of patients in ICU, which is used to improve oxygenation and optimise diaphragm position (Hoste et al 2005). Patients are spending increasing periods of time in upright positions not only to improve respiratory function, but also during early rehabilitation and mobilisation (Schweickert et al 2009). There is a growing body of evidence for early rehabilitation and mobilisation of patients in ICU, which has been translated into everyday practice (Schweickert et al 2009, Morris et al 2008, Bailey et al 2007). The most common rehabilitative intervention employed by physiotherapists on ICU is upper and lower limb exercises, as demonstrated in a survey undertaken by Skinner et al (2008). In their survey of

physiotherapists working in ICU in Australia, they found that active assisted or free active exercises were the most common intervention, with ninety-seven percent of physiotherapists applying the treatment. The focus of these exercises in ICU, especially upper limb exercises, is usually function based and consist of wide ranging movements, with little emphasis on correction of the scapula and humerus, which is in direct contrast to management of the hemiplegic patient.

If the position of the scapula and humerus are not corrected before initiating shoulder elevation, the movement of the humeral head will pinch the capsule against the acromium as the arm moves into flexion or abduction causing pain (Gustafsson and Mckenna 2006).

This is an important concept to consider during upper limb exercise and rehabilitation as one of the suggested causes for HSP is thought to be vigorous ROM to the involved upper extremity. Lynch et al (2005) state that aggressive exercises within wide range of movement provoke much more intense pain than that experienced when doing exercises within a more limited ROM. Gustafsson and McKenna (2006) agree, suggesting that while active exercises are preferable to passive ones, exaggeratedly aggressive programmes may result in a higher incidence of HSP compared with more moderate exercise programmes. Kumar et al (1990) analysed the occurrence of HSP in patients treated with 3 different exercise programmes; therapy lead ROM, skate forward, overhead pulley. The therapy led group had their upper limb supported throughout by the therapist, which was similar to the skate forward group who also had their shoulder supported throughout. The patients in the overhead pulley group did not have their upper limbs supported and took the shoulder

through the greatest range of movement (ROM). The incidence of HSP was 8% in the therapy led group, 12% in the skate group and 82% in the pulley group. This demonstrates the importance of supporting the upper limb during ROM exercises, however the number of patients in the study was small (n= 28) and the applicability to current practice is limited as overhead pulleys are no longer used in upper limb rehabilitation following CVA. Repeated upper limb exercise with uncorrected GHJ position in ICU patients may result in microtrauma causing shoulder dysfunction as seen in the hemiplegic population. There is no discussion in the ICU rehabilitation literature regarding specifics of upper limb exercises, therefore these exercises may be causing, or at least contributing to, shoulder dysfunction. Early exercise in ICU shoulder therefore be reviewed as a potential risk factor for shoulder dysfunction in ICU survivors.

2.3 Impact of Shoulder Dysfunction on Long Term Function

Shoulder dysfunction in ICU survivors may impair the function of the upper limb and lead to disability. In a survey of 1,960 UK working age adults in the general population, Walker-Bone et al (2004) reported an incidence of shoulder dysfunction of 8.2% in men and 10.1% in women. It is common for symptoms of shoulder dysfunction to persist for months and even years, negatively impacting on quality of life and function (Hand et al 2008). Chakravarty and Webley (1990) randomly selected 100 patients over the age of 65 from three General Practices in Aylesbury, UK. Patients with rheumatoid arthritis, inflammatory arthropathies, polymyalgia rheumatic and symptomatic cervical spondylosis were excluded. History of illness, pain and functionality were assessed for each patient. Of the 100 patients, 34 were experiencing shoulder pain that impaired functionality.

The authors did not discuss the randomisation process which is a source of sampling bias (Grimes and Schulz 2002a), and did not use a validated outcome measure to assess pain and functionality decreasing the reliability of the results. Chard et al (1991) undertook a community survey of 644 patients over 70 years old attending GP practices. Patients underwent an interview and physical examination which included: documentation of muscle wasting, ROM, weakness, deformity or tenderness, presence of a painful arc and pain on resisted movements. In this random sample the prevalence of identifiable symptomatic shoulder disorders was 21%. However, the authors did not describe the process of assessing ROM which could be a source of observation bias (Sabari et al 1998). Despite the varying standard in methodology, the studies do identify shoulder dysfunction as a potential source of disability in the general population.

Patients with frozen shoulder experience loss of function in activities of daily living and difficulty sleeping on the affected side, with pain that wakes in the night often one of the primary complaints (Schaffer et al 1992). Impaired sleep is also a common symptom in ICU survivors, and can lead to cognitive impairment (Jackson et al 2009). ICU survivors are prone to depressive mood states following discharge from hospital, which is often accompanied with and/or exacerbated by sleep deprivation (Desai et al 2011). It is therefore important to identify any sources of sleep deprivation in ICU survivors, including shoulder pain.

Patients recovering from critical illness may show persisting organ dysfunction that could impair functional status with an associated reduced HRQOL. Several

reviews have investigated HRQOL in general ICU patients, sepsis patients, or patients with ARDS and reported that survivors have worse HRQOL, compared with matched general populations, at pre-admission and follow up (Oyen et al 2010). Cuthbertston et al (2010) investigated HRQOL in ICU survivors in the first 5 years after discharge from ICU, and compared this to the general population. They prospectively studied 300 patients admitted to a single ICU in the UK. They evaluated HRQOL at 3, 6 and 12 months and 2.5 and 5 years post discharge from ICU. They reported lower physical scores in HRQOL outcomes at all time points compared to the population norms. Cuthbertson et al evaluated HRQOL alone and made no physical examination or assessment of ICUAW, therefore they were unable to speculate as to the cause of the increased physical impairment in the 5 years post discharge from ICU.

Fan et al (2014) undertook a longitudinal prospective follow-up study of 222 survivors of acute lung injury (ALI) over 3, 6, 12 and 24 months. At each of the follow-up points they undertook clinical evaluations of extremity, hand grip strength, respiratory muscle strength, anthropometrics, 6 minute walk test (6MWT) and Short Form 36 HRQOL questionnaire. They found that the proportion of patients with ICUAW declined over time; 36% at hospital discharge, 22% at 3 months, 15% at 6 months, 14% at 1 year and 9% at 2 years. On multivariable regression analysis they found that duration of bed rest was the single risk factor consistently associated with prolonged ICUAW. They also reported that muscle weakness directly correlated with substantial impairments in physical function and HRQOL that persisted at 2 years post discharge. This demonstrates that objectively measured ICUAW has an

association with the substantial and persistent impairments in physical function and HRQOL. However, strength testing alone does not reliably evaluate other neuromuscular factors that may have an important impact on physical function such as pain or endurance. Therefore, evaluating functional outcomes longitudinally is important to review the long term effects of ICUAW. As with all observational studies, due to the lack of randomisation, causality of the associations reported cannot be assessed. The authors were also unable to obtain prospective baseline measurements of muscle strength and physical function, therefore the degree of weakness and reduction in physical function in relation to the individuals is unknown. Finally, the authors also did not account for any post-hospitalisation interventions that may have affected the recovery process.

Other long term follow-up studies of ICU survivors included more detailed assessments of physical function. Herridge et al (2011) prospectively studied ARDS survivors over a 5 year period. They undertook a prospective longitudinal evaluation of 109 survivors of the acute respiratory distress syndrome (ARDS). They undertook physical examinations, HRQOL questionnaire and 6MWT for patients at 3, 6 and 12 months, and at 2, 3, 4, and 5 years after discharge from the intensive care unit. They found that scores for physical role and functioning domains of HRQOL improved dramatically over 12 months which corresponded with an increase in 6MWT. However, scores remained below that of an age and sex matched population, and this deficit persisted over 5 years. At 12 months after discharge, Herridge et al report that 49% of survivors had returned to employment. Some of the reasons reported for not returning to employment

included; persistent fatigue and weakness, poor functional status due to immobility of large joints. The authors also reported frozen shoulders and finger contractures in 4% of survivors. However, they do not discuss how the shoulders were assessed, how frozen shoulder was diagnosed or what proportion of the 4% had frozen shoulder. This large multicentre study does demonstrate that the long term physical complications of critical illness negatively impact on HRQOL up to 5 years after discharge from ICU.

The wider socio-economic impact of impaired physical function in ICU survivors has also been investigated. Griffiths et al (2013) undertook a multi-centre questionnaire based study of ICU survivors at 6 and 12 months after ICU discharge. They investigated changes in family circumstances and social and economic stability, and what additional care needs were required in the context of HRQOL at each time point. They recruited 293 patients from 22 UK ICU's over an 18 month period. They reported a 50% reduction in the number patients reporting employment as their sole source of income at 12 months, with 25% requiring care at 6 months and 22% at 12 months. They also confirm the findings of other large HRQOL studies with lower HRQOL physical functioning scores at 6 and 12 months compared to population norms. However, they didn't identify any relationship between decreased HRQOL and socio-economic impact.

Increasingly, survivors of critical illness are being recognised as a population with profound residual disability. The magnitude of neuromuscular impairment in the increasing population of ICU survivors has come to the attention of healthcare providers, patients and families (Kress and Hall 2014). The negative

effects of ICUAW have been shown to impact on patients long after their survival from critical illness with recovery of functional ability taking time and may ultimately be incomplete. Substantial activity limitations are common and can persist for years after discharge from the ICU, and overall participation and HRQOL may be compromised with limitations persisting long after ICU discharge (Nordon-Craft et al 2012). The long term effect of a certain condition, such as shoulder dysfunction, on QOL is cohort specific and may be the residua of any severe critical illness. It will also depend on the follow up period – and will probably be a mixture of severity of illness, previous health status, pre-morbid QOL, age, gender and diagnostic category (Oeyen et al 2010). None of the longitudinal studies investigating long HRQOL in ICU survivors discuss or identify potential causes of the impaired physical function. However, the complex nature of the shoulder combined with the inflammation, immobility, muscle atrophy and weakness associated with critical illness, makes shoulder dysfunction a potential source of disability in ICU survivors. It is important to identify if shoulder dysfunction is a source of disability in ICU survivors to best direct treatment.

2.4 Aims of the Study

This review has established that despite a small number of studies of varying quality identifying shoulder dysfunction in ICU survivors, its prevalence is unknown. Hospital LOS and sepsis may be associated with shoulder dysfunction in ICU survivors, but there are multiple other potential risk factors that have not been investigated. Impaired physical function in ICU survivors that negatively impacts on their HRQOL is common, persisting for months and years

after discharge from hospital. There are no studies to date investigating the potential causes, or what constitutes this limitation in physical function despite an increasing ICU survival rate. Against this background the aims of this study are:

- To identify the prevalence of shoulder dysfunction in adult ICU survivors within 6 months of discharge from hospital.
- To identify the risk factors for the development of shoulder dysfunction in adult ICU survivors.
- To identify the impact of shoulder dysfunction on upper limb function in adult ICU survivors.

Chapter 3: Methodological Approach

The aims of the study were to identify the prevalence of shoulder dysfunction in ICU survivors, evaluate its impact on upper limb function and to identify any risk factors for its development. To understand the patterns of and cause and effect relationships surrounding shoulder dysfunction in ICU survivors, numerical data was required to be collected. Therefore, an objective approach that reduced the risk of bias was adopted, placing the research methodology of the study within a positivist framework (Crossan 2003).

The study design undertaken was that of an observational cohort study, using both prospective and retrospective data. A consecutive sampling method was used to recruit patients from a single ICU with an ICU length of stay (LOS) of greater than three days. Information regarding potential risk factors for the development of shoulder dysfunction was collected prior to the participants undergoing four separate shoulder assessments over the first six months following hospital discharge. The research design, methods, process and subsequent data analysis will be discussed in detail in the following chapter.

3.1 Design

In order to identify the prevalence of shoulder dysfunction and its impact on upper limb function in ICU survivors, an observational study design was adopted. The prevalence of a disease or disorder tells us what proportion of a population actually has the problem at a specific point in time and is reported simply as a proportion or percentage (Webb and Bain 2011). In this study this was the number of ICU survivors with shoulder dysfunction up to six months

after discharge from hospital. Once a problem, such as shoulder dysfunction has been identified, it is important to investigate the factors that are associated with the problem. Therefore, an analytic observational study was undertaken to observe and assess the strength of the relationship between multiple exposures on ICU and shoulder dysfunction (Song and Chung 2010). This took the form of a cohort study.

The modern epidemiological definition of cohort means a “Group of people with defined characteristics who are followed up to determine incidence of, or mortality from, some specific disease, all causes of death, or some other outcome” (Song and Chung 2010 p2235). Of all the observational designs, cohort studies have been highlighted as providing the most information concerning the causes of a disease or dysfunction and the most direct measurement of the risk of developing the problem (Webb and Bain 2011). A cohort study involves following individuals over time, comparing the experience of a group exposed to some factor with another group not exposed to that factor (Grimes and Schulz 2000). Information on exposures is collected prior to the development of a disease or dysfunction, with the participants being free of the outcome of interest at the start of the follow-up, making it easier to be sure that the exposure preceded the outcome (Webb and Bain 2011). In this study, the population from which the sample was obtained was ICU survivors, therefore admission to ICU was not the exposure under investigation. Multiple exposures present on ICU were investigated (Table 1) and participants with and without the exposures studied to identify any association with shoulder dysfunction.

Cohort studies measure disease occurrence and its association with an exposure by performing a temporal dimension i.e. a prospective or retrospective study design (Song and Chung 2010). Collecting exposure information before people develop disease allows for this temporal framework, resulting in the measurement of exposure not being biased by knowledge of the outcome status (Webb and Bain 2011). To evaluate shoulder dysfunction in ICU survivors, a mixed prospective and retrospective study design was used. Prospective studies are carried out from the present time into the future with specific data collection methods tailored to collect specific exposure data, and are deemed to be level two quality evidence (Chung et al 2009). However, cohort studies can require a large sample size, and using a prospective design to achieve this can be expensive due to the prolonged follow up and difficulty in maintaining follow up (Song and Chung 2010). Due to the limited resources, and therefore time, available to undertake this study, retrospective data was also collected. It is common place to establish a retrospective cohort to decrease to the long follow-up period associated with cohort studies, thereby decreasing the cost (Webb and Bain 2011). This is especially true when examining samples from smaller populations (ICU survivors) and rare exposures as those seen in ICU (Song and Chung 2010).

The main disadvantages of retrospective data collection are the susceptibility to recall bias and the limited control over the variables studied, which results in it being categorised as level 3 quality evidence (Chung et al 2009). A successful retrospective cohort study requires accurate records of exposure status for a group of individuals who can then be traced to determine their current status

(Webb and Bain 2011). These factors were mitigated for as the appropriate information was available retrospectively through established physiotherapy appointments for ICU survivors aimed at reviewing shoulder dysfunction. The exposures under investigation were also recorded as standard for all patients admitted to ICU.

3.1.1 Data Collection

The study consisted of two types of data collection. The first part of the data collection was an initial assessment of patient demographic and admission information, subsequent length of stay (LOS) information and daily collection of information relating to the patient's condition on ICU. The aim of this part of the data collection was to retrieve information that could be associated with patients developing shoulder dysfunction. The potential risk factors identified prior to the study for developing shoulder dysfunction are presented in Table 1.

Several of the risk factors that were assessed were identified by Clavet et al (2008) and Battle et al (2013) as potentially contributing to the presence of decreased shoulder ROM or pain. These included age, ICU LOS, hospital LOS and infection and were therefore included. Other risk factors that were assessed by Clavet et al (2008) and Battle et al (20013) but not identified as having a statistically significant association were also included. These were: comorbidities, admission diagnosis and severity, duration of mechanical ventilation and the use of neuromuscular blocking agents (NMBA).

Table 1 Potential Risk Factors for Developing Shoulder Dysfunction

Demographic Characteristics	Daily Data Collection
Age Gender APACHE II severity score Reason for admission Comorbidities ICU LOS Hospital LOS Limb Dominance Previous shoulder dysfunction Previous neck dysfunction	Invasive mechanical ventilation NMBA Infection CVC (including vascath) presence RRT Patient position MRC SS Rehabilitation ICD Tracheostomy Thoracotomy Hard collar

Note: APACHE= Acute Physiology and Chronic Health Evaluation, LOS= Length of stay, NMBA= Neuromuscluar blocking agents, CVC= Central venous catheter, RRT= Renal Replacement Therapy MRC SS= Medical research council sum score, ICD= intercostal drain

Severity of critical illness has been associated with critical illness polyneuromyopathy (CIPNM) (Hermans et al 2008) which may be a contributing factor to the development of shoulder dysfunction. Severity of critical illness was recorded using the Acute Physiology and Chronic Health Evaluation (APACHE) II severity score, which is a recognised method of scoring illness severity in intensive care (Giangiuliani et al 1989), and is in common use. However, the APACHE II severity score only assesses severity of critical illness on admission to ICU, and unlike the Sequential Organ Failure Assessment (SOFA), does not provide and ongoing assessment of severity of illness throughout the ICU stay (Haddadi et al 2015). The SOFA score was not routinely collected on the ICU therefore only the APACHE II severity score was used for the study. Formal diagnosis of CIPNM would require electrophysiology and muscle biopsy testing

which was beyond the scope of this study (Hermans et al 2008). However, the Medical Research Council Sum Score (MRC SS), is a commonly used method for diagnosing and recording ICU acquired weakness (ICU-AW) (Nordon-Craft et al 2012), and was used in addition to the level of mobility on discharge from ICU as an assessment of weakness. The time to instigate rehabilitation was assessed as a marker of duration of immobilisation. It was also used to identify those patients that received early upper limb exercises, which is associated with shoulder dysfunction in individuals with a hemiplegia (Lynch et al 2005).

There are several conditions associated with shoulder dysfunction (Robinson et al 2012) and therefore comorbidities and admission diagnosis were recorded. There has also been some documentation of an association between prolonged intravenous infusion, chest drains and frozen shoulder (Wadsworth 1986). Therefore, central venous catheter (CVC), vascath and chest drain position was recorded. The other risk factors identified in Table 1 were selected as they may result in the patient being left in a single position repeatedly or for prolonged periods, resulting in prolonged glenohumeral joint (GHJ) immobility and therefore shoulder dysfunction (Topp et al 2002). These included; duration of renal replacement therapy (RRT), the presence of a hard collar, patient position, position of the ventilator and the presence of a tracheostomy.

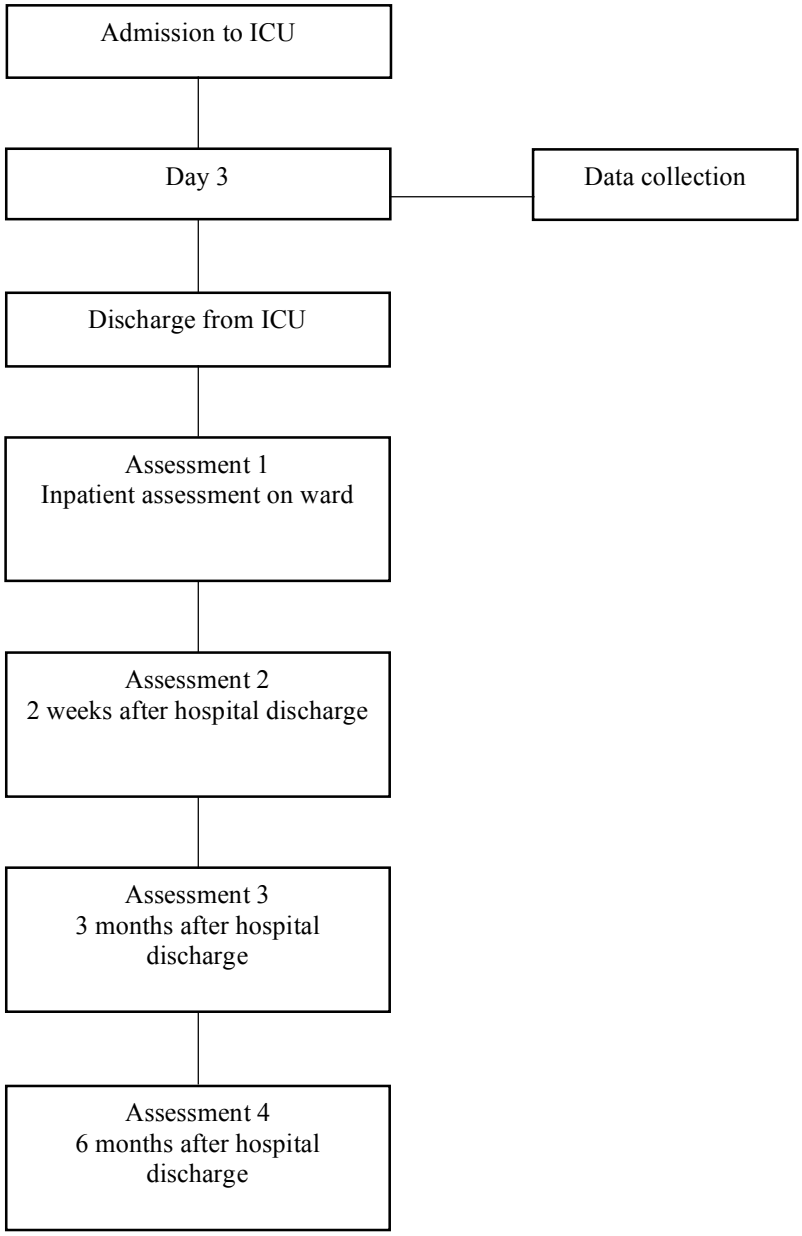
The second part of the data collection was undertaken during clinical assessments of the participant's shoulders. The prevalence, time of onset and course of shoulder dysfunction has yet to be established in studies to date, therefore assessments were undertaken at multiple time points. Assessing the participants at multiple time points also maintained a regular contact with

participants, which is a recognised strategy for reducing the loss to follow up rate (Song and Chung 2010).

A significant source of bias in cohort studies is attrition bias, therefore it is important to minimise the loss to follow-up rate (Webb and Bain 2011). This is particularly important in longitudinal cohort studies investigating ICU survivors, as loss to follow-up rates have been reported up to 70 percent (Jackson et al 2007, Griffiths et al 2013). The shoulder assessments were completed on four separate occasions, with the first assessment undertaken following discharge from ICU to a lower dependency ward. The subsequent assessments took place as outpatient assessments two weeks, three months and six months after discharge from hospital. The final assessment was limited to six months due to the increased cost associated with longer follow up periods.

As previously discussed, there is no single agreed definition of shoulder dysfunction. Therefore, factors that contribute to shoulder dysfunction were assessed. The initial assessment consisted of assessing; shoulder pain and shoulder range of movement (ROM). The subsequent outpatient assessments additionally included assessment of shoulder and upper limb function through patient reported outcome measures. The outcome measures used will be discussed in detail later in the chapter. In addition to the prospective data collection previously outlined, retrospective data was collected through follow up physiotherapy appointments for ICU survivors that were established in February 2013. A study flow diagram is illustrated in Figure 1.

Figure 1 Study Flow Diagram



3.2 Methods

The following chapter describes and discusses the methods that the study adopted. The population and sampling approach, inclusion and exclusion criteria and outcome measures used will be discussed. Shoulder dysfunction will be defined and the research process will be described in detail. Finally, the data analysis design and ethical considerations will be discussed.

3.2.1 Population and Sampling Approach

The population under investigation in this study were individuals admitted to ICU, who survived to discharge from the ICU. It was beyond the scope of the study to undertake a population study investigating all ICU survivors, therefore a representative sample was required for a cohort study. A disadvantage of a cohort study is its susceptibility to selection bias, which can occur when the exposed and unexposed groups are recruited separately (Song and Chung 2010, Webb and Bain 2011), which was not an issue with this study as all participants irrespective of exposure were recruited at the same time. Also, a key feature of a cohort study is defining the selected group of patients by exposure status at the start of the study with both the exposed and unexposed groups selected from the same source population (Webb and Bain 2011). The sample was taken from a single centre due to financial and time constraints, therefore the source population was a single ICU. This ICU is a large general ICU in a university teaching hospital, admitting patients with a variety of emergency medical, surgical and trauma conditions comparable to other general ICU's in the UK.

A sample is expected to mirror the population from which it comes, however there is no guarantee that any sample will be precisely representative of that population. Sampling error compromises the differences between the sample and the population that are due solely to the participants that happen to have been selected (Sedgwick 2013). One source of sampling error is through chance (type I error), where an abnormally large number of participants with natural variation within the population are selected to create that sample (Grimes and Schulz 2002). The risk of chance can be offset by using a random sampling technique, however true random sampling can be very difficult to achieve (Sedgwick 2013). A random sampling technique was not feasible for this study due to the relatively low numbers and difficulty in accessing patients on ICU. The time and cost taken to achieve a sufficient sample size from a single centre using a random sampling technique would have been prohibitive in addressing the research questions. Therefore, it was necessary to use a nonprobability sampling technique, which does not involve random selection. With nonprobability sampling there is a risk that the sample selected will not have the correct proportions because all members of the population do not have an equal chance of being selected (Lunsford and Lunsford 1995).

A consecutive sampling method was used to recruit participants to the study. Consecutive sampling seeks to include all accessible subjects as part of the sample, with every subject meeting the criteria of inclusion selected until the required sample size is achieved, or for the duration of the recruitment period (Lunsford and Lunsford 1995). All patients who were admitted to the single ICU where recruitment took place between February 2013 and September 2014

were included in the sample. The recruitment period was limited to 18 months due to the high costs associated with a prolonged recruitment period. Consecutive sampling is regarded as the best choice of non-probability sampling techniques for limiting sampling error since by studying everybody available, a good representation of the overall population is possible in a reasonable period of time (Lunsford and Lunsford 1995).

In addition to an association developing as a result of chance, a true relation can be missed by chance. It is possible that an exposure is linked to an outcome but a study can be too small to detect this reliably (type II error) (Webb and Bain 2011). To avoid type II error a study needs to have sufficient power to detect a true association with sufficient precision (Grimes and Schulz 2002). The power of a study is the probability that the study will detect an association of a particular size if it truly exists in the general population (Webb and Bain 2011). Peduzzi et al (1995) suggested that the number of patients needed to ensure sufficient power in a retrospective study is equivalent to ten events per variable (EPV) being investigated. There were 22 variables or risk factors investigated in this study (Table 1), however due to the low number of encounters of some risk factors, it was anticipated that a maximum of ten risk factors would undergo further analysis. Therefore, a minimum of 100 events (incidents of shoulder pain) were required. The four studies highlighting shoulder dysfunction in ICU survivors (Battle et al 2013, Clavet et al 2008, Herridge et al 2011, Gustafson 2012) identify incidences ranging from 5 to 80%. The study by Gustafson (2012) estimated an incidence of 80% and was the only study to evaluate and discuss shoulder dysfunction. The study was also

conducted in the same centre as this investigation, therefore an estimated incidence for shoulder dysfunction of 80% was used. This meant that a total sample size of 125 was required. This sample size was deemed achievable over an 18 month recruitment period, as approximately 200 patients with an ICU LOS of three days or more are admitted per year to the ICU where recruitment was taking place. A CONSORT diagram illustrating the flow of patients through the study is displayed in Figure 2.

3.2.2 Inclusion and Exclusion Criteria

The inclusion criteria (Table 2) for the study was deliberately broad due to the lack of previous studies or information regarding shoulder dysfunction in ICU survivors. An ICU LOS of greater than three days was chosen for two reasons. Firstly, it would exclude patients with a brief stay on ICU, whose development of shoulder dysfunction would unlikely be related to their stay on ICU. Secondly, patients with an ICU LOS of greater than three days are automatically invited to attend the ICU follow-up clinic, three months after discharge from hospital. This was a deliberate tactic to decrease loss to follow up rates by providing an additional set point of contact with the participants. A higher ICU LOS would also result in a lower recruitment rate, requiring a longer study period which was beyond the scope of this study.

The aims of this study were to identify the prevalence of shoulder dysfunction in ICU survivors, the impact on upper limb function and the risk factors for ICU related shoulder dysfunction. As previously discussed there are several conditions that are independently associated with shoulder dysfunction.

Therefore, patients whose admitting condition would independently predispose them to developing shoulder dysfunction, irrespective of their stay on ICU, were excluded (Table 2).

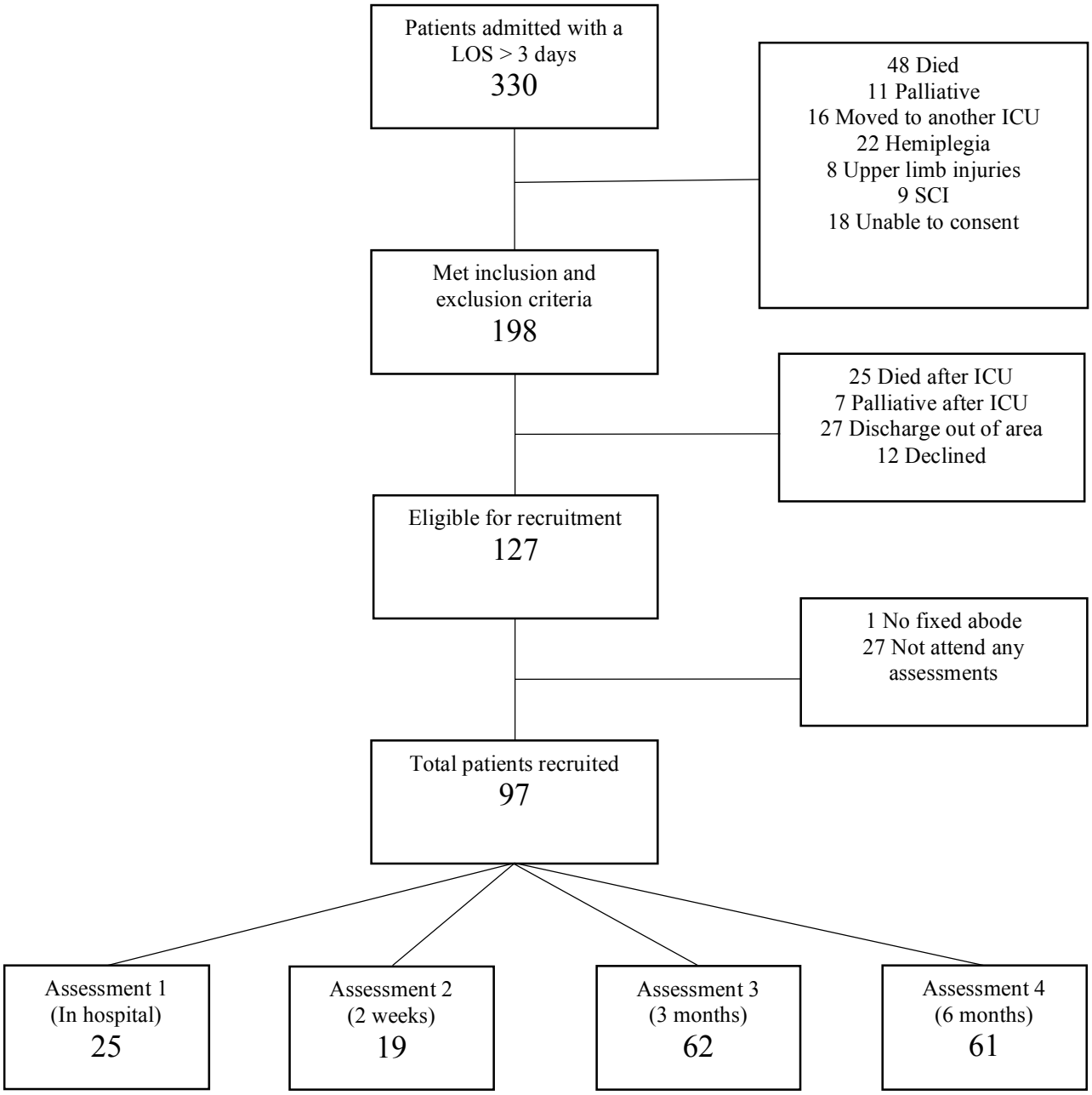
Table 2 Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
ICU LOS > 3 days Over 18 years old	Upper limb fracture Spinal cord injury Upper motor neuron injury or comorbidity resulting in hemiplegia Palliative diagnosis/treatment pathway

Note: LOS= Length of stay

These included patients who were admitted with an upper limb fracture or with new onset or history of hemiplegia (Lindgren et al 2006, Edwards et al 1992, Hessmann et al 1999). Patients with a new or long term spinal cord injury (SCI) were also excluded because of their well documented long term incidence of shoulder dysfunction (Subbarao et al 1995). Patients with known active shoulder dysfunction, present pre-admission to ICU, were included, however only their unaffected shoulder was assessed. Patients with a palliative diagnosis or treatment pathway were excluded due to the complex ethical issues surrounding their follow-up, which were beyond the scope of this study. Finally, patients who were discharged out of area from ICU and the subsequent wards were not included due to the cost implications of their follow-up as their long term care would take place at another hospital.

Figure 2 CONSORT Diagram



Note: LOS= Length of Stay, SCI= Spinal Cord Injury

3.2.3 Outcome Measures

The aims of the study were to identify the prevalence of shoulder dysfunction in ICU survivors, evaluate its impact on upper limb function and to identify any risk factors for its development. To achieve these aims, reliable and and accurate measures of shoulder dysfunction were needed, as information or observation bias results from incorrect determination of exposure or outcome or both (Grimes and Schulz 2002). There are numerous outcome measures that are used to assess shoulder dysfunction, and the components of shoulder dysfunction. Measures specifically evaluating shoulder dysfunction and upper limb function were used in conjunction with measures evaluating pain and ROM, as they are the two main components of shoulder dysfunction (Robinson et al 2012). The subsequent sections describe each outcome measure used and discusses the rationale for their selection.

3.2.3.1 Visual Analogue Scale

Pain may be defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Payne 1989). It is a key component of shoulder dysfunction as it can be generated from a number of different mechanisms including tissue ischaemia, muscle contraction and direct tissue damage from trauma (Ho et al 1996). Pain is a subjective and individual sensation, and health care providers should resist from judging patients based on preconceived notions of the severity (Galvin et al 2014), as there are not accurate physiological or clinical signs that can be used to objectively measure

pain (Ho et al 1996). Therefore, patient reported outcome measures are used to evaluate pain.

The level of pain has historically been measured with a standard categorical scale (none, mild, moderate, severe), however now the methodology most commonly used for the evaluation of pain severity and relief, and the one chosen for this study, is the visual Analogue scale (VAS) (Collins et al 1997, Kelly 2001, Ho et al 1996). The VAS pain score is often used in the belief that the measurement continuum produces greater sensitivity than the discrete points of the categorical scale (Collins et al 1997). Wallenstein et al (1980), have demonstrated a clear correlation between visual analogue scales and categorical scales.

The scale compromises of a 10cm line with descriptive phrases at either end. In most pain studies the range is from “no pain” to “severe pain” or “worst pain ever”. Patients estimate their level of pain by placing a mark on the line; the distance from the “no pain” point is then measured. No intermediate marks should be out on the line as this leads to clustering of responses (Ho et al 1996). A 10cm horizontal line is the most widely used version and the most widely validated, and was therefore chosen to evaluate shoulder pain (Jensen and McFarland 1999).

The VAS was the measure used to assess shoulder pain in the study. The version with a 10cm horizontal line was used as part of the shoulder assessment document (Appendix 1). During each assessment in the study participants were asked to mark on the horizontal line where they felt their level

of pain was. They were asked to rate their pain at rest and during each movement in the assessment. The distance from zero to the mark was measured and patients were then given a pain rating of none (0), mild (less than 3), moderate (3 to 6.9) or severe (7 or greater). The pain ratings of mild (less than 3), moderate (3 to 6.9) and severe (7 or greater) were used as they are the scores with the most agreement amongst previous studies (Kelly 2001, Collins et al 1997, Seymor et al 1996).

The popularity of the VAS stems from its simple construction and ease of use (Ho et al 1996, Kelly 2001, Todd 1994, Carlson 1983). The VAS has also been extensively reported as having a high level of reproducibility, sensitivity, validity and reliability in measuring both acute and chronic pain (McCormack et al 1988, Bijur et al 2001, Downie et al 1978, Scott and Huskisson 1979, Libman et al 2000 and Gaston-Johansson 1996). The VAS has been used to measure pain in a variety of practice settings, is sensitive to treatment effects and has a low failure rate when used in the adult population (Todd 1994, Bird and Dickenson 2001, Jensen and McFarland 1999). Studies suggest that many critically ill patients experience pain, with one study reporting moderate to severe pain in 50% of patients surveyed (Desbiens et al 1996). It has been suggested that ICU staff should use validated methods and assess pain scores frequently, with the VAS identified as an appropriate measure (Galvin et al 2014).

3.2.3.2 Goniometry

The universal goniometer was used to measure shoulder range of movement (ROM). It is the most commonly used instrument in clinical practice for

measuring ROM at large joints such as the shoulder, and has been widely used due to its portability and low cost (Gajdosik and Bohannon 1987, Riddle et al 1987, Kilber and Hanney 2012, Mullaney et al 2010). The shoulder has the greatest ROM of all the joints in the human body, and assessment of shoulder mobility is an integral component of physical examination (Kilber and Hanney 2012). Recognising impairments in joint mobility may assist clinicians in making diagnoses, measuring improvements or deteriorations in mobility, and determining functional limitations (Hayes et al 2001, Gajdosik and Bohannon 1987). Therefore, it is essential for clinicians to have reliable and valid measurement instruments to objectively monitor disease progression, outcomes and mobility impairments (Sabari et al 1998).

Active and passive shoulder ROM was assessed at each of the four assessments using a standard long arm plastic universal goniometer. A standardised testing procedure was used with details of the instructions given to the testers for the measurements using the goniometer available in Appendix 2. Shoulder flexion, abduction and external rotation (ER) were measured using a goniometer, with internal rotation (IR) measured to the vertebral level as demonstrated by Hayes et al (2001) and in the Constant-Murley Score (Appendix 4). All movements were measured with the participant in sitting with their feet on the floor as standard. The participants were encouraged to sit back in the chair to minimise trunk movement and achieve a standardised position. For flexion and abduction, the participant was asked to raise both arms together, with measurements taken one side at a time. The measurements for flexion were taken from the side of the body with the centre of the goniometer

positioned in the centre of the deltoid muscle bulk. For abduction the measurements were taken from behind with the centre of the goniometer positioned in the posterior body of deltoid. External rotation was measured with the participants elbow at their side with their hand pointed straight ahead and their elbow flexed to 90^{o}. The participant was asked to externally rotate the hand as far as possible with the elbow held against the trunk. The measurements were from in front of the participant with the centre of the goniometer on the olecranon process of the ulna. The stationary arm of the goniometer remained at a right angle to the patient while the moveable arm moved parallel to the longitudinal axis of the ulna pointing towards the styloid process. All movements were demonstrated by the tester prior to any verbal instruction.

Goniometry has been extensively investigated regarding its validity and reliability as a method of measuring ROM. The validity of a measurement constitutes the degree to which and instrument measures what it is purported to measure, which, in goniometry, is to measure ROM at a given joint (Kilber and Hanney 2012). The goniometer was designed as a modification of the protractor, therefore if accuracy, and consequently validity of goniometers are in question, the degree units can be compared simultaneously against known angles. The validity of representing movement of body parts by units of a circle can be challenged, however this limitation is accepted and the ROM measured closely approximates movement around a central point, that is, that the ROM measurements are clinically valid (Gajdosik and Bohannon 1987). The reliability of the standard universal goniometer as used in the study is well established,

and this method of measuring ROM is widely accepted (Mullaney et al 2010). Reliability in goniometry means the consistency or repeatability of the ROM measurements, that is, whether the application of the instrument and the procedures produces the same measurements under the same conditions (Gajdosik and Bohannon 1987). Several studies have shown high levels of intrarater reliability when using goniometry to measure ROM at joints in the upper limb (Helbrandt et al 1949, Greene and Wolf 1989, Riddle et al 1987, Sabari et al 1998).

When using goniometry to assess shoulder ROM, Riddle et al (1987) found high intrarater reliability and a variable interrater reliability, recommending using the same size goniometer for all assessments and that a large goniometer should be used for joints with long bones. Mullaney et al (2010) found that the intrarater reliability of the goniometer for assessing shoulder ROM was excellent, reporting intra-class correlations (ICC) between 0.91 and 0.99. Hayes et al (2001) evaluated the reliability of goniometry in measuring shoulder ROM in patients with shoulder dysfunction. They chose the four key movements of the shoulder: flexion, abduction, external rotation and internal rotation (hand behind back measured to the vertebral level). Participants were seated upright on the edge of a treatment table with feet supported on a foot stool and the position of the goniometer was standardised. They found that the hand behind the back measure was less reliable than goniometry for both inter and intrarater reliability, which may be a reflection of the complexity of the movement itself. However, the interrater reliability of goniometry to assess shoulder ROM was

good with an ICC of 0.69 for flexion and abduction, and 0.64 for external rotation.

Other studies have shown that intrarater reliability of goniometric assessments is consistently greater than interrater reliability (Riddle et al 1987, Sabari et al 1998). Riddle et al (1987) found that interrater reliability was high (not as high as intrarater reliability) for shoulder flexion and lateral rotation with ICCs of 0.89 and 0.88 respectively. They found poor interrater reliability for shoulder extension and abduction with ICCs of 0.27 and 0.3 respectively. Mullaney et al (2010) found that the interrater reliability was significantly worse than intrarater reliability, and suggested using a digital level was an alternative to the goniometer with similar intrarater reliability. However, they still reported an intertester ICC of 0.8 which demonstrates a high level of interrater reliability. Kilber and Hanney (2012) demonstrated that the goniometer possessed intrarater reliability and good concurrent validity with the digital inclinometer presenting ICCs of 0.85. However, there was a degree of variability between the instruments and therefore they should not be used interchangeably. Goniometry was chosen to measure shoulder ROM over the digital inclinometer because it was cheaper and more readily available

A limitation of goniometry is that it requires the clinician to use both hands, making stabilisation of the extremity more difficult, and increasing the risk of error in reading the instrument. (Kilber and Hanney 2012). When a tester is measuring active assisted ROM, it may be difficult to keep the reference arm of the goniometer stationary while rotating the joint. It also may be difficult to read the goniometer at the end ROM, and removing the goniometer from the joint to

read the value can result in an unintended movement of the goniometer (Mullaney et al 2010), therefore active assisted ROM was not measured during the study. In addition, measurements of active range of movement (AROM) tend to be more reliable than measurements of passive range of movement (PROM) (Gajdosik and Bohannon 1987). Passive movements may have additional sources of examiner related error as the amount of force applied by the therapist to move the arm can affect the final PROM. However, reliable measures of passive lateral ROM can be obtained when using the plastic universal goniometer (Macdermid et al 1999).

A standardised testing procedure was used when assessing shoulder ROM with a goniometer, as inaccuracies during their use is mainly from their faulty application which increases the potential for greater variations and subsequently decrease reliability Gajdosik and Bohannon 1987). Classic movements at the shoulder include flexion/extension, adduction/abduction and external/internal rotation. These movements are measured at the glenohumeral joint (GHJ), however each of them is dependent on synchronous mobility at the sternoclavicular, acromioclavicular and scapulothoracic joints. In addition, the positions of the thoracic spine and the pelvis influence total mobility of the shoulder (Sabari et al 1998). To negate these additional sources of movement, assessment of ROM was undertaken in a high backed chair with the participant sitting as far back in the chair as possible and their feet on the floor.

3.2.3.3 Constant-Murley Score

The Constant-Murley Score (CMS) was used in the study to assess shoulder function and is available in Appendix 4. Despite the lack of consensus regarding a definition of shoulder dysfunction, there are several outcome measures that aim to specifically evaluate shoulder function, of which the CMS is one of the most commonly used (Rocourt et al 2008). The CMS was undertaken at the three outpatient assessments and not at the inpatient assessment as it includes questions regarding the participants function at home. To ensure high intra and interrater reliability a standardised position was used for the strength measurement component (Appendix 5) using the original recommendations of Constant and Murley (1987).

The Constant-Murley Score (CMS) was introduced by the European Society of Shoulder and Elbow Surgery (ESSE) as a comprehensive and comparable assessment to determine functional outcome after treatment of shoulder injury (Constant and Murley 1987, Rocourt et al 2008). The score is widely used and accepted throughout the ESSE community as a gold standard for the assessment of shoulder function, with new assessments often validated by comparing them with the CMS (Rocourt et al 2008). The CMS is divided into four subscales including pain (15 points maximum), activities of daily living (20 points maximum), range of movement (40 points maximum), and strength (25 points maximum). The greater the score, the greater the quality of function (minimum 0, maximum 100) (Hirschmann et al 1999).

The CMS has demonstrated high intrarater reliability, excellent responsiveness for a variety of shoulder conditions and strong construct validity, with correlation established between the CMS and numerous other shoulder scales (Roy et al 2010, Hirschmann et al 1999, Rocourt et al 2008, Blonna et al 2012). However, the interrater reliability of the CMS has been questioned with Rocourt et al (2008) and Conboy et al (1996) suggesting decreased interrater reliability compared with intrarater reliability for individual components of the score. The lack of interrater reliability has been attributed to the strength measurement component, which represents one quarter of the CMS (Johansson and Adolfsson 2005).

The importance of the strength subscale has been debated, especially for the elderly, but in younger persons, strength has an important impact on work or recreation (Johansson and Adolfsson 2005). Different positions during strength measurement are likely to influence the results and therefore any comparison of the clinical data from different studies. There has been some argument over the appropriate measurement tool and position of the upper limb for the strength test position, with reports using the CMS often lacking details regarding how strength measurement was performed, which may have an important impact on the results obtained (Hirschmann et al 1999). In the initial CMS (Constant and Murley 1987), strength was measured with a digital dynamometer in a test position of 90^{o} abduction and 30^{o} horizontal flexion, with the elbow extended and forearm pronated. Patients who were not able to reach 90^{o} of abduction were assigned a strength score of zero. This test position has been reaffirmed by Constant et al (2008) with Hirschmann et al (1999) also establishing highest

intrarater reliability with the arm in 90^{o} abduction. Johansson and Adolfsson (2005) reviewed the measure used for strength assessment, and found that the standardised strength test in the CMS can be performed with either a digital or a mechanical dynamometer, demonstrating intra and interrater reliability. In their attempt to improve the reliability of the CMS, Blonna et al (2012) showed that standardisation of the items significantly improved both the intrarater and interrater reliability. The level of expertise of the tester also had less of an effect on reliability when the score is applied with a higher level of standardised statement.

3.2.3.4 QuickDASH

The final aim of the study was to evaluate to impact of shoulder dysfunction on upper limb function in ICU survivors. Evaluating function through patient reported outcome measures is an important part of both clinical and research environments, in order to assess patient perceived levels of disability and the impact of disease on daily activities (Mintken et al 2009). To achieve this, an outcome measure specifically tailored to evaluating upper limb function was required. The QuickDASH (QD) was the outcome measure chosen as it is a validated and reliable measure, commonly used throughout the UK. Participants were asked to complete the QD (Appendix 3) at each of the three outpatient appointments, and were given as much time as required to complete the questionnaire. Participants were not asked to complete the QD during the inpatient assessment as the QD asks questions related to the participants' functional ability at home.

The QD is a self-reported regional questionnaire designed to measure physical function and symptoms in patients with musculoskeletal disorders of the upper limb (Kolber et al 2014). The QD questionnaire is an example of an outcome measure focused on function that can be used across conditions affecting the entire upper limb (Polson et al 2010, Beaton et al 2005, Matheson et al 2006). The QD has been developed using a “concept-retention” approach from the original Disabilities of the Arm Shoulder and Hand (DASH), which is a measure used to assess symptoms and physical function in disorders of the upper limb (Gummsson et al 2006). The DASH was designed with a five point Likert scale ranging from one to five, with each of the five points on the scale anchored by an adjective of the level of severity or function. It consisted of 30 items, with high scores for the items corresponding to reduced function and increased severity (Matheson et al 2006). The QD consists of 11 items from the original 30 item DASH with each item allocated five response options (Gummesson et al 2006). Scoring of the instrument requires a three step calculation and ranges from 0 to 100 with zero indicating no perceived symptoms or disability. A score of 100 would imply a completed perceived absence of functional ability with severe symptoms (Kolber et al 2014). To calculate the QD score at least 10 of the 11 items must be completed.

The QD may be more appealing to use than the DASH because a shorter questionnaire is associated with less burden on the responder as well as less administrative burden (Gummesson et al 2006). The QD takes approximately two minutes to complete, takes less time for administration, scoring and interpretation when compared to the DASH (Matheson et al 2006). The QD

offers a more efficient means of identifying baseline function and monitoring outcomes (Kolber et al 2014). However, the QD should be responsive enough to identify changes in function when a true change has occurred (Mintken et al 2009). Both the DASH and QD possess desirable clinimetric properties including reliability, validity and responsiveness (Kolber et al 2014). The shorter version has been found to have excellent fidelity with respect to the original questionnaire (Matheson et al 2006). Macdermid et al (2015) reported that the QD had identical estimates of construct validity as the DASH. The QD has demonstrated good reliability, validity and responsiveness when used for patients with upper extremity disorders (Hunsaker et al 2002).

Reliability refers to the reproducibility of the results from an instrument on different occasions and whether consistent results can be obtained when different testers are involved (Mintken et al 2009, Kolber et al 2014). The QD has high levels of reliability and internal consistency, specifically when used for patients with shoulder disorders (Gummesson et al 2006, Kolber et al 2014). An instrument such as the QD should possess both construct and content validity for deeming clinical usefulness (Mintken et al 2009, Kolber et al 2014). The QD demonstrates good construct validity, with scores similar to those provided by the full DASH, and therefore is a good alternative (Gummersson et al 2006, Kolber et al 2014). Responsiveness refers to the accurate detection of change, with the QD demonstrating responsiveness with a range of upper limb pathologies (Polson et al 2010), specifically responsive to change in patients with shoulder pain (Gumesson et al 2006).

3.2.4 Definition of Shoulder Dysfunction

Due to the lack of consensus in the literature on a definition of shoulder dysfunction, for the purposes of the study a definition was created using the four outcome measures previously discussed (Table 3). The purpose of the study was to identify shoulder dysfunction, not to diagnose pathology, therefore no tests for specific shoulder pathology were included. A classification of shoulder dysfunction was allocated if any of the measurements seen in Table 3 were achieved

Table 3 Definition of Shoulder Dysfunction

Pain	Range of Movement	Upper Limb Dysfunction	Shoulder Function
Moderate/Severe Pain (VAS 3 to 10)	Flexion <150^{o} ER <45^{o} IR >T10	QD of 16 or greater	CMS < 80

Note: VAS= Visual analogue scale, ER= External rotation, IR= Internal rotation, QD= QuickDASH, CMS= Constant-Murley Score

Moderate pain was chosen to exclude those patients with minor shoulder discomfort, which was also the case with ROM. Loss of shoulder ROM could be defined as; flexion < 164^{o} (Donatelli 1997), ER < 50^{o} (Robinson et al 2012), IR >T8 (Constant and Murley 1987), and was used to describe a reduction in ROM. However, this does not take into account the age related changes in ROM discussed previously (Hussain et al 2016, Roy et al 2009). A review of shoulder ROM in patients with shoulder impairment by Hayes et al (2001) idnetified mean values as; Flexion 132^{o}, IR T10, ER 46^{o}. Therefore, greater

reductions in ROM were required for shoulder dysfunction to be classified in the study. Although measured, abduction was not included in the definition due to its lack of interrater reliability when measured using goniometry (Riddle et al 1987). A reduction in any individual movements would result in a classification of shoulder dysfunction due to the presence of reduced ROM in individual movements seen with some shoulder pathologies e.g. reduced ER in frozen shoulder (Robinson et al 2012).

The normal values for the QD have been proposed as a score of 15 or less (Angst et al 2011), however this figure has varied in other studies of QD in the general population. Hunsaker et al (2002) et al report a normal value of 8 or less, with Aasheim and Finsen (2014) reporting mean scores of 9 for males younger than 80 and 15 for females younger than 70. Several studies of QD values in patients with known shoulder pathology report mean scores varying between 34 and 50 (Gummesson et al 2006, Polsen et al 2010, Fayad et al 2009). Angst et al (2011) further categorise the QD scores. They report scores of 16 to 40 as having upper limb impairment but the ability to continue to work, and a score of greater than 40 resulting in the inability to work. Therefore, for the study shoulder dysfunction was classified with a QD of 16 or higher. For further analysis of the level of upper limb impairment, all patients with a QD of 40 or higher were classified as having severe upper limb impairment.

There is no clear agreement on the normal values for the CMS (Angst et al 2011) due to the wide variations in population norms. However, Katolik et al (2005) studied the general population in the USA with no shoulder symptoms. The lowest mean CMS they reported was in females over the age of 70, which

was 81. Yian et al (2005) found similar scores in their study of a large healthy population in Zurich. They also reported a mean lowest CMS of 81 for females over the age of 71. Therefore, shoulder dysfunction in the study was classified when a CMS of less than 80 was achieved.

3.2.5 Procedures and data collection methods

All the data collected in Table 1 was retrieved from an electronic database used in ICU called CareVue. The data collected was already being collected by the ICU physiotherapy team as part of their daily assessment of patients. The information was recorded on a separate form to allow for a further reduction in information bias (Sedgwick 2013). The initial assessment form is available in Appendix 6 and the daily assessment form in Appendix 7. Data collection began when a patient was admitted to ICU when an initial assessment sheet was completed (Appendix 6). Daily data collection (Appendix 7) was recorded for a 24 hour period from 10:00 am each day from the CareVue database until the patient was discharged from ICU. At day three of their ICU stay patients meeting the inclusion and exclusion criteria (Table 2) were given a participant identification number and recorded in the case report form (CRF). Where possible, consent was gained prior to the patients discharge from ICU (Appendix 9 and 10). Copies were made of the consent form with the patient keeping a copy, the original kept by the researcher and a copy put into the medical notes. The recruitment period for the study was between February 2013 and September 2014.

Following discharge from ICU to a lower dependency ward, patients underwent the first shoulder assessment by one of two ICU physiotherapists (Appendix 1). Shoulder ROM was measured in a standardised position using a standardised set of instructions (Appendix 2). The distribution of shoulder pain was recorded to assess for pain referral patterns. Cervical spine pain and ROM were assessed to rule out any cervical source of shoulder dysfunction. If consent was not gained in ICU then there was a further attempt to gain consent at this point. If consent was unable to be obtained at this time the patient was not assessed and consent was gained at the next assessment point following a telephone conversation with the patient.

Following discharge from hospital patients were contacted by letter to arrange an initial outpatient appointment at two weeks after discharge. This assessment was arranged to coincide with any other appointment the participant had at the hospital. The assessment at three months after discharge took place at the ICU follow-up clinic, and a further assessment was arranged via post for six months after discharge. All assessments took place in the physiotherapy department, however if the patient was unable to travel to the hospital then the patient was assessed at their home. At the three outpatient appointments, in addition to shoulder assessment undertaken at the inpatient appointment, the QD (Appendix 3) and CMS (Appendix 4) were undertaken. The CMS strength assessment was completed in a standardised position (Appendix 5).

All patients presenting with shoulder dysfunction at any of the outpatient assessments were given basic shoulder ROM exercises as appropriate and advised to attend their general practitioner. All patients presenting with shoulder

dysfunction at 6 months were given the option of being referred to an orthopaedic shoulder consultant or local musculoskeletal physiotherapy services. The referral to the orthopaedic consultant was made via one of the ICU consultants, which was the process agreed as part of ICU follow-up. All outcome measures and data collected prospectively was available retrospectively through the established physiotherapy outpatient appointments for ICU survivors. All outcome measures were undertaken using the same instructions by the same physiotherapists. The final six month assessment of participants was completed in March 2015.

3.3 Statistical Design

The first research aim was to identify the prevalence of shoulder dysfunction in ICU survivors. The prevalence identifies the proportion of a population with a disease or disorder at a specific time point (Webb and Bain 2011), and therefore will be analysed using descriptive statistics and presented as percentages and total numbers. All statistical analyses were performed using SPSS Version 22. The prevalence will be reported as an overall figure up to six months after discharge from hospital, and at each of the four assessment points. The prevalence of the individual components of shoulder dysfunction will also be reported at each of the four assessment points, along with the distribution of dysfunction.

The second research aim was to identify any risk factors for the development of shoulder dysfunction in ICU survivors. Initially, all continuous variables identified in Table 1 were assessed for normality. The Shapiro-Wilk Test was used, as it

is a well know test used for all sample sizes up to two thousand, with results greater than 0.05 considered normally distributed (Laerd Statistics 2015a). All risk factors identified in Table 1 were then analysed using descriptive statistics with categorical variables presented as numbers and percentages, and means and standard deviations (SD) or medians and interquartile ranges (IR) for continuous data depending on their distribution.

A univariate analysis was then undertaken using a variety of different statistical tests. Continuous variables that were normally distributed were regarded as parametric data and therefore analysed for differences between the groups of participants with and without shoulder dysfunction using the Independent-Samples t-Test, including Levene's test for equality of variances (Laerd Statistics 2015b, Myers et al 2010). Continuous variables that were not normally distributed along with ordinal variables were regarded as non-parametric data and analysed using the Mann-Whitney U Test (Lehmann 2006). The means and standard deviations will be presented for the results of the Independent-Samples t-Test (Altman and Bland 2005) and the differences medians will be presented for the Mann-Whitney U Tests (Hart 2001). Nominal variables were analysed for association with shoulder dysfunction using the Chi-Squared Test for association (Agresti 2013), except where cells had a count of less than five where Fisher's Exact Test was used (Laerd Statistics 2016). For all tests, results were deemed statistically significant at $p < .05$.

It is not possible to identify which variables are independently associated with shoulder dysfunction through univariate analysis alone due to the built in bias that cohort studies have as a result of confounding (Grimes and Schulz 2002).

A confounding variable is associated with the exposure, but is not a link in the process of causation between an exposure and outcome (Grimes and Schulz 2002). Confounding variables should be controlled for, with multivariate analyses being the most common methods used as they can control for more factors than stratification (Grimes and Schulz 2002). To ensure all known confounders were controlled for, all variables that reached a statistical significance of $p < .15$ in the univariate analysis were included for multivariate analysis (Sauerbrei et al 2006). As the dependant variable of shoulder dysfunction is dichotomous, and the independent variables are continuous or categorical, the multivariate analysis undertaken was a Binomial Logistic Regression (Laerd Statistics 2015c). Linearity of the continuous independent variables with respect to the logit of the dependant variable were assessed using the Box-Tidwell procedure with application of a Bonferroni correction (Campbell et al 2007). Outliers were tested for using case diagnostics (Laerd Statistics 2015c). Statistical significance for the identification of independent risk factors for the development of shoulder dysfunction was set al $p < .05$ (Webb and Bain 2011).

In addition to identifying associations between the variables and shoulder dysfunction, the strength of the association was also identified. As the prevalence of shoulder dysfunction is being investigated, the the strength of association is presented as unadjusted and adjusted odds ratios (OR) for the univariate and multivariate analyses respectively (Webb and Bain 2011). Accompanying the OR, a confidence interval of 95% (95% CI) was chosen (Grimes and Schulz 2002). Although there is no universal agreement, the

association is generally considered moderate when the OR is greater than 2.0 and strong when it is greater than 5.0 (Webb and Bain 2011).

The final aim of the study was to evaluate the impact of shoulder dysfunction on upper limb function in ICU survivors. This was assessed using the QD, with a score of 16 and greater indicative of functional impairment and 40 or greater severe functional impairment (Angst et al 2011). Descriptive statistics were used to analyse the QD scores and results presented as numbers and percentages for each of the three outpatient assessments

3.4 Ethical Considerations

The protocol for the study, informed consent form (Appendix 10) and participant information sheet (Appendix 9) were submitted to the Coventry University Ethics board and the Oxford University Hospitals NHS Trust Research and Development Department. Coventry University ethical approval was obtained in July 2014 (Reference P23945), and the Oxford University Hospitals NHS Trust Research and Development Department did not need to issue management approval (Appendix 8).

All patients were given a study information document (Appendix 10) informing them of the methods of data protection and anonymity, also informing them of their right to decline or withdraw from the study at any time with no consequences. The study staff ensured that the participants' anonymity was maintained throughout the study. The participants were identified only by a participant ID number on all study documents and the electronic database, with the exception of the CRF. The patients' name and allocated participant ID

number were held on a separate password protected CRF. All documents were stored securely and only accessible by study staff. All data collection sheets were kept in a locked filing cabinet in a locked physiotherapy office. All electronic data was anonymised and stored on an encrypted Excel Database, on a password protected computer in the physiotherapy department. All information will be retained for five years.

Chapter 4: Results

The main results reported in this chapter are the prevalence of shoulder dysfunction, the risk factors associated with shoulder dysfunction and the impact of shoulder dysfunction on upper limb function. Before these results are presented the baseline characteristics of the analysed sample are described including the distribution of the potential risk factors for shoulder dysfunction.

4.1 Participant Characteristics

A total of 97 participants that survived to discharge from ICU were recruited to the study and underwent at least one shoulder assessment. The number of participants excluded according to the criteria set out in Methods was 84, a further 32 died or entered a palliative care pathway after discharge from ICU, 28 were discharged out of area or to no fixed abode and 39 declined or failed to attend any appointments. At the first assessment after discharge from ICU 25 participants were assessed, 19 at the second assessment, 62 at the third assessment and 61 at the fourth and final assessment. The follow-up rate at 6 months was 48%

In total, 57% of the participants were male with a median age of 63 for both males and females combined. The majority of participants were right hand dominant (84%) and only 2% were ambidextrous. The reported history of both previous shoulder and neck dysfunction were low, with 13% and 9% respectively. The vast majority of participants were admitted to ICU as an emergency (96%) and only 7% were a readmission to ICU. The reason for admission to ICU was predominantly due to an acute medical complaint (56%)

or following surgery (32%), with a small proportion admitted as a result of trauma (12%). The APACHE II severity score was collected for 96 participants giving a mean score on admission of 19. The full details of the demographic characteristics of the participants are contained in Table 4.

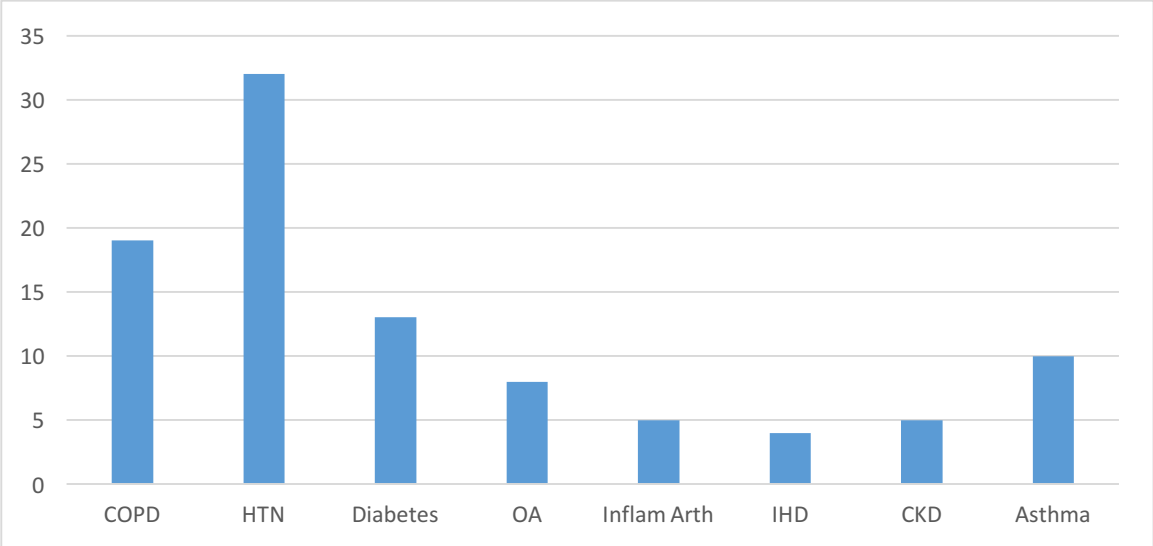
Table 4 Demographic Characteristics of the Participants

Variable	**No. (%) of patients* N= 97**
Age, median (IR)	63 (24)
Gender	
Male	55 (57)
Female	42 (43)
APACHE II severity score†, mean (SD)	19 (6.46)
Admission	
Emergency	93 (96)
Elective	4 (4)
Reason for Admission	
Surgical	31 (32)
Medical	54 (56)
Trauma	12 (12)
ICU LOS, median (IR)	9 (7)
Hospital LOS, median (IR)	25 (31.5)
Readmission to ICU	
Yes	7 (7)
No	90 (93)
Limb Dominance	
Right	84 (87)
Left	11 (11)
Ambidextrous	2 (2)
Previous Shoulder Dysfunction	
Yes	13 (13)
No	84 (87)
Previous Neck Dysfunction	
Yes	9 (9)
No	88 (91)

Note: IR= Interquartile range, SD= Standard deviation, APACHE= Acute Physiology and Chronic Health Evaluation, LOS= Length of Stay.
*Unless stated otherwise
†n= 96

The most common comorbidity present among participants was hypertension (HTN), which was evident in 32 of the 97. This was followed by chronic obstructive pulmonary disease (COPD) and diabetes with 19 and 13 respectively. Full details of the most common comorbidities present amongst participants are illustrated in Figure 3.

Figure 3 Frequency of Comorbidities Present in the Sample

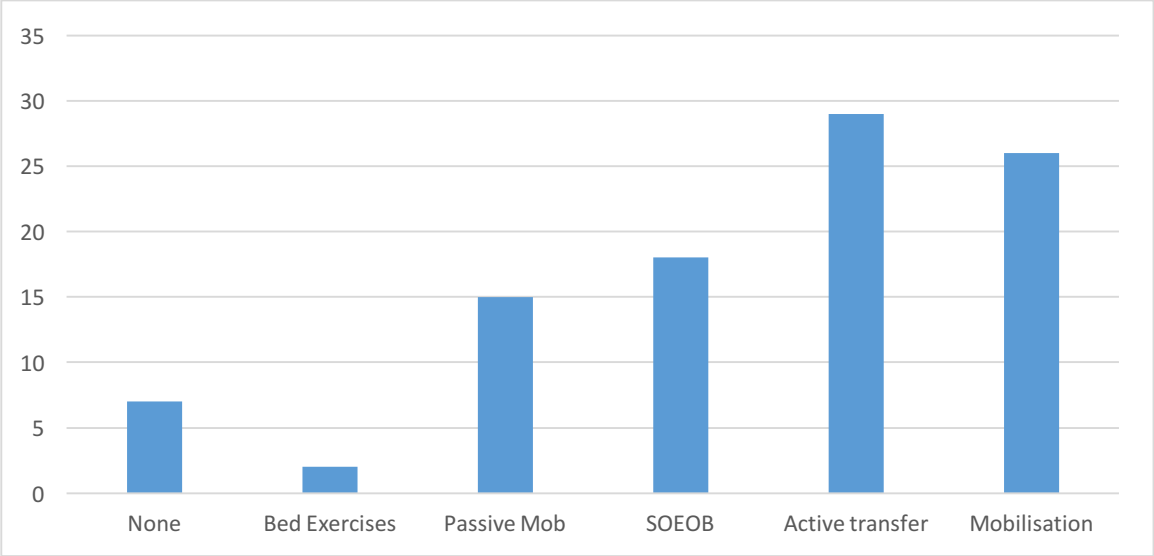


Note: COPD= Chronic Obstructive Pulmonary Disease, HTN= Hypertension, OA= Osteoarthritis, Inflam Arth= Inflammatory Arthritis, IHD= Ischaemic Heart Disease, CKD= Chronic Kidney Disease.

Details of the variables collected as potential risk factors for the development of shoulder dysfunction are outlined in Table 5. The majority of participants (74%) received invasive mechanical ventilation for a duration of 1 to 62 days, with the ventilator positioned on the left for only 3 participants. More than one third (36%) of participants received neuromuscular blocking agents (NMBA), however very few received an ongoing infusion of NMBA (10%) that varied in duration (1 to 44 hours). An infection was treated with or without microbiological

evidence in 94% of participants. All 14 participants who had a vascath inserted had an additional central venous catheter (CVC), however only 12 went on to receive renal replacement therapy (RRT). Of the 85 participants who received a CVC, 28% received more than 1. None of the participants were ever positioned in prone, however 6 participants were limited to supine for a period of time due to spinal precautions. Of the 97 participants, 69 underwent a formal assessment of weakness using the medical research council sum score (MRC SS), of which 52% (36) had a score of 48 or less and therefore a diagnosis of intensive care acquired weakness (ICUAW). The vast majority of participants underwent rehabilitation prior to discharge from ICU (90), with 61% (55) of those actively mobilising out of bed as illustrated in Figure 4.

Figure 4 Level of Mobility Achieved by ICU Discharge



Note: Mob= Mobilisation, SOEOB= Sat On Edge Of Bed

Table 5 Risk Factors Analysed for Developing Shoulder Dysfunction

Variable	**No. (%) of patients* N= 97**
Mechanical Ventilation	72 (74)
Days, median (IR)	3 (7)
NMBA	
Infusion	10 (10)
Bolus	31 (32)
Infection	
Present	40 (41)
Presumed	51 (53)
None	6 (6)
CVC	85 (88)
Vascath	14 (14)
RRT	12 (12)
Patient Position	
Usual	91 (94)
Other	6 (6)
MRC SS†, median (IR)	48 (27)
Rehabilitation Undertaken	90 (93)
Day Commenced, median (IR)	5 (6)
ICD	7 (7)
Tracheostomy	11 (11)
Thoracotomy	2 (2)
Hard Collar	3 (3)

Note: IR= Interquartile Range, NMBA= Neuromuscular Blocking Agents, CVC= Central Venous Catheter, RRT= Renal Replacement Therapy, MRC SS= Medical Research Council Sum Score, ICD= Intercostal Drain.
*Unless stated otherwise
†n= 69

4.2 The Prevalence of Shoulder Dysfunction

The overall prevalence of shoulder dysfunction amongst ICU survivors within six months of hospital discharge was 76%, and is presented in Table 6. Shoulder dysfunction persists to 6 months after hospital discharge with a prevalence of 42%. The prevalence as a proportion of each assessment point was also high

with 80%, 89%, 73% and 67% presenting with shoulder dysfunction at assessments 1 to 4 respectively.

Also presented in Table 6 is the prevalence of pain, loss of range of movement (ROM) and Constant-Murley scores (CMS) for shoulder dysfunction as set out in Methods. A total of 86 participants experienced pain, however only 47 (48%) experienced moderate or severe pain which was the criteria for shoulder dysfunction. The number of participants presenting with moderate or severe pain increased from 3 (12%) participants at inpatient assessment to 30 (49%) participants assessed 6 months after hospital discharge. The distribution of shoulder pain in the 97 participants assessed was even, 18 (19%) for both the right and left shoulder, and 11 (11%) experiencing bilateral shoulder pain. The proportion of participants with decreased shoulder ROM remained high throughout the assessments, with 64% (39) of patients assessed at 6 months post hospital discharge presenting with decreased ROM. The vast majority of the 75 patients with decreased ROM had a bilateral presentation (58). The total number of participants with an abnormal CMS was 62 (64%) and the proportion at each assessment was very similar with 68%, 66% and 61% at assessments 2 to 4 respectively. Table 7 presents the distribution of shoulder dysfunction, showing that the majority of the 74 participants with shoulder dysfunction had a bilateral presentation (84%). At 6 months after hospital discharge, the prevalence of bilateral shoulder dysfunction was 32% (31).

Table 6 Prevalence of Shoulder Dysfunction and its Separate Components

	No. (%) of patients N= 97			
	Pain	**Decreased ROM**	**CMS**	**Shoulder Dysfunction**
Assessment 1 Inpatient (n= 25)	3 (3)	19 (20)	Not assessed	19 (20)
Assessment 2 2 weeks (n= 19)	5 (5)	18 (19)	17 (18)	17 (18)
Assessment 3 3 months (n= 62)	14 (14)	48 (50)	41 (42)	45 (46)
Assessment 4 6 months (n= 61)	30 (31)	39 (40)	37 (38)	41 (42)
Total	47 (48)	75 (77)	62 (64)	74 (76)

Note: ROM= Range of Movement, CMS= Constant-Murley Score

Table 7 Distribution of Shoulder Dysfunction

	No. (%) of patients N= 74		
	Right	**Left**	**Bilateral**
Assessment 1 Inpatient (n= 19)	2 (11)	2 (11)	15 (79)
Assessment 2 2 weeks (n= 17)	2 (12)	2 (12)	13 (76)
Assessment 3 3 months (n= 45)	3 (7)	9 (20)	33 (73)
Assessment 4 6 months (n= 41)	1 (2)	9 (22)	31 (76)
Total	4 (5)	8 (11)	62 (84)

4.3 Risk Factors Associated with Shoulder Dysfunction

The results of the univariate analyses that reached statistical significance to warrant inclusion in the multivariate analysis ($p < .15$) are presented in Table 8. The number of participants with diabetes (13), receiving a tracheostomy (11) and NMBA infusion (10) were all low and not present in participants without shoulder dysfunction. Participants with shoulder dysfunction were older, weaker and more unwell on admission, as demonstrated by the median age (66), MRC SS (48) and APACHE II severity score (19.7) respectively.

A Fisher's Exact test was conducted between all categorical variables in Table 8 and shoulder dysfunction in ICU survivors within 6 months of hospital discharge. A Fisher's Exact test was undertaken as all variables has at least one cell frequency of less than five. There was a statistically significant association between the presence of infection, diabetes, HTN and shoulder dysfunction with $p = .027$, $p = .023$ and $p = .034$ respectively. The strength of the association between infection and shoulder dysfunction was strong (OR 7.6) and moderate between HTN and shoulder dysfunction (OR 4.3). The presence of a tracheostomy and NMBA infusions did not reach statistical significance. The OR for the association between tracheostomies, NMBA infusions, diabetes and shoulder dysfunction was calculated as infinity due to all variables having one cell frequency of zero.

An independent-samples t-test was run to determine if there were differences in illness severity as measured by the APACHE II severity score in participants with and without shoulder dysfunction. APACHE II scores for participants with

and without shoulder dysfunction were normally distributed, as assessed by Shapiro-Wilk's test ($p > .05$), indicating that the data was appropriate to be analysed using a parametric test. The APACHE II score was higher in participants with shoulder dysfunction (19.7 ± 6.6) than those without (16.83 ± 5.4). A difference of 2.87, $p = .062$ was sufficient to be included in the subsequent multivariate analysis, but did not reach the statistically significant threshold of $p < .05$.

Age and MRC SS were not normally distributed, as assessed by Shapiro-Wilk's test ($p < .05$), therefore a Mann-Whitney U test was run to determine if there were differences between participants with and without shoulder dysfunction. Median age was statistically significantly higher in participants with shoulder dysfunction (66) than in those without (57), $p = .008$. Median MRC SS was statistically significantly lower in participants with shoulder dysfunction (48) than in those without (52), $p = .042$.

There was no difference in the prevalence of shoulder dysfunction based on gender, reasons for admission, history of shoulder or neck dysfunction, ventilation, presence of CVC or vascath, receiving RRT or NMBA boluses, patient position or instigation of rehabilitation. All these variables were analysed using a Fisher's Exact test or chi-squared test for association, the results of which were not statistically significant. The presence of a thoracotomy, hard collar and ICD were only evident in participants with shoulder dysfunction. However, on a Fisher's Exact test there were no statistically significant association. A history of COPD, OA, CKD and asthma was more prevalent in participants with shoulder dysfunction, however there was no statistically

significant association on a Fisher's Exact test. The median ICU LOS was higher in participants with shoulder dysfunction, and both the time to instigate rehab and hospital LOS higher in participants without shoulder dysfunction. None reached statistical significance on a Mann-Whitney U test. The details of all risk factors assessed that did not reach statistical significance for association with shoulder dysfunction are available in Appendix 11.

Table 8 - Results of the Univariate Analysis

	Shoulder Dysfunction n= 74		**No Shoulder Dysfunction n= 23**			
Categorical variables	**n**	**%**	**n**	**%**	**p value**	**Unadjusted OR (95% CI)**
Infection	72	97	19	83	0.027†	7.6 (1.3-44.5)
Tracheostomy	11	15	0	0	0.062	∞
NMBA Infusion	10	14	0	0	0.111	∞
HTN	29	39	3	13	0.023†	4.3 (1.2-15.8)
Diabetes	13	18	0	0	0.034†	∞
Continuous and ordinal variables	**Median***	**IR***	**Median***	**IR***	**p value**	
Age	66	24.3	57	27	0.008†	
MRC SS	48	32	52	12	0.042†	
APACHE II severity score, mean and SD	19.7	6.6	16.8	5.4	0.062	

Note: NMBA= Neuromuscular Blocking Agents, HTN= Hypertension, MRC SS= Medical Research Council Sum Score, APACHE= Acute Physiology and Chronic Health Evaluation
*Unless stated otherwise
†significant at $p < .05$
∞infinity

A summary of the results of the multivariate analysis are presented in Table 9.

Table 9 Risk Factors for the Development of Shoulder Dysfunction in ICU Survivors: Results of the Multivariate Analysis

Risk factor	p value	Adjusted OR (95% CI)
Infection	.998	-
Tracheostomy	.999	-
NMBA Infusion	.999	-
HTN	.063	7.96 (.90 – 70.7)
Diabetes	.998	-
Age	.392	1.02 (.98 – 1.07)
MRC SS	.640	.99 (.93 – 1.04)
APACHE II severity score	.577	1.03 (.92 – 1.12)

Note: NMBA= Neuromuscular Blocking Agents, HTN= Hypertension, MRC SS= Medical Research Council Sum Score, APACHE= Acute Physiology and Chronic Health Evaluation

A binomial logistic regression was performed to ascertain the effects of infection, tracheostomy, NMBA infusion, HTN, diabetes, age, MRC SS and APACHE II severity score on the likelihood that participants develop shoulder dysfunction. For the logistic regression analysis to be valid, the linearity of the continuous variables with respect to the logit of the dependent variable was assessed via the Box-Tidwell procedure. As the logistic regression analyses multiple comparisons and therefore hypotheses being tested, the chance of a rare event is increased. To counteract this a Bonferroni correction was applied to the results of the Box-Tidwell procedure using all nine terms in the model. This correction resulted in statistical significance being accepted when $p <$ .00556. Based on this assessment, all continuous independent variables were found to be linearly related to the logit of the dependent variable. Outliers that could skew the results were tested for, resulting in one outlier identified by

studentised residual with a value of 3.771 standard deviations, which was kept in the analysis. The logistic regression model was statistically significant, $p < .0005$. The model explained 49.7% (Nagelkerke R^2) of the variance in shoulder dysfunction and correctly classified 75% of cases. Sensitivity was 87.8%, specificity was 42.1%, positive predictive value was 79.6% and negative predictive value was 57.1%. None of the predictor variables were statistically significant (as shown in Table 9), however a history of HTN had 7.96 higher odds of developing shoulder dysfunction. As with the univariate analysis, OR and 95% CI was unable to be reported for some of the variables due to low cell values.

4.4 Upper Limb Function

The impact of shoulder dysfunction on upper limb function in ICU survivors is presented in Table 10. There was evidence of upper limb dysfunction at all 3 outpatient assessments with 48% of participants assessed presenting with upper limb dysfunction. The proportion of participants presenting with upper limb dysfunction at each assessment point was similar with 42%, 48% and 46% at assessments 2 to 4 respectively. Of the participants assessed at 6 months after hospital discharge, 16% presented with severe upper limb dysfunction.

Table 10 Prevalence and Severity of Upper Limb Functional Impairment as Measured by the QuickDASH

	No. (%) of patients N= 97		
	Impaired	**Severely Impaired**	**Total Impaired**
Assessment 1 Inpatient (n= 25)	NA	NA	NA
Assessment 2 2 weeks (n= 19)	5 (5)	3 (3)	8 (8)
Assessment 3 3 months (n= 62)	21 (22)	9 (9)	30 (31)
Assessment 4 6 months (n= 61)	18 (19)	10 (10)	28 (29)
Total	30 (31)	17 (18)	47 (48)

Note: NA= Not Assessed

5: Discussion

5.1 Summary of findings

The overall prevalence of shoulder dysfunction in ICU survivors assessed was high at 76%, with 84% of those presenting with bilateral shoulder dysfunction. Shoulder dysfunction persisted to six months after hospital discharge in 42%, with a loss to follow-up rate of 44%. Moderate or severe shoulder pain was present in 48% of ICU survivors and limitations in shoulder range of movement (ROM) in 77%.

Multiple different variables were assessed for their association with shoulder dysfunction. Several variables were associated with shoulder dysfunction following univariate analysis including; increasing age (p = .008), infection (p = .027), weakness (p = .042), hypertension (p = .023) and diabetes (p = .034). Subsequent multivariate analysis demonstrated that none of the variables were independently associated with shoulder dysfunction.

Impairment of upper limb function as assessed by the QuickDASH was reported in 48% of ICU survivors, with 29% reporting persistent impairment at 6 months after hospital discharge. Upper limb function was severely impaired in 18% of ICU survivors.

5.2 Strengths and limitations of the study

Before comparing these findings to the results from other studies, the strengths and limitations of the study are discussed.

5.2.1 Selection of participants

Participants were selected from a single general ICU using a consecutive sampling method due to time and financial constraints, which can question the generalisability of the findings to the ICU survivor population across the UK. The characteristics of a sample obtained using a non-probability sampling method is at risk of not representing the population as all members of the population did not have an equal chance of being selected (Sedgwick 2013, Lunsford and Lunsford 1995). Assessing the generalisability is then especially difficult when the characteristics of the population are unknown (Sedgwick 2013), however, there are multiple longitudinal follow-up studies of ICU survivors describing the characteristics of their sample. The admission diagnoses of the participants in the study were similar to those in other studies identifying shoulder dysfunction in ICU survivors (Battle et al 2013, Clavet et al 2008, Herridge et al 2011). The characteristics of the participants in the study, including APACHE II score, age, ICU length of stay and gender were also similar to several other longitudinal follow-up studies of ICU survivors (Cuthbertson et al 2010, Griffiths et al 2013, Vesz et al 2013). Consecutive sampling is also regarded as the best choice for limiting sampling error and is regularly used in the longitudinal follow-up of ICU survivors (Lunsford and Lunsford 1995).

Who is selected into the cohort can influence the generalisability of its findings since they may apply only to the sorts of people who agreed to take part (Webb and Bain 2011). The study sought to identify shoulder dysfunction related to an ICU admission, and therefore the exclusion criteria documented in the Methods deliberately set out to exclude ICU survivors with conditions that are already

known to predispose them to shoulder dysfunction. This may have resulted in under reporting of shoulder dysfunction. Conversely, the participants attending the shoulder assessments may have been those presenting with shoulder dysfunction, and that those not attending were not experiencing shoulder dysfunction. This volunteer bias may have resulted in over reporting of the prevalence shoulder shoulder dysfunction (Junghans and Jones 2007). However, the high incidence of critical illness on the mental health of ICU survivors is increasingly evident, with presentations of depression, anxiety and post-traumatic stress disorder (Jackson et al 2009). This can result in participants not attending healthcare appointments, and therefore could have resulted in participants with shoulder dysfunction not attending assessments.

These apparent weaknesses do not, however, invalidate comparisons with the ICU survivor population as a whole, as participants of the study are unlikely to be fundamentally different to ICU survivors in general. Some caution is required, as the prevalence of shoulder dysfunction in ICU survivors not assessed is unknown.

5.2.2 Sample size and confounding

The sample size calculation set out in the Methods indicated that based on an expected prevalence of shoulder dysfunction of 80%, a sample size of 125 was required to analyse 10 variables for association (Peduzzi et al 1995). The total number of patients recruited to the study was 97, with a prevalence of shoulder dysfunction of 76% (n = 74). Following univariate analysis, 8 variables were chosen for subsequent multivariate analysis. The number of participants with

shoulder dysfunction was therefore 6 below the recommended 10 events per variable for multivariate analysis.

The overall sample size of 97 is larger than the 20 participants in the study by Gustafson (2012) which is the only other study specifically investigating shoulder dysfunction in ICU survivors. It is also comparable to the longitudinal follow up study of ICU survivors by Herridge et al (2011) that identifies shoulder dysfunction, however the sample size is smaller than the studies by Battle et al (2013) and Clavet et al (2008). These studies did have different methodology in that Battle et al used a questionnaire method and Clavet et al undertook a retrospective review of medical notes.

Although the overall sample size is comparable to other single centre follow-up studies of ICU survivors, the number of participants presenting with several of the variables analysed for association was low. Ten of the variables that underwent univariate analysis for association with shoulder dysfunction presented in 15 participants or less. Several of these variables were not present in participants without shoulder dysfunction therefore resulting in an odds ratio (OR) of infinity. This is misleading, as it implies that shoulder dysfunction is certain to happen in participants with these variables. This is not the case, as odds ratios do not approximate well to the relative risk when the prevalence of the outcome of interest is high, as it is in this study (Davies et al 1998). Of those 10 variables, 4 reached sufficient statistical significance to be included in the multivariate analysis.

A multivariate analysis was undertaken to address for confounding in identifying associations with shoulder dysfunction (Webb and Bain 2011). Following univariate analysis 8 variables were analysed, 4 of which were not present in participants without shoulder dysfunction and presented in 15 patients or less. A logistic regression analysis was undertaken, which was valid as all continuous independent variables were linearly related to the dependent variable which was assessed using the Box-Tidwell procedure with a Bonferroni correction applied to account for the effect of the multiple comparisons (Laerd Statistics 2015). There was only one outlier evident in the results which was kept in the analysis. The logistic regression model was statistically significant, indicating that when compared to no independent variables, the logistic regression model was good at predicting shoulder dysfunction and correctly classified 75% of cases. The model showed high levels of sensitivity, correctly predicting 88% of cases with shoulder dysfunction, but low levels of specificity only correctly predicting 42% of cases without shoulder dysfunction. Despite the logistic regression model demonstrating good fit and sensitivity, the lack of specificity and statistical significance in independent variables can be attributed to both low variable occurrence and a high prevalence of shoulder dysfunction.

5.2.3 Loss to follow-up

One of the major problems with a follow-up study of ICU survivors is the loss to follow-up rate. If a high number of participants are lost to follow-up in a study, it is impossible to know if they experienced the health outcome under investigation, and subsequently the results of the study may be exposed to attrition bias, decreasing the internal validity of the study (Webb and Bain 2011).

The rate of loss to follow-up has been recommended not to exceed 20% (Song and Chung 2010). However, in longitudinal cohort studies investigating ICU survivors the loss to follow-up rate often far exceeds this recommendation, often reported between 10 and 70% (Jackson et al 2007).

There is great heterogeneity in the methods of calculating loss to follow-up amongst the follow-up studies of ICU survivors. The method suggested by Dettori (2011) was applied to this study and resulted in a loss to follow-up rate at 6 months after hospital discharge of 52%. This initially appears high, however this is similar to the 6 month rates of 53% and 46% in the studies by Griffiths et al (2013) and Eddleston et al (2000) when the same methods for calculation are applied. To add further context, Griffiths et al and Eddleston et al, like the majority of ICU follow-up studies used questionnaires in their studies that did not involve the participants attending an appointment.

The follow up rates for this study were lowest at 2 weeks after hospital discharge, with a rate of only 15%. This has also been demonstrated in other ICU follow up studies. In their study of HRQOL in ICU survivors, Graf et al (2003) reported a loss to follow-up rate of 44% at 1 month and then 16% at 9months after ICU discharge. This change in follow-up rate may reflect the relief that patients feel at being discharged after a period of critical illness, and associated reticence in engaging with any further healthcare until they deem it necessary.

The follow up rate at the initial in hospital assessment was also low (19%). Gaining access to participants to undertake the shoulder assessment at this

point was hampered by patient availability, as patients were commonly undergoing other procedures or were away from their bed space. Also, due to the regional nature of the hospital, patients were often quickly discharged home or to another care facility, limiting the period of time available for assessment and recruitment.

5.2.4 Assessment and definition of shoulder dysfunction

One of the strengths of the study is that unlike other studies identifying shoulder dysfunction in ICU survivors, shoulder dysfunction was assessed using several validated outcome measures. Shoulder ROM was assessed using goniometry which has good intrarater but variable interrater reliability (Sabari et al 1998). To improve interrater reliability, ROM was measured using the same goniometer in a standardised position with a standardised set of instructions (Appendix 2). Pain was assessed using the standard visual analogue scale (VAS) and upper limb dysfunction via the QuickDash. The Constant-Murley score (CMS) was used as a specific measure of shoulder dysfunction, and was the most controversial outcome measure used. The intrarater reliability of the measure has been questioned by several authors, and has been attributed to the inconsistent methods of undertaking the strength measurement component (Rocourt et al 2008, Johansson and Adolfsson 2005). To address this, the strength measurement procedure was performed as per the original instructions by Constant and Murley (1987), using a standardised set of instructions and position (Appendix 5).

The study used a mixed data collection method of both prospective and retrospective design, which puts it at risk of information and recall bias (Grimes and Schulz 2002). This was minimized due to the same outcome measures being used to the same set of instructions in the follow-up appointments where the retrospective data was retrieved. The data collected from the ICU is recorded prospectively by a variety of healthcare staff as part of usual practice, therefore also minimising the recall bias.

The definition of shoulder dysfunction that was based on a measurable criteria was also a strength of the study. Shoulder dysfunction was recorded based the results of the outcomes discussed above, ensuring that unlike other studies, patients presenting with only one symptom of shoulder dysfunction were included. The level of pain, severity of loss of ROM and scores on the CMS and QuickDASH were set so that minor shoulder dysfunction would not be included in the study, and only clinically relevant shoulder dysfunction was reported.

In summary, the main strengths of the study include: the standardised method of assessing shoulder dysfunction using validated outcome measures, which provided accurate and reliable identification of shoulder dysfunction; and the comprehensive definition of shoulder dysfunction, which allowed for clear diagnosis of clinically relevant shoulder dysfunction. The main limitations include: the low frequency of several variables under analysis, which resulted in the lack of reliability in identifying factors associated with shoulder dysfunction; and the high loss to follow-up relate, although common in ICU follow-up studies, may have resulted in under or over reporting of shoulder dysfunction.

5.3 Consistency with published literature

5.3.1 Prevalence

The prevalence of shoulder dysfunction in ICU survivors described in this thesis is higher than is reported in the majority of the studies identified in the Literature Review. The exception is the study by Gustafson (2012), which is the only other study specifically investigating shoulder dysfunction in ICU survivors. Gustafson (2012) reported shoulder pain or loss of ROM, that was not present prior to ICU admission, in 80% of participants assessed. Despite the overall prevalence of shoulder dysfunction being similar, the definitions of pain and decreased ROM may differ. Gustafson (2012) did not describe either the methods for assessing pain and ROM or how decreased ROM was classified, therefore mild pain and a slight loss of shoulder ROM would have been included in their definition of shoulder dysfunction. If the strict classification of shoulder dysfunction set out in the Methods were applied to the participants in the study by Gustafson (2012), the prevalence of shoulder dysfunction may have been less.

Herridge et al (2011) reported the presence of frozen shoulder in 3% of the 64 ICU survivors assessed in their study. This is substantially lower than the prevalence described in this thesis, however the follow-up by Herridge et al (2011) was conducted at 5 years after discharge from ICU. This may have been sufficient time for any shoulder dysfunction exhibited in the first 6 months after discharge, as assessed in this thesis, or in the subsequent year to resolve. Herridge et al (2011) also did not explain how frozen shoulder was assessed or defined, or who conducted the assessments. It is reasonable to infer that the

patients identified with frozen shoulder had a loss of shoulder ROM, however it is unclear if other participants exhibited shoulder pain or loss of ROM that was deemed not to be significant by the assessors. Therefore, the incidence of shoulder dysfunction may have been higher than the reported 3% both at 5 years after ICU discharge and 6 months after hospital discharge.

Battle et al (2013) reported shoulder pain at least 6 months after ICU discharge in 22% of 196 ICU survivors undertaking their questionnaire assessing chronic pain. This is lower than the 31% of participants presenting with shoulder pain at 6 months after hospital discharge in this thesis. Battle et al (2013) did not identify the severity of shoulder pain in their questionnaire, and therefore could possibly have included responses indicating any level of pain. For this thesis only moderate or severe pain as described in the Methods were recorded, therefore if this was applied to the participants in the study by Battle et al (2013) then the prevalence of shoulder pain may have been lower. Battle et al (2013) also included participants with a history of spinal cord injury (SCI), which is a patient population known to have a high incidence of shoulder pain and dysfunction (Subbarao et al 1995). Although it is not clear from the study how many patients with SCI were included, this could have increased their rate of shoulder pain compared to this thesis. The participant characteristics were also different in the study by Battle et al (2013) when compared to this thesis. Participants in the the study by Battle et al (2013) were less unwell on admission to ICU with a mean APACHE II score of 15, and subsequently had a lower ICU length of stay (mean of 6.2 days) and hospital length of stay (mean of 17.8 days). This is compared to this thesis where the mean APACHE II score

was 19 and subsequent median ICU and hospital length of stays were 9 and 25 days respectively. This difference in severity of illness and subsequent length of stay could be a contributing factor to the differing prevalence of shoulder dysfunction.

Clavet et al (2008) identified contractures in 24 (11%) shoulder joints of 155 patients on discharge from ICU. This is similar to the 19 (20%) participants presenting with decreased shoulder ROM on assessment immediately after ICU discharge in this thesis. It is unclear if the 24 shoulder joints were in different participants in the study by Clavet et al (2008) increasing the prevalence to 15%, or if some of the participants presented with bilateral shoulder contractures. Clavet et al (2008) recorded a shoulder contracture as being present when flexion or abduction was less than 179^{o}. If the classification of decreased ROM as set out in the Methods was applied it is likely that less participants in their study would have been recorded as having a shoulder contracture.

5.3.2 Risk factors

Unlike some of the previous studies identifying shoulder dysfunction in ICU survivors, this thesis was unable to identify any risk factors that were independently associated with shoulder dysfunction. Battle et al (2013) identified sepsis and hospital length of stay as independently associated with shoulder pain in ICU survivors after undertaking a logistic regression analysis. They included factors that were statistically significant at $p < .15$ on univariate analysis which were ICU and hospital length of stay, sepsis, age and a surgical

reason for admission to ICU. They did not explain in any detail the results of the univariate analysis. Clavet et al (2008) identified ICU LOS as independently associated with any joint contracture on discharge from ICU after undertaking a logistic regression analysis. However, they included all the variables that were deemed relevant by the investigators, which included; age, diabetes, APACHE II score, admission diagnosis, ICU length of stay, duration of mechanical ventilation, use of neuromuscular blocking agents (NMBA) and steroids. They also did not explain the results of any univariate analysis undertaken. None of the other studies reporting shoulder dysfunction in ICU survivors undertook an analysis of risk factors.

Several variables analysed in this thesis were associated with shoulder dysfunction on univariate analysis. Age and infection reached a statistically significant association, which were also identified as independently associated with chronic pain and shoulder pain respectively by Battle et al (2013). Diabetes also reached statistical significance, but was not independently associated with joint contractures as measured by Clavet et al (2008). Weakness and a history of HTN both reached statistical significance in the thesis, but were not investigated by either Clavet et al (2008) or Battle et al (2013) as a potential risk factor for pain or joint contracture.

5.3.3 Upper limb function

Upper limb functional impairment was present in nearly half of ICU survivors assessed in this thesis. None of the studies discussed in the Literature Review that identify shoulder dysfunction in ICU survivors either assessed or discussed

the impact on upper limb function. Clavet et al (2008) did differentiate the shoulder contractures that they deemed functionally significant, which was present in 9% of participants assessed at ICU discharge. They deemed a functionally significant contracture as being present when shoulder flexion or abduction was less than 96^{o}. In healthy individuals, the minimum shoulder flexion or abduction required to complete everyday functional tasks is 120^{o} (Khadikar et al 2014), and is likely to be greater in individuals recently discharged from ICU. If this ROM was applied to the study by Clavet et al (2008) then the prevalence of functionally significant contractures is likely to increase.

Physical function in general terms in ICU survivors has been investigated and compared to the general population. Cuthbertson et al (2010) assessed the physical function of ICU survivors at multiple time points, including 6 months after discharge. Their ICU survivors had similar characteristics to this thesis and presented with significantly lower physical function scores at 6 months when compared to the general population. Similarly to other studies investigating health related quality of life (HRQOL) in ICU survivors highlighted in the Literature Review, Cuthbertson et al (2010) do not discuss the reasons or causes of the impairment in physical function. Given the impairment in upper limb function at 6 months after hospital discharge evident in this thesis, it is reasonable to suggest that some of the impairment may be due to shoulder dysfunction.

5.4 Causality

It is evident from this study, and the small number of previous studies, that shoulder dysfunction is a potential complication of critical illness, and a source of functional impairment in ICU survivors. It is not clear, however, which factors are associated with shoulder dysfunction and the cause of shoulder dysfunction is unclear. Data from observational studies cannot be used as the sole evidence to advocate or deny causal link, but are useful in generating hypotheses, by pointing out associations between exposure and diseases (Fang and Shan 2002). There are several variables analysed in this study that warrant discussing further in relation to their contribution to the development of shoulder dysfunction.

5.4.1 Immobility and weakness

There is an agreement in the literature that immobility of the shoulder joint will result in loss of ROM through atrophy of the musculature, capsular tightening and fibrosis of the ligaments (Robinson et al 2012, van de Laar and van der Zwaal 2014). There were a number of variables analysed in the study that were markers of glenohumeral joint (GHJ) immobility and indicated that the GHJ was immobile in the participants who developed shoulder dysfunction. The presence of a chest drain or thoracotomy has previously been suggested as being associated with decreased shoulder ROM and pain (Muller et al 2000, Pineda et al 1990), and were only present in participants who went on to develop shoulder dysfunction in the study. The presence of a hard collar and tracheostomy were

also only present in participants who developed shoulder dysfunction, which could also be markers of GHJ immobility.

The impact of GHJ immobility is more pronounced in the elderly population as a result of age specific increases in collagen stiffness, damage to the articulating surfaces and limited use of the full ROM of the joint (Bassey et al 1989, Roy et al 2009). This was evident in the study where the median age of participants with shoulder dysfunction was 66 and the median age of participants without shoulder dysfunction was 57. Increased age on ICU has also been previously associated with a higher rate of muscle mass loss (Kortbein et al 2007), and as such, the participants presenting with shoulder dysfunction may have had greater muscle mass loss.

Immobility is associated with muscle mass loss, not only in elderly patients but in all patients on ICU, with the rate of muscle mass loss also related to the severity of illness (Lightfoot et al 2009, Puthucheary et al 2013). The enhanced proteolysis and decreased protein synthesis initiated by immobility is then exacerbated by the inflammation associated with critical illness, and has been correlated with a reduction in strength (Fan et al 2009, Bamman et al 1998). In addition to immobility and inflammation, intensive care unit acquired weakness (ICUAW) can be caused by critical illness neuromuscular abnormalities (CINMA) which are present in up to 50% of the most severely critically ill patients (Hermans et al 2008) and can result in prolonged disability (Latronico and Bolton 2011). The presence of ICUAW is diagnosed with a score of 48 on the MRC SS (Nordon-Craft et al 2012). There was a significant difference in MRC SS between participants with and without shoulder dysfunction in the

study. The median score in the shoulder dysfunction group was 48, indicating ICUAW, compared to 52 in the group without shoulder dysfunction.

With the complex nature of the GHJ, and the majority of the joints stability arising from dynamic stabilisers, weakness and atrophy of the rotator cuff group will result in displacement of the humeral head and therefore, shoulder dysfunction. This is evident in patients with hemiplegia following CVA. There are several theories on the pathophysiology behind this hemiplegic shoulder pain (HSP). During the flaccid stage post CVA, the shoulder adopts an inferior, rotated position since the serratus anterior muscle is paretic and the upper part of the trapezius muscle no longer supports the scapula (Carr and Kennedy 1992). Inferior subluxations develop in the acute phase of recovery, with the weight of the patients' arm exerting a downward force on the upper trunk and the scapula, rotating the scapula downwards with the slope of the glenoid fossa becoming less oblique. This change disrupts the passive locking mechanism of the shoulder as the labrum and inferior portion of the fossa can no longer provide inferior support (Bender and McKenna 2001). The weight of the arm stretches the non-elastic shoulder capsule, causing it to become taught. Initially intrinsic tension in the shoulder capsule, ligaments and the shoulder musculature may be adequate to maintain the humeral head in the glenoid, however over time, the superior portion of the capsule becomes permanently lax, and the rotator cuff and deltoid muscles lengthen (Walsh 2001).

In the shoulder, the presentation of ICUAW can mimic that of the paresis seen in hemiplegia. This also occurs when patients receive an infusion of neuromuscular blocking agents (NMBA), which results in temporary paresis of

the patient. In this study all participants undergoing NMBA infusion developed shoulder dysfunction. There is little focus on the care of the upper limb when the ICU patient is in the upright position, unlike in the CVA patient population where the maintaining the upper limb in the correct position to prevent excessive GHJ subluxation is seen as fundamental in managing HSP (Bender and McKenna 2001).

The negative impact of weakness and joint immobility on shoulder dysfunction in ICU survivors could suggest that early rehabilitation would be a benefit. However, this was not the case as participants with shoulder dysfunction started rehabilitation a day earlier than participants without shoulder dysfunction. It is likely that these patients spent more time in an upright position during rehabilitation and mobilization (Schweickert et al 2009), with little emphasis on maintain GHJ position as previously highlighted. Early rehabilitation using wider ranging upper limb exercises without correcting GHJ position could also exacerbate shoulder dysfunction in ICU survivors, and is no longer undertaken in the hemiplegic patient due to the association with HSP (Gustafsson and McKenna 2006).

5.4.2 Infection

The presence of infection was found to have a statistically significant association with shoulder dysfunction on univariate analysis (p = .027), also demonstrating a strong association with an OR of 7.58. This is consistent with Battle et al (2013) who identified sepsis as being independently associated with shoulder pain. Sepsis is a systemic illness caused by infection of the normally

sterile parts of the body (Lever and Mackenzie 2007), therefore is directly related to infection.

In sepsis, an exaggerated immune response to the invading pathogen results in the release of widespread inflammatory cytokines, leading to the multiple systemic symptoms associated with the condition (Mossie 2013). Following the initial cytokine storm in the first few days of sepsis, a state of immunosuppression develops, potentially increasing the risk of new infection in patients with prolonged critical illness (Boomer at al 2011). The patient may develop “immune exhaustion”, a proposed term to describe the potentially disabling effects of depleted, dysfunctional, or inhibited immune resources that may impair defence against pathogens (Kalb and Lorin 2002). A prolonged critical illness leads to accumulation of other debilities which hamper the immune response to infection, including nutritional deficiency, micronutrient deficiency, protein depletion and mitochondrial dysfunction (Kalb and Lorin 2002, Boomer et al 2011). Ultimately, abnormalities in the resolution of inflammation may lead to unresolved inflammation and worsen long term outcomes (Boomer et al 2011).

The inflammatory cytokines seen in sepsis, and subsequent chronic inflammation are a key component of the development of frozen shoulder (Leow et al 2005). There is has also been some suggestion of an autoimmune basis for frozen shoulder in the general population, and that some patients have a genetic predisposition to develop it (Bulgen et al 1978). Clinical evaluation of the frozen shoulder, is similar to the presentation of ICU survivors assessed in this study, with pain present over the deltoid muscle, occasionally radiating

down to the elbow (Robinson et al 2012). Pain is followed by a gradual loss of shoulder function with activity above the head and behind the back becoming difficult (Bunker et al 200). As the shoulder stiffens there is a progressive loss of glenohumeral joint (GHJ) motion, with the most significant loss of external rotation followed by abduction and internal rotation (Chambler and Carr 2003).

The natural history of frozen shoulder suggests three phases. Phase one lasts for two to nine months and consists of pain with progressive stiffness (freezing). Phase two lasts for four to twelve months, consisting of established stiffness with a rigid end feel and reduced pain (frozen). Phase three lasts for 12 to 42 months and is associated with increasing range of movement and minimal pain (thawing) (Robinson et al 2012 and Haanafin and Chiana 2000). As pain characteristically precedes stiffness it is suggestive of an evolutionary process, from inflammation to fibrosis, which would also match the chronic inflammation seen in sepsis (Robinson et al 2012). It is possible, therefore, that in ICU survivors, the initial period of inflammation associated with frozen shoulder begins in ICU as a result of the systemic inflammation and immunosuppression associated with sepsis and immobility. If the shoulder dysfunction present in ICU survivors is frozen shoulder, then symptoms are likely to continue past the 6 month follow up period undertaken in this study.

The variables analysed in the study also consistently demonstrated that shoulder dysfunction presented in the more severely unwell participants, who were more likely to develop the chronic inflammation and immune exhaustion discussed previously. The APACHE II score was higher in participants with shoulder dysfunction (19) compared to those without (16), and they also had a

longer ICU length of stay, 9 days compared to 8 days. The other variables that could be suggestive of severity of illness were the presence of a tracheostomy and a readmission to ICU, both of which only presented in participants with shoulder dysfunction.

5.4.3 Systemic conditions

A history of diabetes was only present in participants with shoulder dysfunction and was significantly associated with shoulder dysfunction on univariate analysis, but not independently associated on multivariate analysis. Individuals with diabetes have a 10-20% lifetime risk of developing frozen shoulder due to microvascular disease causing abnormal collagen repair (Anton 1993, Robinson et al 2012). There is also some suggestion that abnormal blood glucose levels without the development of diabetes can predispose individuals to developing frozen shoulder (Tighe and Oakley 2008), which could contribute to the high prevalence of shoulder dysfunction seen in ICU survivors. Illness or injury increases hepatic glucose production with ongoing glucogenesis despite hyperglycaemia and abundantly released insulin (Van den Berghe 2004). High glucose levels in critically ill patients are associated with poor outcome, however controversy exists on the optimal level of glucose in critically ill patients, as multicentre trials could not replicate the previously demonstrated overall benefit effects of tight glucose control on mortality, and even pointed to potential harm (Van Den Berghe et al 2009). Therefore, altered blood glucose levels in patients on ICU are common, and persist for prolonged periods of time. Although a history of diabetes was analysed, abnormal blood glucose levels

were not considered for this study and therefore could have been a contributing factor to shoulder dysfunction.

A history of hypertension was present in the majority of participants with shoulder dysfunction and was associated with shoulder dysfunction on univariate analysis only, with a moderate strength of association (OR 4.3). The pathophysiological explanation for this is unclear, and may be as a result of chance as hypertension was the most common pre-existing condition in participants in the context of a high prevalence of shoulder dysfunction.

In summary, shoulder dysfunction in ICU survivors is most likely as a result of a combination of factors, which may include: chronic inflammation and immunosuppression, which is associated with critical illness and sepsis; weakness and joint immobility, as a result of ICUAW or more local GHJ constricting interventions; and diabetes.

5.5 Clinical implications and recommendations for further research

The results of this study has important clinical implications for healthcare professionals working with ICU patients. There is an increasing body of evidence surrounding early rehabilitation in ICU, with little specific detail of the content of the rehabilitation practices (Schweickert et al 2009). This increased time in an upright position, with or without wide ranging upper limb exercises, may be resulting in shoulder dysfunction in ICU survivors. The provision of rehabilitation for ICU survivors after they leave hospital is variable (McWilliams et al 2009, Denehy and Elliott 2012), and as such there is a possibility that

untreated shoulder dysfunction is contributing to the high levels of physical impairment seen in ICU survivors.

Therefore, the high prevalence of shoulder dysfunction in ICU survivors demonstrated in this thesis has important implications for clinical practice. Firstly, healthcare professionals should have an increased awareness of GHJ position when handling and positioning the patient to ensure that repetitive joint subluxation is avoided. Secondly, early rehabilitation of the upper limb in patients with severe ICUAW should mirror the rehabilitation provided to hemiplegic patients, with an increased focus on GHJ stability prior to wide ranging movements. Thirdly, an increased awareness of this potential problem amongst healthcare professionals in contact with ICU survivors after hospital discharge could improve their access to rehabilitation and musculoskeletal services.

The analysis of risk factors related to shoulder dysfunction in this thesis would have benefited from a greater number of participants experiencing the risk factors. In particular, there were several risk factors that were only present in participants with shoulder dysfunction but were a rare occurrence: tracheostomy, thoracotomy, hard collar, chest drain, readmission to ICU, NMBA infusion, inflammatory arthritis, ischaemic heart disease and diabetes. Further investigation into the risk factors for the development of shoulder dysfunction would evaluate which were independently associated with the condition.

Future research could either further investigate the prevalence of shoulder dysfunction in other centres or investigate the prevention and treatment of

shoulder dysfunction in ICU survivors. Further investigation into the prevalence would require a multicentre prospective cohort study, which would improve the generalisability of the findings to the ICU survivor population across the UK. Investigation into the prevention and treatment of shoulder dysfunction could include: education on GHJ handling, shoulder specific rehabilitation interventions on ICU and post-ICU rehabilitation. It would be difficult to create a control group for some of these interventions, as they involve cultural changes in practice for large groups of ICU staff. Therefore, a cluster randomised study approach could be used, where the control and intervention groups are recruited from separate ICUs.

5.6 Conclusion

This is the first cohort study specifically investigating shoulder dysfunction in ICU survivors. The prevalence of shoulder dysfunction within 6 months of hospital discharge was found to be 76%, and presents predominantly as bilateral dysfunction. This rate is greater than previous studies investigating components of shoulder dysfunction. Impairment of upper limb function was evident in 48% of participants with 18% experiencing severe impairment, and has not previously been reported in ICU survivors. There was no association found between shoulder dysfunction and the risk factors analysed collectively, and warrants further investigation.

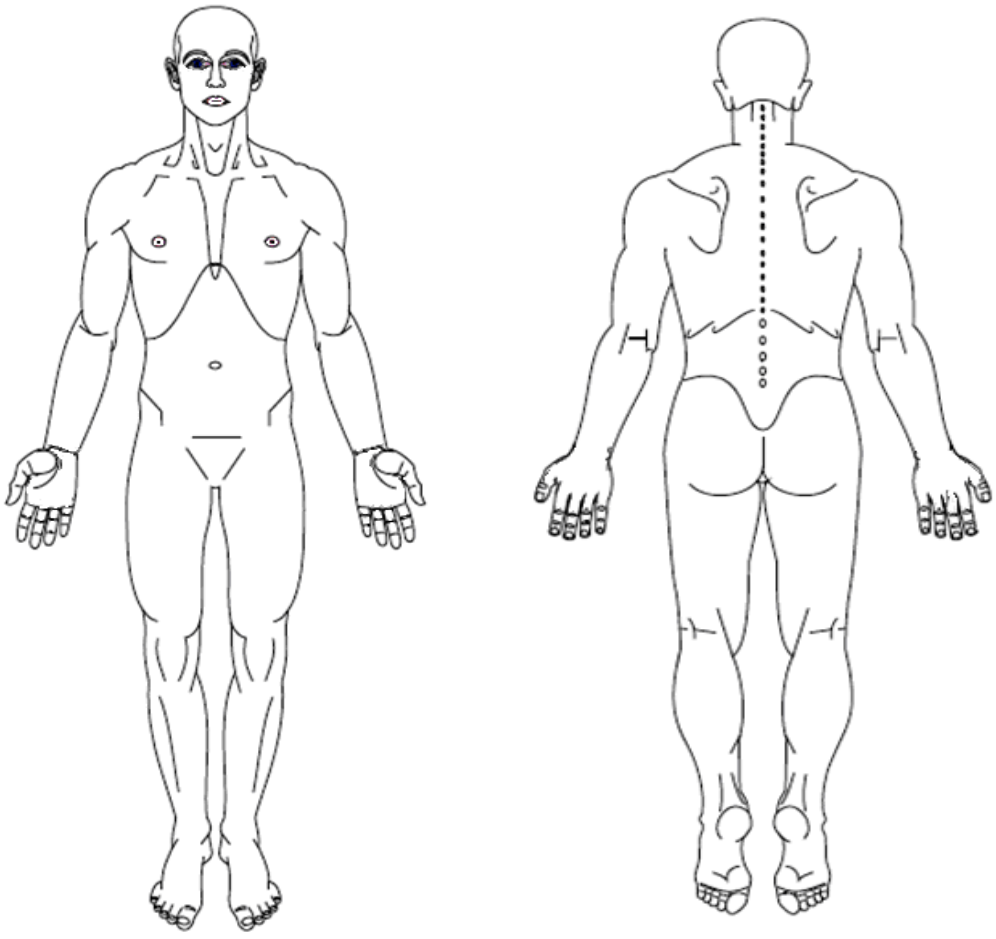
Appendix 1
Shoulder Assessment Form

Identifier: ..... Hosp N°: .....

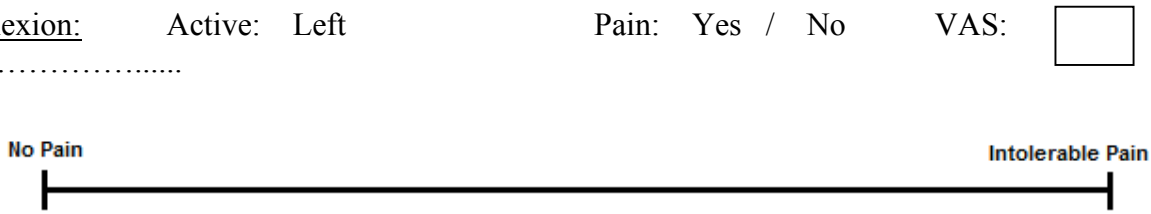
Date: ..... Assessment N°: 1 / 2 / 3 / 4

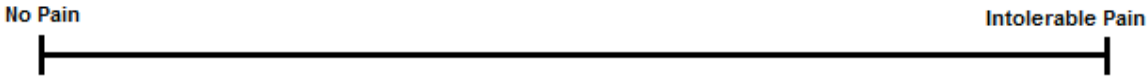
Pain: Left / Right / Bilateral / None VAS Score:

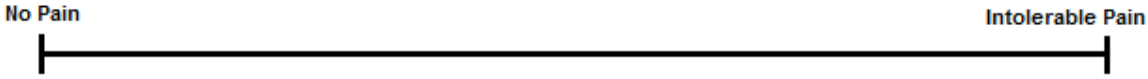
No Pain — Intolerable Pain



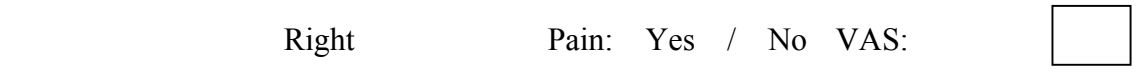
*Please shade the area of pain as described by the patient. Please annotate if there are multiple areas of pain

Flexion: Active: Left Pain: Yes / No VAS: ……..... 

Right Pain: Yes / No VAS: ……..... 

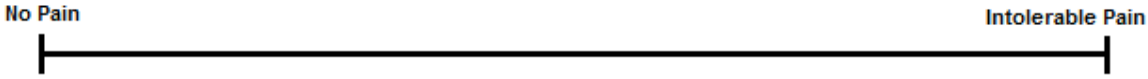
Passive : Left Pain: Yes / No VAS: …… 

Stiffness limiting PROM: Yes / No

Right Pain: Yes / No VAS: …… 

Stiffness limiting PROM: Yes / No

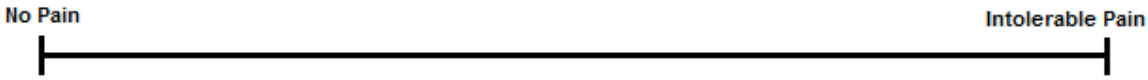
Abduction: Active: Left Pain: Yes / No VAS: ……..



Right Pain: Yes / No VAS: ……..

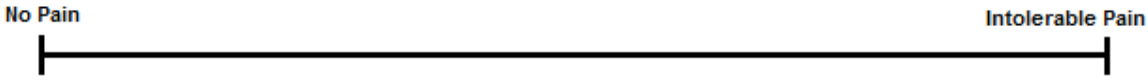
Passive : Left Pain: Yes / No VAS: ……

Stiffness limiting PROM: Yes / No



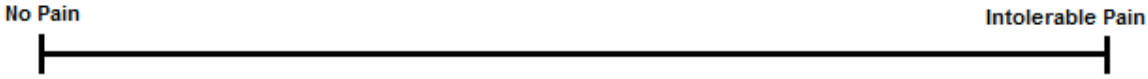
Right Pain: Yes / No VAS: ……

Stiffness limiting PROM: Yes / No



Lat Rot^{n}: Active: Left Pain: Yes / No VAS: ☐

……..



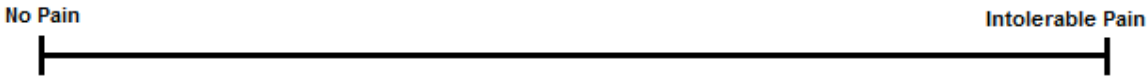
Right Pain: Yes / No VAS: ☐

……..

Passive : Left Pain: Yes / No VAS: ☐

……

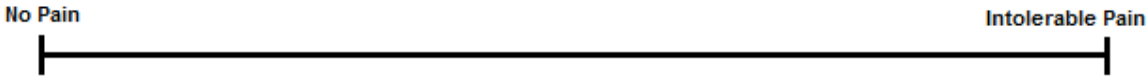
Stiffness limiting PROM: Yes / No



Right Pain: Yes / No VAS: ☐

……

Stiffness limiting PROM: Yes / No



Scapula Elevation: Left Full / Limited / Absent

Right Full / Limited / Absent

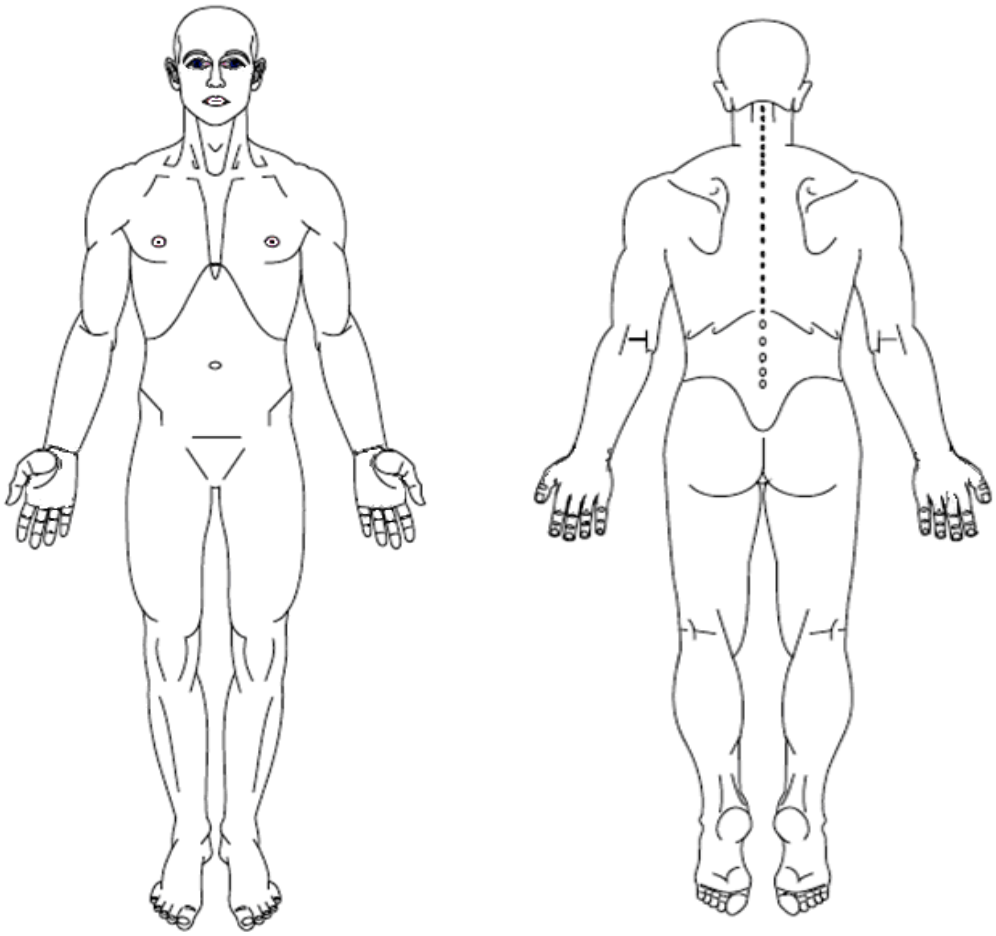
On assessment 2, 3 or 4:

Quick Dash UL Score: ☐ *Please attach completed sheet

Constant Murley Score: ☐ *Please attach completed sheet

Neck clearance:

No Pain — Intolerable Pain



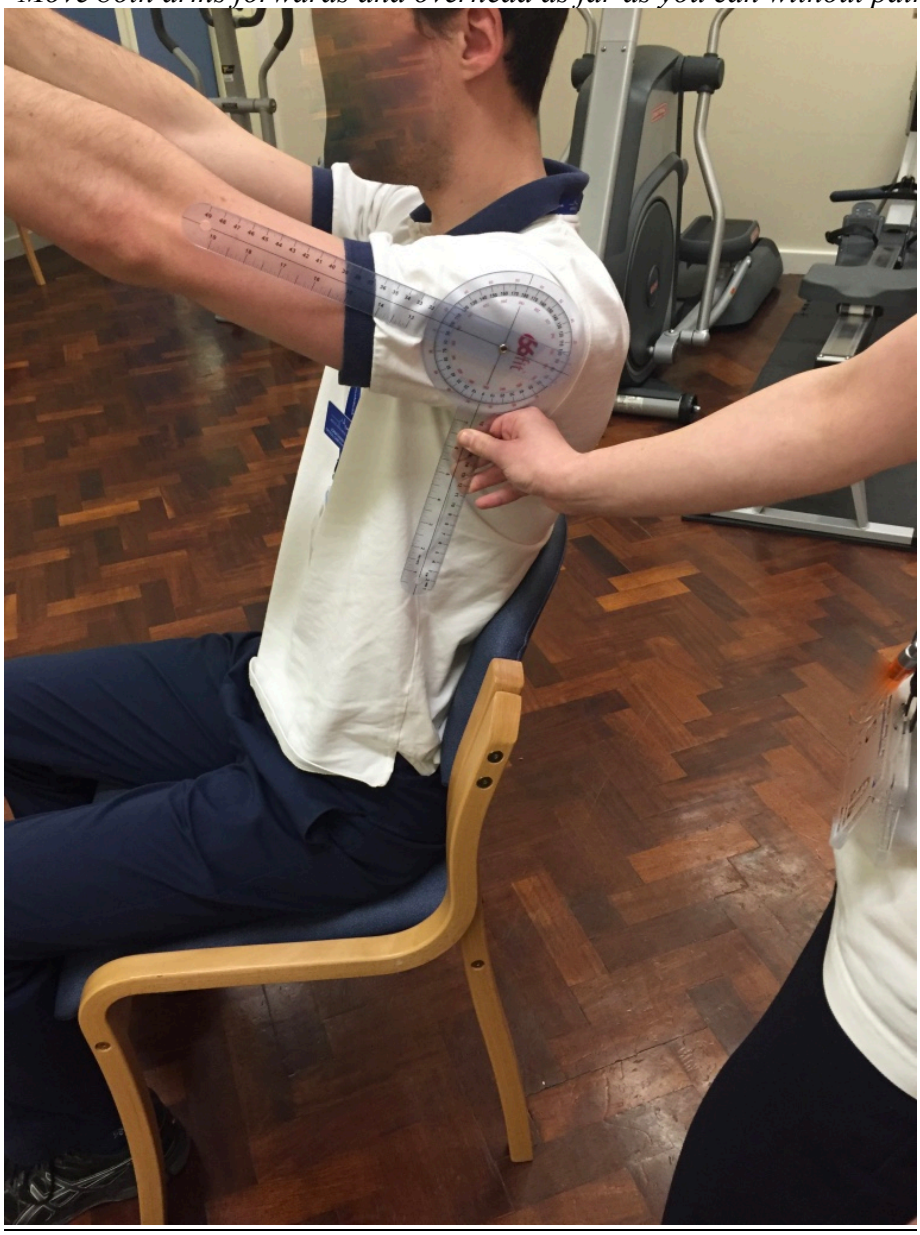
*Please shade the area of pain as described by the patient. Please annotate if there are multiple areas of pain

Comments

Appendix 2
ROM Assessment Instructions

1. Flexion: movement of the arms forward in front of the body.
The patient is sitting for the physical examination. Ideally have the patient's feet on the floor as standard. The patient should be sitting back in the chair so any trunk movement is minimised and the position is standardised. Ask the patient to raise both arms together, measuring on side at a time (see instruction below). Demonstrate the movements once yourself, before you give the verbal instruction. The measurements should be taken with a goniometer from the side of the body with the centre of the goniometer positioned in the centre of the deltoid muscle bulk.

"*Move both arms forwards and overhead as far as you can without pain"*



2. Abduction: the movement of arms out to the side, in line with the body
The patient is sitting for the physical examination. Ideally have the patient's feet on the floor as standard. The patient should be sitting back in the chair so any trunk movement is minimised and the position is standardised. Ask the patient to raise both arms together, measuring on side at a time (see instruction below). Demonstrate the movements once yourself, before you give the verbal instruction. The measurements should be taken with a goniometer from behind the patient with the centre of the goniometer positioned in the posterior body of deltoid. The patient should be sitting nearer the painful side of the chair to allow the goniometer to be next to the body.

"Move both arms out to the side as high as you can without pain"

3. Lateral Rotation: rotation away from the centre of the body

The patient is sitting for the physical examination. Ideally have the patient's feet on the floor as standard. The patient should have their elbow at their side with their hand pointed straight ahead and their elbow flexed to 90^0. Ask the patient to externally rotate the hand as far as possible with the elbow held against the trunk (see instruction below). Demonstrate the movements once yourself, before you give the verbal instruction. The measurements should be taken with a goniometer from in front of the patient with the centre of the goniometer on the olecranon process of the ulna. The stationary arm should remain at a right angle to the patient while the moveable arm should move parallel with to the longitudinal axis of the ulna pointing towards the styloid process.

"*Keep your elbows at your side and rotate your forearm outwards as far as you can without pain"*

All movements should also be measured passively with the placement of the goniometer in the identical position as in active ROM.

Appendix 3

QuickDASH

*Quick*DASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

*Quick*DASH DISABILITY/SYMPTOM SCORE = $\left(\left[\frac{(\text{sum of n responses})}{n}\right] - 1\right) \times 25$, where n is equal to the number of completed responses.

A *Quick*DASH score may <u>not</u> be calculated if there is greater than 1 missing item.

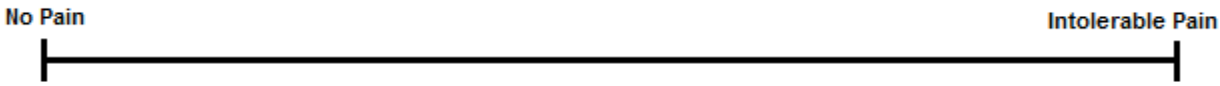
Appendix 4
Constant Murley Score

1. Pain **(Max =15)**

a) Describe the worst pain you have on everyday activities during the last 24hours

☐ No pain (15)
☐ Discomfort (13)
☐ Slight pain (10)
☐ Moderate pain (7)
☐ Severe pain (5)
☐ Unbearable pain (0)

b) Please mark on the line below the worst pain you have felt in your shoulder on everyday activities during the last 24 hours?



Research staff will measure line in cms & provide (eg. 3.2) number between 0 & 15, where 0 =no pain and 15 =intolerable pain.
This then needs to be inverted (15 =no pain, 0= intolerable pain)
Pain score will be the MEAN of these two scores?

2. Activities of Daily Living. **(Total Max for activities daily living =20)**

a) **How much is your sleep disturbed by your shoulder (Max = 2)**

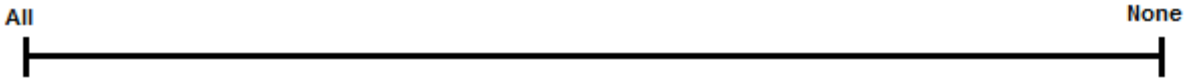
☐ Undisturbed (eg. the shoulder affects my sleep rarely or does not affect my sleep) (2)

☐ Occasional disturbance (eg. the shoulder affects my sleep sometimes or only if I sleep on the affected shoulder) (1)

☐ Every night is disturbed (eg. the shoulder affects my sleep most nights) (0)

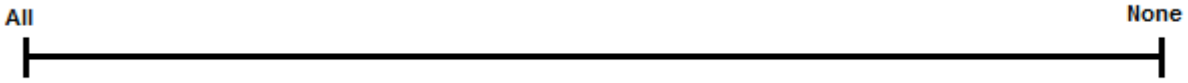
b) Please mark on the line below how much of your usual work does your shoulder allow you to do? **(Max = 4)**

(If you are not working, consider your everyday activities)



Research staff will measure line in cms & provide (eg. 3.2) number between 0 & 15, where 0 =no pain and 15 =intolerable pain.
This then needs to be inverted (15 =no pain, 0= intolerable pain). The score is recorded as 0 to 4 scale (eg 0-3 =0, 3.1-6=1, 6.1-9=2, 9.1-12=3, 12.1-15=4)

c) Please mark on the line below <u>how much of your usual recreational activity/hobby</u> does your shoulder allow you to do? (Max =4)



Research staff will measure line in cms & provide (eg. 3.2) number between 0 & 15, where 0 =no pain and 15 =intolerable pain.
This then needs to be inverted (15 =no pain, 0= intolerable pain). The score is recorded as 0 to 4 scale (eg 0-3 =0, 3.1-6=1, 6.1-9=2, 9.1-12=3, 12.1-15=4)

d) How high can you comfortably use your arm?

☐ Below waist level (0)

☐ At waist level (eg.wash dishes, cut meat, perform typing, clean a table) (2)

☐ Up to chest (eg. perform ironing, open a closed door, drive) (4)

☐ Up to neck (eg. drink with a glass, tie a tie, hang a jacket) (6)

☐ Up to top of head (eg. wash hair, comb hair, use a hairdryer) (8)

☐ Above head (eg. change a light bulb in a ceiling light) (10)

3. Assessment of active movement **Total max for Range of Movement = 40**

Patient is seated (back against the chair, feet on the ground, measure with

*'Move both arms **forwards and overhead** as high as you can **without pain**'*

*'Move both arms **out to the side and overhead** as high as you can **without pain**'*

i) **Flexion** (degrees) **(Max=10)**

ii) **Abduction** (degrees)

☐ 0 - 30 (0)	(0)	☐ 0 – 30 (0)
☐ 31 – 60 (2)	(2)	☐ 31 – 60 (2)
☐ 61 – 90 (4)	(4)	☐ 61 – 90 (4)
☐ 91 – 120 (6)	(6)	☐ 91 – 120 (6)
☐ 121 – 150 (8)	(8)	☐ 121 – 150 (8)
☐ ≥151 (10)	(10)	☐ ≥151 (10)

iii) **Functional External Rotation** **(Max =10)**

'Llift your hand above the top of your head with your elbow out to the side. If possible try NOT to touch your head'
See figs A, B,C, D & E in notes, demonstrate position D yourself

☐ Unable to get hand to head (0)

Hand to back of head – elbow forward
☐ Hand touching (1)

☐ Hand not touching (fig A) (2)

Hand to back of head - elbow back
☐ Hand touching (3)

☐ Hand not touching (fig B) (4)

Hand to top of head - elbow forward
☐ Hand touching (5)

☐ Hand not touching (fig C) (6)

Hand to top of head - elbow back

☐ Hand touching (7)

☐ Hand not touching (fig D) (8)

☐ Lift hand above head, elbow straight (fig E) (10)

iv) Functional Internal Rotation (Max = 10)

Sitting at the front of chair or side-on so can visualise – use thumb as pointer
See notes for figures for each position
'Take your arm behind your back as high as you are able without pain'

☐ To lateral thigh (0)
☐ Behind buttock (2)
☐ Sacroiliac joint (4)
☐ Level of waist (6)
☐ 12th thoracic vertebrae (8)
☐ Interscapular (10)

4. Strength (Max = 25)

Patient is in sitting with arm at 90^{0} abduction in scapular plane (30 ° forward from the body), holding the 'Balanzza^{TM}', palm facing the floor. Examiner stands on the belt so that it is taut & directly under the patient's hand.

'Pull up in the air against the belt and maintain the pull as much as you can without pain. Keep it there until you hear the beep'.

3 repetitions – with 1 minute rest between reps

☐ Unable to get into test position or get a score. ie.no bleep (score 0 and abandon this part of the test)

First pull (maximum score): _____ lb.
Second Pull (maximum score: _____lb.
Third pull (maximum score): _____lb.

HIGHEST MAXIMUM SCORE in lbs_____≥25lbs = 25 (0 – 25)

Appendix 5

CMS Strength Assessment Procedure

Patient is in sitting with arm at 90^0 abduction in scapular plane (30 ° forward from the body), holding the 'Balanzza^{TM}', palm facing the floor. Examiner stands on the belt so that it is taut & directly under the patient's hand.

'Pull up in the air against the belt and maintain the pull as much as you can without pain. Keep it there until you hear the beep'.

Appendix 6
Initial Assessment

Identifier: .....

Consent: ☐

Hosp N°: .....

DOA ICU: .....

Age: .....

Gender: M / F

Routine / Emergency .....

Medical:

Surgical:

..... .

APACHE Score ☐

Trauma:

.....

Other:

……..

PMH:

……..

……..

Neck pain/dysfunction requiring medical input: Yes / No

Upper Limb Dominance: Right / Left / Ambidextrous

Previous shoulder dysfunction: **Yes**: Attendance at: GP / Physio / Orthopaedics

Frozen shoulder: Right / Left / Bilateral / No

Surgery: Right / Left / Bilateral / No

Pain: Right / Left / Bilateral / No

No

AICU LOS ☐

Readmission: Yes / No

Hosp LOS 

Appendix 7
Daily Assessment

Identifier: ..... Hosp N°: .....

Date: ..... Day: ☐

Ventilation: MV / NIV / SV Position: Right / Left

RASS: Lowes ☐ Highest ☐ Current ☐

NMBA: Bolu ☐ Infusion ☐

Infection: Proven: BC ☐ BA ☐ Oth ☐

Presumed: ☐

No: ☐

Central Line: Yes / No Position: ..... Left / Right

Vascath: Yes / No Position: ..... Left / Right CVVH ☐

ICD: Yes / No Lef ☐ Right ☐

Position: Routine / Prone / Other.....

.....

MRC Sum Score: ☐ NA

Mobility: None / Bed Ex / Passive mob / SOEOB / Active sit out / Mobilised

Tracheostomy: Yes / No

Thoracic Incision: Yes .....

No

Hard Collar: Yes / No

Appendix 8

OUH NHS Trust Ethical Exemption

Oxford University Hospitals NHS
NHS Trust

FP/ JF

Mr John Mckenna
Clinical Healthcare Masters Student
Faculty of Health and Life Sciences
Oxford Brookes University
Jack Straw Lane
Marston, Oxford
OX3 0FL

OUH Research & Development
Joint Research Office
Block 60, Churchill Hospital
Old Road, Headington
Oxford OX3 7LJ
Tel: (01865) 572231
Fax: (01865) 222648
Email: Fiona.Parker@ouh.nhs.uk

Thursday 20th March 2014

Dear Mr Owen Gustafson

Re: Shoulder dysfunction in intensive care survivors study

Thank you for your enquiry about Trust Management Approval.

The Oxford University Hospitals NHS Trust Research and Development Department have reviewed your application.

I can confirm that as this project would not be classified as research the OUH NHS Trust do not need to issue Management Approval on this occasion.

I wish you every success with the study.

Yours sincerely,

Fiona Parker
Research Support Services Manager

Appendix 9

Participant Information Sheet

Participant Information Sheet

Shoulder Dysfunction in Intensive Care

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve, so please take time to read the following information carefully. Talk to others if you wish.

What is the purpose of the study?
The study is designed to look at the incidence of shoulder pain and/or shoulder decreased movements in patients who have spent time in an Intensive Care Unit.

Why am I being invited to participate?
You are being invited to participate because you have spent 3 or more days on the Intensive Care Unit.

Do I have to participate?
No, you can choose whether or not to participate, there is no obligation to take part in this study. If you decide to participate you will be given this information sheet to keep and you will be asked to sign a consent form. If you decide to agree you are still free to change your mind at any time without giving a reason. A decision not to take part or to withdraw will not affect your standard of care.

What will happen if I don't participate?
If you decide not to participate in the study you will receive the same medical care. Your legal rights will not be affected.

What does participation involve?
Every patient in the Intensive Care Unit receives a comprehensive daily assessment by a physiotherapist. In addition to this you will receive a specific shoulder assessment by a physiotherapist or doctor on 4 additional occasions. These assessments will take place on the ward after discharge form the Intensive Care Unit, 2 weeks after your discharge from hospital, 3 months after your discharge from hospital and at 6 months after discharge from hospital. If you have evidence of any shoulder pain or decreased movement at 6 months after discharge from hospital then you will be referred to a specialist orthopaedic shoulder consultant at the Nuffield Orthopaedic Centre.

How long will I be in the study for?
Until you have had your assessment at 6 months after you are discharged from hospital.

Will I be paid?
No you will not receive any payment for participating in this study.

What if I change my mind?
You can withdraw your consent to be in the study at any time. If you decide to agree you are still free to change your mind at any time without giving a reason. A decision not to continue or to withdraw will not affect the standard of care given.

What risks are there through participating?
There are no risks through participating in this study.

What are the benefits of participating?
A pilot study has shown that a number of patients who have spent time on Intensive Care have developed shoulder pain that has limited their ability to complete every day tasks. This study will identify how many patients have shoulder pain and how this is affecting their every day life at home. This study will assist us in identifying the need to provide treatment for this shoulder dysfunction. Patients who agree to take part in the study will receive a referral to an orthopaedic shoulder specialist if they have shoulder pain and /or reduced movement at the 6 month assessment.

Who will know that I am in the study?
The person who asked your permission to be in the study and the physiotherapist or doctor who provides your shoulder assessments will know.

What if I want to complain?
The Patient Advice and Liaison Service (PALS) in the hospital will be happy to help. Their contact details are:

Patient Advice and Liaison Service (PALS)
Level 2
John Radcliffe Hospital
Headley Way
Headington
Oxford
OX3 9DU
Tel: 01865 (2)21473

Will my taking part be confidential?
Yes. All information obtained during the course of this study will be kept confidential. The data collected will be kept for 15 years after the end of the study under secure conditions.

What will happen to my data?
Your data will be anonymised and only delegated responsible people will be allowed to access the one book with your personal details on it. The on book with your details on it will be kept in a locked filing cabinet in a security accessed room. All other sheets will have a participant number, rather than your details on them. All the anonymised data will be stored on a data stick that is password protected and that is in a locked filing cabinet in a security accessed room, along with the anonymised data sheets. The anonymised data will be collected together and statistically analysed. The results of the statistical analysis will be published in a scientific journal.

What will happen to the results of the study?

Once the study is completed the results will be published in a Medical journal and presented at meetings of health professionals. It may take 1 year after the study is entirely completed for results to be published. You can request a copy of the published results from the Principal Investigator.

Will I ever be contacted again in the future about this?
No you will not be contacted in the future with regards to this study.

Who can I contact for more information?
If at any time during the study you have questions or concerns regarding the study you can contact Principal Investigator, who is in charge of the research:

Owen Gustafson
Physiotherapy Team Leader
Adult Intensive Care Unit
Level 1
John Radcliffe Hospital
Headley Way
Headington
Oxford
OX3 9DU
Tel: 01865 (2) 20624

If you would like to speak to an independent doctor about this study then please contact:

Dr Julian Millo
Adult Intensive Care Unit
Level 1
John Radcliffe Hospital
Headley Way
Headington
Oxford
OX3 9DU
Tel: 01865 (2) 20621

Thank you for taking the time to participate in this study.

Appendix 10

Participant Consent Form

Participant Consent Form

Shoulder Dysfunction in Intensive Care

Name of Investigators: Owen Gustafson, Dr Stuart McKechnie, Dr Toby Thomas.

Participant Study Number:
……..

Name of Participant: …….

Please initial box

I confirm that I have read the participant information sheet dated 28/2/13 (version 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily and understand what is involved. ☐

I understand that my participation is voluntary and I may withdraw at any time, without giving any reason and without my medical care or legal rights being affected. ☐

I understand that relevant sections of my medical notes and data collected during this study may be looked at by the study investigators, regulatory authorities or form the NHS organisation, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

I understand that all information will be anonymised by the allocation of codes and that information will remain confidential and only be used for research. ☐

I agree to take part in the above study. ☐

Name of participant	Date	Signature

Name of researcher	Date	Signature

Appendix 11

Non-Significant Univariate Analysis Results

Table 11 Non Statistically Significant Results of the Univariate Analysis

	Shoulder Dysfunction n= 74		**No Shoulder Dysfunction n= 23**			
Categorical variables	**n**	**%**	**n**	**%**	**p value**	**Unadjusted OR (95% CI)**
Male	42	57	13	57	0.984	1.0 (0.4-2.6)
Female	32	43	10	43	0.984	1.0 (0.4-2.6)
Emergency admission	71	96	22	96	1.0	1.1 (0.1-10.9)
Readmission	7	9	0	0	0.192	-
Shoulder dysfunction	10	14	3	13	1.0	1.0 (0.3-4.2)
Neck dysfunction	8	11	1	4	0.68	2.7 (0.3-22.5)
Ventilation	55	74	17	74	0.969	1.0 (0.4-2.9)
NMBA	27	36	8	35	0.882	1.1 (0.4-2.9)
NMBA Bolus	24	32	7	30	0.858	0.9 (0.3-2.5)
CVC	66	89	19	83	0.470	1.7 (0.5-6.4)
Vascath	10	14	4	17	0.733	0.7 (0.2-2.6)
RRT	9	12	3	13	1.0	0.9 (0.2-3.7)
Patient position	4	5	2	9	0.625	0.6 (0.1-3.5)
Rehab undertaken	69	93	21	91	0.668	1.3 (0.2-7.3)
ICD	7	9	0	0	0.192	-
Thoracotomy	2	3	0	0	1.0	-
Hard collar	3	4	0	0	1.0	-
COPD	16	22	3	13	0.549	1.8 (0.5-7.0)
OA	6	8	2	9	1.0	0.9 (0.2-4.9)
Inflam Arth	5	7	0	0	0.335	-
IHD	4	5	0	0	0.570	-
CKD	3	4	2	9	0.589	0.4 (0.1-2.8)
Asthma	9	12	1	4	0.443	3.1 (0.37-25.4)
Continuous and ordinal variables	**Median**	**IR**	**Median**	**IR**	**p value**	
ICU LOS	9	7	8	7	0.702	
Hospital LOS	25	32.2	28	27	0.647	
Days ventilated	3	8	3	5	0.589	
RRT Hours	0	0	0	0	0.859	
Days to commence rehab	4	6	5	6	0.905	

Note: NMBA= Neuromuscular Blocking Agents, CVC= Central Venous Catheter, RRT= Renal Replacement Therapy, ICD= Intercostal Drain, COPD= Chronic Obstructive Pulmonary Disease, OA= Osteoarthritis, Inflam Arth= Inflammatory Arthritis, CKD= Chronic Kidney Disease, LOS= Length of Stay.

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