Long-Term Outcomes and Health-Related Quality of Life in Post-ICU Patients: a Mixed Methods Study

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Long-Term Outcomes and Health-Related Quality of Life in Post-ICU Patients: A Mixed Methods Study

PhD Thesis

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Abstract:

Background: The management of patients in Intensive Care Units (ICU) remains complex, however advances in critical care medicine have resulted in a growing population of survivors of critical illness. There is increasing evidence to demonstrate the long-term burden associated with critical illness and the ICU experience, and the term Post-Intensive Care Syndrome (PICS) has emerged to describe the domains of physical, cognitive, and psychological impairments that occur after ICU discharge. The recovery for these patients after ICU is challenging and the literature outlining causes and predictors of PICS outcomes is inconclusive. Further research is needed to understand the long-term outcomes and health related quality of life (HRQoL) of critically ill patients and to explore the predictors that, if addressed, could optimize patients' recovery. No research studies have been conducted in Saudi Arabia regarding long-term outcomes and HRQoL of post-ICU patients.

Aim: The aim of this thesis was to examine the long-term outcomes and HRQoL of post-ICU patients in Saudi Arabia using a mixed methods approach.

Methods: Phase I involved examining long-term outcomes and HRQoL in the post-ICU population in the literature by conducting a systematic review. A conceptual framework was developed based on previously proposed frameworks and the systematic review conducted in Phase I. In Phase II, the long-term outcomes and HRQoL of patients in Saudi Arabia were investigated by conducting a prospective cohort study (Life-ICUS study). Incidence of and predictors for PICS were examined. In Phase III, a qualitative approach was undertaken to explore the lived experiences of post-ICU patients in this cohort (Life-ICUS-Q study).

Results: A review of 13 studies identified key characteristics of long-term outcomes (physical, cognitive, and psychological) and HRQoL in post-ICU patients highlighting the main predictors for PICS. In-ICU factors such as ICU delirium, ICU length of stay, mechanical ventilation, and ICU diagnosis were found to be key predictors for PICS. Factors related to patients' characteristics such as younger age, female gender, unemployment, education, and pre-existing diseases were found to be associated with PICS as well. The Life-ICUS experiment studied 94 patients from the time of their ICU admission to 3 months after discharge.

Outcome data were examined at the time of discharge and at 3 months follow-up. At discharge, a large proportion of patients demonstrated PICS impairments (n=63, 93%). At 3 months follow-up all domains of PICS (physical, cognitive, psychological) and HRQoL significantly improved (in all domains and HRQoL $p<0.001$). However, a large proportion of patients (n=44, 74%) demonstrated sustained mild cognitive impairments at 3-months follow up. Non-modifiable and modifiable predictors for PICS were identified. These included younger age, female gender, education (with higher levels having a protective effect), ICU diagnosis, and pre-existing cognitive impairments. In the Life-ICUS-Q study, a total of six patients were interviewed. They perceived their recovery journey challenging with predominantly physical and psychological difficulties in the immediate post-ICU discharge period (first few days after ICU discharge). However, they perceived improvements in the long-term recovery period (several weeks to months after ICU discharge), and they related their psychological wellness to the improvements in their physical status. Several factors played a role in the trajectory of the long-term recovery of patients, and these included patients' coping, resilience, faith, gratitude, and the presence of healthcare providers and family.

Discussion: This thesis has described the long-term outcomes and HRQoL in ICU patients and the patients' experiences throughout their recovery journey. The process has provided an important first insight into the understanding of PICS in the Saudi context. This study confirmed that PICS is a common phenomenon that affects patients in different settings and cultures. A large proportion of the patients in the Life-ICUS study experienced PICS impairments. Compared to existing literature, however, Life-ICUS cohort experienced less physical and psychological impairments but higher incidents of cognitive disabilities, especially in executive functioning. Several novel findings were conferred in this study such as higher level of education having a protective role in the physical impairments, and younger patients being more predisposed to anxiety and depression. Despite acquiring PICS difficulties, patients scored their HRQoL highly and their HRQoL improved significantly over time; a finding which was also novel in this study. In the qualitative Life-ICUS-Q study, the accounts covering the entire trajectory from the time patients were in the ICU until several months after discharge depicted a challenging recovery process especially in the immediate post-ICU period. Physical and psychological aspects of PICS were the most debilitating during

this period. In the long-term post-ICU period, a strong positive outlook toward the recovery from critical illness was adopted, which was a remarkably novel finding in this study. Several personal attributes, such as resilience and a sense of gratitude, and personal efforts, such as self-care and activation of coping mechanisms, were found to be positive factors that facilitated better long-term outcomes. From a cultural perspective, the values and teachings of Islamic faith and the presence of a social and family environment played an important role in the successful navigation of the recovery phase.

Conclusions: This thesis has presented the investigation of the long-term outcomes and HRQoL of post-ICU patients in Saudi Arabia. A new and more comprehensive conceptual framework for PICS was proposed. Findings of this thesis have provided important insights into the outcomes and experiences of post-ICU patients in Saudi Arabia. Several recommendations have been proposed mainly for the enhancement of ICU practices, post-ICU research, and the development of post-ICU clinics. While critical illness and the ICU experience were associated with substantial recovery burden, there are opportunities to optimize outcomes of Saudi patients through in-ICU and post-ICU assessments and interventions.

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Author Declarations

The work presented in this thesis is my original work, except where properly acknowledged. All sources used have been duly acknowledged and referenced. Any contributions made by others have been appropriately acknowledged. This thesis has not been submitted for any other degree or diploma at this or other university or institution.

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ACLS	Advanced Cardiac Life Support
ADL	Activities Of Daily Living
A-IQCODE	Arabic-Short Form Informant Questionnaire on Cognitive Decline in the Elderly
AKI	Acute Kidney Injury
ALI	Acute Lung Injury
ANCC	American Nurses Credentialing Centre
APACHE	Acute Physiology And Chronic Health Evaluation
ARDS	Acute Respiratory Distress Syndrome
ATLS	Advanced Trauma Life Support
BLS	Basic Life Support
BMI	Body Mass Index
BPS	Behavioural Pain Scale
CAM-ICU	Confusion Assessment Method for ICU
CAUTI	Catheter-Associated Urinary Tract Infection
CCU	Critical Care Unit
CDC	Centres for Disease Control and Prevention
C. Diff	Clostridium difficile
CIM	Critical Illness Myopathy
CIP	Critical Illness Polyneuropathy
CLABSI	Central Line-Associated Bloodstream Infection
COPD	Chronic Obstructive Pulmonary Disease
CPOT	Critical Care Pain Observation Tool
CRRT	Continuous Renal Replacement Therapy
EDD	Extended Daily Dialysis
EGDT	Early Goal Directed Therapy
FGI	Facility Guidelines Institute
HADS	Hospital Anxiety and Depression Scale
HAI	Health care-associated infection
HRQoL	Health Related Quality of Life
IADL	Instrumental Activities of Daily Living
ICDSC	Intensive Care Delerium Screening Checklist
ICF	International Classification of Functioning, Disability and Health
ICU	Intensive Care Unit
ICUAW	ICU-Acquired Weakness
ICNARC	Intensive Care National Audit & Research Centre
IHI	Institute for Healthcare Improvement
ITU	Intensive Therapy Unit
KSA	Kingdom of Saudi Arabia
Life-ICUS	Long-term outcomes and Health related Quality of **Life** in **I**ntensive **C**are **U**nit Patients: a prospective cohort study in **S**audi Arabia
Life-ICUS-Q	Long-term outcomes and Health related Quality of **Life** in **I**ntensive **C**are **U**nit Patients: a prospective cohort study in **S**audi Arabia-Qualitative
MCI	Mild Cognitive Impairment

MCS	Mental Component Summary
MoCA	Montreal Cognitive Assessment
MOH	Ministry of Health
MRSA	Methicillin-Resistant Staphylococcus Aureus
NICE	National Institute of Health and Clinical Excellence
PA	Physical Activity
PCL-C	PTSD Checklist- Civilian
PCS	Physical Component Summary
PICS	Post-Intensive Care Syndrome
PICS-F	Post-Intensive Care Syndrome
PROM	Patient Reported Outcomes Measure
PSQI	Pittsburgh Sleep Quality Index
PTSD	Post-Traumatic Stress Disorder
RCT	Randomized Control Trial
SATs	Spontaneous Awakening Trials
SBTs	Spontaneous Breathing Trials
SCCM	Society of Critical Care Medicine
SCCS	Saudi Critical Care Society
SF-36	Short Form-36
SSU	Surgical Site Infection
TBI	Traumatic Brain Injury
UK	United Kingdom
VAE	Ventilator-Associated Event
VBHC	Value-Based Healthcare
WFSICCM	World Federation of Societies of Intensive and Critical Care Medicine
WHO	World Health Organization

1. Chapter 1: Introduction and Background

1.1. Chapter overview

The impetus for this study stemmed from the absence of evidence in Saudi Arabia regarding long-term outcomes of post-ICU patients. In the pursuit to understand what happens to patients in the long-term, it is important to recognize how patients are cared for in the ICU and the context of the ICU environment. This chapter introduces the topic of long-term outcomes of ICU patients. It then follows with a description of the background of the study. A case presentation is used in this section to illustrate a patient's journey throughout his critical illness. The background section is divided into a description of the ICU, both in terms of structures and processes of care to provide a context for the study. The chapter then continues to describe the background to outcomes of ICU patients focusing on the long-term sequelae of critical illness. Gaps in literature are highlighted to provide a justification for this study. Key terms are defined to provide a common and standardized understanding throughout the thesis.

1.2. Chapter aims and objectives

This chapter aims to provide an overview and background to the thesis and key concepts that underpin post-ICU long-term outcomes. The objectives are:

- To introduce the topic of long-term outcomes of post-ICU patients.
- To provide an overview of intensive care in general and services provided in Saudi Arabia in specific.
- To describe critical illness and the current clinical structures and processes of ICU care.
- To provide a synthesis of current knowledge surrounding outcomes and post-discharge care of ICU patients.
- To highlight the gaps in the research on post-ICU patients that provide a justification for this thesis.

1.3. Introduction

Traditionally, effectiveness of critical care in hospitals has been measured by survival rates which measure whether patients have survived the ICU alive or not (Iwashyna et al., 2012). As intensive care as a speciality has evolved in the past several decades, survival has improved with technological advances, organ failure prevention and reversal, new care delivery methods, and better patient-centred ICU designs (Fuke et al., 2018; Howard et al., 2019; Inoue et al., 2019).

More recently, the quest to identify the effectiveness of ICU has shifted towards investigating what happens to those who survive the ICU (Angus and Carlet, 2003; Desai et al., 2011; Needham et al., 2012). In the past two decades, clinicians and researchers have been increasingly interested in exploring the long-term effects of critical illness. In its first clinical guidelines on rehabilitation after critical illness in 2009, the National Institute of Health and Clinical Excellence (NICE) advocated for "optimization after recovery" to be included as a therapeutic objective for critically ill patients rather than mere survival rates (Tan et al., 2009). In 2010, the Society of Critical Care Medicine (SCCM) held a stakeholders' conference with the aim of understanding long-term outcomes of post-ICU patients and exploring how stakeholders can contribute to generating knowledge, awareness and education, as well as research in this area (Needham et al., 2012). In this conference, the long-lasting consequences of ICU experience were discussed and characterized by physical, cognitive, and psychological disturbances (Needham et al., 2012). Physical impairments were described as ICU-acquired physical deconditioning and inability to perform activities of daily living (ADL); cognitive impairments were defined as poor memory, inattention, and sub-optimal executive functions; and psychological sequelae were described as including depression, anxiety, and post-traumatic stress disorder (PTSD). In the SCCM conference, the stakeholders agreed to adopt a common nomenclature to describe the multiple impairments after critical illness and thus the term Post Intensive Care Syndrome (PICS) was recommended (Needham et al., 2012). The term PICS was defined as "*new or worsening impairments in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization*" (Needham et al., 2012, p. 505). This definition of PICS will be adopted and applied throughout this thesis.

The physical, cognitive, and psychological disturbances of PICS have been shown to lead to poor quality of life and raise a significant public health concern by putting a burden on society in terms of morbidity, productivity, and financial cost (Davydow et al., 2009; Gerth at al., 2018). Since the reports of NICE and SCCM, although awareness has been growing about PICS and its devastating consequences, the literature on epidemiological studies remains scarce (Hiser et al., 2023; Marra et al., 2017). Despite calls for standardized assessments for all ICU patients in relation to their risk of physical, cognitive, and psychological morbidity, clinical practice lags in adoption of these practices (Tan et al., 2009). PICS problems are often unrecognized, and there is no consensus regarding the optimal screening and assessment tools for their identification (National Institute for Health and Care Excellence, 2018). The definition and the scope of post-ICU impairments are not yet fully described, and evidence regarding risk factors and specific patient populations who are at greatest risk for specific impairments is limited (Elliott, et al., 2014). Are certain groups of patients at risk because of their vulnerabilities prior to critical illness, such as chronic diseases, cognitive and psychiatric predispositions, age, gender, or socio-economic factors? Or is the nature of the critical illness and the course of ICU stay that puts them at risk? These questions remain to be fully understood. It is well known that in the ICU, patients undergo sedation, mechanical ventilation, organ-support treatments, and poly-pharmacology. They are often unable to communicate due to intubation, and they may experience delirium due to either sensory deprivation or overload (Howell et al., 1999). The relationship of these ICU-related experiences and the development of PICS is not yet fully understood. Factors relating to post-ICU transfer to wards, hand-off communication, and immediate post-ICU recovery and their effect on PICS are not well researched and understood. Literature is still lacking regarding factors that affect trajectories of recovery after hospital discharge and evidence that supports rehabilitation efforts is scarce.

In the Kingdom of Saudi Arabia (KSA), very little is known about ICU outcomes, and data on long-term outcomes and quality of life does not exist. To date, there are no publications in the current literature from Saudi Arabia and the entire Middle East regarding post-ICU outcomes or PICS. It is known from anecdotal observations that patients are discharged from ICUs without assessment of long-term sequelae. Follow-up occurs in the primary physicians' clinics, focusing on respiratory status, infections, and post-operative surgical care. Targeted

rehabilitation services for these patients are scarce in Saudi Arabian communities. Follow-up ICU clinics, recently gaining support in the US and Europe, do not exist in Saudi Arabia and the region. The lack of longitudinal studies on long-term outcomes of ICU patients deprives Saudi Arabian critical care professionals from opportunities to improve care practices within the ICU and after ICU discharge.

1.4. Background: Understanding the intensive care unit

1.4.1. Overview of intensive care

This section provides an overview of the nature of critical illness and the interventions that occur in the ICU. This will enhance the understanding of the care setting and the care modalities used in the ICU to facilitate insight to some of the underlying factors that might play a role in the development of adverse post-ICU outcomes. A case presentation approach will be taken in this section to illustrate a patient journey in the ICU; this case will be re-visited at the end of the thesis in Chapter 7.

The history of how intensive care evolved as a speciality since its inception, and the developments that led to the modern quest for post-ICU outcomes are intriguing topics and the author has embarked on illustrating them in a narrative piece titled: History of Critical Care Medicine (**Appendix 1.1**).

1.4.2. Definition and scope of intensive care

Case presentation 1.4.2 A 68-year-old male patient, HK, is admitted to the adult medical-surgical ICU of a 400-bed tertiary care private hospital in Eastern Province of Saudi Arabia. The patient is diagnosed with septic shock due to pneumonia.

Intensive care is defined by the World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM) as a "*multidisciplinary and interprofessional specialty dedicated to the comprehensive management of patients having, or at risk of developing, acute, life-threatening organ dysfunction*" (Marshall et al., 2017, p.271).

The ICU is defined as: "*an organized system for the provision of care to critically ill patients that provides intensive and specialized medical and nursing care, an enhanced capacity for monitoring, and multiple modalities of physiologic organ support to sustain life during a period of acute organ system insufficiency*" (Marshall et al., 2017, p.274).

Although some critical care services are delivered beyond the walls of ICU premises, designating a distinct geographic location within a hospital where the most acutely ill patients are cared for is central to the definition of an ICU. The allocation of a discrete physical space enables efficient communication, sharing of knowledge and expertise, and provision of specialized care to these patients.

Intensive care services utilize an array of technologies to provide life support, in particular to failing respiratory, cardiovascular, and renal systems. Patients admitted to intensive care typically require support for hemodynamic instability, airway and respiratory management, acute renal failure, and other organ dysfunctions. The primary goal of intensive care is to prevent further physiologic deterioration while treating underlying diseases (Thimmapur et al., 2018).

ICUs are also known as Intensive Therapy Units (ITUs) and critical care units (CCUs). In the United Kingdom (UK), the term critical care encompasses intensive care (highest of 4 levels of care) and high dependency care, which provides for the next higher level of care. These units can be general or specialized and can be organized by specific systems, pathologies, or problems (e.g., neurological, burn, or trauma ICUs, and medical or surgical ICUs) or by age groups (e.g., adult or paediatric ICUs).

Prior to the Covid-19 pandemic, approximately 164,000 patients were admitted in ICUs in the UK, with a survival rate of 79% (WFSICCM, 2016). In the United States (US), there were 5.7 million annual admissions to the ICUs, of which approximately 4.8 million (84%) patients survived (SCCM, 2022). Comparative data for low- and middle-income countries are not readily available.

In 2020, there were 4130 adult critical care beds in the UK (The King's Fund, 2021 A), with an occupancy rate of 83% (The King's Fund, 2021 B). Unlike other categories of hospital beds in the NHS, the total number of intensive care beds has increased over time. Cardiovascular and respiratory support account for the largest share of critical care activity, with the vast majority being discharged to general wards (The King's Fund, 2021). In the USA, there are 59,281 of intensive care beds with 67% occupancy (American Hospital Association, 2022). Internationally, for every 100,000 people, Germany has 24.6 ICU beds, Canada 13.5 ICU beds, the UK 3.5 ICU beds, South Africa 8.9 ICU beds, Sri Lanka 1.6 ICU beds, and Uganda 0.1 ICU beds (Picetti et al., 2019).

The number of critical care beds and admissions rose substantially worldwide during the Covid-19 pandemic (Institute for Health Metrics and Evaluation, 2022). Data are not yet available and conclusive to show whether these increases have been sustained or whether they have started to return to pre-pandemic levels.

ICUs play a crucial role in managing patients with acute, life-threatening organ dysfunction, providing specialized medical and nursing care alongside advanced monitoring and life support technologies (Marshall et al., 2017). In Saudi Arabia, like in many countries, ICUs are designated areas within hospitals dedicated to the care of critically ill patients, characterized by their ability to deliver intensive therapies and continuous monitoring essential for stabilizing and supporting organ function during acute crises.

The utilization of ICUs in Saudi Arabia reflects global trends, with a growing emphasis on providing specialized care to patients at high risk of mortality due to severe illnesses like sepsis and acute respiratory distress syndrome (Institute of Medicine, 2001; Kohn et al., 2000). While specific mortality rates and causes of death within Saudi Arabian ICUs may vary, similar challenges in managing critically ill patients persist, necessitating ongoing advancements in ICU design, staffing, and technology adoption.

The availability of ICU beds in Saudi Arabia, relative to its population, reflects international variations. Although precise statistics for Saudi Arabia were not detailed in the current literature, international benchmarks underscore the importance of adequate ICU capacity

to meet healthcare demands during routine periods and health crises, such as the COVID-19 pandemic (Picetti et al., 2019; Institute for Health Metrics and Evaluation, 2022).

1.4.3. Critical care in the Kingdom of Saudi Arabia (KSA):

This section provides an overview of healthcare in KSA, specifically in relation to critical care. This will provide the reader a context of where the PhD study was conducted.

The KSA is a land approximately 2.1 million km^2 and is the largest country in the Middle East (The World Bank, 2021). The population of Saudi Arabia is estimated to be over 35 million, of which over 13 million are expatriates. In 2020, the annual population growth was 2.38% (The World Bank, 2021). The consistent annual growth has placed a significant demand on the healthcare sector, which has received considerable amount of attention from the country's leadership. According to the World Health Organization (WHO), the Saudi health care system is ranked 26^{th} among 190 of the world's health care systems (World Health Organization, 2000).

The Kingdom's population has a life expectancy of 75 years (73.7 for males and 76.4 for females) (Ministry of Health, 2020). There is a high prevalence of adult overweight and obesity rates in KSA. In 2020, it was estimated that 69.7% of the adult population were overweight and 35.5% were obese, which placed a huge burden on the country's healthcare system (Ministry of Health, 2020).

Currently, there are 470 hospitals in KSA. Of these, 274 are operated by the Ministry of Health (MOH), 44 by other governmental sectors, and 152 by the private sector. In 2020, the patient care services provided a total of 78,596 beds, of which 3,546 were critical care beds. The occupancy in critical care beds were around 65% in MOH hospitals with an average of 7.28 days of length-of-stay (Ministry of Health, 2020).

Regarding the healthcare workforce, there are 2,645 intensive care physicians and 54 newly enrolled physicians in intensive care fellowship programs in KSA. Training courses such as Basic Life Support (BLS), Advanced Cardiac Life Support (ACLS), Advanced Trauma Life Support

(ATLS), and Covid-19 crash courses are readily available to healthcare providers (Ministry of Health, 2020).

Intensive care units in KSA vary in size, function, capability, and staffing. Primary care hospitals (the majority in number) are in remote areas and villages, and they have relatively small ICUs with limited equipment and expert healthcare providers. Secondary care hospitals, found in small cities, have larger ICUs and better equipment, typically with a coverage of an intensivist. Tertiary care hospitals have well-equipped specialized ICUs. Most are closed units (one where the intensivist is the admitting physician and the specialty teams collaborate with ICU staff) and covered by on-site certified intensivists, and well-trained nurses in a 1:1 or 1:2 nurse to patient ratios (Al-Omari et al., 2015).

Similar to the trend globally, there has been a considerably rising demand for critical care services in the Kingdom. An increasingly ageing population, rising levels of comorbidities such as hypertension and diabetes, better survival of once incurable diseases, and advances in medical technology and procedures have necessitated the need for acute and critical care services (Ministry of Health, 2020). In the past, people needed to travel outside of the country to receive critical care; however, these services are now available locally. Physicians and surgeons, having completed their postgraduate training in the USA and European countries, have returned home introducing new modalities of care (Ministry of Education, 2023).

In August 2020, the MOH increased the ICU bed capacity in the capital city of Riyadh by 43% to reach 3,500 beds in order to respond to the needs posed by the COVID-19 pandemic (Ministry of Health, 2020). During the Haj season, and prior to the Covid-19 pandemic, nearly two million pilgrims used to come to Mecca from more than 100 countries. During these times, and due to the overcrowding, the risk for falls, trauma, and communicable diseases increases. If the season falls during summertime, heatstroke is a major concern. The government mobilizes health services in 14 permanent hospitals and seven seasonal hospitals with a total of more than 5000 beds, of which 30% are critical care beds, with specialized physicians, nurses, and healthcare providers (Arabi et al., 2006).

The cost for caring for a critically ill patient in KSA is not clear since most ICUs are

governmental and cost is not calculated per patient; however, it is estimated that around 1200-1500 USD (around 1200-1500 GBP) are spent per day per patient in the ICU (Arabi et al., 2006).

The Saudi 2030 vision is an ambitious and aspirational endeavour targeting the transformation of healthcare in the country. This includes a comprehensive streamlining of strategies and restructuring initiatives in the country. As part of the transformation and adoption of the Value-Based Healthcare (VBHC) model, in 2016, the MOH developed a nation-wide project called "*Ada'a*" ("*performance*" in English), in which districts and various medical centres and hospitals compete to demonstrate superior outcomes. As a result, waiting times and other major indicators have improved drastically (Ministry of Health, 2021).

Individual hospitals may currently own internal databases and measures of critical care such as reason for admission, acuity, severity indices, complications, infection rates and mortality. However, critical care disease profiles and national outcome data are not evident in the Saudi literature.

The Saudi Critical Care Society (SCCS) was established in 2006 to serve the Saudi critical care community with its extensive educational and professional programs (SCCS, 2023). It is one of the largest professional societies in the Middle East and it caters to both adult and neonatal critical care. The SCCS provides staffing, training, and support to the services provided during the Haj season. The society holds strong bonds with the Society of Critical Care Medicine in the US, the European Society of Intensive Care Medicine, and many other regional and international societies (Al-Omari et al., 2015).

Research in critical care has been slowly growing over the past two decades in KSA. Topics such as heatstroke management, severity prediction and mortality, end-of-life, and resource utilization are being well represented in the Saudi medical literature (AlDorzi et al., 2013; Al-Shimemeri et al., 2020; Arabi et al., 2002). However, the medical community considers that research has not yet expanded, especially in areas such as critical care. The reasons behind this lag are considered to be lack of research funding, absence of databases, expertise in research methods, and a general poor acceptance of research - socially and culturally. Despite

this, there is a noticeable drive towards research in leading centres and academic hospitals (Al-Omari et al., 2015).

Saudi Arabia's healthcare system is characterized by a commitment to providing comprehensive medical services, including critical care in ICUs, aimed at managing acute and life-threatening conditions effectively. This infrastructure supports the research aim of exploring the long-term outcomes of ICU patients by highlighting the foundational healthcare framework within which these outcomes are assessed. Understanding Saudi healthcare's capabilities and resources is crucial for contextualizing the study findings on ICU patient outcomes, ensuring insights are applicable and relevant to the local healthcare context.

Saudi Arabia's healthcare system, characterized by significant investment and expansion, plays a crucial role in supporting the research aim of investigating the long-term outcomes of ICU patients. With a growing population exceeding 35 million and substantial annual healthcare advancements, including the increase in critical care beds and advancements in medical technologies, Saudi healthcare infrastructure provides a robust foundation for studying patient outcomes in intensive care settings. The country's commitment to healthcare transformation under initiatives like the Saudi Vision 2030 and the adoption of Value-Based Healthcare models further underscores the relevance of this research within the evolving Saudi healthcare landscape.

1.4.4. Critical illness and ICU services:

Case presentation 1.4.5 Upon admission to the ICU, an initial assessment of HK was conducted by the physician and the nurse, revealing a history of COPD and renal failure in this patient. Vital signs were documented as: Temperature 36.6 degrees Celsius; heart rate 121 beats per minute; blood pressure 83/42 mmHg; respiratory rate 32 breaths per minute; and oxygen saturation 86%. The patient was confused, and his words were incomprehensible. A family member, his sister, was present to provide information about the patient.

1.4.5. Critical illness admissions:

Critical illness is characterized by life-threatening organ dysfunction leading to excess morbidity and mortality (Kahn et al., 2010). General ICUs host a heterogeneous group of critically ill patients who all share the need for frequent assessment and a greater need for technological support than that provided in general wards or high dependency areas. Intensive care services are best utilized for those with potentially recoverable conditions who can benefit the most from the detailed observation and invasive treatment (Nates et al.,2016). General medical-surgical units host an array of conditions. In the UK, the top 3 ICU admission diagnoses for adults are (Intensive Care National Audit and Research Centre, 2022):

- Acute kidney injury
- Sepsis
- Pneumonia

In the US, the top three primary ICU admission diagnoses for adults are (SCCM, 2022):

- Respiratory insufficiency/failure with ventilator support,
- Acute myocardial infarction,
- Intracranial haemorrhage or cerebral infarction

In KSA, national data of ICU admissions is lacking (Arabi et al., 2006), however based on reports from two large hospital systems in the country, the following are the top three admission diagnoses (Alharthy et al., 2019):

- Trauma
- Cardiopulmonary failure
- Sepsis

Other medical conditions frequently encountered in the ICU are: poisoning and toxic effects

of drugs, pulmonary edema and respiratory failure, heart failure and shock, cardiac arrhythmia and conduction disorders, renal failure with major complication or comorbidity, gastrointestinal haemorrhage with complications or comorbidity, and diabetes with complications or comorbidity.

Surgical indications for ICU admission include acute emergencies such as haemorrhagic strokes, ruptured aortic aneurysms, and acute abdomen.

Understanding the diverse and severe nature of conditions leading to ICU admissions is essential for appreciating the subsequent challenges faced by ICU survivors. The intensity and complexity of care required in the ICU may often result in long-lasting effects and can significantly impact patients' quality of life and functional status long after discharge. By exploring these outcomes, critical areas for intervention can be identified and addressed to improve the overall prognosis and quality of life for ICU survivors.

In Saudi Arabia, where specific data on ICU admissions is sparse, there is a growing recognition of the need to address long-term outcomes of ICU patients. The country is witnessing a surge in the incidence of conditions requiring critical care, such as trauma and cardiopulmonary failure, partly due to rapid urbanization and an increase in chronic diseases. Studying the long-term outcomes of ICU patients in this context is crucial for developing targeted healthcare policies and rehabilitation programs that can cater to the unique needs of the Saudi population.

1.4.5.1. ICU interventions:

Case presentation 1.4.5.1 An urgent x-ray demonstrated right middle and lower lobe pneumonia in HK. A point of care testing of blood gases showed severe hypoxia and hypercapnia. The patient was immediately sedated by a benzodiazepine (Midazolam) and was intubated in a rapid sequence method. He was placed on mechanical ventilation to provide high oxygen and high respiratory rate to properly oxygenate and wash off the carbon dioxide from the body. Pain assessment, using the nonverbal pain assessment tool indicated that the patient is not in pain. A fluid bolus of 500 ml of normal saline increased the patient's

blood pressure to 92/62 mmHg. Vasopressors were not started, awaiting response and further improvements in blood pressure. An indwelling urine catheter was inserted with a urine output of 120 ml. Haemodialysis was not considered; however, the urine output of the patient was monitored on an hourly basis. A nasogastric tube was inserted, and the ICU nutritionist was consulted for dietary recommendations.

The goal of ICU interventions is to preserve life and to prevent or minimize damage to vital organs while treating the underlying cause of disease (Marshall et al., 2016). In this regard, the key interventions are targeted towards optimizing respiratory and cardiovascular function in order to maintain systemic perfusion and prevent organ dysfunction. There is lack of rigorous, conclusive scientific evidence regarding the clinical effectiveness of many interventions carried out in ICUs (Auriemma et al., 2019). This is probably due to the nature of critical illness, heterogeneity of patients, and feasibility and ethical considerations in carrying out large-scale randomized control trials in ICU populations. Alternatively, observational studies, adjusting for case mix (e.g., accounting for age and severity of illness) have been used to determine the outcomes of interventions (ICNARC, 2022). The following are key interventions carried out in the ICU; evidence regarding their effects on outcomes of patients are mentioned.

A. Respiratory support:

Most ICU patients require some form of respiratory system support in the form of oxygen therapy, endotracheal intubation, and mechanical ventilation, in order to keep the airway patent and treat hypoxemia. Complications of respiratory support include ventilator associated events (VAE) and hospital/ventilator acquired pneumonia (National Healthcare Safety Network, 2024). The nursing act of suctioning and providing oral/endotracheal care puts the patient at risk for hypoxemia and feelings of discomfort, suffocation, and anxiety (Grap et al., 2002; Rotondi et al., 2002; Samuelson et al., 2011). Patients needing mechanical ventilation are often sedated with benzodiazepines such as midazolam or anaesthetics such as propofol, in order to ameliorate the patients' intolerance to the endotracheal tube (Grap et al., 2012). Opiates such as morphine and fentanyl are often prescribed to alleviate pain. Both benzodiazepines and opiates however are potentially disruptive to sleep (Kamdar et

al., 2012). Benzodiazepines provide sedation through GABA-ergic pathways but disturb the stage of “deep” sleep (N3) which is essential for restoration and memory consolidation (Kamdar et al., 2012). Opiates such as morphine and fentanyl on the other hand, promote sleep onset in healthy adults, but inhibit REM and “deep” sleep stages, cause nocturnal awakenings, and can precipitate central apnoea (Dimsdale et al., 2007; Shaw et al., 2005). Even when administered at low doses, both benzodiazepines and opiates are associated with delirium in critically ill patients (Figueroa-Ramos et al., 2009; Pandharipande et al., 2007). There is clear evidence from several randomized control trials that sedation with benzodiazepines leads to deleterious outcomes, including oversedation, delirium, delayed extubation, and prolonged and costly ICU stays (Breen et al., 2005; Carson et al., 2006; Pandharipande et al., 2007). A propensity-matched, retrospective cohort analysis using the Project IMPACT database, Lonardo and colleagues have proved that sedation with propofol rather than benzodiazepines is associated with a shorter ICU stay and duration of mechanical ventilation, as well as a reduced short-term mortality (Lonardo et al., 2014). Effective weaning off of the ventilator has been advocated to occur in coordinated efforts with spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs) (Girard et al., 2008). When paired, SAT and SBT reduce the number of mechanical ventilation days, which in turn reduce the length of ICU stay (Girard et al., 2008). More recently, the SCCM ICU Liberation Collaborative, a US nationwide quality improvement initiative that implemented the ICU Liberation Bundle in 68 ICUs involving over 15,000 patients, showed that a thorough implementation of the ICU Liberation Bundle is associated with improvements in delirium, use of physical restraints, ICU readmission, and hospital death within 7 days (Pun et al., 2019). This Bundle will be discussed further in section E.

B. Cardiovascular support:

Circulatory support is often required in critically ill patients to treat hypotension and different types of shock, and to prevent complications of decreased tissue perfusion. This type of support occurs in the form of volume replacement by crystalloids, colloids, and blood and blood products (Singer et al., 2016). If shock persists despite volume replacement, vasoactive drugs are used to restore cardiac output and tissue perfusion (Singer et al., 2016). If not treated early and effectively, shock states can lead to significant morbidity and

mortality (Angus et al., 2006; Quenot et al., 2013; Vasu et al., 2012). In refractory shock states, high doses of vasopressors may be needed to maintain mean arterial pressure above 65 mmHg (Levy et al., 2010), however high-dose vasopressor therapy has been associated with increased mortality (Benbenishty et al., 2011; Dopp-Zemel et al. 2013; Jenkins et al., 2009). Regarding fluid resuscitation, it had been long established, by the guidelines of Early Goal Directed Therapy (EGDT), to resuscitate hemodynamic instability by aggressive fluid replacement (Rivers et al., 2001). However, over the last decade, several studies have shown that aggressive fluid resuscitation is associated with increased morbidity and mortality in patients with severe sepsis, Acute Respiratory Distress Syndrome (ARDS), as well as trauma and surgical patients (Wiedemann et al., 2006). Several randomized control trials and cohort studies across diverse patient populations have demonstrated that a conservative fluid strategy is associated with significantly fewer complications and lower mortality (Marik, 2015)

C. Renal support:

Renal impairment is often not due to primary renal disease, but secondary to poor perfusion, renal vascular occlusions, and pharmacological treatments in the ICU (Chen et al., 2018). The most common contributing factor to acute kidney injury (AKI) in critically ill patients is septic shock (Uchino et al., 2005). Management of AKI consists of optimization of circulation and oxygenation, and renal replacement therapy (Chen et al., 2018). The latter is performed either by intermittent haemodialysis (IHD) or continuous renal replacement therapies (CRRT). Patients with acute critical illness have significantly higher risks for acute kidney injury and there is a higher mortality risk among patients who subsequently need dialysis and develop end-stage renal disease (Chen et al., 2018; Coca et al., 2012; Wald et al., 2009). Common complications of dialysis for acute kidney injury patients in ICUs are hypotension, and coagulation and electrolyte imbalances (Chen et al., 2018). Hypotension is the most frequent complication and may occur in over 20% of AKI patients (Albino et al., 2014). A hybrid therapy called extended daily dialysis (EDD) has emerged as an alternative to CRRT in the management of hypotensive and haemodynamically unstable patients with AKI (Fliser et al., 2006; Kielstein et al., 2010). More research is being conducted regarding the efficacy of this new modality.

D. Patient monitoring:

Most patients in ICU require continuous invasive and non-invasive monitoring for heart rate, respiratory rate, oxygen saturation, blood gases, arterial blood pressure, central venous pressure, urinary output, and temperature (Marik, 2015). In some cases, patients may need assessments for abdominal pressures, intracranial pressures, cardiac output and pulmonary artery pressures, and other point-of-care testing (Marik, 2015). Patient monitoring is essential in establishing a diagnosis, identifying severity of illness, recognizing early changes in condition, guiding diagnostic tests and treatments, and following the progression of the critical illness.

E. Other supportive interventions:

- Most patients would need some type of nutritional support in the form of enteral or parenteral feeding in order to reduce muscle waste and enhance wound healing (Marik, 2015). Current evidence suggests that in critically ill patients the approach to nutritional support directly impacts outcomes. Critically ill patients loose large amounts of lean body mass, which can have a drastic effect on weaning from mechanical ventilation and long-term recovery (Marik, 2015). Emerging data suggests for: early nutritional feeding; intermittent rather than continuous tube feeds; preventing overfeeding; and a formula which is low-osmolarity, low-carbohydrate, high-fibre, and containing whey protein, omega-3 fatty acids, and structured lipids. This is the preferred type of feeding except for patients with kidney disease, severe pancreatitis, and those on propofol (Marik 2015).

- Patients also require chest physiotherapy, turning, repositioning, and mobilization to prevent respiratory complications and to counter muscle weakness and pressure injuries. Many studies in the recent decades have demonstrated that early mobilization in the ICU for patients with respiratory failure and mechanical ventilation is feasible and safe (Bailey et al., 2007; Morris et al., 2008). In a study where individually tailored exercise training protocol was initiated during the early ICU days of patients requiring

mechanical ventilation, exercise training proved to enhance recovery of exercise capacity, self-perceived functional status, and muscle strength (Burtin et al., 2009). Similarly, in a Randomized Control Trial (RCT) by Schweickert and colleagues, patients who were ventilator dependant for more than 3 days were randomized to early physical and occupational therapy, coupled with daily awakenings (Schweickert et al., 2009). Patients in the intervention group demonstrated better outcomes in terms of more ventilator-free days, shorter duration of delirium, and enhanced independent functional status at discharge compared to the standard care group (Schweickert et al., 2009).

- Health care-associated infections (HAIs) are leading causes of morbidity and mortality among hospitalized patients (Burke et al., 2003). In its 2020 National and State Healthcare-Associated Infections Progress Report, the Centers for Disease Control and Prevention (CDC) stated that "*each day, approximately one in 31 U.S patients contracts at least one infection in association with his or her hospital care*" (CDC, 2020). Similar data have been reported in European prevalence surveys where 5 to 10% of patients admitted to acute care wards acquire one or more infections during their stay (Kaoutar et al., 2004; Lizioli et al., 2000; Lyytikainen et al., 2008,). The World Health Organization states that, one in ten patients get an infection while receiving care (WHO, 2011). The most common HAIs are central line-associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), ventilator-associated events (VAEs), surgical site infections (SSIs), methicillin-resistant Staphylococcus aureus (MRSA) bloodstream events, and Clostridium difficile (C. difficile) events (CDC, 2020). It is evident that HIAs increase length of stay and hospital costs (Lambert et al., 2011; Zimlichman et al., 2013). The effects of HAIs on attributable mortality however are less clear; since HAIs are more common in patients with higher acuity illnesses and thus higher mortality and length of stay, it has therefore been unclear as to whether HAIs independently contribute to adverse outcomes (Lambert et al., 2011). In 2001, the Institute for Healthcare Improvement (IHI) started initiating a series of "bundles" to redesign care in intensive care through the institution of highly reliable processes and to enhance outcomes related to HAI (Resar et al., 2012). A bundle was defined as "*a small set of evidence-based interventions for a defined patient segment/population and care setting*

that, when implemented together, will result in significantly better outcomes than when implemented individually" (Resar et al., 2012, p.2). Bundles were created for all device-associated infections. A growing body of published results demonstrate the effectiveness of this method in improving care and subsequently outcomes (Furuya et al., 2011). To successfully implement bundles with high reliability, the IHI advocates for redesign of work processes and infrastructure, interdisciplinary communication, and sustained measurement and vigilance (Resar et al., 2012).

The interventions described above, while crucial for immediate survival, have significant implications for the long-term outcomes of ICU patients. For instance, complications arising from respiratory support, such as ventilator-associated events and disruptions to sleep due to sedation, can contribute to prolonged recovery periods and impact overall quality of life post-ICU. Cardiovascular support, especially aggressive fluid resuscitation and high-dose vasopressor therapy, has been associated with increased morbidity and mortality, which highlights the need for careful management to improve long-term health outcomes. Similarly, the management of acute kidney injury and the risks associated with renal replacement therapies can affect long-term renal function and overall survival.

In the context of Saudi Arabia, it is essential to consider the specific healthcare infrastructure and patient population characteristics. With the growing prevalence of chronic diseases such as diabetes and cardiovascular conditions in the Saudi population, ICU interventions need to be tailored to address these comorbidities effectively. Additionally, the integration of evidence-based practices, such as the ICU Liberation Bundle, within the Saudi healthcare system can enhance patient outcomes by reducing the incidence of delirium, physical restraints, and ICU readmissions. The establishment of national databases to track ICU admissions and outcomes, similar to those in the UK and the US, would be invaluable in providing data-driven insights and improving the standard of care in Saudi ICUs.

By understanding the immediate and long-term impacts of ICU interventions, healthcare providers can develop more effective strategies to enhance patient recovery and quality of life, ultimately contributing to better long-term outcomes for ICU survivors.

- The ABCDEF bundle: Evidence based practices in the ICU include the assessment and management of pain, sedation, delirium, mobility (Devlin et al., 2018), and family engagement in care (Davidson et al., 2017). These practices have been delineated in the Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the ICU (PADIS), first initiated in 2013, and updated and expanded in 2018 (Devlin et al., 2018). The guidelines have been endorsed by American, Australian, Canadian, and European critical care nurse associations (Devlin et al., 2018). This evidence-based set of guidelines, rigorously instituted by professionals from three continents, stipulates the foundations for minimizing potential risks and maximizing better outcomes for critically ill patients (Devlin et al., 2018). For the purpose of enabling the implementation of these guidelines, the SCCM has established a pragmatic tool, the ICU Liberation Bundle, otherwise known as the ABCDEF bundle (SCCM, 2023) to be implemented in ICUs (**Figure 1.1**).

  When the ABCDEF bundle has been implemented in hospitals in a multidisciplinary approach and in quality improvement processes, it has been proven to decrease ICU stay, duration of mechanical ventilation, occurrence of delirium, and subsequent costs (Kram et al., 2015). It is undisputable that coordinated care using bundles of care or interventions have a role in enhancing outcomes of patients (Lavallée et al., 2017), and the ABCDEF bundle has provided sufficient evidence that its implementation reduces mortality and short-term morbidity (Mart et al., 2021). It has been therefore recommended to be used as the standard of ICU care (Olsen et al., 2012). An extensive elaboration of the evidence behind each item of the bundle is demonstrated below:

  The "**A**" element of the Bundle describes assessment, prevention, and management of pain. Recognizing the inherent difficulties of assessing pain in predominantly mechanically ventilated or sedated patients in the ICU, the bundle advocates for a stepwise approach of first seeking self-report of pain, followed by alternatives such as considering behavioural changes and asking proxies to identify such behaviours, and finally, if all not possible, assuming that pain is present (SCCM, 2023). For adult ICU patients, the use of behavioural pain scale (BPS) and Critical Care Pain Observation Tool (CPOT) have been

recommended (Gelinas et al., 2013; Nordness et al., 2021). One of the core preventive measures for pain is identified to be nurses' diligence during routine nursing procedures and interventions, as such nursing acts have been recognized to be a source of pain (Puntillo et al., 2014). Such interventions have been recommended to be treated with prior analgesics and non-pharmacological methods (Barr et al., 2013).

The "**B**" element of the Bundle integrates both SATs and SBTs. Effective liberation from the ventilator in interdisciplinary and coordinated efforts by daily cessation of sedation and assessment of patients' breathing efforts reduces the number of mechanical ventilation days, which in turn reduces the occurrence of delirium and length of ICU stay (Girard et al., 2008). Additionally, the routine assessment of sedation levels using the RASS tool (Ely et al., 2003) and the application of the "Wake up and Breathe Protocol" (Crookes et al., 2022) have been recommended to enable the efficient and safe practices of awakening and breathing of ICU patients.

The "**C**" stands for the choice of analgesic and sedation medications (SCCM, 2023). The use of intravenous opioids, titrated to pain levels, and accompanied by non-opioid alternatives, have been recommended, with special considerations to opioid-induced adverse effects and complications. In regard to sedation, light, propofol or dexmedetomidine-induced sedation has been recommended (Hughes et al., 2021), to reduce ventilator (Carson et al., 2006) and delirium days (Pandharipande et al., 2007).

The "**D**" element of the ABCDEF bundle refers to assessment, prevention, and management of delirium (SCCM, 2023). The short-term and long-term effects of ICU delirium are deleterious to patients, and as such using screening tools such as the Confusion Assessment Method for ICU (CAM-ICU) or Intensive Care Delerium Screening Checklist (ICDSC) have been advocated (Devlin et al., 2018). For effective preventive and management strategies for delirium, the memory-aide "Stop, THINK, and lastly medicate" has been recommended, to first identify aetiologies behind the delirium, then apply non-pharmacologic interventions, and lastly consider medications (SCCM, 2023). The non-pharmacologic aspect has been described with several elements, such as removing catheters as soon as their use is not indicated, optimal nutrition, and hydration.

Furthermore, conducting daily and routine orientation of patient to the ICU environment, having family and familiar objects around the patient, providing visual or hearing aids for those patients who need them, enhancing sleep at night and exposing to daylight during the day, and maintaining an ICU diary have been incorporated. Although strong evidence behind these interventions in the ICU setting could not be attributed to short-term and long-term outcomes, these could be considered as best practices and benefits of exercising them may greatly outweigh their potential risks. The only non-pharmacological modifiable factor that has been systematically evidenced to protect patients from delirium is early mobilization in the ICU (Schweickert et al., 2009; Vasilevskis et al., 2012).

The "**E**" element in the ABCDEF bundle refers to early mobilization. This modality of care remains the cornerstone for the efforts in early rehabilitative measures in the ICU. In addition to the physical benefits of muscle strengthening and developing stamina, early mobilization has been evident to reduce duration of ventilator days and functional disability at discharge (Bailey et al., 2007; Schweickert et al., 2009). In the Liberation of ICU bundle, specific mobility steps and considerations have been elaborated with patient safety in mind (SCCM, 2023). Incremental increases in movements, passive in the beginning, and then active mobility in varying degrees later, are safe and feasible to be conducted in the ICU (Bailey et al., 2007, Morris et al., 2008). Barriers to engage healthcare providers to adopt these practices have been identified to include lack of training and availability of staff, inaccessibility of mobility equipment, and prohibitive unit culture (Babazadeh et al., 2021; Dub et al., 2016). It is strongly recommended that critical care leaders in organizations exert efforts to reduce these barriers and to strive for a culture of mobility in a supportive and rewarding environment.

Finally, the "**F**" element, that denotes family engagement and empowerment, advocates for family presence, involvement, and activation at the point of care (SCCM, 2023). Nurses, being at the critical point of juncture between the patients' families and the ICU, have a vital opportunity to identify key family members, utilize personal, social, and cultural information provided by family, and engage them in goal setting during the patient's critical illness. They can also enhance the presence of family by enabling flexible visitation, family conferences, and provision of resources to families (Davidson et al.,

2017; SCCM, 2023). As critical care nurses may often be preoccupied with day-to-day clinical priorities of patients, a good initiative would be for ICU nurse leaders to provide time and resources for their teams to assess their culture of family engagement and identify strategies to enhance it. Davidson and colleagues have provided a practical tool to conduct a gap analysis and identify priorities and barriers in fully implementing family-centred approaches in the ICU (Davidson et al., 2017). This tool (**Appendix 1.2**) can facilitate discussion among team members and help systematically overview the current ICU practices related to families. Its use is also suggested to help in the development of a practical set of actions, tailored to the specific local ICU environment, and implementation of the Guidelines for Family-Centred Care (Davidson et al., 2017; SCCM, 2023).

The ABCDEF bundle's comprehensive approach directly impacts long-term outcomes by addressing critical aspects of ICU care that extend beyond immediate survival. Effective pain management, reduced delirium incidence, and early mobilization contribute to better physical and cognitive recovery, reducing the risk of PICS. Implementing the bundle has shown to improve long-term functional status, quality of life, and decrease healthcare costs associated with prolonged ICU stays and readmissions.

In Saudi Arabia, where ICU practices and patient outcomes can vary significantly, the implementation of the ABCDEF bundle can standardize care and improve long-term outcomes for critically ill patients. Given the increasing burden of chronic diseases and trauma cases in the region, adopting evidence-based practices such as the ABCDEF bundle can enhance the quality of ICU care. Training and resources could be allocated to ensure healthcare providers are equipped to implement these practices effectively, ultimately benefiting patient outcomes and healthcare systems across the Kingdom.

Figure 1.1. ABCDEF Bundle. (Adopted from SCCM website, 2023, https://www.sccm.org/iculiberation/abcdef-bundles).

1.4.6. The ICU setting, environment, and organization of care:

Case presentation 1.4.6 The patient HK remained in the ICU for 5 days. He received care in a private, single-bed, room. His care was led by the primary intensivist of the unit and the care was provided by the nurse in a 1:2 nurse to patient ratio. The family was informed of the patient's condition and his response to treatment and was encouraged to spend time at the patient's bedside.

The ICU design and how the care is organized greatly influence the patient/family experience and outcomes.

1.4.6.1. ICU design:

The full description of the optimal adult ICU design is beyond the purpose of this paper and certainly ICUs may differ based on location and culture, however due to the global nature of the care provided, a few best design practices will be mentioned here.

Evidence shows that the physical environment of a healthcare setting shapes the experience of those who encounter it and impacts the processes of care and patient outcomes (Ferri et al., 2015). The optimal goal of an ICU design is to cater for a healing environment, which is defined by measurable improvements in the physical and psychological wellbeing of patients, families, and caregivers (Hamilton et al., 2010). This environment should consist of materials and floor plans that consider several elements such as reduction of noise levels and support of infection control. Furniture, equipment, and other features that may enhance effectiveness and efficiency of patient care and minimize workplace injury should also be well chosen. Stress-alleviating features that incorporate daylight and views of nature, and mindful provisions of material and colours that promote the comfort of patients, families, and staff should be integrated (Donchin et al., 1995; Ulrich et al., 2000; Ulrich et al., 2008). Literature shows that evidence-based ICU designs can help improve outcomes, reduce errors, decrease length of stay and costs, and enhance family engagement and social support for patients (Hamilton et al., 2010; Ulrich et al., 2004).

A. **General unit layout**:

In its latest edition of Guidelines for Design and Construction of Hospitals, the Facility Guidelines Institute (FGI) provides descriptions of design standards and codes for healthcare settings (FGI, 2018). These include prescriptive standards for appropriate ICU floor plans, square footage, unit access modes, and safety risk assessment approaches (infection control, patient transport, fall prevention, medication safety, and others). Other features such as acoustics, wayfinding, lighting, lab and pharmacy services, waste management, medical gas, electrical outlets, and other features of a critical care unit have also been described. Many members in the critical care society have been participants in the guideline development and revision (Thompson et al., 2019)

Traditionally, ICU designs have been characterized by the use of paper medical records, and central monitors and workstations from which all beds within the unit can be observed. However, these conditions have changed over time. In modern times, technology and information systems allow communication at multiple places at the same time, care is provided in multidisciplinary teams, work processes have changed, nursing has moved closer to the patient, families are encouraged to be more engaged in patient care, and overall functions that had been centralized have become decentralized (Thompson et al., 2019).

It is now recommended that the overall ICU space be small enough for caregivers to be aware of all activities on the unit and to be able to observe the patient from many points, yet large enough to comfortably accommodate the patients, their families, the healthcare team, and the equipment used in the care (Teltsch et al., 2011). Direct visualization of the patient is paramount. Staff should be able to easily see the patient's face and body from the decentralized work areas and through the ICU corridor. Poor visualization of patients by ICU staff is associated with patient mortality (Leaf et al., 2010).

B. **Patient care zone**: Ideally, each patient should be cared for in a single-bed room for better patient safety and privacy (Cepeda et al., 2005; Chaudhury et al., 2005; Chaudhury

et al., 2006; Harris et al., 2006; Teltsch et al., 2011). Enclosed rooms have been shown to enhance quality of sleep (Gabor et al., 2003). Each bed needs access from all sides to allow patient assessment and treatment and effective and reliable implementation of infection control measures. Each room should have a sink and materials should be easy to clean to prevent the growth and spread of pathogens (Carling et al., 2010). Built-in mechanical lift devices incorporated into the ceiling or access to mobile lifts enhance both patient and staff safety (Evanoff et al., 2003; Li et al., 2004).

To create a personalized environment for patients and families, rooms should include a clock to prevent patient confusion, and surfaces should be provided where greeting cards and photos could be posted. Whiteboards should also be provided to allow patients and their families to be aware of their care team. Critically ill patients often suffer from delirium and evidence suggests that abstract art or geometric images should be avoided in patient care rooms (Thompson et al., 2019). For ICU patients, who spend most of their time in bed, the ceiling is most often what they see; thus, incorporating images and positive distractions into ceilings is desirable (Thompson et al., 2019). A source of natural daylight is essential for patient and staff wellbeing. There is evidence that patients exposed to natural sunlight perceive less stress and less depression, they use fewer analgesics, and have improved sleep quality and quantity (Olofsson, 2004; Ulrich et al., 2004; Walch et al., 2005,). Views to the outside may help relieve anxiety and stress, enhance comfort, and improve patient orientation (Ulrich et al., 2008).

C. **Family zone**: The presence of family of the critically ill patient has been recognized to have a significant role in recovery and reduced mortality (Page, 2016). Families may be given accommodation in designated areas inside or near the unit, inside patient rooms, or in some combination of the two. These spaces should be mindfully designed and coordinated for appropriate furniture, storage, colour palettes, artwork, daylight, privacy, and other calming features (Thompson et al., 2019). Consultation or family education/conference rooms should also be readily available inside or near the ICU.

D. **Staff zone**: Regarding staff support spaces, ICU unit design should accommodate for workstations, and multidisciplinary rounding and team conference areas. Having a large

number of caregivers in these rounds and the use of mobile devices such as computers on wheels, can create increased level of noise, therefore careful considerations should be given to unit layout (Anderson et al., 2016). Medication preparation and dispensing can be performed in either a centralized or decentralized fashion. In either way, space designs should consider reducing interruptions and noise, and providing proper lighting in order to reduce medication errors (Anderson et al., 2016). Staff support areas should also consider on-call rooms, staff lounges, lockers, and other support functions.

E. **Noise**: ICUs have been found to have noise levels above recommended decibel levels (Blomkvist et al., 2005; Hagerman et al., 2005; Jastremski et al., 1998). Increased noise levels can disrupt sleep and increase perception of pain in critically ill patients (Hagerman, 2005). Conversations, alarms, movement, and other unit activities are often disturbing to patients (Walder et al., 2000; Monsén et al., 2005). Eliminating voice paging systems by alternatively using personnel tracking systems can reduce noise and possibly stress levels (Konkani, 2012).

F. **Technology:** ICUs are differentiated from general wards by their ability to perform continuous monitoring of patient physiologic parameters. Invasive and non-invasive monitoring has been described in a previous section in this review. Staff should have access to continuously displayed patient data so that trends are identified, and interventions instituted in a timely manner. Other uses of technology such as bar coding, pneumatic tube system, laboratory processing, handheld and wireless devices, and others should be counted for (Thompson et al., 2019).

G. Relationship between ICU Design and Long-Term Outcomes of Patients

- Impact on Patient Recovery: The optimal design of ICU environments, focusing on factors like reduced noise levels, infection control measures, and stress-alleviating features such as natural daylight and views of nature, can significantly impact patient recovery. Studies suggest that a healing environment can contribute to improved psychological well-being, reduced stress, and potentially better long-term outcomes for ICU patients (Hamilton et

al., 2010; Ulrich et al., 2004).

- Patient Safety and Privacy: Single-bed rooms with easy access for patient assessment and infection control measures are crucial for patient safety. Enhanced privacy and reduced exposure to pathogens can potentially lower the risk of infections, which can influence both short-term recovery and long-term health outcomes (Carling et al., 2010).

- Family Engagement and Support: Design elements that facilitate family zones and accommodation near ICU units can enhance family engagement in patient care. Research indicates that family involvement can positively influence patient outcomes, including reduced mortality rates and improved long-term recovery prospects (Page, 2016).

- Staff Efficiency and Care Quality: Effective ICU design that includes decentralized work areas, supportive staff zones, and technology, can improve workflow efficiency and reduce stress among healthcare providers. This setup may contribute to better care coordination and adherence to protocols, potentially impacting patient outcomes over the long term (Thompson et al., 2019).

H. Cultural Considerations in Saudi Arabia:

In Saudi Arabia, it is essential to consider cultural norms and preferences in the design of healthcare facilities, including ICUs. For example, incorporating elements that respect Islamic culture, such as privacy considerations for both patients and families, and ensuring appropriate gender segregation where necessary, are crucial. Integrating Islamic cultural values of privacy and modesty in patient care settings can also enhance patient and family satisfaction, which may indirectly influence long-term recovery outcomes.

In Saudi Arabian cultures, family involvement and support for the hospitalized patients are highly important. For example, the Saudi "care partner program" is a culturally ingrained practice where family members are often expected to stay with patients during their

hospital stay to provide care and support. This program, which consists of identifying a family member to be actively engaged in the care of hospitalized patients, is practiced in most healthcare settings and ICUs. Family members wear a wristband to be identified, and assist with basic care needs, provide emotional support, and often act as intermediaries between the patient and healthcare providers. This program highlights the important role of family in patient care, reflecting the deep-rooted values of family solidarity and responsibility in Saudi society. As this program offers significant emotional and practical benefits to patients while in the hospital, it also presents opportunities for family engagement in the post-ICU setting, particularly in the context of critical care transitions where family support is crucial for ensuring optimal long-term outcomes. Integrating professional post-ICU care models with this culturally significant partnership program could enhance patient recovery and long-term health outcomes in Saudi Arabia.

1.4.6.2. The intensive care team:

Intensive care is delivered by a specialized and skilled interprofessional team. The care provided in the ICU is more intensive than other areas of the hospital, because of the nature of acuity of patient conditions, close interaction between healthcare providers, and close observation and immediate interventions for the patient (Marshall et al., 2017). Ideally, members of the team should have advanced specialty qualifications and experience in intensive care medicine. In addition to staff nurses, nurse practitioners, and physicians, team members may include other professionals as well. These may include respiratory therapists who manage ventilation, physiotherapists who support mobility and rehabilitation, a nutritionist skilled in the enteral and parenteral feeding needs of complex patient populations, a pharmacist with particular knowledge and expertise in pharmacology used in the ICU and optimal dosing in the critically ill patient, a microbiologist to assist with the diagnosis and management of infection, and a social worker and spiritual care services who can support patients and families during a time of crisis (Marshall et al., 2017).

The expertise of the team is not confined to their clinical knowledge and patient management skills, but it extends to the support of the family and the provision of compassionate care at the end of life, and this team if often characterized to be working in

physically and emotionally challenging environments (Ervin et al., 2018).

A. **Physician staffing**: A "closed ICU" model is characterized by an intensivist being primarily responsible for the management of the ICU patient, while an "open ICU" is managed by a primary physician with access to elective consultation to an intensivist. An abundant amount of evidence points to the superiority of "closed ICUs" in terms of outcomes (Gajic et al., 2009; Haupt et al., 2003; Manthous, 2004; Pronovost et al., 2002; Pronovost et al., 2006). A systematic review and meta-analysis of ICU physician staffing models has showed that when compared with low-intensity staffing (open ICU), the high intensity model (closed ICU) was associated with lower hospital and ICU mortality (Wilcox et al., 2013). In addition, patients receiving care under the intensivist staffing model were more likely to receive evidence-based care for deep vein thrombosis and stress ulcer prophylaxis, in addition to spontaneous breathing trials (Kahn et al., 2007). The evidence supporting 24/7 intensivist staffing in the ICU has not been substantial in terms of reducing mortality and other beneficial outcomes such as family satisfaction, and the practice has not been widely adopted because of staffing, feasibility, and cost issues (Nates, 2016). The utilization of nurse practitioners and physician assistants, and telemedicine have been considered to be feasible alternatives (Gajic et al., 2009; Gershengorn et al., 2011).

B. **Nursing staffing**: The topic of nursing staffing in relation to patient outcomes is an intricate one and has been a matter of serious consideration for over several decades. In its largest scale of examining nursing staffing ratios and patient outcomes, The RN4CAST project has generated two decades of global nursing-outcomes research and has been successfully implemented in 30 countries (Aiken et al., 2018). Over 70 scientific papers were published from the RN4CAST-EU study in leading nursing and interdisciplinary journals, making it "*the most productive study ever funded by the European Commission*" (Aiken et al., 2018, p.322). The following are key points or findings from all RN4CAST studies:

- Across all countries studied, significant associations have been found between lower patient-to-nurse ratios and lower risk-adjusted mortality (Aiken et al., 2018; West et al., 2014). Two systematic reviews have confirmed this finding (Kane et al., 2007; Shekelle et al., 2013).

- Each one patient added to a nurse's workload is associated with a 7% increase in risk-adjusted mortality following general surgery (Aiken et al., 2018).

- Hospitals with the best nurse staffing had 30% fewer HAIs than hospitals with poor nurse staffing, taking into account patient risk factors and characteristics of hospitals such as size, technology, and teaching status (Aiken et al., 2018).

- Every one additional patient added to nurses' workload is associated with a 6-9% increase in readmissions for patients with pneumonia, heart failure, and acute myocardial infarction (McHugh et al., 2013); 8% increase in readmissions after hip and knee replacement (Lasater, 2016); 3% increase in readmissions after general surgery (Ma et al., 2015). About half of the nurses reported rationing complete discharge planning and patient teaching in this scenario (Ma et al., 2015).

- Every 10% increase in the proportion of professional nurses among all nursing care personnel was associated with 11% lower odds of mortality after general surgery and 10% lower odds of poor hospital ratings from patients (Aiken et al., 2018).

- In hospitals with a higher proportion of professional nurses, adverse patient outcomes (pressure ulcers, falls with injuries, and urinary tract infections) occurred significantly less frequently (Aiken et al., 2018).

- Most adverse patient outcomes substantially increase the overall per patient cost of care in terms of needing additional surgical procedures, more diagnostic testing, more use of expensive drugs and supplies, more days of intensive care, and longer lengths of stay in addition to pain and suffering for patients (Dall et al., 2009).

- Considerable variations were found in patient-to-nurse ratios across hospitals within the same country (Aiken et al., 2018).

The results of this research program have been influential in changing clinical practice, and organizational and governmental policies in many countries, such as US (California), Australia (Victoria and Queensland), Ireland, and Wales, where safer nursing staffing regulations were adopted based on the findings of these studies (Aiken et al., 2018). In addition, Magnet hospitals in the US have set a target to achieve at least an 80% bachelor's educated nursing workforce based on this study (ANCC, 2023), and the European Parliament approved a bachelor's pathway for nurse education for the first time to enhance the educational background of nursing (Aiken et al., 2018).

It is worth mentioning that nurse staffing ratios do not only affect patient outcomes, but they also affect nurse outcomes. In a recent systematic review, worse nurse staffing was associated with adverse nurse outcomes such as high burnout, fatigue, emotional exhaustion, depersonalization, and stress (Bae et al., 2021).

In Saudi Arabia, optimizing nurse staffing levels could potentially improve long-term patient outcomes by mitigating complications and enhancing quality of care delivery. Implementation of evidence-based staffing standards, as seen in global initiatives influenced by RN4CAST findings, could be beneficial in Saudi Arabian healthcare settings, ensuring better patient recovery and reduced readmission rates. These staffing considerations are not only crucial for improving clinical outcomes but also for addressing the well-being of healthcare providers, mitigating burnout, and ensuring sustained quality care delivery in Saudi Arabia's evolving healthcare landscape.

C. Other considerations related to the critical care team:

Clinical psychologists play a unique role in addressing patients' and their families' psychological wellbeing and recovery. Research shows that patients who receive care by a clinical psychologist in the ICU have lower rates of anxiety, depression, and post-

traumatic stress (Novoa et al., 2006).

Case presentation 1.4.6.3 During the five days spent in the ICU, the patient HK was successfully treated for his pneumonia and multi-organ failure was prevented. He was weaned off the sedation and mechanical ventilation by the third day. In the afternoon of the third day, he demonstrated signs of delirium, however after several trials to re-orient the patient to time, place, and the conditions he was in, he was assisted to start early mobilization, and by the nightfall of the third day the patient slept well and delirium signs subsided. Complications of ICU stay, such as HAIs, did not occur and the patient was planned for transfer to the medical ward.

1.4.6.3. Mortality and cost:

While overall mortality in hospitalized patients is reported to be less than 5%, 10% to 29% of patients die after admission to the intensive care unit (ICU), depending on age, comorbidities, and severity of illness (Coopersmith et al., 2012; Nates et al., 2016). Mortality may exceed 50% in cases of sepsis and acute respiratory distress syndrome, which are the severe forms of critical illness (Institute of Medicine, 2001; Kohn et al., 2000). The 10-year mortality for ICU survivors is greater than those of the same age who have never been admitted to the ICU (SCCM, 2022).

In the US, the leading causes of ICU death are sepsis and multiorgan system failure. Sepsis affects more than 1.7 million people with a mortality of around 16% (SCCM, 2022). It is also the major cause of readmissions to the hospital within 30 days. Of patients who are diagnosed with sepsis, up to 51% develop acute renal failure, and up to 20% have acute respiratory failure requiring mechanical ventilatory support. Length of stay in the ICU has been estimated at 3.8 days in the US. However, it varies depending on patient and ICU attributes (SCCM, 2022). In 2008, the estimated cost of critical care in the US ranged between $121 and $263 billion (approximately between 100 to 220 billion pounds), reaching up to 38% of hospital costs and 11 % of national healthcare expenditures (Coopersmith et al., 2012).

According to the Intensive Care National Audit and Research Centre (ICNARC) 2019-2021 report on Key Statistics for the Case Mix Programme in the UK (ICNARC, 2022), ICU mortality ranged between 14 and 18% with a hospital mortality of 19-24%. Similar to the US, the leading cause of death was sepsis with a high mortality of 26-33%. Patients spent on average 5-9 days in the ICU. Cost data is not available.

As discussed, ICUs play a crucial role in managing critically ill patients, with mortality rates varying widely depending on factors such as age, comorbidities, and the severity of illness. Research indicates that ICU mortality rates can range from 10% to 29%, with higher rates observed in cases of severe conditions like sepsis and acute respiratory distress syndrome (Coopersmith et al., 2012; Nates et al., 2016). In Saudi Arabia, while specific data on ICU mortality and leading causes of death are not readily available, similar patterns are likely observed due to the global nature of critical care practices.

In the US, sepsis and multiorgan system failure are cited as leading causes of ICU mortality, highlighting the critical need for effective management strategies in these conditions (SCCM, 2022). The financial burden of critical care is also substantial, with estimates indicating that ICU costs can constitute a significant portion of healthcare expenditures in developed countries like the US (Coopersmith et al., 2012). While data specific to Saudi Arabia's ICU mortality and cost profiles are lacking, understanding these global trends can inform local healthcare strategies and resource allocation in the Kingdom.

This contextualization ties the global ICU mortality trends and cost implications to the research aim of investigating long-term outcomes among ICU patients, while acknowledging the need for localized data in Saudi Arabia.

1.4.6.4. Transition from ICU to ward:

Case presentation 1.4.6.4 The patient was transferred to the medical ward. The nurse provided hand over verbally and by a written note in the patient’s electronic medical record. The emphasis was put on monitoring temperature and breathing patterns. Continuing ambulation in the ward was also highlighted to the ward nurse and to the patient and family.

An automatic follow up appointment to the primary care doctor's clinic was set in the electronic health system and the patient and family were informed that they will be reminded of the visit date two days prior to the appointment.

Most patients transition to general wards after their critical illness has been stabilized and the need for close monitoring has subsided. This transitional period is critical for patients in terms of continuity of care and follow-up, and modern critical care teams should consider innovations regarding the care needed for patients in care-transitions. ICU consult teams have been utilized to assist ward staff in the management of deteriorating patients and reduce rates of readmission to ICU (National Guideline Centre, 2018). A model used in Australia and in the UK, where an ICU liaison nurse assisted in the transition of patients from the ICU to the ward and acted as a member of the rapid response team, has demonstrated a significant impact in preventing ICU readmissions (Eliott et al., 2012) and decrease in discharge delays (Chaboyer et al., 2006; Mellinghoff et al., 2012). In addition, prevention of adverse events (Endacott et al., 2010), decrease in unplanned ICU admissions/readmissions (Endacott et al., 2009; Green et al., 2004; National Guideline Centre, 2018), and reduced mortality rates (Priestley et al., 2004) have been achieved with this model. In addition to patient outcomes, ward staff has also reported positive experiences and perceptions of the ICU liaison role (Baker-McClearn et al., 2008). The liaison nurse also provided support and education for patients and families who had been recently discharged from the ICU (Endacott et al., 2009). Although this role is a recognized clinical service role in Australia, further robust research is needed to relate it to patient outcomes after hospital discharge. This role could potentially be instrumental in identifying and following up on patients who demonstrate risk for developing post-intensive care syndrome, and act as a resource person for patients and families after hospital discharge.

In Saudi Arabia, as in many countries, the transition of ICU patients to general wards represents a critical phase impacting their long-term outcomes. This transitional care period is pivotal for ensuring continuity of care and minimizing adverse events post-discharge. In the Saudi healthcare context, where there is a growing emphasis on improving critical care services and patient outcomes, adopting and further researching transitional care models could be instrumental. Establishing robust protocols for post-ICU care transitions, supported

by trained ICU liaison nurses, could enhance patient follow-up, support families during the recovery process, and contribute to better long-term outcomes for ICU survivors in Saudi Arabia. This approach aligns with global efforts to optimize ICU patient care beyond the acute phase, addressing the specific needs and challenges within the Saudi healthcare system.

1.5. Long-term outcomes:

Case presentation 1.5 The patient followed up with his primary care doctor after one week of hospital discharge. Information about the ICU admission was accessible to the doctor from the medical record. The discharge note indicated the treatment of pneumonia in the ICU and the need for monitoring of the patient for the risk of recurring infections. No data was recorded regarding the patient's abilities to conduct activities of daily living, and cognitive and psychological status upon discharge from the ICU. The primary doctor evaluated the patient for his pulmonary status by auscultating his lung sounds and ordering a follow-up x-ray. The patient complained of difficulty in sleeping because of intrusive memories of severe breathing difficulties and suffocation. The patient was reassured. No formal assessments were done at this point to evaluate the patient's abilities in conducting activities of daily living, cognition, mental wellbeing, and HRQoL, and no further referrals for rehabilitation were made.

Survival rates from intensive care have improved over time (Zimmerman et al., 2013). Better understanding of the nature of critical illness and the technology used in assessment and immediate intervention have led to a decline in mortality for conditions such as sepsis and acute respiratory distress syndrome over the past two decades (Iwashyna et al., 2012; Martin et al., 2003). A significant number of patients survive their critical illness to hospital discharge (Wunsch et al., 2010). As with other serious illnesses, such as those studied in cancer (Mullan, 1985), survivors of critical illness can encounter profound changes in their lives due to their illness and hospitalization experience.

As described in the introductory section of this chapter, the long-term outcomes of intensive care therapy have been defined as new or worsening impairments in three main domains: physical, cognitive, and/or psychological, collectively known as PICS (Needham et al., 2012).

Problems in these areas arise after critical illness and may persist for a long time after discharge from the acute care setting (Rawal et al. 2017). Family members may also suffer with depression and other emotional problems. This is recognized as PICS-Family (PICS-F). Families may experience acute and chronic psychological morbidity, including symptoms that are experienced during the critical illness as well as those that occur following death or ICU discharge of a loved one (Davydow et al., 2012; Sullivan et al., 2012). For survivors, these physical, mental, and cognitive morbidities are frequently severe, adversely affect an individual's functioning (e.g., employment and quality of life), and may persist for months or years after hospital discharge (Barnato et al., 2011; Ehlenbach et al., 2010; Herridge et al., 2011; Iwashyna et al., 2010; Needham et al., 2014).

The following is a brief synthesis of current evidence focusing on the three domains of PICS long-term outcomes: Physical, cognitive, and psychological. In each domain, a preliminary review of the prevalence, predictors, and risk factors of these disturbances will be discussed, highlighting gaps in the literature.

1.5.1. Physical disability:

It has been reported that the major physical impairment after critical illness occurs in the form of neuromuscular weakness (De Jonghe et al., 2002; Herridge et al., 2003; Stevens et al., 2007). An expert consensus recommended the use of the term ICU-Acquired Weakness (ICUAW), defined as "*diffuse, symmetric, generalized muscle weakness (detected by physical examination and meeting specific strength-related criteria) that develops after the onset of critical illness without other identifiable causes*" (Stevens et al., 2013 p.30).

Within the definition of ICUAW, this consensus framework identifies the components of ICUAW as "critical illness polyneuropathy (CIP)" and "critical illness myopathy (CIM)", which are primarily based on electromyography and nerve conduction studies (Stevens et al., 2007). Both CIP and CIM usually present as flaccid and symmetric paralysis, as well as lower limb and respiratory muscle weakness (Zhou et al., 2014). The term critical illness neuromyopathy is recommended for patients with coexisting CIP and probable or definite CIM. The pathogenesis of CIP and CIM is complex, involving alterations in microcirculatory, metabolic,

and electrical levels, as well as bioenergetic failure (Zhou et al., 2014).

ICUAW has been reported to occur in 25-90% of ICU patients even if patients were fully independent at baseline (Fan et al., 2014; Jackson et al., 2014; Marra et al., 2018; Needham et al., 2014). However, these studies have been widely heterogenous in terms of methodology, sample size, and mode of evaluation of ICUAW. Other studies have reported that the physical weakness after ICU results in problems with mobility, falls, and ADLs (Fan et al., 2014; Iwashyna et al., 2012). One multicenter study in UK reported that 64% of ICU survivors had problems with mobility at six months; 73% reported moderate or severe pain; and one quarter of patients reported themselves in need of care for more than 50 hours per week, the majority of which was provided by family members (Griffiths et al., 2004). Furthermore, a third of the patients were disabled in their activities of daily living (ADL), and another third were disabled in instrumental activities of daily living (IADL) at three months. Impairments in ADL and IADLs were prominent in those with and without pre-existing functional disability, and these impairments persisted in most patients when assessed at 12 months (Griffiths et al., 2013). Although this more recent study was a comparatively large study involving multiple sites, it carried significant risks for bias related to selection and recall. In addition, standardized instruments to measure outcomes were not used, making assessments inconsistent and generalization of outcomes inconclusive.

Research activities investigating predictors and risk factors of physical problems after ICU have found various factors to be associated with ICUAW, such as prolonged mechanical ventilation, immobility, prolonged ICU stay, sepsis, and the use of corticosteroids (Herridge et al., 2003; Latronico et al., 2005; Stevens et al., 2009). A systematic review by Stevens and colleagues has suggested that intensive glycaemic control might decrease the risk of ICUAW (Stevens et al., 2007), however this finding was not validated in other studies.

A systematic review and meta-analysis conducted by Yang et al (2022) aimed to identify and quantify risk factors for ICUAW from existing literature. Key findings from the analysis indicated that female gender (OR = 3.62, 95% CI: 1.79 to 5.44), mechanical ventilation days (OR = 6.33, 95% CI: 5.05 to 7.61), length of ICU stay (OR = 3.39, 95% CI: 1.76 to 5.03), and age (OR = 6.33, 95% CI: 5.05 to 7.61) are significant risk factors for ICUAW. The heterogeneity

observed across studies suggests variability in study designs and populations, affecting the consistency of findings. The sensitivity analyses conducted revealed that excluding studies with small sample sizes did not substantially alter the estimates, although some heterogeneity persisted. Factors like renal replacement therapy (OR = 1.59, 95% CI: 1.11 to 2.28) and infectious diseases (OR = 1.67, 95% CI: 1.20 to 2.33) were also identified as risk factors, with consistent literature findings supporting these associations. However, the use of corticosteroids and neuromuscular blockers did not show statistically significant associations with ICU-AW, indicating the need for further high-quality research to elucidate their roles. The study's limitations include potential publication bias, heterogeneity among studies due to differences in sample sizes and case selection, and the exclusion of gray literature. Despite these limitations, the review provides valuable insights into the multifactorial etiology of ICUAW and underscores the need for comprehensive clinical strategies to identify and mitigate these risk factors. Future research should focus on large-scale, multicenter studies to validate these findings and explore additional risk factors, ensuring a more robust understanding of ICUAW to inform clinical practice and improve patient outcomes. The study concludes with recommendations for healthcare providers to enhance early warning systems and interventions to prevent ICUAW, emphasizing the importance of early identification and risk stratification in critically ill patients.

Overall, more studies are required to delineate the risk factors associated with ICUAW and long-term physical disabilities. Further data is also needed to identify contributions of ICUAW to long-term outcomes, such as ADLs, functionality, and work-related reintegration in the months or years following the acute illness. Finally, the adoption of standardized and uniform diagnostic criteria and assessment tools are needed to enhance communication of assessments between clinicians and promote well-designed epidemiological studies (Stevens et al., 2007).

1.5.2. Cognitive dysfunction:

There is no widely adopted terminology for cognitive impairments after critical illness. They are commonly referred to as “long-term cognitive impairments” (Needham et al., 2012). The severity of cognitive impairment has been found to vary from mild to severe; from subtle

difficulties in accomplishing complex tasks to a profound inability to conduct one's daily activities. The most affected domain has been reported to be memory, followed by executive functioning and attention (Hopkins et al., 2005; Sukantarat et al., 2005). These problems prohibit individuals from engaging in purposeful, goal-directed behaviors which are necessary for effective daily functioning. For example, patients may find difficulty adhering to a discharge plan (compliance to medication regimen, dietary restrictions, scheduling and maintaining appointments, etc…), which in turn may further impair recovery. Impaired cognition may also contribute to communication difficulties, in addition to functionality such as returning to work (Pandharipande et al., 2013).

The pathogenesis of cognitive impairment after critical illness is complex and multifactorial. Possible mechanisms have been hypothesized such as ischemia, neuroinflammation, and disruption of the blood-brain barrier and white matter integrity in areas involving executive functioning and memory (Hopkins et al., 1999; Marra et al., 2018).

In the largest post-ICU cognitive impairment study, the BRAIN-ICU (Bringing to light the Risk factors And Incidence of Neuropsychological dysfunction in ICU Survivors), provided substantial information regarding the incidence and risk factors of cognitive dysfunction in ICU survivors (Ely et al., 2004; Girard et al., 2010; Pandharipande et al., 2013). Several publications have resulted from this study and the following is a summary of the findings:

- At baseline, 6% of ICU survivors had cognitive impairment.

- At 3 months post discharge, 40% had deficits that were similar to patients with moderate traumatic brain injury (TBI), and 26% had deficits that were similar to mild dementia.

- At 12 months post discharge, deficits persisted for most patients, and over one-third of ICU survivors (without pre-existing dementia) demonstrated new cognitive impairments resembling moderate to severe Alzheimer’s Disease and Related Dementias (ADRDs).

- Of people admitted emergently to ICU in respiratory failure or shock, 50-70% developed

delirium.

- The duration of delirium independently predicted earlier death, longer hospital stays, and higher healthcare expenses.

- Delirium in ICU patients was suggested to be the strongest potentially modifiable risk factor for development of long-term cognitive impairment.

Since the first BRAIN-ICU study, some developments have happened in this area with pilot neuroimaging (MRI) data showing that acute ICU delirium is associated with atrophy of the whole brain, frontal lobe, and hippocampus (Hopkins et al., 2012). Hence, a second BRAIN-ICU study has been undertaken to determine the "*main paths to decline, maintenance, or recovery of brain function*" in ICU patients (Ely et al, 2020). In the protocol of this study, it is explained that patients from the first cohort will be followed-up and new patients will be enrolled for complete cognitive testing of neuroimaging and cerebrospinal fluid sampling. The aim will be to reveal locations and mechanisms of injury in ICU patients beyond what has been shown in the first study. Furthermore, a partnership has been established with the Rush Alzheimer's Disease Research Centre brain bank program so that patients will be given the choice to donate their brains to science and further pathological studies. The ultimate purpose of this project is to gain knowledge that would develop interventions against ICU-related dementia (Ely et al., 2020).

Several other studies have been conducted in the cognitive domain of PICS. The reported prevalence of cognitive impairments has varied among studies, ranging between 30 to 80% (Brummel et al., 2012; Hopkins et al., 2006; Marra et al., 2018; Wolters et al., 2013). Some studies have investigated predictors of cognitive dysfunction and confirmed that duration of ICU delirium is strongly associated with decline in cognitive function (Davidson et al., 1999; Girard et al., 2010; Larson et al., 2007; Pandharipande et al., 2013). The type and dose of sedatives (Girard et al., 2007; Jackson et al., 2010) and duration of mechanical ventilation (Barr et al., 2013; Jackson et al., 2003) have also been identified as predictors. In one study, long term cognitive abilities were found to be better if sedation in the ICU was stopped on

daily basis for spontaneous awakening and breathing trials (Hopkins et al., 1999). Sepsis survivors have been found to be 3 times more likely to develop moderate to severe cognitive impairments, which have been found to persist until 2 years or more after ICU discharge (Pandharipande et al., 2013).

Other predisposing conditions have also been hypothesised to have an association with cognitive impairments. These include: acute brain dysfunction (e.g., alcoholism, stroke), hypoxemia (e.g., ARDS, cardiac arrest), hypotension (e.g., sepsis, trauma), glucose dysregulation, respiratory failure (e.g., prolonged mechanical ventilation, chronic obstructive pulmonary disease [COPD]), congestive heart failure, cardiac surgery, obstructive sleep apnea, blood transfusions, and use of renal replacement therapy (Girard et al., 2010; Larson et al., 2007).

Patients who are at higher risk to develop cognitive impairments have been reported to be those with pre-existing cognitive deficit, poor cognitive reserve prior to critical illness, and high disease-severity index at admission. Conversely, attaining a higher level of education (i.e. cognitive reserve) has been associated with a greater likelihood of being PICS-free at 3- and 12-months (Barr et al., 2013). These findings pose an important foundation for more studies to be conducted in this area to establish the causality and risk related to cognitive impairments.

The systematic review conducted by Wolters et al (2013), according to the Institute of Medicine's 2011 standards, has aimed to summarize evidence on long-term cognitive impairment in ICU survivors. A comprehensive search of multiple databases from January 1980 to July 2012 identified 1,664 publications, with 19 articles meeting the selection criteria. These studies varied in sample size, follow-up duration, and cognitive assessment methods, with most involving young ICU survivors and a few focusing on the elderly. The incidence of cognitive impairment ranged from 4% to 62%, with studies using extensive neuropsychological tests reporting higher rates. The most frequently impaired cognitive domains were memory, attention, verbal fluency, and executive functioning. The review found significant variations in study designs and methods, preventing pooled data presentation and highlighting the complexity of defining cognitive impairment. Cognitive

impairment in ICU survivors is likely multifactorial, involving factors like multi-organ failure, neuroinflammation, hypoxemia, hypotension, and medication effects. Future studies should standardize cognitive impairment definitions and adjust for premorbid cognitive status to improve long-term outcomes after ICU admission. The review underscores the need for standardized definitions and assessment methods for cognitive impairment, awareness among clinicians, and early interventions like mobilization programs. Given the growing use of ICUs and the aging population in Saudi Arabia, these findings are particularly relevant for improving long-term outcomes and reducing healthcare costs. Further research in the Saudi context is essential.

A more recent scoping review by Alrø (2023) investigated the long-term cognitive challenges faced by patients who have survived critical illnesses and were treated in intensive care units (ICUs). Through a systematic review of 11 qualitative and quantitative studies, the research identified four key themes: experiencing poor memory, managing everyday life, feeling unsupported by the healthcare system, and employing strategies for recovery support. The findings highlighted that cognitive impairments significantly disrupt patients' quality of life, necessitating various coping mechanisms to regain independence. However, the study also revealed a profound sense of abandonment by the healthcare system, which failed to provide adequate support post-discharge. The study's strengths lied in its comprehensive literature review and thematic analysis, offering valuable insights into patient experiences. Nevertheless, it was limited by the heterogeneity of included studies and potential publication bias.

Although, as described, many efforts have been made to understand the cognitive aspect of PICS over the past several years, strong evidence that synthesizes the predictors, risk factors, and mechanisms of cognitive impairments remains lacking. To be able to discern “new impairments” in cognition, as described in the PICS definition, it is important to design longitudinal studies that control for the presence of pre-existing cognitive diseases. And to be able to identify “worsening impairments”, it is important to establish baseline cognitive function. The lack of both concepts is the major limitation in most of the above-mentioned literature. Establishing baseline cognitive impairments is very challenging in patients admitted in ICU as they may not be in a condition to be assessed cognitively (e.g. on mechanical

ventilation or sedation), or they may not be able to give an accurate report of prior cognitive difficulties. In this case, the report of proxies and their assessment of the patient's cognitive status prior to ICU admission may be helpful. More on proxy reports will be described in the methods section.

1.5.3. Psychological morbidity:

The psychological aspect of PICS has also received attention in the literature. Prevalence of clinically significant depression and PTSD is reported up to 33% and 22% of post-ICU patients respectively, and prevalence of anxiety has been reported to reach 48% (Davydow et al., 2008; Davydow et al., 2009; Marra et al., 2018). Depression is found to be four times more prevalent than PTSD (Jackson et al., 2014; Marra et al., 2018).

Depression, mostly in the form of somatic complaints, has been reported to persist for a year after ICU discharge, both in young and older patients. Patients with symptoms of depression have been reported to complain of fatigue, loss of interest, poor appetite, sense of hopelessness, and insomnia (Jackson et al., 2014; Marra et al., 2018). In these patients, ssymptoms suggestive of PTSD included affective and behavioral responses to stimuli, flashbacks, hyperarousal, and delusional memories (Jackson et al., 2014; Marra et al., 2018). Problems with intrusive recollections and avoidance of experiences that evoke memories have also been reported (Jackson et al., 2014; Marra et al., 2018). The most common symptoms of anxiety have been reported to include excessive worry, irritability, restlessness, and fatigue (Pattison et al., 2009).

Predictors of long-term psychiatric morbidity and those who may be at higher risk of developing it have been investigated in the past. Predictors have been reported to include presence of prior psychiatric disease (Long et al., 2014; Schandl et al., 2013), sleep deprivation, and prolonged mechanical ventilation (Jubran et al., 2010). Those at greater risk have been found to be the elderly with chronic diseases, women, the unemployed, and those with lower educational and socio-economic status (Eisendrath et al., 2006; Wade et al., 2012). However, as in the case of the investigation of cognitive disabilities, most longitudinal studies have not controlled for the presence of pre-existing psychiatric diseases to be able to discern

"new impairments" of mental health, and baseline mental health assessments in ICU have not been done to identify "worsening impairments".

1.5.4. Co-occurrence of impairments:

As mentioned earlier, PICS is defined when disabilities occur in one or more of the three domains: physical, cognitive, and psychological. To date, there are few studies that have investigated PICS in all its domains. One study, conducted by Marra, et al., that showcased the co-occurrence (two or more domains) of PICS impairments is one of the rare trials to investigate PICS in all its domains. Although this study carried some methodological limitations, however it laid a good foundation for future studies to investigate PICS as a whole phenomenon. In this study, authors showed that most patients demonstrated a single PICS problem at 3 months and then at 12 months follow up (39% and 35% respectively). Two problems of PICS were present in less than one fifth of the patents at both time points. And only around 5% of patients had problems in all three domains at the two points of the study (Marra et al., 2018). In this setting, more years of education was shown to be a protective factor for developing new long-term impairments, and frailty was identified as a risk. Survivors who were PICS-free also tended to be younger and had fewer comorbidities than those with PICS. Socioeconomic status was not associated with being PICS free (Marra et al., 2018).

It is hypothesized that the co-occurrence of PICS problems can cause deleterious effects on the perceptions of patients about their HRQoL (Estrup et al., 2022). Difficulties in conducting one's ADLs and impairments in cognitive and emotional wellbeing can potentially affect one's daily routines, roles, and social interactions. These hypotheses have not been fully studied in the post-ICU population. Although more research has been conducted in recent years regarding the three domains of PICS, its broader impact on a person's life has not been equally explored. Existing literature in inconsistent and varies in the way assessments of HRQoL have been conducted, the timing of assessments, and the tools used. For example, in one study, physical, mental and HRQoL measures did not improve from 3-months follow up to one year after ICU discharge, and the scores of the HRQoL tool used in the study showed the physical domain to be the most affected (Estrup et al., 2022). In contrast, in another study, physical and mental components of HRQoL were both affected but improved significantly from the

time of 1 month follow up to 6 months post discharge (Rai et al., 2020). No studies exploring the HRQoL of post-ICU patients exist in Saudi Arabia and there is a great opportunity to examine this aspect of the post-ICU journey in this specific geographic and cultural context.

1.5.5. Early rehabilitation:

Early mobilization and physiotherapy in the ICU were discussed in previous sections in terms of their feasibility, safety, and efficacy, and their effect on better outcomes. A systematic review by Parry et al (2017) comprehensively evaluates barriers and enablers to physical activity (PA) for survivors of critical illness, focusing on the ICU and post-ICU settings. The review identified five major themes: (1) patient physical and psychological influences, including pain, fatigue, sedation, and delirium, which hinder PA, and factors like patient trust and adequate sleep that promote it; (2) safety influences, where physiological stability, medical contraindications, and concerns about the safety of lines and endotracheal tubes were barriers, while guidelines for safe rehabilitation and proper planning were enablers; (3) culture and team influences, highlighting barriers such as resistance to change and poor interprofessional communication, and enablers like team collaboration, visible goals, and leadership for PA; (4) motivation and beliefs about PA, where patients and caregivers recognized the benefits of PA, though there was a discrepancy in the perceived benefits and challenges of PA in different settings; and (5) environmental influences, noting barriers like lack of resources and time constraints, and enablers such as mobility protocols, dedicated rehabilitation teams, and institutional support. The review's strengths include its rigorous methodological approach, including adherence to established guidelines and a broad, international scope covering diverse study designs and settings. The synthesis of both quantitative and qualitative data provided a nuanced understanding of the multifaceted nature of PA interventions. However, the review also faced limitations, such as the potential for publication bias due to the inclusion of only English-language studies and the challenge of comparing studies with different designs and methodologies. The thematic analysis did not quantify the prevalence of identified barriers and enablers, which may limit the ability to generalize findings. Despite these limitations, the review offers valuable insights for improving PA practices for ICU survivors by emphasizing the need for targeted education, the development of behaviour change models, and the exploration of innovative and low-cost

interventions. Future research should address the gaps identified, particularly the transition from ICU to community care and the implementation of effective PA strategies. Overall, this review advances the understanding of the complex barriers and enablers affecting PA in ICU settings and beyond, setting the stage for future improvements in patient care and rehabilitation.

While early physical activity has been advocated for and often integrated in evidence-based guidelines for ICU practices, psychotherapy and cognitive therapy have not received equal attention in clinical practice and in research. One of the reasons for not engaging in the integration of the psychological and cognitive rehabilitative aspects of care in the ICU is probably due to its labour-intensive nature. Providing counselling or psychological interventions have not yet been widely used in ICUs, although some evidence exists that psychological morbidity can be reduced by early psychological intervention. In one study, significant reductions of PTSD incidence were generated from an early intervention where clinical psychologists provided sessions of counselling, coping strategies and support to patients (Peris et al., 2011). Other research shows that patients who receive care by a clinical psychologist in the ICU have lower rates of anxiety, depression, and post-traumatic stress (Novoa et al., 2006).

Diaries kept in the ICU have been hypothesized to foster the formation of factual memories of the ICU stay and hence assist in the psychological recovery of patients (Knowles et al., 2009). The clinical use of ICU diaries traces back to the 1980s, Scandinavia, and has spread to European countries and US since (Ewens et al., 2014). Diaries have been used for patients in the ICU from the time of admission or mechanical ventilation/sedation and throughout the ICU stay (Ewens et al., 2014). Records of the patients' stay are usually captured by family members and nurses by written material and/or photographs. Sharing this type of information with the ICU patients after their acute illness has been found to be beneficial for the reconstruction of the patients' understanding of their ICU journey, and promoting a discussion that has been helpful for their psychological recovery (Ewens et al., 2014). Small prospective or randomized studies have shown that the use of an ICU diary maintained prospectively during the patient's ICU stay by family members, healthcare providers, or both, decreases symptoms of PTSD (Knowles et al., 2009). A large, randomized trial, however, has

failed to confirm this benefit (Garrouste-Orgeas et al., 2019). Further research is needed in this area.

Similar to the trend of infrequent implementation of early psychological help in the ICU, cognitive interventions in the ICU have also rarely been recognized and implemented in clinical practice and research. In a randomized control study at Vanderbilt University, US, a combination of early physical and cognitive therapy was found feasible and safe in ICU patients (Brummel et al., 2014). Cognitive therapy in this study was administered twice a day by a protocol consisting of a series of activities. These included orientation, digit span calculation (forward and reverse), matrix puzzles, "real world", noun list and paragraph recall, letter-number sequences, and pattern recognition (Brummel at el., 2014). This protocol was found to be doable on nearly all days while the patients were in ICU, even if the patients were on mechanical ventilator (Brummel et al., 2014). As the aim of this study was not to detect the outcomes of such a treatment, efficacy and effect on long-term outcomes could not be established. In a more recent study in Netherlands, a group of multidisciplinary members of the ICU team developed and tested the feasibility of a cognitive training program for ICU patients (Wassenaar et al., 2018). This pilot study also showed feasibility (in terms of practicability and burden) of implementing such a program from both patients' and nurses' perspectives. The complete program, consisting of exercises for attention, memory, and executive function, is published (Wassenaar et al., 2018). Hence, there are some efforts to test and establish cognitive therapy regimens for ICU patients, however, such as the case in these two studies, efficacy has not been established so far. Further and large studies are needed to identify the type, the intensity, the time, and the duration of such therapies, and their effect on long-term cognitive outcomes.

1.5.6. After-care:

The potential public health burden of PICS is substantial due to the presence of neuropsychological and functional disability that occurs in association with this syndrome. Post-ICU care programs, including rehabilitative services, pose a potential opportunity to improve the health of critically ill patients after they overcome their acute illness and hospitalization. However, uncertainty exists regarding the best approaches for providing this type of post-ICU care, and research is lacking regarding outcomes of rehabilitative services. A small noncontrolled UK study of ICU survivors demonstrated that a 6-week program consisting of a 2-hour outpatient class and two unsupervised home-based exercise sessions per week was feasible and showed improvement in walk tests and anxiety and depression scores (McWilliams et al., 2009). A randomized trial conducted by Jones and colleagues in the UK examined the use of a rehabilitation manual consisting of self-directed exercises, psychological advice, and information about the effects of critical illness and the importance of smoking cessation. This trial demonstrated improved physical function at 6 months, a trend toward decreased depression symptoms, and increased smoking cessation in the control group. However, there were no differences in levels of anxiety and PTSD-related symptoms between the usual-care and the intervention groups (Jones et al., 2001; Jones et al., 2003). Another randomized trial of home-based physical rehabilitation (including a handbook, in-person evaluation, and personalized rehabilitation program) in an Australian setting demonstrated no benefits in physical function-related quality of life or secondary outcomes (Elliot et al., 2011). Furthermore, a randomized trial of a nurse-led intensive follow-up program after ICU in the UK demonstrated no benefit in quality of life or secondary outcomes (Cuthbertson et al., 2009). These studies have generated inconsistent results and the nature of rehabilitative programs in terms of optimum timing, duration, setting (outpatient versus home-based), delivery mode (self-paced versus nurse-led), and content, remain inconclusive.

The integrative review by Connolly et al. (2012) investigates the rehabilitation needs of ICU survivors following hospital discharge, focusing on exercise rehabilitation. The authors synthesize evidence from various studies on the effectiveness of exercise interventions initiated after hospital discharge, noting that while early mobilization in the ICU is well-supported by evidence, there is a notable lack of consistent and robust data for post-

discharge rehabilitation. They highlight critical gaps in the field, such as the unclear optimal timing, dosage, and specific types of interventions required for effective long-term rehabilitation. The review identifies ICUAW as prevalent, suggesting that patients suffering from it at discharge might benefit the most from continued rehabilitation. However, screening based solely on muscle strength might miss other critical functional impairments and non-physical complications, pointing to the need for comprehensive assessments. The review critically identifies the limitations in existing guidelines and the variability in study methodologies, which hinder the formulation of clear clinical recommendations. The identification of ICUAW as a key criterion for post-discharge rehabilitation is a strength, yet the authors rightly criticize the reliance on muscle strength alone as a screening tool. Additionally, the review's emphasis on early ICU mobilization and the need for post-discharge interventions reflects significant insights into the field, but it also reveals the challenges of translating early successes into effective post-ICU care strategies. The review suggests that future studies should stratify patients based on ICUAW and other relevant criteria to better understand the impact of tailored rehabilitation programs. Overall, Connolly et al.'s review serves as a valuable resource for identifying research gaps and guiding future efforts to improve rehabilitation outcomes for ICU survivors, it provides valuable insights into the challenges and opportunities in exercise rehabilitation for ICU survivors and calls for a more innovative approach to patient assessment and a stronger evidence base to support clinical practice.

1.6. Conclusion:

This chapter has introduced the topic of long-term outcomes of ICU patients. In a case presentation method, the structure and the processes underpinning ICU care have been presented. Specific information relating to the Saudi context of critical care has been provided. This chapter has identified the gaps in literature relating to the investigation of long-term outcomes of ICU patients. These relate to the examination of predictors, and the overall experience of patients with PICS in Saudi Arabia. As trends in patient survival from ICUs have been improving, and as modern critical care is evolving, it is clear now that long-term outcomes should be included in the definition of successful critical care. Excellence in care should be addressed not only in mortality indexes, but in outcome driven approaches, where

evaluation of ICU care doesn't cease when the patient leaves the ICU, but rather continues to measure overall health and functionality over the trajectory of critically illness recovery. Understanding the determinants of PICS, its occurrence, and the perceptions of patients on its effect on their lives in the post-ICU period should be the focus today and in the future of critical care medicine. In the following chapters, the examination of these concepts will be demonstrated, first by demonstrating the specific aims and then by detailed explanations of each of the phases of this thesis.

2. Chapter 2: Methodology

2.1. Chapter overview:

The introduction and background chapter presented an overview of the ICU structures and processes, and long-term outcomes of critically ill patients. Gaps in the literature were highlighted regarding investigations of PICS and HRQoL in post-ICU patients and the lack of outcomes data in Saudi Arabia. This chapter illustrates the aims, the research questions, and the overall methodology applied in this research. Specific methods of each phase of the thesis will be elaborated in subsequent chapters corresponding to each phase of the study. Finally, a section explaining the involvement of patients and the public in the research process of this study is included in this chapter.

2.2. Overall aims of the thesis:

The aims of this PhD thesis were:

- To establish what is already known regarding the nature of ICUs and the post-ICU long-term outcomes (Chapter 1).

- To determine the predictors of long-term outcomes and HRQoL by conducting a systematic review of the literature (Chapter 3).

- To add to existing evidence by conducting a high-quality prospective cohort study in a sample of ICU patients in Saudi Arabia, investigating long-term outcomes and HRQoL, and to identify the most important risk factors in this cohort (Chapters 4 and 5).

- To explore ICU survivors' lived experiences after their ICU discharge by conducting a qualitative study (Chapter 6).

- To develop an overall understanding of the post-ICU journey in a cohort in Saudi Arabia

by integrating findings of all phases of the thesis (Chapter 7).

2.3. Research questions

The aims of the thesis were derived from the following research questions:

- What is already known about the nature of critical illness and the long-term outcomes of post-ICU patients? (Chapter 1: Background)

- What is already known about long-term outcomes in Saudi Arabia? (Chapter 1: Background)

- What are the predictors of long-term outcomes and HRQoL of post-ICU patients? (Chapter 3: Systematic review)

- What are the concepts underpinning PICS and what are the elements of a framework that captures all aspects of PICS? (Chapter 4: conceptual framework).

- What are the long-term outcomes and HRQoL in post-ICU patients in Saudi Arabia? (Chapter 4 and 5: Prospective cohort study).

- How do patients perceive their experiences after discharge from the ICU? (Chapter 6: Qualitative study).

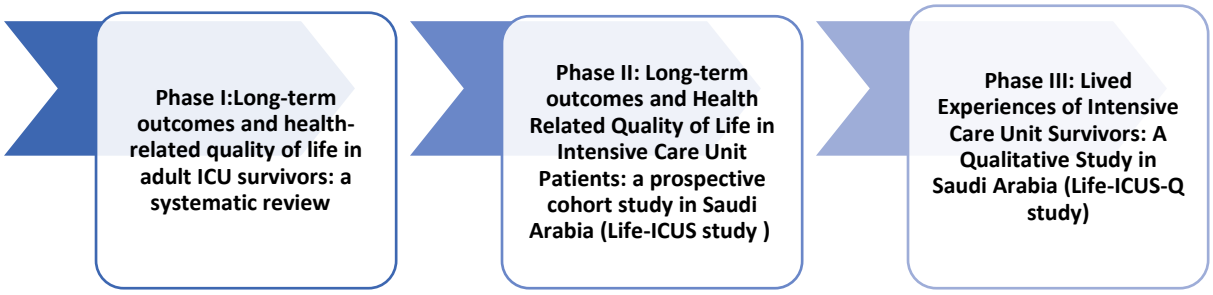
- What could be learned from integrating quantitative and qualitative findings about long-term outcomes of post-ICU patients? (Chapter 7: Integrative discussion).

2.4. Brief overview of the study phases:

This PhD study was conducted in three phases. First a systematic review was conducted as an initial step, followed by a quantitative cohort study, and concluded with a qualitative study (see **Figure 2.1**). The phases were undertaken in a sequential manner to provide a robust and

comprehensive approach to understanding the complex experiences and outcomes of post-ICU patients.

Figure 2.1: Thesis phases



Starting the study with a systematic review allowed the researcher to gather and synthesize existing evidence from multiple studies, providing a broad overview of the available literature. This step was considered crucial for the establishment of a solid foundation of knowledge regarding post-ICU outcomes and for identification of knowledge gaps and inconsistencies. It also allowed for the development of a comprehensive conceptual model for PICS that informed subsequent research steps. This phase is described in Chapter 3.

Following the systematic review, and in light of non-existing evidence in the Saudi population, conducting a quantitative study allowed for the examination of a sample of Saudi post-ICU patients. The longitudinal design of this study permitted the collection of quantitative data on the three domains pertaining to PICS (physical, cognitive, and psychological) in addition to HRQoL, over two points in time (at discharge from ICU and 3 months following discharge from ICU). By using standardized measurements and statistical analysis, the quantitative cohort study provided valuable insights into the occurrences and associations of these specific health outcomes within the sample of Saudi post-ICU patients. This phase is presented in Chapter 4 and 5.

While quantitative data provided important statistical evidence, it was not found sufficient to capture the nuances in the experiences and perceptions of patients. Hence, integrating a

qualitative study into the research sequence helped delve into the lived experiences, emotions, and perspectives of post-ICU patients. Through semi-structured interviews, this phase allowed for in-depth exploration of patients' experiences, coping mechanisms, and their perceptions of health and recovery. This qualitative approach helped complement the quantitative findings, providing a richer understanding of the complexities and contextual factors that influenced the recovery journey of the post-ICU patients. This phase is presented in Chapter 6.

The overall sequential methodology of this thesis allowed for the integration of existing evidence, rigorous examination of clinical outcomes, and exploration of patients' lived experiences, ultimately contributing to a more holistic understanding of the post-ICU patients and the PICS phenomena within the Saudi context.

2.5. Thesis design:

2.5.1. Mixed methods approach to research:

Mixed methods research involves the combination of quantitative and qualitative designs to address specific research aims. It is defined as "*the class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts, or language into a single study*" (Johnson and Onwuegbuzie, 2004, p.17). This approach is adopted often in health-related research to explore complex health phenomena (Johnson and Onwuegbuzie, 2004). The mixed method design is best suited when biomedical data is needed in quantitative form (e.g. ICU outcomes) coupled with social data captured in qualitative form (e.g. perspectives of patients on ICU outcomes) (Johnson & Turner, 2003). Thus, this design has emerged as an attractive and pragmatic counterpart to the conventional mono-methodological form of conducting research by applying more than one method of data collection for specific research questions in hand (Johnson and Onwuegbuzie, 2004).

2.5.2. Rationale for using mixed methods in this thesis:

A mixed methods approach was adopted as the best possible means to obtain useful answers for the research questions that were formulated in the earlier stages of this thesis. A quantitative approach was considered best for the purpose of gathering standardized data, conducting statistical analyses, investigating predictors, and identifying trends and patterns related to post-ICU outcomes (Johnson and Onwuegbuzie, 2004). A qualitative approach was considered to provide deeper insights into individual experiences, perceptions, and cultural variations of post-ICU patients which could not have been captured by quantitative methods alone (Johnson and Onwuegbuzie, 2004). Thus, the use of multiple strategies and approaches were considered to maximize what Johnson and Turner call the "fundamental principle of research", where the combination of methods is "likely to result in complementary strengths and nonoverlapping weaknesses" (Johnson and Turner, 2003). This principle stipulates that using mixed methods can balance the disadvantages that one method can have by itself (Molina-Azorín, 2007).

In the context of this thesis, the "complementary strengths" of mixing quantitative and qualitative designs were carefully explored and identified as:

1) Depth and breadth of understanding: While the quantitative method offers a broad view of occurrences, patterns, and statistical relationships, the qualitative method provides individual insights, perceptions, and context to the experiences of patients (Molina-Azorín, 2012).

2) Triangulation: in this method, the quantitative approach corroborates qualitative results ensuring a more robust interpretation, and the qualitative approach validates, refutes, or compliments the quantitative findings enhancing the overall validity of the study (O'Cathain et al., 2010).

3) Enhanced validity and credibility: while the quantitative data contributes to the validity and objectivity of findings, the qualitative methods add depth and context, adding to the credibility of the study (Creswell and Clark, 2011).

4) Practical utility: quantitative data can be used to assess the generalizability of findings and inform evidence-based decision-making and policy making; qualitative data can complement towards the development of outcome measures in the future, ensuring that quantitative measures are contextually relevant and sensitive to participants experiences (Johnson and Onwuegbuzie, 2004).

While the notion of mixing methods presented compelling strengths for the investigation of the research phenomenon in hand, it was important to explore the "non overlapping weaknesses" related to this type of methodology. These included:

1) Generalizability: as quantitative research can establish general patterns of understanding of the research topic in hand, qualitative studies may lack generalizability due to the small, non-random samples used in research (Creswell and Clark, 2011).

2) Complexity: quantitative data may oversimplify a complex phenomenon, missing the depth provided by qualitative insights, while qualitative data can be complex and subjective, making it challenging to quantify and generalize (Molina-Azorín, 2012).

3) Integration challenges: integration of both quantitative and qualitative findings can be challenging due to differing paradigms and methodologies (Molina-Azorín, 2012).

Recognizing these "complementary strengths" and "nonoverlapping weaknesses" was crucial in the planning phase of this thesis. With thoughtful design and mindful execution, the benefits of both approaches were balanced so that a robust methodology can be adopted and a comprehensive understanding of the complex research questions of the study can be achieved.

2.5.3. A mixed methods typology:

In the development of the mixed methods study design, several dimensions should be considered. These are:

1) *Stages of the study*: whether mixing quantitative and qualitative methods would be conducted within or across the different stages of the research (Johnson and Onwuegbuzie, 2004).

2) *Emphasis of the paradigm*: whether to give the quantitative and qualitative approaches equal weight or give one paradigm the dominant weight (Creswell and Clark, 2011).

3) *Time ordering*: whether to carry out the quantitative and qualitative components concurrently or sequentially (Creswell and Clark, 2011).

4) *Degree of mixture*: deciding to which degree the methods would be mixed on the continuum of single method to fully mixed methods (Johnson and Onwuegbuzie, 2004).

5) *Stage of mixing*: this refers to the phase in the research process where the mixing would occur, for example during setting the objectives, data collection, data analysis, or data interpretation (Mason, 2006).

Based on the above five dimensions of the mixed method research typology, this PhD study was planned to engage in predominantly quantitative methods (emphasis and degree), sequentially followed by a qualitative component (staging and time ordering), concluding in an integrated interpretation of findings (stage of mixing). The rationale for choosing this typology was because the research question "What are the long-term outcomes and HRQoL in post-ICU patients in Saudi Arabia?" could be best explored using a quantitative approach. As the impetus of this research was the lack of evidence regarding ICU patients' outcomes in Saudi Arabia, this quantitative approach was given a predominant stance in the research design. To answer the research question "How do patients perceive their experiences after discharge from the ICU?", the qualitative method was opted best. This approach was considered to be complimentary to the understandings of the post-ICU patients' experiences found in the quantitative phase of the study.

A multitude of research designs can be produced by combining different features of the mixed method dimensions. For example, nine different mixed-methods designs can be

produced by arranging the dimensions of *emphasis* and *time ordering*, and this is illustrated in **Figure 2.2**. The aim of the mixed-methods researcher should focus on the research questions in hand and be creative in adopting a model that best addresses those questions. In this thesis, the QUAN → qual design was chosen and the justification for this has been provided above.

Figure 2.2: Mixed methods design matrix (Johnson and Onwuegbuzie, 2004. Permission to use from Sage Publications)

		Time order decision	
Paradigm emphasis decision		*Concurrent*	*Sequential*
	Equal status	QUAL + QUAN	QUAL → QUAN QUAN → QUAL
	Dominant status	QUAL+ quan QUAN + qual	QUAL → quan qual → QUAN QUAN → qual Quan → QUAL

"qual" stands for qualitative, "quan" stands for quantitative, "+" stands for concurrent, "→" stands for sequential, capital letters denote high priority weight, and lower-case letters denote lower priority or weight. The blue highlighted area denotes to the type of design adopted by this thesis.

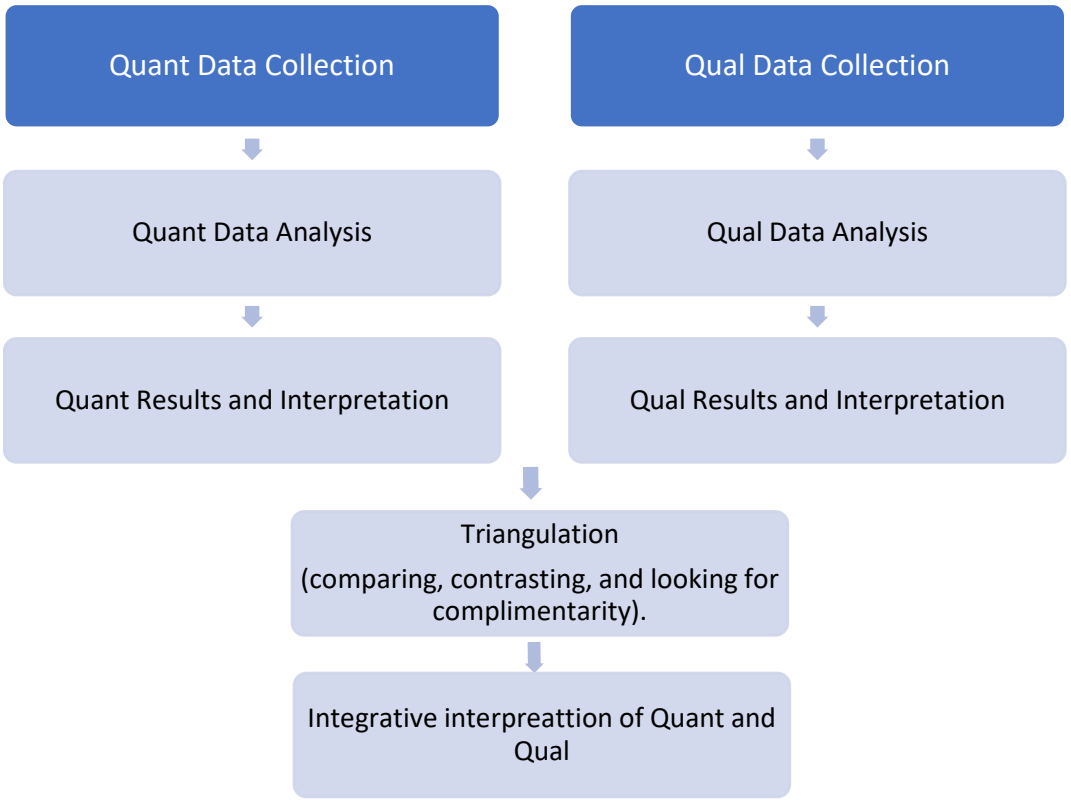
2.5.4. Results integration:

Integration of results derived from mixed studies is a very important component of the mixed method approach to studies. The primary focus of mixed methods studies is the combination of quantitative and qualitative approaches in understanding a complex phenomenon and a series of research questions, that one method would not be able to address alone (Creswell and Clark, 2007; Johnson and Onwuegbuzie, 2004).

The main objective of combining the results of the two methods in this thesis was to achieve an in-depth understanding of the long-term status and predictors of long-term outcomes of post-ICU patients. In order to achieve this objective, result integration was planned to be conducted in a triangulation method. Triangulation means that the same phenomenon was studied by using two different methods in order to gain a complete picture (O'Cathain et al., 2010). It is defined as the "*convergence and corroboration of findings from the two methods that examined the same phenomenon*" (Molina-Azorín, 2012). The adoption of this method of result integration necessitated that quantitative data be collected and analysed

separately from qualitative data in this thesis (O'Cathain et al., 2010). Whilst each of the empirical phases of this thesis will be reported separately and the designs of each phase will be discussed in detail in their corresponding chapters (Chapter 4 for quantitative and Chapter 6 for qualitative), the integrated discussion chapter (Chapter 7) will incorporate the integration of both studies. **Figure 2.3** illustrates the data integration approach adopted in this thesis.

Figure 2.3 Data integration process (O'Caithan et al., 2010. Permission to use from BMJ Publishing Group Ltd)



2.6. Public and Patient Contribution to the research study:

Evidence shows that engaging the public and the patients throughout the process of clinical research has an impact on the quality of the research and can be beneficial to both the researcher and the patient/public (Tomlinson et al., 2019). Therefore, more Public and Patient Involvement (PPI) has been advocated for adoption in doctoral studies (Tomlinson et al., 2019). The benefits of this involvement have been reported to have a positive effect on mutual learning (Staley and Barron, 2019), accessibility of research language to the public (Tomlinson et al., 2019), effective dissemination of research findings (Baxter et al., 2016), and a sense of empowerment and satisfaction for both parties (Hanson and Hanson, 2017).

In this study, service users were involved in the conceptualization of the study, data analysis, interpretation of data, and dissemination of results.

In the systematic review phase, one nurse (VT) was involved in the systematic review protocol development, search strategy, data collection, data extraction, quality assessment, manuscript writing, and dissemination of results. Other service users (AM, ZA) were also engaged as advisors to the project. These engagements from the PPI were found to be helpful for the overall quality of the study.

In the quantitative phase of the study, two intensivist physicians (SZ and SQ), and two nurses (HM and FA) were involved in the conceptualization of the study and discussed with the lead researcher domains related to PICS, inclusion and exclusion of patients, timing of outcome measurements, and the tool used for measurement of PICS domains. This engagement was found to be beneficial both to the researcher and the involved individuals. For the researcher, the diversity of experiences that the clinicians had in their daily work with critically ill patients helped the researcher make important methodological considerations. For example, Dr SQ (who is a local Saudi doctor) explained that, due to cultural and religious reasons, do-not-resuscitate orders were not commonly used in the clinical setting in Saudi Arabia. Hence, some patients stayed in the ICU in a chronic condition, few of which were diagnosed to be in vegetative state. This information helped the researcher review the inclusion and exclusion criteria of the study and list patients in persistent vegetative state under exclusion criteria

since these patients were deemed incapable of undergoing physical, cognitive, psychological, and HRQoL assessments. Another perspective communicated by the nurse FA (who is a local Saudi nurse) was that culturally, when patients are asked a health question, they usually evade giving a direct answer. For example, she mentioned that when patients are asked if they are in pain, they usually answer with a “al hamdu lillah” (praise be to Allah) rather than directly answering the question. This cultural difference helped the researcher set realistic expectations for the challenges that might have been faced with the data collection phase. From the perspective of the involved PPI members, their engagement had positive effects on them individually; they expressed great satisfaction from the discussions about the study as it raised their awareness about PICS and helped them appreciate their daily work with critically ill patients. The nurse HM was inspired to do his master’s degree project on delirium management in the ICU, and the nurse FA has repeatedly expressed how her engagement in the discussion of PICS has widened her understanding of her role as a nurse and her impact on the outcomes of ICU patients. She is currently on her path to commence her masters degree in critical care nursing in Australia, with an emphasis on outcomes of post-ICU patients.

In the qualitative phase of the study, two service users (AM and ZA) acted as advisors to the project. They discussed with the researcher their experiences with conducting qualitative studies in Saudi Arabia. The information provided was helpful for the design of the procedures of the study. For example, the researcher learned that visiting a patient in their homes after a hospitalization, including for research purposes, was culturally welcomed, as it was recognized as a sign of respect and caring. This information assured the researcher of the appropriateness of the procedures adopted in both the quantitative and qualitative phases of the study since home visits were part of these procedures.

It was very challenging to involve patients in the research process of the study due to the researcher’s location in an under-researched area in Saudi Arabia. In this area, early school enrolment is very low and engagement in research design and conduction is almost unheard of. Through an internet search and networking with researchers and critical care clinicians, it was evident that established PPI groups do not exist in the region. Due to the nature of critical illness and the inability of patients to focus on research related matters while they were

treated, patients were not approached in the clinical setting for the purpose of PPI. Ethical considerations and the possibility of coercion to have PPI conversations while patients were in the clinical setting was another reason why the hospital was not considered as a medium for PPI involvement. Accessing support groups for the purpose of PPI was also considered, however, this was not available. Although patient engagement in the development of the research could not be attained, patients could be potentially involved in the dissemination of results in the future. As the organization where the researcher is employed is in the phase of establishing patient support groups, some of the study patients could be involved in a peer-support program for intensive care unit survivors. Findings of this study could be referred to and used as catalysts to raise awareness on the topic and enhance the recovery experience of the patients.

2.7. Conclusion:

This chapter presented the aims, the research questions, and the key methodological methods used in this thesis. A mixed methods design was adopted to provide rigor to the research process of investigating post-ICU outcomes and lived experiences of critically ill patients. In the subsequent chapters, the systematic review and the phases of the empirical studies will be presented.

3. Chapter 3: Systematic review of PICS and HRQOL in adult ICU survivors

3.1. Chapter Overview:

The preceding chapters described the need to better understand the long-term outcomes of ICU patients and the determinants that play a role in the development of PICS. This chapter describes the first phase of the thesis which is an undertaking of a systematic review of literature. The review spanned over a long period of time (24 years), dating back to the years before PICS was defined as a syndrome. It covered the most important long-term outcomes and HRQoL in post-ICU patients. This step of the thesis process was important to identify gaps and inconsistencies in the literature and inform the subsequent steps of the thesis. This chapter provides the background for the systematic review, followed by a detailed description of the methods undertaken for the conduction of the review. The results section describes the ICU-related and patient-characteristics related factors that were predominantly associated with post-ICU outcomes. A discussion section describes the findings and contextualizes them relating to previous literature and evidence. Important insights were derived from this process regarding trends, patterns, and inconsistencies in the literature, which informed the next phases of the empirical studies of this thesis.

3.2. Background

With advances in medical technology and care delivery, every year millions of patients survive critical illness and are discharged from ICUs (Kim et al., 2019; Lee et al., 2020; Mikkelsen et al., 2020). Over the past two decades, studies measuring the outcomes of critically ill patients have moved from mortality and morbidity outcomes to non-mortality indices, with a focus on long-term functional status, health status, and HRQOL (Lee et al., 2020; Needham et al., 2012). These studies have been conducted in various ICU settings, patient populations, and diagnostic groups (Desai et al., 2011; Gaudry et al., 2017; TessaDamm et al., 2019). They have been addressed in various quantitative and qualitative designs and explored various predictors, contributing factors, and functional, health, and quality-of-life outcomes at different time points after ICU discharge (Desai et al., 2011; Haines et al., 2020).

Through studies that examined health and functionality after discharge from the ICU, it has been evident that after patients survive their critical illness, they can develop new or worsening health issues in three specific domains: physical, cognitive, and psychological functions, which, individually or collectively, affect HRQoL (Davydow et al., 2009; Gerth et al., 2019; Rawal et al., 2017). As described in Chapter 1, the SCCM termed the combination of these impairments as PICS in a 2010 stakeholders conference (Needham et al., 2012). The use of the term "syndrome" and the categorization in the three domains was intended to enhance clinicians' knowledge and attention to the long-term effects of critical illness and promote research to address their prevalence, predictors, and contributing factors (Needham et al., 2012).

Many studies were conducted to understand patient characteristics and pre-illness conditions that may put a patient at risk for PICS (De Jonghe et al., 2007; Herridge 2011). For example, preexisting cognitive impairment and high disease severity index at admission (Barr et al., 2013) were found to be associated with long-term cognitive impairments. Prior psychiatric disease was associated with psychiatric morbidity after the ICU (Schandl et al., 2013). Those who appeared to be at greater risk for psychological disturbances were the elderly with chronic diseases, women, the unemployed, and those with lower educational and socio-economic status (Eisendrath et al., 2006; Wade et al., 2012).

Many others explored ICU practices, possible factors, and post-discharge interventions that might mitigate the negative long-term outcomes of intensive care (Fiest et al., 2021; Mikkelsen et al., 2020). Prolonged mechanical ventilation and ICU stay, sepsis, and multi-organ failure were associated with long-term physical disabilities (Latronico et al., 2005; Stevens et al., 2009). Immobility in the ICU and the use of corticosteroids were associated with neuromuscular sequelae (Herridge et al., 2003). In regards to cognitive dysfunction, duration of ICU delirium (Girard et al., 2010; Larson et al, 2007; Pandharipande et al., 2013), type and dose of sedatives (Girard et al., 2007; Jackson et al., 2010), and duration of mechanical ventilation (Barr et al., 2013; Jackson et al., 2003) were found to be risk factors. Long-term cognitive abilities were found to be better if sedation in the ICU was stopped every day for spontaneous awakening and breathing trials (Hopkins et al., 1999). In relation to psychiatric morbidity, sleep deprivation and prolonged mechanical ventilation in the ICU

seemed to be predictive factors (Jubran et al., 2010).

Several review studies have been published on the topic of post-ICU outcomes; however, most are either undertaken in an integrative or narrative manner, while others were unable to provide a meta-analysis of suspected risk factors due to heterogeneity (Haines et al., 2020; Robinson et al., 2017). None of the studies included all three domains of PICS and HRQoL outcomes (Hiser et al., 2023). This has created a significant gap in identifying evidence-based predictors of PICS (Hiser et al., 2023). Therefore, we have undertaken a systematic review investigating the predictors of PICS, encompassing all three domains of outcomes (physical, cognitive, and psychological), in addition to HRQoL.

Including HRQoL in this systematic review was essential due to the profound impact that PICS can have on patients' overall well-being. HRQoL encompasses a broad range of factors, including physical, psychological, and social dimensions, all of which can be significantly affected by the sequelae of critical illness. While the clinical outcomes of PICS, such as physical, cognitive, and psychological impairments, have been more extensively studied, their broader impact on patients' daily lives, routines, and social interactions remains underexplored (Estrup et al., 2022). Assessing HRQoL provides a comprehensive understanding of the long-term consequences of ICU care and offers insights into how these impairments disrupt patients' ability to function and engage in life post-discharge. Furthermore, inconsistencies in the existing literature regarding HRQoL outcomes highlight the need for a more standardized approach to evaluate these impacts across different populations and contexts (Rai et al., 2020). By including HRQoL in this review, we aimed to address gaps in knowledge, particularly within underrepresented regions such as Saudi Arabia, and ultimately contribute to improving the holistic management and support of post-ICU patients (Davydow et al., 2009; Gerth et al., 2019; Rawal et al., 2017).

This review was undertaken to answer the question: In adult ICU patients, what are the prognostic factors for PICS and HRQOL?

3.3. Methods

A protocol (PROSPERO registry ID: CRD 42019143023) (Tashjian et al., 2018) was written to perform a systematic review of the literature, based on the Cochrane Handbook (Higgins et al., 2019) and the checklist of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (Page et al., 2021). This method was chosen as it is most rigorous in selecting, evaluating, and synthesizing primary research articles addressing a specific clinical subject (Higgins et al., 2019). This review examined primary studies of adult patient outcomes in physical, cognitive, psychological, and HRQOL domains, following an admission to a general ICU.

3.3.1. Eligibility Criteria

The eligibility criteria for the patient population were derived from the research question, combined with types of studies that address the question (O'Connor et al. 2008).

Inclusion criteria:

- Adult ICU patients (age>18 years)
- randomized-controlled trials, non-randomized studies, observational studies.

Exclusion criteria:

- Paediatric patients (age<18 years); cardiac; stroke, Traumatic Brain Injury and neurology/neurosurgery; obstetric; Covid-19; chronically critical patients on long-term ventilation. These patient populations were excluded because they differ clinically from the general ICU population (Ahmad et al., 2021; Gupta et al., 2021), and would have added further heterogeneity in the findings.
- Qualitative studies, descriptive studies (case series and case reports), reviews, expert opinion, feasibility/quality improvement studies, tool validity studies, abstracts/conference proceedings that do not provide sufficient information.

3.3.2. Search Strategy

Using the PPOTS framework, the **p**opulation/**p**atient group, **p**rognostic factors, **o**utcome, **t**iming, and **s**etting/**s**tudy design elements of the research question were identified (Agency for Healthcare Research and Quality, 2018) (see **Table 3.1** for a complete description). This framework has been adopted to guide the formulation of a clear and well-framed research question pertaining to evidence-based practice, and to the identification of a comprehensive range of key terms and synonyms, which in turn provide comprehensive literature when applied in the search strategy (Agency for Healthcare Research and Quality, 2018).

Table 3.1 PPOTS Framework

Acronym	Descriptor	Description
P	Patient group	Adult critically ill patients
P	Prognostic factors	All potential pre-ICU and in-ICU factors: age, sex, co-morbidities, severity of illness, length of stay, mechanical ventilation, delirium, medications, and others
O	Outcome	Long-term outcomes: physical, cognitive, psychological, HRQoL
T	Timing	Long-term defined as more than 3 months
S	Setting/study design	Empirical quantitative observational studies; conducted in adult general ICUs. No qualitative, descriptive studies (case series and case reports), reviews, and expert opinions.

ICU, Intensive Care Unit, HRQoL, Health Related Quality of Life

A comprehensive search strategy was devised and executed with the assistance of a specialist librarian on the following bibliographic databases: MEDLINE, Embase, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), and PsycINFO. Furthermore, reference lists, citation tracking, and hand-search were performed. OpenGrey was searched for grey literature.

The search strategy included key terms, MeSH terms, synonyms, and abbreviations such as “critical care”, “ICU survivor”, “intensive care”, “ICU”, “PICS”, “post-intensive care syndrome”,

"cognitive function", "physical function", "psychological assessment", "health-related quality of life", "long-term outcomes", and others (see **Table 3.2** for a complete description of the search strategy). Boolean operators "OR" and "AND" were used to merge search results. Results were limited to studies on adults ≥ 18 years old, humans, English language, and to studies published since 1999. The years were limited to the past 24 years to capture contemporary publications that would represent the current state of the topic in review (Hiser, 2023). The search was performed in July 2019 and updated in July 2023 (Tashjian et al., 2018).

The outcomes of interest were physical, cognitive, psychological, and HRQOL outcomes. The outcomes were defined as "long-term" according to the timing of their evaluation post-ICU (evaluated at any point ≥ 3 months after discharge from ICU).

Table 3.2 Search Strategy

	Population	**Exposure**	**Outcome**
MeSH	Critical illness	ICUs	Quality of life
		Critical care	Critical care outcomes
		Mechanical ventilation	Activities of daily living
		Sedation	Cognitive dysfunction
			Anxiety
			Depression
			Post-traumatic stress disorder
Key words/ Free text	Critically ill	Intensive care	Quality of life
	ICU survivor	Aftercare	Quality of life
		Critical care	health-related quality of life
		Long-term care	Post-intensive care syndrome
		Rehabilitation	Post Intensive Care Syndrome
		Acute disease	Physical function
		Catastrophic illness	Physical outcome
		Artificial ventilation	Physical disability
		Mechanical ventilation	Physical impairment
		Intensive therapy	Physical weakness
		Intensive treatment	Functional outcome
		ICU	Functional impairment
		Intensive Therapy Unit	Functional disability
		Acute care	ICU acquired weakness
		ICU sedation	ICUAW
			Activities of daily living
			ADL
			Polyneuropathy

			Myopathy
			Muscular weakness
			Muscle atrophy
			Muscular disease
			Cognitive assessment
			Cognitive function
			Cognitive outcome
			Cognitive disability
			Cognitive impairment
			Psychological function
			Psychological disability
			Psychological outcome
			Psychological assessment
			Psychological impairment

3.3.3. Screening and selection process

The reference manager/bibliographic software, Endnote X8 (Endnote X8, 2013), and the data extraction and quality appraisal tool, Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia; www.covidence.org., 2022), were used. Duplicates were removed. Titles and abstracts of the remaining records were screened against the eligibility criteria by two reviewers independently (HT and VT). Full-text articles of relevant studies were retrieved and evaluated for eligibility against the inclusion and exclusion criteria by two reviewers (HT and VT). In case of discrepancies, a third reviewer was consulted (AK) for independent assessment, and conflicts were resolved by consensus among the reviewers. The total number and reason for exclusions were documented. Results are presented in a PRISMA flowchart (**Figure 3.1**).

3.3.4. Data extraction and quality analysis

A form was devised and used to extract study elements (author, year, country, study design, sample description, number enrolled) and aims of the review question (inclusion and exclusion criteria, exposure, outcome measure, assessment time, and tool) (This tool is provided in **Appendix 3.1**). The extraction form was then customized to be used in Covidence. Data were extracted primarily from the following sections of the papers: introduction/background, results, and discussion. Where applicable, available online

appendices were used. Data extraction was performed by two reviewers (HT and VT), independently. In case of discrepancies, a third reviewer was consulted (AK) for independent assessment, and conflicts were resolved by consensus among the reviewers.

The risk of bias in each study was assessed by two reviewers (HT and VT), independently, utilizing the Cochrane risk-of-bias assessment tool, ROBINS-I (Higgins et al., 2019). This tool is optimum in evaluating for risk of bias in non-randomized studies (Higgins et al., 2019). Differences in opinion were discussed and resolved, with occasional arbitration by a third assessor (AK). The following categories were evaluated: confounding bias, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of reported results (Higgins et al., 2019). Eventually, the overall bias of each study was identified. Studies were of "low" overall risk if all categories were evaluated as "low risk" (Higgins et al., 2019). If more than one category was evaluated as "moderate", then the study was considered as "moderate" overall risk (Higgins et al., 2019). If a study was assessed to be "serious" in at least one category, but not "critical" in any category, then it was considered as "serious" overall risk (Higgins et al., 2019). A study was assessed to be "critical" risk in at least one category (Higgins et al., 2019). "No information" was assigned to a study if there was insufficient information in at least one category (Higgins et al., 2019).

3.3.5. Data Synthesis

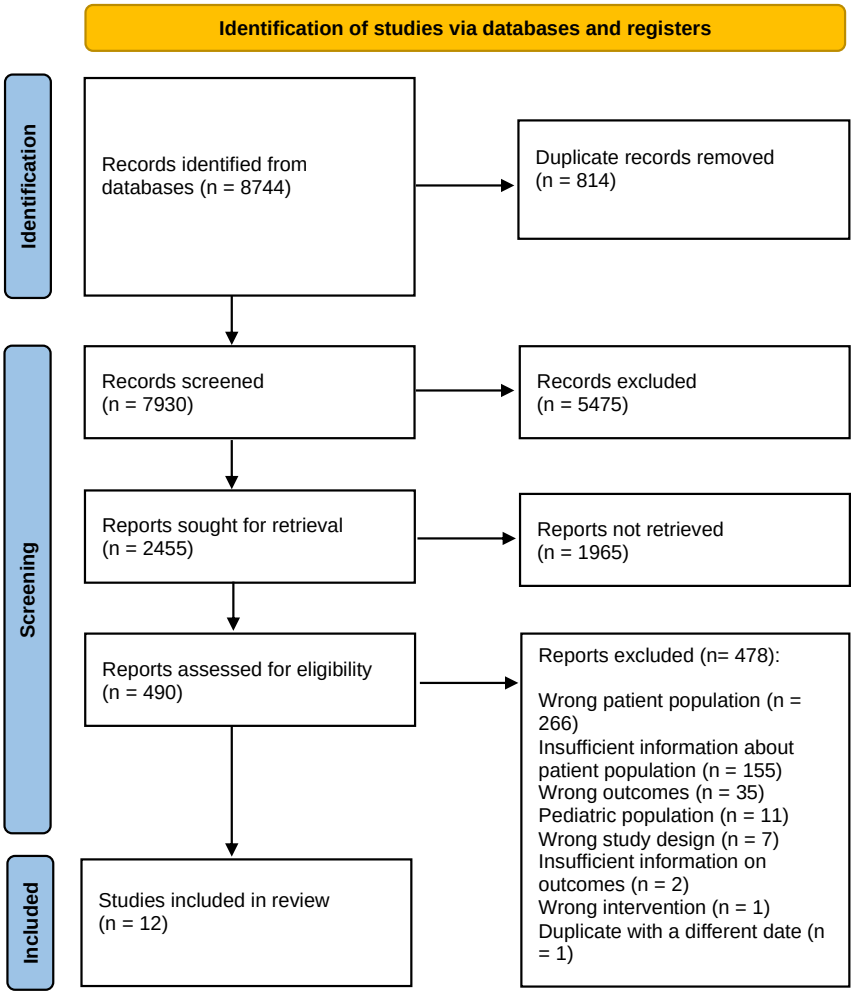
Due to substantial methodological heterogeneity (differences in exposures and outcome measurements), meta-analysis could not be performed. Instead, best-evidence synthesis was performed, and results presented in narrative format. Patient outcomes were categorized under four sections: physical outcomes, cognitive outcomes, psychological outcomes, and HRQOL. Data aggregation was not possible across studies in all categories due to the mentioned variabilities in methodology. All risk factors related to every domain in each study were explored. Only data incorporating multivariate analysis to identify predictors were reported. Every eligible study had at least one factor that was reported by a risk ratio (RR) or odds ratio (OR). For the purposes of this synthesis, a predictor or factor was identified and reported in the results if it was deemed significantly associated with an outcome.

Including only data incorporating multivariate analysis to identify predictors in the systematic review is crucial for several reasons. Multivariate analysis allows for the simultaneous examination of multiple variables, accounting for potential confounding factors that could skew the results. This provides a more accurate and robust identification of predictors of PICS outcomes. Given the substantial methodological heterogeneity across studies, relying on multivariate analysis ensures that the predictors reported are not influenced by isolated variables but rather reflect a comprehensive understanding of the factors contributing to PICS. Additionally, multivariate analysis yields risk ratios (RR) and odds ratios (OR), offering clear and quantifiable measures of association that enhance the reliability and comparability of findings across different studies. By focusing on these rigorously analysed data, the review aims to provide the best possible evidence on predictors of PICS, thus facilitating more informed clinical decision-making and targeted interventions to improve long-term outcomes for post-ICU patients.

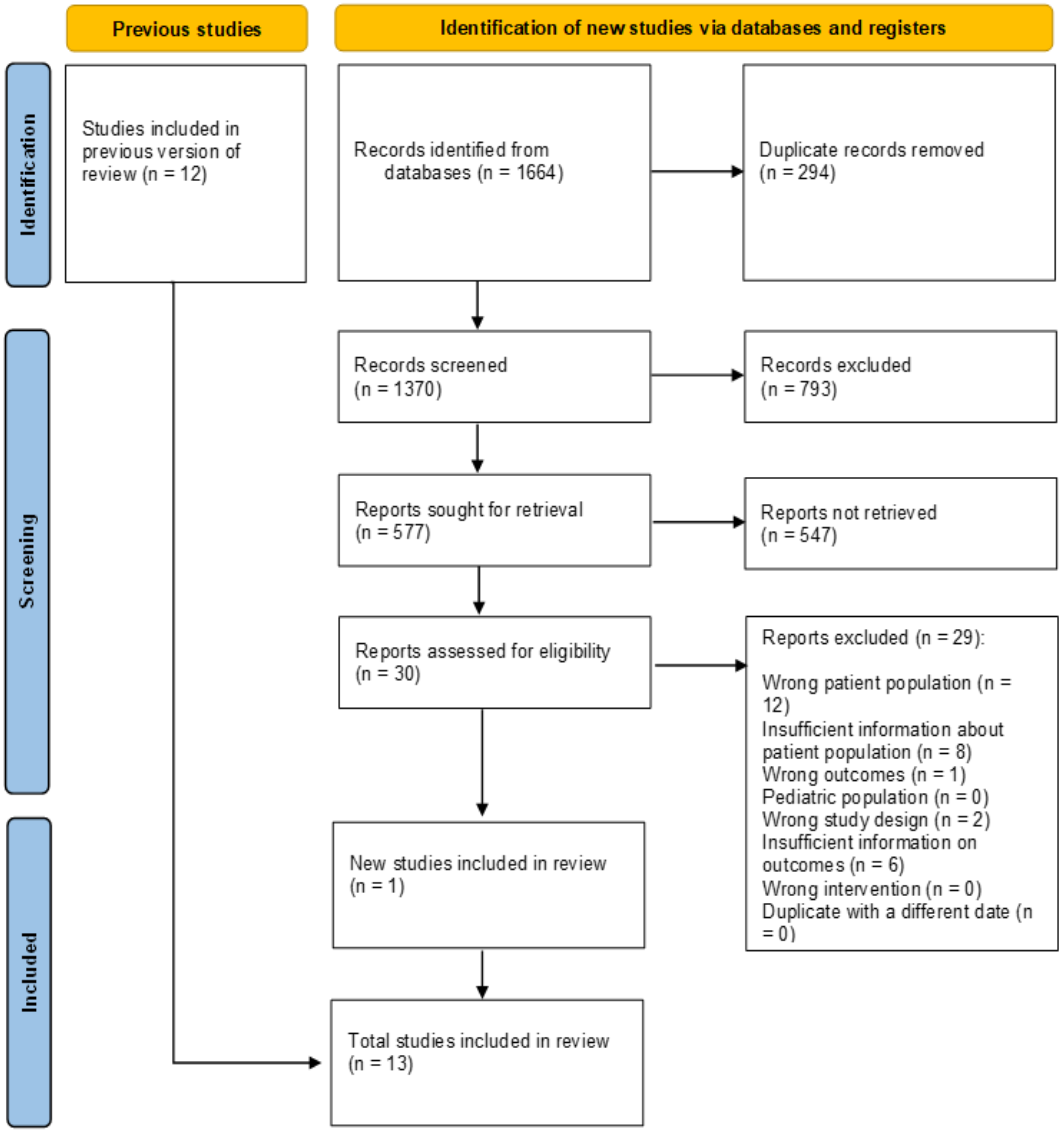
Prognostic papers that did not use multivariate analysis were handled differently. These studies were still included in the narrative discussion to provide a comprehensive overview of the current state of research. However, their findings were not reported to distinguish them from those studies employing more rigorous multivariate methods. This approach ensured that all relevant data were considered while clearly indicating the varying levels of analytical robustness. The insights from these prognostic papers helped to contextualize the quantitative findings and highlight areas where further research using more advanced statistical techniques is needed.

Figure 3.1 PRISMA flow diagram of search result

The following PRISMA diagram refers to the first search conducted in 2019.



The following PRISMA diagram refers to the updated search conducted in 2023.



3.4. Results

A total of 10,414 titles and abstracts from database searches, hand searching, and grey literature were identified. After removal of duplicates, 3,032 articles were screened for title and abstracts. Full-text review of 520 articles was conducted, 507 of which were excluded based on population, outcomes, study design, or intervention. One duplicate study was found at this stage because of a different publication date. Thirteen studies were identified to be eligible (Table 3.3). All studies were non-randomized, observational studies.

3.4.1. Assessment of risk of bias

Using the ROBINS-I tool as described earlier, risk of bias was identified to each study. Table 3.4 describes the assessment of bias in each domain of the ROBINS-I tool for each study article in detail. Below is a description of the overall evaluation of risk of bias of these articles.

In regard to the study by Altman et al (2018), the study employed robust methodologies and validated instruments, however, the moderate risk in participant selection and missing data, and to a lesser extent, the potential for bias in outcome measurement through surrogate interviews, contributed to an overall moderate risk of bias.

The overall risk of bias of the study by Bienvenu et al (2012) was considered moderate. The primary concerns were residual confounding and the potential for detection bias due to the lack of blinding of outcome assessors. However, the study used robust statistical methods and sensitivity analyses to address missing data and confounding, which supported the credibility of the findings.

The overall judgment of the study by Bienvenu et al (2013) was assessed as having moderate risk of bias. While the study demonstrated rigorous methodology in many areas, potential biases due to selection and missing data warranted a moderate overall risk rating. The prospective design, comprehensive adjustments for confounders, and validated outcome measures enhanced confidence in the findings despite these limitations.

The article by Boyle et al (2004) was evaluated as follows having moderate overall risk of bias.

The study was well-conducted with clear methodology and efforts to minimize bias. The primary limitation was the lack of pre-ICU HRQOL data, which introduced some uncertainty regarding the true impact of the ICU stay on chronic pain and HRQOL outcomes. However, the study's robust design and use of validated measures provided confidence in its findings.

The article by Bruck et al (2018) was evaluated for moderate overall risk of bias. The study addressed many potential sources of bias through adjustments and validated measures. However, the moderate response rate, exclusion criteria, and lack of baseline cognitive function data contributed to an overall moderate risk of bias.

The study by Fan et al (2014) appeared to be well-conducted with reasonable efforts to minimize bias, particularly in the measurement of interventions and outcomes, and the handling of data. However, as with all observational studies, there remained a moderate risk of bias due to confounding and the potential impact of missing data from non-participants.

The study by Huang et al (2016) on psychiatric symptoms in ARDS survivors demonstrated thorough consideration and adjustment for potential confounders, consistent and standardized data collection methods, minimal missing data, and appropriate handling of outcomes using validated instruments. Given these factors, the study was assessed to have a low risk of bias across all domains.

Overall, the study by Needham et al (2014) demonstrated a moderate risk of bias primarily due to concerns related to confounding variables, deviations from intended interventions, and potential biases in outcome measurement. Efforts to control biases were noted, including adjustments for confounders in statistical analyses and efforts to minimize missing data. However, variability in clinical practices and potential biases in outcome assessments may have affected the internal validity of findings.

The study by Orwelius et al (2011) demonstrated a generally low risk of bias across most domains assessed by the ROBINS-I tool. However, due to the moderate risk related to missing data, the overall risk of bias was assessed as moderate. This assessment should be considered when interpreting the study's findings, particularly regarding the generalizability of results to

the broader ICU population.

The study by Orwelius et al (2008) appeared to have a moderate risk of bias overall. The primary concerns were related to potential biases due to missing data and uncertainties regarding deviations from intended interventions. These factors may have impacted the generalizability and robustness of the study's findings. This suggests that while the study provided valuable insights, particularly into the prevalence of sleep disturbances post-ICU, caution is warranted in interpreting results, especially in contexts requiring robust data on interventions and outcomes.

The study by Orwelius et al (2010) presented moderate to serious risk of bias across several domains, particularly in confounding, selection bias, and attrition bias. The validity of outcomes measured longitudinally in ICU survivors was crucial but may have been affected by these biases.

The assessment of the article by Solverson et al (2016) suggested that while the study provided valuable insights into the long-term outcomes of ICU patients, there were moderate risks of bias primarily related to confounding factors, variability in the implementation of interventions, and the potential impact of missing data.

Overall, the study by Timmers et al (2011) demonstrated a moderate risk of bias. The main concerns arose from potential confounding due to unmeasured variables, the moderate proportion of missing data, and the lack of blinding in outcome assessment. While the study made considerable efforts to mitigate these biases through statistical adjustments and thorough follow-up, the inherent limitations of observational studies and the potential for residual confounding and measurement bias could not be completely eliminated.

3.4.2. Results of PICS domains

Each of the three PICS domains (physical, cognitive, psychological) and HRQoL were examined as follows.

Physical Outcomes: Five articles examined physical outcomes (Altman et al, 2018; Bienvenu et al., 2012; Boyle et al., 2004; Fan in the ICU, even after two years (Fan et al., 2014). In one study, the occurrence of ICU delirium showed an association with worse functional ability (point estimate 0.903; 95% CI -0.090-1.896) (Altman et al., 2018). Prior depression was a predictor for impaired physical function (OR 2.7; 95% CI 1.2–6.0) in another study (Bienvenu et al., 2012). Ventilator hours (OR 1.094; 95% CI 1.007-1.189) and hospital length of stay (OR1.272; 95% CI 1.004-1.610) were associated with risk of chronic pain (Boyle et al., 2004). Physical weakness was evident in patients who endured long periods of bed rest in the ICU, even after two years (Fan et al., 2014). Two studies reported that corticosteroids correlated with muscular weakness (Fan et al., 2014; Needham et al., 2014). Muscular weakness was also associated with the use of neuromuscular blockers (Fan et al., 2014) and ICU length of stay (Needham et al., 2014).

Cognitive Outcomes: Three articles investigated cognitive outcomes (Altman et al., 2018; Brück et al., 2018; Orwelius et al., 2008). The incidence of delirium was higher in patients with severe sepsis/septic shock (OR 3.7; 95% CI 1.7-8.1); however, sepsis or delirium could not be associated with long-term cognitive function (Altman et al., 2018). A positive association was found between psychological symptoms and cognitive function ($r = 0.53$; $p < 0.001$) (Brück et al., 2018). No associations were found between cognitive function and ICU stay, patient acuity, or ICU diagnosis (Brück et al., 2018). In relation to sleep, total days of ICU delirium (RR 1.114; 95% CI 1.023-1.212), younger age (RR 0.990; 95% CI 0.982-0.998), and pre-existing depression (RR 1.335; 95% CI 1.036-1.720) were significantly associated with higher Pittsburgh Sleep Quality Index (PSQI) scores (sleep disturbances) at follow-up (Altman et al., 2018). Observed rate ratio (1.11) suggested that each additional day of ICU delirium was associated with poorer sleep, evidenced by an increase in the PSQI score by 11% (Altman et a.l, 2018).

Psychological Outcomes: Four papers explored psychological outcomes (Bienvenu et al., 2012; Bienvenu et al., 2013; Huang et al., 2016; Sivanathan et al., 2019). Risk factors for depressive symptoms included education of 12 years or less (OR 3.1; 95% CI 1.5–6.6), baseline disability or unemployment (OR 1.78; 95% CI 0.86–3.69), higher baseline medical comorbidity (OR 1.10; 95% CI 0.98–1.23), and lower blood glucose (OR 1.42; 95% CI 0.74–2.70) in the ICU

(Bienvenu et al., 2012).

Risk factors for PTSD symptoms included prior depression (hazard OR 1.96; 95% CI 1.06–3.64), ICU length of stay (OR 1.39; 95% CI 1.06–1.83), proportion of ICU days with sepsis (OR 1.08; 95% CI 1.00–1.16), high ICU opiate doses (OR 2.13; 95% CI 1.02–4.42) and proportion of ICU days on opiates or corticosteroids (OR 0.83; 95% CI 0.74–0.94) (Bienvenu et al., 2013).

Younger age was significantly associated with anxiety (PR 1.16, 95% CI 1.07-1.26) and PTSD (PR 1.23, 95% CI 1.08- 1.41). Greater opioids use was significantly associated with depression and anxiety (PR 1.11, 95% CI 1.03-1.20; PR 1.08, 95% CI 1.01-1.15 subsequently) (Huang et al., 2016).

The following were significantly associated with all three areas of psychiatric symptoms (depression, anxiety, and PTSD): Female sex (PR 1.26, 95% CI 1.01-1.58; PR 1.43, 95% CI 1.18,-1.74 and PR 1.80, 95% CI 1.31- 2.48 subsequently); unemployment (PR 1.35, 95% CI 1 1.09-1.69; PR 1.26, 95% CI 1.05-1.52, and PR 1.40, 95% CI 1.03-1.90 subsequently); and alcohol misuse (PR 1.39, 95% CI 1.09-1.77; PR 1.45, 95% CI 1.18-1.79, and PR 1.79, 95% CI 1.31- 2.46 subsequently). No associations were found with severity of illness and ICU length of stay (Huang et al., 2016).

Health Related Quality of Life: Three articles investigated HRQOL (Orwelius et al., 2010; Orwelius et al., 2011; Timmers et al., 2011). In one study, the level of intensive care survivors' social integration after hospitalization was reported to affect their HRQOL, and to a larger extent than age, sex, and the ICU -related factors (Orwelius et al., 2011). Reported quality of life scores were reduced in patients with pre-existing diseases (Mean 0.55-0.63, $p < 0.001$), but no significant effect was evident by ICU-related factors, such as diagnosis and length of stay (Orwelius et al., 2010). Oncological surgical cancer patients had the best quality of life scores (EQ utility score 0.83, SD 0.20) (Orwelius et al., 2011). Vascular patients had the worst quality of life scores (EQ utility score 0.72, SD 0.22) (Orwelius et al., 2011). Increased incidence of problems related to mobility, self-care, usual activities, and cognition were found in trauma (OR 2.47-3.47) and vascular surgery (OR 2.27-5.37) patients (Orwelius et al., 2011).

Table 3.3 Study Characteristics

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
Altman 2018	US	Observational cohort study	Medical ICU patients 422 enrolled	Patients with expected ICU LOS >24 h	None specified	- Age - Female - Preexisting depression - APACHE II - Hospital LOS - MV - Time to interview in days - Total days of delirium	Change in disability	145 days	BADL/IADL PSQI
Bienvenu 2012	US	Prospective, longitudinal cohort study	Mechanically ventilated patients with ALI 520 enrolled	None specified	- neurologic disease or head trauma - preexisting illness with a life expectancy of less than 6 months - pre-existing cognitive impairment or communication/language barriers - no fixed address - transfer to a study site ICU with preexisting ALI of greater than 24 hours' duration - more than 5 days of MV before ALI - a physician order for no escalation of ICU care	- Education <12 years - Disability or unemployment - Charlson Comorbidity Index (per point) - Mean daily minimum glucose < 100mg/dl - Impaired physical functionality last follow-up	Incident depressive symptoms Incident impaired physical function	2 years	HAD IADL

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
Bienvenu 2013	US	Prospective, longitudinal cohort study	Mechanically ventilated patients with ALI 520 Patients enrolled	None specified	- primary neurologic disease or head trauma - pre-existing illness with a life expectancy of <6 months - pre-existing cognitive impairment or communication/language barriers - no fixed address - transfer to a study site ICU with pre-existing ALI >24h - >5 days of mechanical ventilation before ALI - a physician order for no escalation of ICU care (e.g. no vasopressors or hemodialysis)	- age 40-54, age ≥55 - Education - Overweight (BMI > 25 kg/m2) - Ever depression - Ever smoking - Ever illicit drug use - Days in ICU - Delirium (% of ICU days) - Days of sepsis (per 10% of ICU days) - Max midazolam equivalent ≥100mg/day - Mean morphine equivalent ≥100 mg /day - Days of opiate use (per 10% of ICU days) - Days of corticosteroid use (per 10% of ICU days)	Symptoms of PTSD	2 years	IES-R
Boyle 2004	Australia	Prospective repeated measures observational study	Elective surgery, emergency surgery, medical 99 patients	ICU LOS of at least 48 hours	- under 18 years of age - unable to respond to a written English language questionnaire	- Gender - Type of surgery	Chronic pain	6 months	10 points pain scale

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
					- suffering from neurological impairment - patients admitted with a spinal injury				
Brück, 2018	Sweden	Prospective observational cohort study	General ICU patients 125	Patients with an ICU LOS > 24	- Patients who were mentally impaired (including dementia) - had serious auditory or visual disorders - were unable to understand Swedish - suffered from serious aphasia - Patients transferred to other ICUs as the presence of or total duration of ICU delirium could not be assessed. - Patients with a Richmond Agitation and Sedation Scale−4 or more during their entire ICU stay	Self-rated cognitive function	Cognitive Failure	3 months	CFQ
Fan 2014	US	Prospective, longitudinal cohort study	Mechanically ventilated patients with ALI 520 patients	None specified	- primary neurologic disease or head injury - pre-existing illness with a life expectancy of less than 6 months. - preexisting cognitive	- Age - Sex - Functional comorbidity (per FCI point) - APACHE II score (per 5 points) - Proportion of ICU days septic (per 10% change)	Muscle weakness	3-24 months	ICUAW

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
					impairment or communication/language barriers - no fixed address - transfer to a study site ICU with preexisting ALI of greater than 24 hours duration - greater than 5 days of MV before ALI - greater than 4 days between ALI diagnosis and enrolment - prior lung resection - a physician order for no escalation of ICU care (e.g., no vasopressors or hemodialysis)	- Mean blood glucose over ICU stay >150mg/dL - Need for dialysis (ever vs. never) - Total ICU dose of benzodiazepine (per 500 mg midazolam-equivalent) - Total ICU dose of narcotic (per 500 mg morphine-equivalent) - Any NMB received - Proportion of ICU days alert (per 10% change) - Proportion of ICU days comatose (per 10% change) - Proportion of ICU days delirious (per 10% change) - Cumulative ICU steroid dose (per 500 mg hydrocortisone) - Physical therapy in ICU (ever vs. never) - Days until PT started (per 5 days) - Duration of bed rest (per day)			
Huang 2016	US	Prospective, longitudinal cohort study	ARDS patients 1,176 patients	Within 48 hours of ARDS onset and within 72 hours of initiation of	- severe comorbid malnutrition	- Female - Unemployed - Hemodialysis	Symptoms of Depression	1 year	HADS IES-R

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
				MV	- lung, liver or neuromuscular diseases - limitations in life support at time of eligibility - potential cognitive impairment prior to admission - non-English speaking, homeless, or younger than 18 years old.	- alcohol misuse - APACHE III, per 20 unit - number of organ failures - % of days with opioids, per 20% - ICU LOS, per week - Change at 12 vs 6-month follow-up	Symptoms of Anxiety PTSD		
Needham 2014	US	Prospective, longitudinal cohort study	Survivors of Acute Respiratory Distress Syndrome Network (ARDSNet) trials 419		- severe comorbid malnutrition - lung, liver, neuromuscular diseases - limitations in life support at time of eligibility - potential baseline cognitive impairment - non-English speaking, homeless, or younger than 18 years old.	- Age - Sex - Body mass index - Living independently at home - Functional Comorbidity Index - Charlson Comorbidity Index - Psychiatric comorbidity - Substance abuse - Pulmonary comorbidity - Rheumatologic comorbidity - Cardiac comorbidity - APACHE III score - Brussels score - Proportion of days with catecholamine use	Muscle strength QoL	6 and 12 months	MMT 6MWT SF-36 Physical Function

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
						- Any neuromuscular blocker - Mean corticosteroid dose* (per 10 mg of prednisone-equivalent increase in mean dose when mean ,40 mg) at ICU LOS= 14 - ICU LOS among patients with no corticosteroid use, per week			
Orwelius 2011	Sweden	Prospective, controlled	medical and surgical ICU 1,663 patients	- 18 years and older - remained in the ICU for more than 24 h - were alive 6 months after discharge from hospital	- primary coronary disease - those recovering after heart surgery and neurosurgery - patients with burns	- APACHE II score (per 5 points) - LOS ICU - LOS hospital - Diagnosis - Time on ventilator - Marital status (living alone) - Basic school - High school/university - Born in Sweden - Sex - Age - Availability of social integration (AVSI) - Pre-existing disease	HRQOL	6 months	PCS SF-36 MCS SF-36
Orwelius 2008	Sweden	Prospective, controlled 1625 patients 6,093 reference	General ICU patients	- 18 years and older - remained in the ICU for more than 24hours - who were alive 6 months after	- Postoperative patients, those after open-heart surgery and neurosurgery - primary coronary disease	- Concurrent disease - APACHE II score 0 to 15 - APACHE II score 16 to 25 - APACHE II score 26 to 43 - LOS in ICU<37 hours	Difficulties in falling asleep Poor quality of sleep	6 and 12 months	Swedish version of the Basic Nordic

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
		group		discharge from hospital	- burn patients	- LOS in ICU 38 to 52 hours - LOS in ICU 53 to 144 hours - LOS in ICU >144 hours - LOS in hospital <5 days - LOS in hospital 6 to 13 days - LOS in hospital >13 days - Diagnosis at admission	Sleep deficit		Sleep Questionnaire
Orwelius 2010	Sweden	Prospective, controlled 1625 patients 6,093 reference group	Mixed med-surg ICUs Reference group: Data from a public health survey (random sample of the general population living in the uptake area)	- Age 18 years and older - remained in the ICU for more than 24 hour - were alive six months after discharge from hospital	None specified	- Preexisting disease - Diagnosis - LOS hospital - Born in Sweden - Sick leave before ICU - Employment before ICU	HRQoL	36 months	SF-36 Bodily pain
Sivanathan, 2019	Canada	Case control	Population-based cohort of hospitalized adults (case: admitted to ICU, control: not admitted to ICU). ICU cohort: 121,101	- Aged 18 years or older - survived a hospitalization	- Patients with evidence of a mental illness diagnosis or dementia in the year prior to hospitalization. - Conditions that are known to increase the risk of	- Pneumonia - COPD exacerbation - Asthma exacerbation - Sepsis - Severe Sepsis	Mental illness	1 year	Medical diagnosis

Author year	Country	Study design	Population description number enrolled	Inclusion criteria	Exclusion criteria	Exposure	Outcome measure	Assessment time	Tool
			Hospital cohort: 1,726,361		subsequent mental illness diagnosis, including traumatic brain injury, cardiac surgery, stroke, cardiac arrest, and pregnancy.				
Timmers 2011	Netherlands	Prospective cohort study	Surgical ICU patients 1882 patients	- Trauma - vascular (aneurysmatic and occlusive disease) - gastrointestinal - oncological - general surgery	- age younger than 18 years - readmission to the ICU during the same hospital admission - multiple admissions to the ICU over the study period - gynecological and non-trauma neurosurgery - cardiac surgery	- Age - Sex - Surgical classification - ICU LOS - Emergency vs elective - MV	HRQoL	6 years	EQ-6D

US, United States; ICU, ICU; APACHE, Acute Physiology And Chronic Health Evaluation; BADL, Basic Activities of Daily Living; IADL, Instrumental Activities of Daily Living; PSQI, Pittsburgh Sleep Quality Index; ALI, Acute Lung Injury; HAD, Hospital Anxiety and Depression; BMI, Body Mass Index; PTSD, Post Traumatic Stress Disorder; IES-R, Impact of Event Scale- Revised; CFQ, Cognition Failure Questionnaire; MV, mechanical ventilation; PT, Physiotherapy; LOS, Length of Stay ; NMB, Neuromuscular blocker; ICUAW, ICU acquired weakness; ARDS, Acute Respiratory Distress Syndrome, QoL, Quality of Life; MMT, Manual Muscle Testing; 6MWT, six minute walk test; SF-36, Short Form-36; HRQoL, Health Related Quality of Life; PCS, Physical Component Summary; MCS, Mental Component Summary; COPD, Chronic Obstructive Pulmonary Disease; EQ-6D, EuroQol 6 Dimensions.

Table 3.4 Risk of bias assessment

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Moderate**	**Low**	**Low**	**Moderate**	**Low**	**Low**
Altman et al., 2018 **Moderate**	The study acknowledged and adjusted for potential confounders such as age, gender, baseline depression, APACHE II score, hospital length of stay, mechanical ventilation status, time to follow-up interview, and total days of ICU delirium. The study appeared to have appropriately identified and adjusted for key confounders.	The cohort included critically ill adults admitted to the medical ICU with an expected ICU stay of more than 24 hours. Patients were excluded if their ICU stay was less than 24 hours, if they had been previously enrolled, or if the follow-up interview was completed more than a year after discharge. Exclusion criteria and a significant proportion of patients who were unable to be contacted or died before follow-up might have introduced some bias in selection.	Delirium was assessed daily using the CAM-ICU and chart review methods, which are well-validated tools. The use of validated assessment tools for classifying delirium minimized bias in this domain.	The study design was observational with no deviations from intended interventions reported.	A considerable proportion of patients were lost to follow-up: 24% were unable to be contacted, and 22% died after hospitalization but before follow-up. The missing data, especially among those who were unable to be contacted or died, could have potentially introduced bias.	Outcomes such as sleep disturbance and functional disability were measured using validated instruments like the PSQI and functional status interviews. Some interviews were conducted with patient surrogates. The use of validated instruments and trained staff for outcome assessment reduced the risk of bias, though surrogate interviews could have introduced some variability.	The study reported on predefined outcomes including sleep disturbance and disability, and the statistical analyses were described in detail. The study appeared to have reported all predefined outcomes and used appropriate statistical methods.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**Low**	**NA**	**NA**	**Low**	**Moderate**	**Low**
Bienvenu et al., 2012 **Moderate**	The study identified several potential risk factors for incident depressive symptoms and impaired physical function, including education level, employment status, comorbidities, ICU-related factors, and blood glucose levels. Multivariable models were used to adjust for these potential confounders. Sensitivity analyses were also performed to evaluate the potential bias due to missing data. Residual confounding cannot be completely ruled out.	Mechanically ventilated patients with ALI were consecutively enrolled from multiple ICUs over a three-year period. Exclusion criteria were clearly stated, and informed consent was obtained once patients regained capacity. The study population was from a specific geographic region (Baltimore, Maryland) and specific hospitals, which may have limited generalizability. The consecutive enrolment and clear inclusion/exclusion criteria reduced the risk of selection bias.	Interventions were not specifically described in the methods section. The primary focus was on the outcomes (depressive symptoms and impaired physical function) rather than on interventions. Since the study did not focus on interventions, this domain was not relevant for this assessment.	Not applicable as no interventions were described.	The study used imputation for missing HAD depression scores based on SF-36v2 Mental Health domain scores and assumed stability of conditions when data were missing. Complete case analyses were performed as sensitivity analyses. Missing data were addressed, and results were consistent between primary and complete case analyses. Appropriate methods for handling missing data were employed, and sensitivity analyses supported the robustness of the findings.	Depressive symptoms were measured using the HAD scale, and impaired physical function was assessed through IADL dependencies. Both measures have been validated in previous studies. There was no mention of blinding of outcome assessors, which could have introduced detection bias. While validated tools were used, the lack of blinding of outcome assessors could have introduced some bias.	The study reported on all the specified outcomes, including the incidence, remission, and recurrence of depressive symptoms and impaired physical function. There was no indication of selective reporting based on the provided information. The study appeared to report comprehensively on the outcomes as pre-specified.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Low**	**Low**	**Low**	**Moderate**	**Low**	**Low**
Bienvenu et al., 2013 **Moderate**	The study appropriately adjusted for potential confounders, such as demographic characteristics (age, sex, education), baseline health characteristics (comorbidities, psychiatric and substance use problems), and critical illness-related factors (ICU severity, length of stay, medication use). Sensitivity analyses were conducted to account for missing data and additional potential biases.	The study included a prospective cohort of mechanically ventilated patients with ALI from 13 ICUs at four hospitals, excluding patients with pre-existing conditions that could confound results. However, some selection bias may have risen from patients who declined or were not contacted for consent, which is common in such longitudinal studies.	The classification of interventions (such as the use of ICU medications) appeared accurate, with data collected prospectively from medical records and standardized assessments (e.g., CAM-ICU, RASS).	The study's observational nature meant there were no deviations from intended interventions that could impact the outcomes. Treatments were administered as per usual care in the ICU.	Although the study employed multiple imputation for missing RASS and CAM-ICU values and conducted sensitivity analyses, missing follow-up data could still have introduced bias. Specifically, the assumption that prior PTSD symptom status remained unchanged for patients with missing data may not always hold true.	PTSD symptoms were measured using the IES-R questionnaire, a validated tool with high internal consistency and reliability. Follow-ups at 3, 6, 12, and 24 months allowed for comprehensive assessment of PTSD symptoms over time.	The study pre-specified its outcome measures and statistical methods, including detailed sensitivity analyses to support the robustness of the findings. Reporting appeared to be complete and transparent.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**low**	**NA**	**NA**	**Low**	**Low**	**Low**
Boyle et al. 2004 **Moderate**	The study adjusted for potential confounders like age, gender, and admission category in the logistic regression model. However, the pre-ICU HRQOL status of the patients was not measured, which was critical for understanding the impact of ICU stay on chronic pain and HRQOL and could be considered as a significant confounder.	The inclusion and exclusion criteria were clearly defined and applied consistently. The choice of excluding patients with ICU LOS less than 48 hours was justified for focusing on critically ill patients.	Not applicable as this was an observational study and there were no interventions classified or compared.	The study was observational with no interventions; thus, there was no risk of bias due to deviations from intended interventions.	The study reported a response rate of 67% at 1 month and 53% at 6 months. Efforts were made to contact participants by phone and mail reminders. Comparisons showed no significant differences between respondents and non-respondents regarding key characteristics. Although there was a substantial loss to follow-up, the study performed a reasonable analysis to ensure that the missing data did not bias the results significantly.	The study used validated instruments (PSEQ, SF-36, CES-D) to measure outcomes related to pain, self-efficacy, HRQOL, and depression. The internal consistency of the SF-36 was confirmed with Cronbach's alpha. The use of validated and reliable instruments reduced the risk of measurement bias.	The study comprehensively reported outcomes related to pain, self-efficacy, HRQOL, and depression, including comparisons at 1 month and 6 months. There was no indication that the study selectively reported results.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**Moderate**	**Low**	**NA**	**Moderate**	**Low to Moderate**	**Low**
Bruck et al., 2018 **Moderate**	Potential confounders like severity of illness (APACHE II score), diabetes mellitus, substance abuse, and history of psychological problems were considered and adjusted for in the logistic regression analysis. However, other potential confounders, such as baseline cognitive function, were not assessed, as most patients were emergency admissions. While several confounders were adjusted for, the lack of baseline cognitive function data introduced potential bias.	Patients were included if their ICU stay was longer than 24 hours. Exclusions included mental impairment, serious sensory disorders, inability to understand Swedish, serious aphasia, and transfer to other ICUs. Patients with a RASS of -4 or more were also excluded. The exclusion criteria, particularly those based on language and sensory impairments, might have limited the generalizability of the findings and introduced selection bias.	The intervention classification (severe sepsis/septic shock) was based on standard definitions and the presence of organ dysfunction or the need for inotropic drugs. The classification of the intervention was well-defined and based on standard criteria.	Not applicable, as the study was observational, so no deviations from intended interventions were reported.	There was a 60% response rate for the questionnaires. Non-responders received a reminder letter, but there were still 74 non-responders and 10 who declined participation. The response rate, although comparable to other ICU follow-up studies, was not complete, which could introduce bias due to missing data.	Outcomes were measured using validated questionnaires (CFQ, PTSS-10, HADS). However, the CFQ is a self-rated test, which may have introduced subjective bias. While the measurement tools are validated, the subjective nature of the CFQ could introduce bias, but it is relevant as it reflects patients' perceived cognitive issues.	The results were reported comprehensively, including both significant and non-significant findings. There did not appear to be selective reporting of results.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**Low to Moderate**	**Low**	**Low**	**Low to Moderate**	**Low**	**Low**
Fan et al., 2014 **Moderate**	The study accounted for a range of confounders, such as age, sex, severity of illness at ICU admission (APACHE II score), organ failure status (SOFA score), and a variety of ICU variables including cumulative corticosteroid use, blood glucose levels, and nutritional intake. These were included in the multivariable regression analyses. While many potential confounders were considered, the observational nature of the study means there could still be residual confounding.	Patients were consecutively enrolled from 13 ICUs across four hospitals, with specific exclusion criteria to avoid primary neurologic disease or head injury and other conditions that could interfere with the study. The use of consecutive enrollment and clear exclusion criteria reduced selection bias.	The primary intervention of interest (cumulative corticosteroid use) and other ICU exposures (e.g., neuromuscular blockers, duration of bed rest) were well-defined and measured consistently. The definitions and measurements of interventions were clear and appropriate.	The study did not involve randomization or intervention by researchers, focusing on observing outcomes based on existing clinical practices. Efforts were made to ensure that the observed associations were not due to deviations from standard care. As the study was observational, there were no deviations from intended interventions by the study design.	The study had a high follow-up rate (99% of eligible survivors were followed longitudinally), and missing data for muscle strength assessments were addressed through imputation methods. However, there was a potential for bias due to non-participation of more severely ill patients who did not survive or participate in follow-up. Although missing data were handled appropriately, the impact of non-participation by the sickest patients was a concern.	Outcome measures included standardized manual muscle testing, hand grip strength, and maximum inspiratory pressure, all conducted by trained assessors with high interrater reliability. The use of standardized and reliable measures reduced the risk of bias in outcome measurement.	The study reported on multiple outcomes and performed a range of statistical analyses, including bivariate and multivariable regression models, to explore associations. The comprehensive reporting and analysis of multiple outcomes suggested that selective reporting was unlikely.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Low**	**Low**	**Low**	**Low**	**Low**	**Low**
Huang et al., 2016 **Low**	The study adjusted for potential confounders (age, sex, baseline unemployment, alcohol misuse, pre-existing psychiatric comorbidities, severity of illness, and ICU-related exposures (e.g., opioid use)). Sensitivity analyses accounted for pre-existing psychiatric comorbidity, which strengthened the robustness of the findings. The use of multivariable regression models to adjust for confounders and the consistency of findings across different analyses suggested thorough handling of confounding factors.	Participants were selected from the ARDSNet Long-term Outcome Study (ALTOS), a prospective cohort study. The study included survivors from three ARDSNet clinical trials, with clear inclusion and exclusion criteria. Exclusion criteria included severe comorbid malnutrition, lung, liver or neuromuscular diseases, and cognitive impairment prior to admission, among others. The high retention rate (≥95%) at follow-up indicated minimal loss to follow-up bias.	The study classified interventions and exposures accurately, utilizing established criteria and validated instruments for measurement. The study relied on well-defined protocols for mechanical ventilation and fluid management, along with validated scales (HADS and IES-R) for psychiatric symptoms. Data collection methods were consistent and standardized.	Patients were managed according to simplified versions of lung protective mechanical ventilation and fluid conservative hemodynamic management protocols, with blood glucose control aimed at specific targets. The study did not indicate any significant deviations from these protocols. Moreover, the focus was on the outcomes of psychiatric symptoms, not the interventions themselves.	The study had minimal missing data, with less than 5% of survivors having incomplete data at each follow-up time point. Given the low rate of missing data, the study conducted regression analyses using available data without imputation, which was acceptable.	Outcomes were measured using the HADS and IES-R, both of which are validated instruments for measuring psychiatric symptoms. Outcomes were assessed via phone, mail, or in-person administration by trained research staff, which ensured consistency. However, self-reported measures can be subject to reporting bias.	The study pre-specified its outcomes and analysis methods. Results were reported for all planned analyses, including bivariable and multivariable regression models. The study's comprehensive reporting and transparency in statistical methods reduced the risk of selective reporting.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Moderate**	**Low**	**Low**	**Low**	**Low**	**Low**
Needham et al., 2014 **Moderate**	The study appeared to adequately control for confounding variables through the use of multivariable regression models. They adjusted for age, sex, comorbidities, and baseline functional status, which are crucial factors influencing physical outcomes. The study's methods for handling confounding factors seemed robust and appropriate.	Participants were selected from ARDSNet trials with clear inclusion and exclusion criteria. However, there were exclusions based on cognitive impairment, non-English speakers, and others, which could potentially limit generalizability. Exclusions might have affected the representation of the general ARDS population, potentially biasing the results.	The study intervention (ICU-related factors like length of stay and corticosteroid use) and outcome measures (physical function tests) were clearly defined and standardized across multiple study sites. The definitions and methods for classifying interventions and outcomes appeared consistent and objective.	There were no major deviations reported from the intended ICU management protocols, such as lung-protective ventilation and fluid management, across study sites. Adherence to protocols reduced the likelihood of bias from deviations in intervention delivery.	The study reported low rates of missed follow-up visits, suggesting efforts to minimize missing data. Sensitivity analyses were conducted to assess the impact of missing data. The study's approach to handling missing data appeared rigorous, enhancing the reliability of the findings.	Physical outcomes were measured using standardized tests (e.g., 6MWT, SF-36 PF), with procedures described in detail. Training and quality assurance measures were implemented for outcome assessments. The use of validated measures and quality control procedures reduced bias in outcome assessment.	The study reported all primary physical outcomes and explored associations across different exposure variables (ICU length of stay, corticosteroid use). There was no evidence of selective reporting; all measured outcomes and relevant associations were reported comprehensively.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Low**	**Low**	**NA**	**Moderate**	**Low**	**Moderate**
Orwelius et al., 2011 **Moderate**	The study appeared to have accounted for confounding factors such as age, sex, APACHE II scores, and other socio-demographic variables in their statistical analyses. They adjusted for these factors in their regression models to evaluate the independent effects on HRQoL.	Participants were consecutively admitted to three ICUs in south-east Sweden and met specific inclusion criteria (age 18+, ICU stay >24 hours, alive 6 months post-discharge). Exclusion criteria were clearly defined (e.g., specific medical conditions). Inclusion and exclusion criteria were clear, and participants were likely representative of the ICU patient population within the specified region.	The study did not involve interventions per se but rather assessed social integration (AVSI) and HRQoL using validated instruments (AVSI and SF-36). These instruments are well-established for measuring social integration and HRQoL. Measurement tools were standardized and validated, reducing the likelihood of bias in measurement.	Not applicable as this study does not involve interventions with specified protocols that could deviate.	The study had a response rate of 59%, and efforts were made to contact non-responders with reminders. Differences between responders and non-responders were noted and discussed. Although efforts were made to mitigate missing data (e.g., reminders), the response rate may introduce potential bias if non-responders differed significantly from responders in terms of social integration or HRQoL.	HRQoL was assessed using the SF-36, a well-validated instrument in Swedish and international contexts. AVSI, used to assess social integration, was also validated for reliability. Established and validated instruments were used, minimizing bias in outcome measurement.	The study reported multiple outcomes related to HRQoL and social integration, including adjusted regression analyses to identify significant predictors. While most domains showed low risk of bias, the moderate risk due to missing data suggested caution in interpreting results, particularly regarding the generalizability to non-responders.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Low	**Low**	**Low**	**Unclear**	**Moderate**	**Low**	**Low**
Orwelius et al., 2008 **Moderate**	The study design, a prospective longitudinal study, included appropriate measures to control for confounding variables such as age, sex, and concurrent diseases. This reduced the risk that these factors significantly confounded the observed associations.	The inclusion criteria were clearly defined (adult patients consecutively admitted to ICUs meeting specific criteria), and efforts were made to ensure consecutive enrolment. This reduced the risk of selection bias.	The interventions (ICU care and subsequent follow-up) were clearly described, and there were no indications that there were systematic errors in how these interventions were classified or applied.	While the study design implied a standard protocol for ICU care, there is no explicit mention of how deviations from this protocol were handled or reported. Without this information, it was unclear whether deviations occurred and how they might have impacted outcomes, posing an unclear risk.	The study reported a significant loss to follow-up (response rates were not fully detailed), which raised concerns about missing data. It was unclear how missing data were handled in the analysis, which could have potentially biased results if they were not appropriately addressed.	The outcomes, including sleep disturbances HRQoL, were assessed using standardized and validated instruments (Basic Nordic Sleep Questionnaire, SF-36). This reduced the risk of bias in outcome measurement.	The study appeared comprehensive in reporting various outcomes related to sleep disturbances and quality of life, which mitigated the risk of selective reporting bias.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Serious	**Moderate**	**Low**	**Low**	**Serious**	**Moderate**	**Low to moderate**
Orwelius et al., 2010 **Serious**	The study included patients from three mixed medical-surgical ICUs in Sweden, focusing on ICU survivors over a long-term follow-up period. There might have been potential confounding due to differences in baseline characteristics (e.g., age, sex, comorbidities) between ICU patients and the reference group. Serious, due to possible confounding from pre-existing diseases and demographic differences.	Patients aged 18 years and older, admitted for more than 24 hours to the ICUs, were included. The reference group was from a population survey in the same region. The selection criteria appeared clear, but there might have been biases from excluding certain patient groups.	The interventions were not directly classified, but patients were managed according to ICU protocols and care practices. The study primarily focused on long-term HRQoL rather than specific interventions.	There was minimal risk as the study observes outcomes longitudinally post-ICU care without intervention deviations specified. The focus on HRQoL measures did not imply significant deviations from intended ICU care protocols.	Follow-up rates decreased over time, with 47% response at 36 months. High attrition rates could have introduced biases, especially if non-respondents differed significantly from respondents.	HRQoL measured using EQ-5D and SF-36 questionnaires, validated but not specifically in ICU populations. Validated instruments but potential limitations in capturing ICU-specific outcomes or long-term changes adequately.	The study reported outcomes based on statistical significance and changes in HRQoL over time. Reporting focused on significant findings without adjustment for multiple testing.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**Low**	**Moderate**	**Moderate**	**Low**	**Low**	**Low**
Sivanathan et al., 2019 **Moderate**	The study was a prospective longitudinal cohort study. Confounding might have risen due to factors like age, sex, comorbidities, and severity of illness, despite attempts to control for these through multivariate regression.	Patients were selected from a specific ICU setting in southern Alberta. Potential selection bias could have risen from the exclusion criteria (e.g., traumatic brain injuries, pre-existing neurocognitive disorders).	The intervention (physiotherapy initiation) was at the discretion of attending physicians. Lack of standardized intervention could have led to variability in treatment received.	There was variability in when and how physiotherapy was initiated. Non-standardized initiation could have impacted outcomes measured (muscle strength, 6MWT).	Four patients declined follow-up, and one was lost to follow-up. Missing data could have led to bias if those lost or declined follow-up differed systematically from those included. However, the proportion of missing data was relatively small.	Outcomes were assessed using validated tools (hand-held dynamometry, 6MWT, SF-36, EQ-5D). Variability in measurement techniques or reliability could have impacted outcome assessment.	The study reported multiple outcomes related to muscle strength, physical function, and HRQoL. Selective reporting of outcomes could have biased the interpretation of study findings.

Article Overall risk of bias	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
	Moderate	**Low**	**Low**	**Low**	**Moderate**	**Moderate**	**Low**
Timmers et al., 2011 **Moderate**	The study adjusted for several potential confounders such as age, sex, type of surgical ICU diagnosis, ICU length of stay, elective or emergency admission, and mechanical ventilation. The study appeared to have made efforts to control for confounding variables by using multivariable linear regression and logistic regression. However, potential confounders such as pre-existing comorbidities and socioeconomic status were not detailed or adjusted for in the analysis.	All consecutive surgical patients admitted to the ICU of the hospital between January 1995 and February 2000 were included, with exclusions based on age, readmissions, multiple ICU admissions, and certain types of surgeries. The inclusion and exclusion criteria were clearly stated and seemed reasonable. The prospective nature of the study helped in minimizing selection bias, though excluding patients with multiple admissions and certain types of surgeries may have limited generalizability.	The intervention of interest (surgical ICU admission) was clearly defined and consistently applied across the study population. There was no indication of misclassification of the type of surgical ICU diagnosis. The classification of interventions appeared straightforward with minimal risk of bias.	The study did not describe any deviations from intended interventions. All patients received standard ICU care.	Follow-up data were collected for a significant proportion of the eligible patients (69% completed the questionnaire). However, 31% did not complete the HRQOL questionnaire. Missing data on HRQOL outcomes could have introduced bias, especially if the reasons for missing data were related to the outcomes. The study did not provide detailed reasons for non-response, though it made an effort to follow up by telephone.	HRQOL was measured using the EQ-6D, which includes cognitive functioning and was adjusted using the EQ-5D US index tariff. The EQ-6D is a validated instrument for measuring HRQOL. Outcome assessors were not blinded, which may have introduced measurement bias.	The study reported on all specified outcomes (HRQOL dimensions, EQ utility score, and VAS score) and provided comparisons with the general population. There was no evidence of selective reporting; all prespecified outcomes were reported.

3.5. Discussion

In this study, the prognostic factors related to long-term outcomes of post-ICU patients were systematically reviewed. Due to heterogeneity of studies (variations in sample size, exposures, and outcomes), statistical inferences of the predictors could not be made, hence a meta-analysis could not be conducted. However, by using alternative synthesis methods described in the "data synthesis" section, several factors were found to be associated with PICS. These were divided into two categories- those "In-ICU factors" that are inherent to the ICU experience, nature, and practices, and those factors that are related to patient characteristics.

In-ICU factors

ICU Delirium: The occurrence of ICU delirium appeared to be a significant factor in increased physical disability and lower cognitive function in this review. Similar results have been reported by many recent studies. ICU delirium, characterized by alterations in cognition and behaviour, inattention, and confusion (American Psychiatric Association, 2000) is highly prevalent in the ICU (Salluh et al., 2015). It has been reported to be associated with multiple adverse outcomes, such as prolonged hospital stay (Thomason et al., 2005), increased health costs (Vasilevskis et al., 2018) and increased mortality (Fiest et al., 2021). A recent large multicenter longitudinal cohort study in Netherlands, reported that delirium caused impairments in all domains of physical, mental, and cognition, and reported a lower quality of life one year after ICU admission compared to patients without delirium (Van der Heijden et al., 2023). Furthermore, a systematic review demonstrated that negative ICU experience and delirium had a moderate effect size for anxiety, PTSD, and global cognitive function (Lee et al., 2020). The overall ICU experience and occurrence of delirium could be considered as modifiable factors and hence should attract attention from the ICU teams through nurse-led measures, and appropriate assessment and management of delirium.

Length of stay: Length of stay in the ICU appeared to be an important factor since it was commonly associated with chronic pain, muscular weakness, new mental disorders, and PTSD

in this review. In relation to pain, a similar finding was supported in a study systemically reviewing the occurrence of pain after ICU discharge, where length of stay exceeding 15 days was identified as a predictor for increased risk of persistent pain (Mäkinen et al., 2020). Regarding ICUAW, it has been consistently identified to be related to long hospitalization in several hallmark studies conducted by De Jonghe and colleagues and several others (De Jonghe et al., 2002; De Jonghe et al., 2004; De Jonghe et al., 2007; Herridge et al., 2011). ICU-Acquired Weakness has been defined as "*clinically detected weakness in critically ill patients where the only plausible aetiology is the critical illness itself, and which may persist long after ICU discharge*" (Lad et al., p. 1). It has been found to be experienced by 25-90% of ICU survivors (Jackson et al., 2014; Lad et al., 2020; Needham et al., 2013). Prolonged bed rest, immobilization, and critical illness lead to muscle atrophy and weakness that may last several years after discharge from ICU (De Jonghe et al., 2002; De Jonghe et al., 2004; De Jonghe et al., 2007; Herridge et al., 2011). The use of corticosteroids (Yang et al., 2018) and neuromuscular blockades (Herridge et al., 2003; Rodríguez-Blanco et al., 2022) also seemed to play a role in muscle weakness and this was evident in this review (Fan et al., 2014; Needham et al., 2014). Nurses can initiate early mobilization, in-bed cycling, nutritional supplementation, and other measures to ameliorate ICUAW during and after ICU stay (Zhang et al., 2019). Regarding the association of length-of-stay with the development of psychological disorders, findings of this review were supported by a recent study in Taiwan utilizing a large national database which was charged with the primary aim of investigating the association between ICU stay and depression (Liao et al., 2020). The authors interestingly found a "U-shaped association" with the risk of depression, being lowest in those staying for 8-14 days, and highest in those staying for 1-3 days and beyond 15 days (Liao et al, 2020). The association between length of stay and symptoms of PTSD is more complex though. Earlier research on ICU outcomes hypothesized that early delusional memories and amnesia in the ICU could be the main causes of PTSD, and since amnesia has been found to be associated with longer stay, it could be a proxy for PTSD (Granja et al., 2008; Jones et al., 2001; Schelling et al., 1998). The assessment and screening of mental disorders while the patients are still in the ICU should be exercised diligently, and non-pharmacological interventions could be explored in their ability to ameliorate long-term mental health disturbances.

Mechanical ventilation: Time spent on mechanical ventilator was found to be associated with

long-term chronic pain, a finding which was not substantiated with other literature. Although the literature is abundant in describing the experiences of pain of ventilated patients during routine nursing interventions such as positioning, tracheal suctioning, and other procedures (Al Sutari et al., 2014; Puntillo et al., 2014), a direct association between days of mechanical ventilation and long-term pain has not been previously established. In this respect, healthcare providers could utilize extensive evidence that have shown that duration of mechanical ventilation can be shortened through evidence-based pain assessment and management practices, and protocolized sedation and liberation of mechanical ventilation by instituting Spontaneous Awaking and Breathing Trials (Marra et al., 2017; Payen et al., 2009).

ICU diagnoses: Severe sepsis and septic shock states were associated with the incidence of delirium in the ICU in this review however, these states could not be directly correlated with long-term cognitive dysfunction. Early sepsis studies reported a 3-fold increase in the incidence of long-term cognitive impairments in sepsis survivors (Iwashyna et al., 2010), and proxy factors such as prolonged mechanical ventilation and length of stay have been previously hypothesized (Brummel et al., 2017; Rengel et al., 2019). The pathogenesis of cognitive impairment after critical illness is complex and multifactorial. Possible mechanisms have been hypothesized such as ischemia, neuroinflammation, and disruption of the blood-brain barrier and white matter integrity in areas involving executive functioning and memory (Hopkins et al., 1999, Marra et al., 2018). However, more studies are needed in this area to determine the exact pathogenesis and mechanisms of cognitive morbidity in sepsis/septic shock patients.

In terms of other ICU admission diseases, the findings of this review suggest that oncology patients reported better quality of life, and those with trauma experienced higher incidence of issues related to mobility, self-care, usual activities, and cognition. This can be partly explained as the care for cancer patients admitted to ICU have improved greatly through proper triaging, management of infections, and other strategies of managing underlying malignancies and support of organ functions, leading to better prognosis and ICU survival (Azoulay et al., 2011; Biskup et al., 2017). Cancer patients may also experience enhanced and integrated resources for social networking and support in the form of support groups, education, and others, which have been well documented to have a positive contribution to

the perceived quality of life in the general cancer patient population (Cheng et al., 2013; Howard-Jones et al., 2022; Kroenke et al., 2013; Soares et al., 2013). On the other hand, the outcomes of trauma patients experiencing PICS is well documented in literature, in terms of cognitive impairments (Wolters et al., 2013), significant physical and psychological disabilities (Sluys et al., 2005), inability to go back to work, chronic pain, symptoms of depression and PTSD (Von Ruden et al., 2013). The long-term consequences that trauma patients endure are detrimental, therefore it is advocated that multidisciplinary team members consider and integrate early physical, cognitive, and psychological rehabilitation in their care plans which have shown to have a positive impact on trauma patients' emotional wellbeing and perceived quality of life (Jackson et al., 2012; Van der Schaaf et al., 2009).

In a review by Oeyen et al (2010), it was found that long-term quality of life after severe illness largely depends on the type of diagnosis. Patients suffering from severe ARDS, extended mechanical ventilation, serious trauma, and severe sepsis experienced the greatest and most prolonged declines in QOL, with physical recovery occurring slowly and mental health often deteriorating. Trauma patients, generally young and healthy before ICU admission, saw significant drops in both physical and psychosocial well-being after their ICU stay, impacted by delusional memories and difficulties in returning to work. On the other hand, survivors of cardiac arrest, older patients, and those with severe pancreatitis or acute kidney injury often reported good or even improved QOL after illness, likely due to a higher acceptance of disability, especially among those with a good socioeconomic background. The review also highlighted that factors presumed to predict poor QOL, such as age or lengthy ICU stays, did not necessarily lead to reduced QOL. Other elements, like cognitive impairments, PTSD, and employment status, significantly influenced QOL. Methodological inconsistencies across studies, such as different follow-up durations and low response rates to QOL surveys, limited the findings' interpretation. The review advocated for optimal assessments of long-term QOL using validated tools in large cohorts with consistent follow-up periods and baseline evaluations prior to ICU admission (Oeyen, 2010).

Factors Related to Patient Characteristics

In this review, associations between patient demographics, such as age, gender, employment

status, and education, and domains of PICS were explored. The findings revealed that patients in the younger age group had a higher incidence of anxiety and sleep disturbances post ICU. Female sex and unemployment were associated with anxiety, depression, and PTSD. Education less than 12 years was found to be a predictor of depression. These findings were partly supported by previous literature (Eisendrath et al., 2006; Marra et al., 2019; Wade et al., 2012). In two ICU outcomes studies, those who appeared to be at greater risk for long-term psychological disturbances were women, the unemployed, and those with lower educational and socio-economic status (Eisendrath et al., 2006; Wade et al., 2012). The elderly with chronic diseases were more prone to experience psychological symptoms than younger ones, contrary to findings in this review. Other studies have also found that younger and more educated survivors were more protected from PICS symptoms than their counterparts (Marra et al., 2019). The exact mechanism by which education may be a protective factor is not clear, however it could be explained by the possibility of having better employment opportunities, income, social support, and ability to access information and conceptualize the post ICU experience (Marra et al., 2019).

Prior diseases, such as depression, were associated with impaired physical function, sleep disturbances, PTSD, and lower HRQOL. This finding was partly supported by the systematic review conducted by Lee, et al. (2020), where previous mental health was found to be a strong predictor of PTSD. In another study, prior psychiatric disease, manifested by episodes of depression, anxiety, or having other psychiatric diagnoses, have been associated with psychiatric morbidity after ICU (Schandl, 2013). In a prospective multicenter study, patients with pre-admission anxiety were more likely to suffer from depression and PTSD one year after ICU discharge (Geense et al., 2021). Pre-existing cognitive impairments have been found to be associated with long-term cognitive impairments (Barr et al., 2013). Pre-existing health disorders are not modifiable factors but could trigger clinicians to assess the risk of PICS before and after ICU discharge.

In this review, it was noted that more studies were published in the last ten years, reflecting an increased interest in the long-term outcomes of ICU survivors. Most studies were conducted in United States and Europe than elsewhere, which may be due to higher ICU survival in these continents and hence an interest in long-term outcomes (Lee et al., 2020).

The timing of post-ICU follow-up varied greatly between studies, ranging between three months to six years. The timeframe also depended on the outcome under consideration, as some outcomes occurred early and improved rapidly, some outcomes manifested themselves later, and others overlapped in many domains and different timespans (Rousseau et al., 2021). The timeframe of outcome measurement in this population is very important as research has demonstrated that post-ICU negative outcomes may persist up to eight years after ICU discharge (Cuthbertson et al., 2010; Herridge et al., 2011; TessaDamm et al., 2019).

Regarding the areas of PICS, almost 85% of studies in this review reported on only one domain and none of the studies reported on all PICS domains. This may be because PICS is a novel and contemporary term, and research is evolving in this area.

A diverse range of measurement tools were applied in the studies, which affected integration of evidence. A great variability was found in the reported tools; for example, 8 different tools were used to assess for physical functioning. In addition, most tools utilized in the studies were not specifically developed to assess post-ICU outcomes. A systematic review by Robinson et al., in 2016, explored the performance characteristics of instruments measuring physical, cognitive, mental, and HRQOL outcomes in ICU survivors. Authors reported insufficient evidence about the measurement quality of the instruments used in the domains of PICS (Robinson et al., 2017). There is clearly a need for empirical studies evaluating the performance of such instruments in the adult ICU survivors, and the development of a comprehensive and unique PICS measurement tool would be beneficial.

Recommendations for future research include addressing the three Rs: the right measurement instruments, the right timing of measurements, and the right outcomes, so that methodological rigor can be reached, and cross-study comparisons and synthesis of recommendations can be made. As interest in long-term outcomes in ICU survivors evolves, more long-term prospective studies are needed to examine the health trajectory and changes in outcomes over time. In addition, as the components of PICS are interrelated and multidimensional, it is recommended that research focuses on identifying risk factors that lead to co-occurrence of PICS disabilities. The development of core patient-reported outcomes through rigorous research, as well as expert and patient/family input, should be

prioritized as they will be important in the future of PICS identification and management.

3.6. Limitations

There are some limitations to this study. Although the study spanned over the past 24 years, and the search was undertaken across five databases, it is possible that some relevant studies were omitted. However, a rigorous search was applied in 2019 and repeated in 2023, and a solid process was followed with stringent criteria for inclusion, selection, and quality evaluation of articles by multiple reviewers. Effect sizes could not be calculated, and thus it was not possible to identify the true risks, predictors, and outcomes of intensive care therapy. Relevant and important outcomes might have been missed, which may have led to bias related to outcomes reporting, however, the study included all major long-term outcomes that may occur after a critical illness (physical, cognitive, psychological, and HRQOL).

In this systematic review, the decision to use the ROBINS-I tool over the PROGnosis RESearch Strategy (PROGRESS) checklist (Riley et al., 2019) was guided by the specific focus and nature of the included studies, which predominantly involved non-randomized intervention studies in PICS literature. ROBINS-I was selected for its structured framework that comprehensively evaluates biases such as confounding, selection bias, and attrition bias, ensuring a rigorous assessment of study quality and reliability of evidence. This choice facilitated a general understanding and interpretation of predictors and outcomes in PICS research, aligning with the review's goal to inform clinical practice and policy recommendations related to interventions. While PROGRESS is valuable for assessing methodological quality and bias in prognostic factor studies, the emphasis on intervention effects in PICS necessitated prioritizing ROBINS-I. However, this approach may have constrained the inclusion of studies solely focused on prognostic factors, potentially limiting the breadth of factors considered. Similarly, as the Quality in Prognostic Studies (QUIPS) tool (Hayden et al., 2013) is designed for prognostic factor studies, emphasizing methodological quality aspects, choosing not to use QUIPS in this systematic review on PICS interventions was deliberate to ensure a robust evaluation of bias in non-randomized intervention studies relevant to the focus of the study. ROBINS-I's applicability across diverse study designs encountered in PICS research allowed for a thorough assessment of study quality and reliability, enhancing the review's rigor and

relevance to clinical practice. While this decision may have limited the inclusion of studies focused solely on prognostic factors, prioritizing ROBINS-I was crucial for achieving the review's objectives effectively. Future reviews incorporating PROGRESS and QUIPS criteria could provide additional insights into prognostic factors impacting PICS outcomes across diverse populations and settings.

3.7. Conclusion

This systematic review shows that, although the notion of PICS has developed and grown over the past two decades, rigorous prognostic research is still lacking for clinicians to draw conclusions from and integrate in practice. Several factors could be potentially strong predictors of PICS, such as delirium, pre-existing depression, and length of stay. It is therefore imperative that critical care communities advocate for rigorous studies about PICS, including meticulously designed prospective follow up methods and the use of uniform assessment tools. Composite models capable of predicting PICS should be the focus of research in the next decade, and along with qualitative studies, the goal should be generating a set of patient-reported or patient-important outcomes. This review covered the most important long-term outcomes and HRQoL in post-ICU patients and identified gaps and inconsistencies in the literature. Important insights were derived from this process which informed the next two phases of the thesis- the quantitative look into PICS and its predictors, and a qualitative approach in exploring the experiences and perceptions of patients. The next chapter will describe the methodology adopted in conducting the prospective cohort study in Phase II.

4. Chapter 4: Methodology of Phase II study

Long-term outcomes and Health related Quality of **Life** in **I**ntensive **C**are **U**nit Patients: a prospective cohort study in **S**audi Arabia (**Life-ICUS study**)

4.1. Chapter overview:

The previous chapter presented a systematic review of long-term outcomes and HRQoL of ICU survivors. Although several studies were identified through this process, and an overall understanding of the prevalence, predictors, and outcomes of PICS was formulated, no studies were identified in the literature from Saudi Arabia and the middle eastern region. This chapter presents the initiation of Phase II and the methodology of the investigation of long-term outcomes and HRQoL in a cohort of ICU patients in Saudi Arabia. This study title was abbreviated as the Life-ICUS study, where "S" refers to Saudi Arabia. The chapter starts with an introduction, followed by a proposal of a conceptual framework which was developed throughout this research process and underpinned the Life-ICUS study. Based on this framework, research aims and questions were developed and are presented in the next section. In the last part of this chapter a detailed methodological description of the Life-ICUS study will be provided, including recruitment procedures, tools utilized throughout the study process, and statistical approaches to this study. The next chapter will present the results of this study with an in-depth discussion of the overall findings.

4.2. Introduction

Traditionally, outcomes of intensive care in hospitals have been studied with physiological, clinical, and mortality endpoints in mind (Curtis, 2002). As described in Chapter 3, the focus has shifted towards those who survive the ICU. Patients experience long-lasting and devastating consequences termed PICS. This is characterized by 1) Physical disabilities, that include ICUAW and inability to perform activities of daily living (ADLs); 2) Cognitive impairments including poor memory, inattention, and inadequate executive functions, and 3) Psychological sequelae such as depression, anxiety, and PTSD. The above disturbances lead to poor quality of life and raise a significant public health concern.

In Saudi Arabia, there are 470 hospitals, of which many have medical-surgical ICUs (Ministry of Health, 2020). Medical and nursing leaders of critical care in the country recognize that research regarding ICU practices and outcomes are lagging due to the absence of national critical care databases and a generally slow growth of clinical research funding (Al-Omari et al., 2015). Through a systematic review conducted earlier and described in Chapter 3, it was evident that little is known about ICU outcomes in KSA and there are no data on PICS. Through interactions with critical care clinicians, it was recognized that patients are not currently assessed for PICS prior to and after discharge from ICU. In the absence of post-ICU clinics, specific physical, cognitive, psychological, and HRQoL evaluations are not conducted for post-ICU patients. Opportunities to improve the care inside and after ICU remain severely under-recognized. To the best of our knowledge, this was the first study on PICS in ICU survivors in Saudi Arabia.

4.3. Conceptual Framework

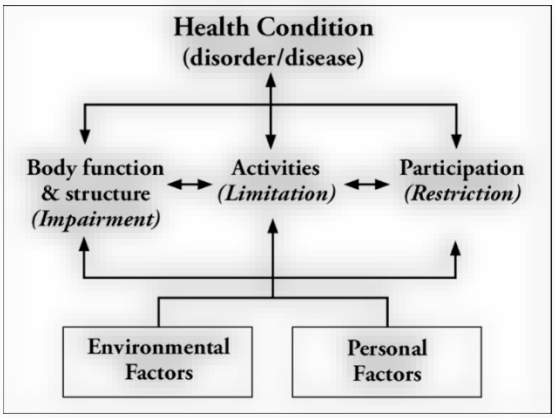
Studying the long-term outcomes of ICU patients in the context of a structured conceptual framework provides an opportunity to broaden and deepen the knowledge about the PICS phenomena and assists in considering all possible determinants and predictors of PICS outcomes. It also guides critical care researchers to explore uncharted territories related to possible causes that may attribute to adverse outcomes. These causes may originate from factors prior to the critical illness episode, during the care of the patient inside the ICU, and after the event of the acute illness. Ultimately, a comprehensive conceptual framework helps widen the horizon for exploring patient-centric outcomes and leads the ICU community to adopt standardized approaches to outcome evaluation. The employment of standardized assessment tools or patient reported outcomes measures (PROMs), and their investigation across studies, enhances comparability of studies. This provides a rich medium for healthcare providers to develop and execute risk mitigation strategies and quality improvement initiatives to improve long-term outcomes for patients and their families.

For the purpose of the current study, a comprehensive conceptual framework for PICS was designed in accordance with 1) The World Health Organization's (WHO) International Classification of Functioning, Disability and Health (ICF) model, 2) The Society of Critical Care

Medicine's PICS framework, and 3) the systematic review conducted in this area and reported in Chapter 3.

The WHO has established the ICF to provide a framework for health and disability definitions and measurements (WHO, 2001). It identifies the role of personal factors, health conditions, and the environment in overall functioning (WHO, 2001) (see **Figure 4.1**). It categorizes sequelae of acute illness into a number of functional elements: "impairment to body function and structure", "limitation in activities", and "restriction in participation in social roles" (WHO, 2001).

Figure 4.1. International Classification of Functioning, Disability, and Health (ICF). (WHO, 2001. Reproduced with permission from WHO)

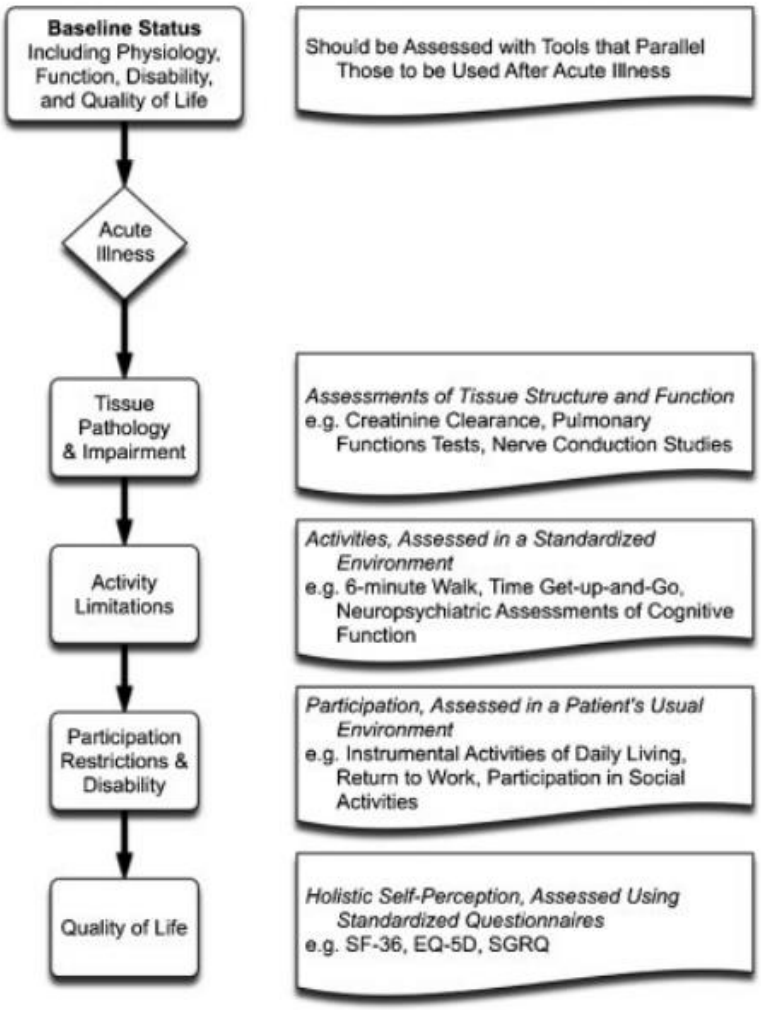


Iwashyna and colleagues have suggested that post-ICU outcomes be considered within the concepts of this framework with a proposition to add a fourth category to the PICS outcomes, which is quality of life (Iwashyna et al., 2012) (see **Figure 4.2**). It is hypothesized that critical illness causes organ failures and subsequent impairments, including those of activity and cognition, which in turn lead to constraints in social engagements and thus influence quality of life (Iwashyna et al., 2012). It is easier to understand this concept in an example. Visualize Mr Abu Zeid, for example, who is mechanically ventilated for pulmonary disease (impairment to body function and structure), who then develops delirium after a three-day period of sedation and experiences cognitive impairments after discharge from the ICU (limitation in activities), and is no longer capable of grocery shopping for his family because he is not able to organize the list fully and navigate to find the items on the racks of the market (restriction

in participation in social roles). He verbalizes deep dissatisfaction with these deficits and diminished quality of life.

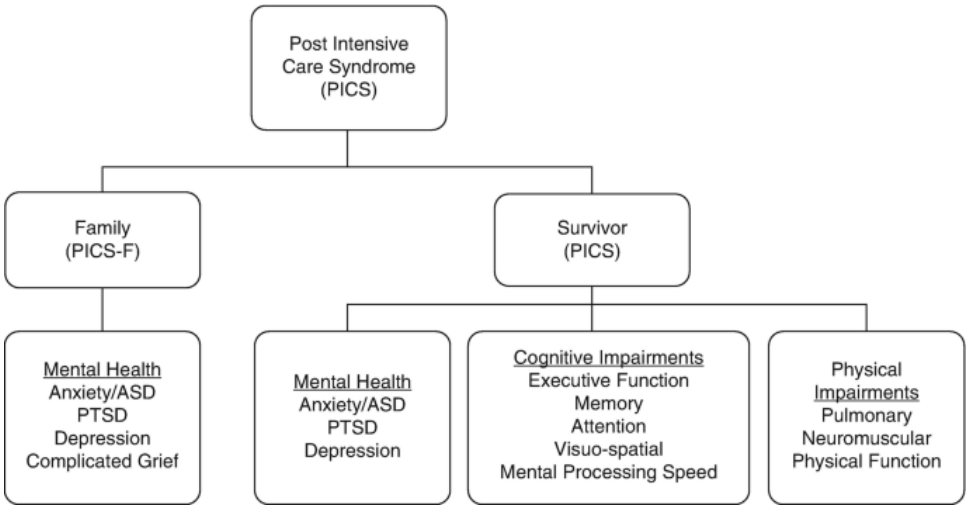
Quality of life, in this context, is proposed to be a "*holistic measure of the extent to which a patient is satisfied with his or her life*" (Iwashyna et al., 2012, p. 329). The WHO provides a broader definition of quality of life as "*individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationship to salient features of their environment*." (WHO, 1993, p.153). In its clinical relevance, the term HRQoL, is defined as "*the relative desirability of measured or estimated health states*" (Gold, et al., 1996, p. 158). HRQoL has been recognised as perhaps the most central outcome in health and disease (Rai et al., 2020). Within this understanding of HRQoL, the extent of disablement is variable and could be considered modifiable (Haines, 2016). For example, the perceived HRQoL of Mr Abu Zeid could be variable and modified relative to whether he underwent spontaneous awakening and breathing trials in the ICU, received less sedation, was cared for in a quiet ICU room, had family present at his bedside to ameliorate his confusion, received early rehabilitation inside the ICU and progressed after discharge, and whether or not he received social support after returning home. Within the premises of Iwashyna's framework that integrated quality of life, modifiable and non-modifiable factors could be considered, studied, and applied to the evidence-based practices inside the ICU.

Figure 4.2. A conceptual model for studying long-term outcomes after critical illness, rooted in the International Classification of Functioning, Disease and Health. (Permission to use from Georg Thieme Verlag KG).



The second aspect of designing the framework of the Life-ICUS study considered the PICS framework developed by Needham, et al. following the SCCM first stakeholders conference in 2010 (Needham et al., 2012) (see **Figure 4.3**). The outline of this framework was established based on research in critical care survivorship, indicating that patients experience long term physical, cognitive, and mental health impairments, collectively recognizing them as PICS for the first time (Needham et al., 2012). The prevalence and predictors of these impairments have been fully described in Chapter 1 and 3. A brief overview and selected references are stated for each domain of PICS as follows:

Figure 4.3. Postintensive care syndrome (PICS) conceptual diagram. (Needham et al., 2012; Permission to use from Wolters Kluwer Health, Inc.).



- Physical domain: Impairments after critical illness occur in the form of ICU-acquired weakness (ICUAW), further classified as “critical illness polyneuropathy (CIP)” and “critical illness myopathy (CIM)”, in addition to long-term pain and disabilities in ADLs. Predictors have been found to be prolonged mechanical ventilation and ICU stay, sepsis, immobility, use of corticosteroids and neuromuscular blockades (De Jonghe et al., 2002; Desai et al., 2011; Herridge et al., 2009; Herridge et al., 2011; Stevens et al., 2007; Stevens et al., 2009).

- Cognitive domain: Disturbances in memory, executive functioning, and attention are the main difficulties for patients in this domain. Predictors include pre-existing cognitive deficit, high disease severity index, sepsis, duration of ICU delirium, type and dose of

sedatives, and duration of mechanical ventilation (Girard et al., 2010; Herridge et al., 2003; Hopkins et al., 2005).

- Mental Health domain: Clinically significant anxiety, depression, and PTSD have been widely reported in the post-ICU period, with predictors such as pre-existing psychiatric disorders, sleep deprivation, and prolonged mechanical ventilation. Those at risk have been identified to be women, the unemployed, and those with lower educational and socio-economic status (Davydow et al., 2008; Hopkins et al., 1999; Hopkins et al., 2010; Jones et al., 2010; Kamdar et al., 2011)

Although the SCCM did not include quality of life in its diagram of the framework (**Figure 4.3**), it made substantial references to the implications that PICS poses on a patient's overall post-ICU experience, recovery, and quality of life (Dowdy et al., 2005; Dowdy et al., 2006). The SCCM advocated for consensus in measuring this fundamental outcome in the post-ICU setting (Needham et al., 2012). It also highlighted some of the measures and structured rehabilitative interventions that could potentially mitigate the negative impact of PICS on quality of life (Elliot et al., 2014; Jones et al., 2003; McWilliams et al., 2009; Schweickert et al., 2009; Needham et al., 2010).

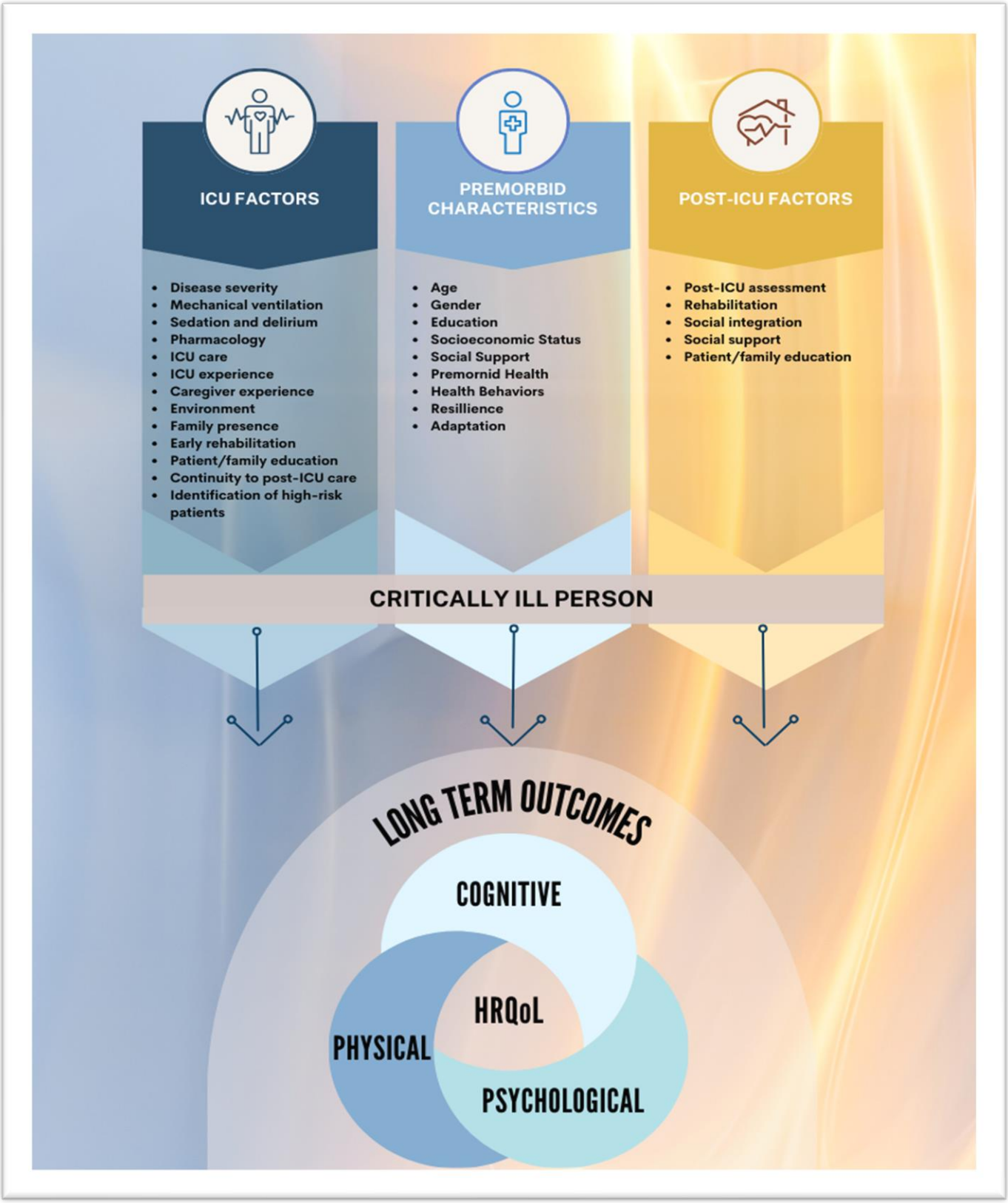
The SCCM framework also recognized that PICS not only affects patients, but it also impacts caregivers and family, dedicating a section of the PICS diagram to PICS-Family (PICS-F). Research has clearly illustrated that caregivers and family of critically ill patients experience similar mental health disturbances as their loved ones, demonstrating symptoms of depression, PTSD, burden, and reduced quality of life (Cameron et al., 2008; Davidson et al., 2007; Davidson et al., 2017; Jones et al., 2004). Although the Life-ICUS study focuses on the ICU patients and does not address PICS-F, its predictors, outcomes, and caregiver/family experiences in the Saudi setting, the dyad patient-caregiver experiences of PICS are of paramount importance, and awareness and research about families' outcomes and challenges should be elevated.

The third aspect that was taken into consideration for the development of the Life-ICUS conceptual framework was the systematic review on long-term outcomes and HRQoL in adult

ICU patients described in Chapter 3. In brief, the predictors for one or more of the PICS domains were divided into two sections: 1) In ICU conditions, including ICU delirium, length of stay, use of corticosteroids and neuromuscular blockades, mechanical ventilation, sepsis, oncological and trauma diagnoses; and 2) patient characteristics, including age, gender, employment status, education, prior disease states including those related to mental health conditions.

In accordance with the above frameworks (Figure 4.1, Figure 4.2, and Figure 4.3) and in conjunction with the knowledge acquired about PICS through a systematic review of literature (Chapter 3), a comprehensive framework was developed to guide this study (**Figure 4.4**).

Figure 4.4. Conceptual Framework of Life-ICUS and Life-ICUS-Q studies.



This framewrok captures all possible elements of PICS that have been identified so far. However, for serious methodological and practical reasons, not all components of this framework were studied in the quantitaive and qualitative phases of this thesis. Not all components of the framework were within the scope and aims of the Life-ICUS and Life-ICUS-Q studies; bolded areas in the below descriptive sections refer to the ones investigated in this thesis.

This proposed framework puts the person in the centre of care, and recognizes the four major domains of long-term outcomes of critically ill patient (PICS) in the following manner:

- **Physical:** these outcomes include **weakness, ADLs, pain**, and **fatigue**.
- **Cognitive:** these outcomes include **memory, attention, executive functioning,** and **sleep**.
- **Psychological:** these outcomes include **anxiety, depression, and PTSD.**
- **HRQoL:** these outcomes include **(physical, cognitive, emotional, social,** relationships, financial, and return to work)

The framework also identifies three major areas where causes, predictors, and determinants of PICS could be hypthesized: a) premorbid characteristcs b) ICU factors, and c) Post ICU factors. Again, bolded words refer to the factors systemtically examined in this thesis.

a. Premorbid characteristics are **age, gender, education, socio-economic status** (e.g. **employment**, **financial**), **premorbid health (e.g. pre-exisiting physical, cognitive, or psychiatric disorders,** frailty), health behaviours (e.g. smoking, alcohol and drug abuse), **social support**, **resilience and adaptation**.

b. In ICU factors include **disease type and severity** (e.g. **sepsis, APACHE II score**), **mechanical ventilation, sedation, delerium, pharmacology used in ICU (e.g. corticosteroids, neuromuscular blockades)**, ICU care (e.g. early ambulation, hand hygiene, prevention of Hospital Acquired Infections, use of restraints, nutrition), ICU experience (e.g. pain, sleep, weight loss, **memories**), caregivers experience (e.g. education, staffing, work

environment), ICU environment (noise, daylight), family presence (e.g. open visitation, ICU diary), early rehabilitation, continuity to post-ICU care, and patient and family education.

c. Post-ICU factors include post-ICU evaluations (e.g. PICS clinics), rehabilitation (physical, cognitive, psychological, and functional), social integration and support (e.g. support groups), and patient and family education.

4.4. Aims

Using the framework as outlined above, the main aims of the life-ICUS study were to:

- Determine the long-term outcomes and HRQoL of a sample of Saudi Arabian adult ICU patients at 3 months after ICU discharge.
- Identify the predictors of long-term (physical, cognitive, psychological), and HRQoL outcomes in this sample.

4.5. Objectives

The objectives of this study were to:

- Identify demographic and clinical characteristics of the study sample.
- Assess the patient's pre-existing ADL and cognitive status.
- Examine the patients' physical, cognitive, psychological, and HRQoL outcomes at discharge from ICU.
- Examine the patients' physical, cognitive, psychological, and HRQoL outcomes at 3-months after ICU discharge.
- Demonstrate the changes in patients' physical, cognitive, psychological, and HRQoL status from discharge to 3-months follow-up.
- Investigate the associations between demographic characteristics and changes in long-term and HRQoL outcomes from discharge to 3-month follow-up.

- Investigate the associations between clinical characteristics and changes in long-term and HRQoL outcomes from discharge to 3-month follow-up.

4.6. Methods

This was a single-center, prospective longitudinal cohort study.

4.6.1. Justification for study design

After carrying out a thorough literature review and later a systematic review on long-term outcomes and HRQoL in ICU patients (Chapter 1 and 3), it was evident that physical, cognitive, and psychological morbidity, and poor HRQoL were prevalent problems after ICU. No studies, as far as we know, however have been conducted in Saudi Arabia and a significant gap was found in the understanding of the long-term consequences and challenges faced by patients after their discharge from the ICU. The need for a high-quality investigation that would generate information on the long-term status of patients and predictors of outcomes was imperative. Selecting the prospective cohort design among other observational studies, such as retrospective cohort or case-control designs, was deliberate, as this type was considered the strongest approach that would address the study aims and objectives.

The following rationale outlines this approach:

- **Minimizing Bias and Confounding**

Prospective cohort studies are advantageous in their ability to minimize bias and confounding, thus enhancing the internal validity of the research findings (Hulley, 2001). It was considered that recruiting participants at the onset of ICU admission and following them longitudinally would allow baseline and ICU data collection before the occurrence of outcomes, thus minimizing the likelihood of selection bias. The prospective nature of the study also reduced recall bias as data were gathered prospectively rather than relying on retrospective recall (Merril, 2006). Additionally, comprehensive baseline data collection, including patient demographics, comorbidities, and severity of illness, allowed for the adjustment of

confounding variables during the analysis phase. This adjustment ensured that the observed associations between exposures and long-term outcomes were not distorted by the influence of other variables, improving the accuracy and reliability of the study findings (Hulley, 2001).

- **Ability to Examine Multiple Exposures and Outcomes**

Prospective cohort studies are useful in examining multiple exposures and outcomes simultaneously (Merril, 2006; Song, 2010). As demonstrated in the systematic review in Chapter 3 and derived from the conceptual framework described above, various factors can influence ICU patients' health outcomes, including their demographics, comorbidities, and ICU interventions. By collecting comprehensive data on these variables, this design enabled the researcher to assess new relationships between exposures and outcomes, and the cumulative effects of multiple exposures on long-term outcomes.

- **Establishing temporal sequence and cause-effect relationship**

Prospective cohort studies are robust in their ability to establish temporal relationship between exposures and outcomes (Song, 2010). By recruiting and enrolling patients at the time of their ICU admission and following them over time, this design allowed exposure data to be obtained before outcomes occurred. This temporal sequencing was essential for inferring causality, as it would enable the researcher to determine whether the exposure preceded the outcomes (Song, 2010). In the context of long-term outcomes of ICU patients, this design was considered ideal for assessing the influence of ICU care, patient demographics, clinical characteristics, and other factors on subsequent outcomes. As the objectives of this study were to capture outcome data at multiple time points (at discharge and at 3-month follow up), this design was deemed best at capturing the evolving nature of critical illness recovery and its consequences.

The decision to follow up patients for three months after their ICU discharge was deliberately made as this was deemed an adequate timeframe where patients would recover and stabilize from their acute illness (Haines et al., 2020). It was also considered as an appropriate time as patients would have had the chance to adjust to their condition and circumstances. Assessing

patients too early, such as within a few weeks of ICU discharge, may not have accurately portrayed their true long-term trajectory as they would still be in early stages of recovery. The three-month time mark has been widely used in critical care research for proper assessment and prognostication, and for cross-study comparisons (Haines et al., 2020).

- **Generalizability and External Validity**

Prospective cohort studies generally demonstrate a higher degree of generalizability and external validity compared to other study designs (Merril, 2006; Song, 2010). By enrolling a representative sample of ICU patients and collecting comprehensive data, the findings would likely be applicable to a broader population of ICU survivors (Hulley, 2001; Song, 2010). This would enhance the external validity of the study, allowing for a better understanding of the long-term outcomes of ICU patients in real-world settings (Hulley, 2001; Song, 2010). The ability to generalize the findings to a wider population would contribute to evidence-based decision-making, policy development, and the improvement of long-term strategies for ICU survivors (Hulley, 2001).

The disadvantages associated with this design were also carefully contemplated. The following describes these drawbacks and the methodological strategies taken to overcome the limitations.

- **Time and Resource Intensive**

Prospective cohort studies can be time and resource-intensive due to the need for long-term follow-up and data collection (Merril, 2006; Song, 2010). The extended duration of the study was a risk for participant attrition and loss to follow-up, potentially introducing bias and compromising the generalizability of the findings (Song, 2010). To overcome this limitation, meticulous planning and time were allocated and re-evaluated periodically. In addition, a strong follow-up system was established with regular contact and reminders to enhance participant retention and minimize attrition and survivorship bias. More on this will be described in the procedures section.

- **Confounding and Variable Control**

Prospective cohort studies are susceptible to confounders, as the exposure-outcome relationship may be influenced by unmeasured or unknown factors (Elwood, 2007). Despite comprehensive data collection at baseline, certain confounders may still be overlooked or not adequately accounted for (Elwood, 2007). To address this concern, rigorous statistical analyses were planned to be employed in this study to adjust for confounding variables during data analysis.

- **Ethical Concerns and Informed Consent**

Generally, prospective cohort studies raise ethical concerns regarding obtaining informed consent and ensuring participants' autonomy and privacy (Song, 2010). Investigating critically ill patients poses further vulnerabilities and challenges due to the nature of the course of their treatment and recovery (Jackson et al., 2021). To mitigate these ethical concerns, the researcher carefully planned the process of obtaining informed consent with allocation of adequate time, space, and informational sheets in Arabic language.

4.6.2. Ethics approval:

Ethics approval was granted for this study from AlMoosa Specialist Hospital Institutional Review Board (ARC-21.07.03) (**Appendix 4.1**) and King's College London Ethics Committee (MOD-21/22-14821) (**Appendix 4.2**). In the process of ethics approvals, both English and Arabic consent forms and information sheets were prepared for patients and families. These forms were revised and modified meeting the requirements set by both organizations.

4.6.3. Setting:

Patients were recruited from the ICU at AlMoosa Specialist Hospital in the Eastern Province in Saudi Arabia. This is a 400-bed university-affiliated medical center with a 45-bed Intensive Care Unit which provides care to general medical and surgical adult patients. The number of admissions in 2022 was 581 patients. The top three reasons for admission in 2022, the year

when data was collected, were respiratory failure, acute kidney dysfunction, and sepsis. The mortality rate in 2022 was 14%. The hospital does not provide post-ICU services in a post-ICU or PICS clinic.

4.6.4. Participants:

Participants were recruited from January 21 to December 31, 2022 from the ICU of the hospital, and were followed up 3 months after discharge.

Inclusion criteria:

- General medical/surgical ICU patients;
- above 18 years of age;
- ICU stay ≥ 48 hours.

Exclusion criteria:

- Documented psychological, cognitive or neurodegenerative diseases at baseline (mental illness, substance abuse, stroke, traumatic brain injury, Parkinson's disease, Alzheimer's disease, severe cognitive deficits);
- Neurology and neurosurgery patients;
- Cardiac and cardiothoracic surgery patients;
- Do-Not-Resuscitate status;
- Those who are not expected to survive for an additional 24 hours or in a persistent vegetative state (as determined by treating physician);
- Post-cardiac arrest with anoxic/hypoxic brain injury;
- Blind, deaf, or unable to speak Arabic or English.

4.6.5. Procedures:

The list of patients meeting the study inclusion criteria was checked every day by the researcher, Sunday through Saturday, except for holidays and annual leave, by calling the ICU

manager or charge nurse.

A two-step approach was adopted for recruitment of potential participants who met the inclusion criteria. First, the participant's treating physician, or another member of the medical team, approached the participant. If he/she demonstrated interest in the study, then the process of providing further information and obtaining informed consent was initiated (see **Appendix 4.3**: Informed Consent and Information Sheet and **Appendix 4.4** Information Sheet for Family).

The informed consent process was conducted in a private setting (in the patient's private room in ICU). Written informed consent was sought from each participant after fully informing him/her of the objectives, benefits, and risks of the study. The consent form was presented in clear and simple language. The participant was given ample time to ask questions, inquire further information and decide whether to participate or not. For those accepting participation, two original consent forms were completed, dated, and signed by the participant. Patient medical records were not reviewed prior to obtaining the signed informed consent.

In some instances, the patient was sedated and/or mechanically ventilated at the time of enrollment. In these situations, to protect the patient's rights, written informed consent was sought from the next-of-kin or the legal guardian of the patient. On the occasion where there was more than one next-of-kin, the consent to participate was obtained in consensus by all members involved. Two original consent forms were completed, dated, and signed by all members.

If consent was initially obtained from the next-of-kin or legal guardian, the patient was consented once his/her capacity was regained in the same approach as described above. The patient's own consent, once his/her capacity was regained, took priority. In the case where the patient refused participation in the study, all previously collected data were destroyed.

Once a participant consented to the study, he/she was assigned a study identification number, which was linked to the patient medical record number (MRN). The MRN was not

included on the data sheet, but only the study ID number was recorded. The sheet linking study ID and patient MRN were stored separately from the data sheets. All forms that contained the participants' names and contact information were saved in a locked cabinet only accessible by the researcher. Data files were saved on the researcher's KCL drive, which was accessed by username and password known only to her.

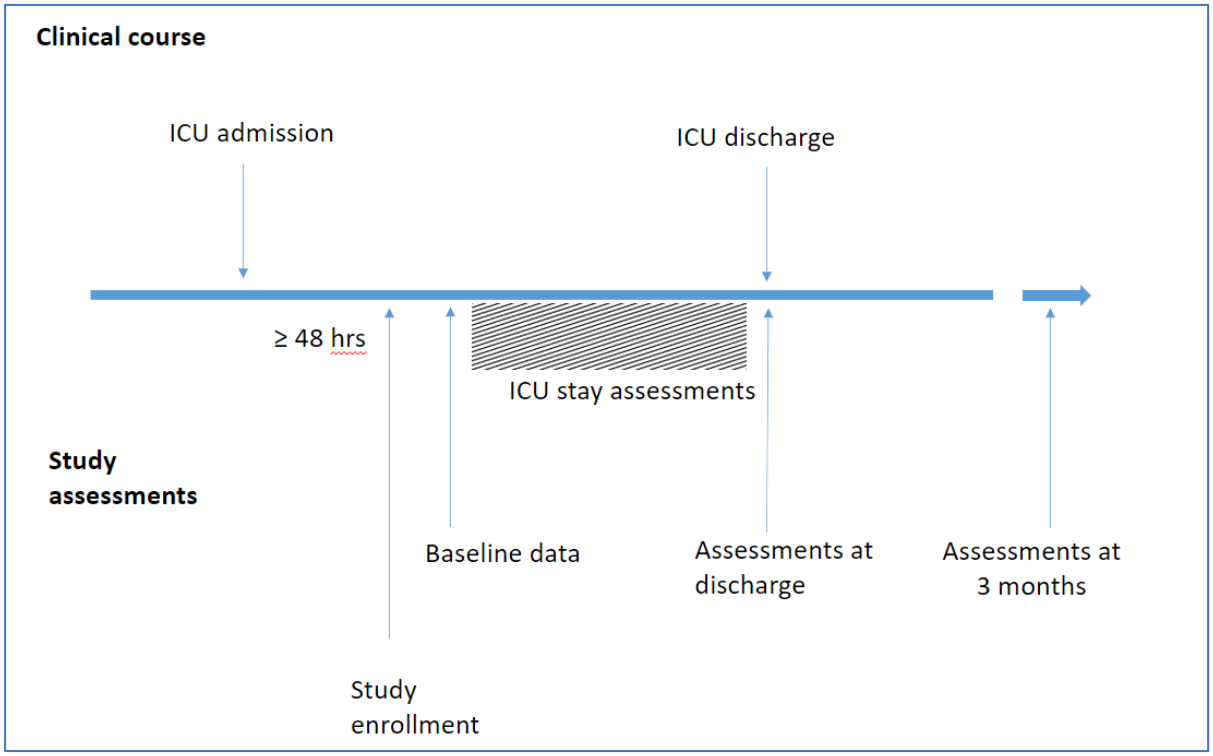
4.6.6. Data collection:

Upon enrollment, baseline data (demographic and clinical) were collected from the medical chart and measures of pre-existing physical and cognitive assessments (ADL and A-IQCODE) were completed by proxy (more on the assessment tools below). Throughout their ICU stay, information about sedation and delirium (RASS and CAM-ICU) was collected daily until the patient discharged from the ICU. Upon discharge from the ICU, outcome measures for physical cognitive, psychological, and HRQoL (ADL, MoCA, HADS, PCL-C, and SF-36) were assessed. See **Figure 4.5** for the timepoints of data collection.

At 3 months' follow-up, the patient was contacted by phone to schedule for an evaluation of outcomes at his/her home. Prior to each contact, the patient's status (living or dead) was checked through the hospital's health information system and/or primary physician to avoid calling deceased patient's family for study follow-up. Follow-up visits were conducted in the patients' homes. A family member was welcome to attend the assessment session, however asked not to help with the surveys.

In the event of a patient scoring low on the cognitive (MoCA < 26), and high on the anxiety, depression, and PTSD scales (11-21 on either aspect of the HADS, and > 45 on PCL-C), a referral was made to the patient's physician demonstrating that the patient had significant risk for cognitive and psychological disturbance on the relevant screening tools.

Figure 4.5. Time points of study data collection.



4.6.7. Tools used in the study:

Table 4.1 is a summary of all the tools used in the data collection process.

Table 4.1. Tools used in the data collection process.

	Measurement	Assessment Tool	Time(s) of assessment	Time required (minutes)
Baseline	Demographics	Medical Record	Enrollment	1
	Severity of illness	APACHE II	Enrollment	7
	Pre-existing physical impairment	ADL	Enrollment	2
	Pre-existing cognitive impairment	A-IQCODE	Enrollment	10
ICU stay	Sedation	RASS	Daily	< 1
	Delirium	CAM-ICU	Daily	1
Outcome	Physical impairment	ADL	At ICU discharge and 3 months	2
	Cognitive impairment	MoCA	At ICU discharge and 3 months	11
	Anxiety and depression	HADS	At ICU discharge and 3 months	6
	PTSD	PCL-C	At ICU discharge and 3 months	5
	HRQoL	SF-36	At ICU discharge and 3 months	12

4.6.7.1. Baseline data: Upon recruitment the following data were collected:

Demographic and clinical information (**Appendix 4.5**)*:* age; gender; BMI; educational level; current occupation; admission diagnosis; admission status (non-surgical, surgical, elective; surgical, emergent); comorbidities; medications prior to admission; length of stay in ICU; length of stay in hospital. In addition, duration of mechanical ventilation (days) and duration of sedation (days) were noted.

Severity of illness: Severity of illness was assessed by the Acute Physiology and Chronic Health Evaluation (APACHE II) scale (**Appendix 4.6**). The rationale for including this was that mortality prediction tools are often used to determine prognosis, help healthcare providers and family members make informed decisions about the care of the patient, and are essential tools used in research studies to assess the characteristics of baseline risk groups compared to others (Keuning et al., 2020). In the critical care setting, several prognostic tools have been utilized, including the Acute Physiology and Chronic Health Evaluation (APACHE) (Knaus et al., 1985) and the Simplified Acute Physiology Scores (SAPS). In research, assessing the long-term outcomes of post-ICU patients, both of these tools have been used, however the APACHE II has been preferred over the SAPS in terms of two objective measures: calibration and discrimination (Gilani et al., 2014; Ko et al., 2018). "*Calibration refers to how closely the estimated probabilities of mortality correlate with the observed mortality over the entire range of probabilities. Discrimination refers to how well the model discriminates between individuals who will live and those who will die*" (Sakr et al., 2008, p. 801). The APACHE II score generates a point score ranging from 0 to 71, by assigning points in 3 domains: acute physiology (Acute Physiology Score [APS]) based on 12 physiologic variables; age; and chronic health (Chronic Health Index [CHI]). Patients with higher APACHE II scores have a higher severity of illness.

Pre-existing physical function: This assessment was done by asking proxies to evaluate the pre-ICU physical function of their patient by using the ADL tool (**Appendix 4.7a** for English version and **Appendix 4.7b** for Arabic version). The rationale for inclusion of this tool was that the ADL is a simple instrument that assesses physical or functional ability (Katz et al., 1963). When used by proxies, this tool can be useful in establishing premorbid physical function of

the patient (Haines, 2016) and some studies have demonstrated agreement between the proxy, when used as a baseline assessment, and the patient, during follow-up (Brummel et al., 2014; Choi et al., 2014). In the absence of other means of establishing pre-existing physical dysfunction (Haines, 2016), this tool was considered most appropriate to be used by proxies in this study due to its simplicity. The tool assesses functional activity in six areas, ordered in the following manner: bathing, dressing, going to toilet, transferring, continence, and feeding (Katz et al., 1963). Each area is assessed with a score of 0 for complete dependence, 0.5 as partial independence, and 1 as complete independence. Hence, the lower the total score, the more severe the dependence. A total score of 0 would indicate very dependent, 1-5 would indicate partially dependent and 6 would indicate totally independent (Katz et al., 1963).

Pre-existing cognitive function: This assessment was done by asking proxies to evaluate the pre-ICU cognitive function of their patient by using the Arabic-Short Form Informant Questionnaire on Cognitive Decline in the Elderly (A-IQCODE) (**Appendix 4.8a** for English version and **Appendix 4.8b** for Arabic version). The rationale to have this tool was that a large proportion of the ICU patients over 65 years are reported to have pre-morbid cognitive impairment (Pisani et al., 2003). Careful screening of these patients is important to identify cases of baseline cognitive impairment and adjust for it as a co-variate during data analysis. Identifying patients with a history of stroke or Alzheimer might be easy, however patients with mild or moderate cognitive impairment who do not have a formal diagnosis might be overlooked and hence, in this study, might increase the chance of over-estimating the incidence of cognitive impairment in the post-ICU setting (Lee et al., 2008). Assessing the patient directly by using traditional screening tools might be difficult in the ICU, since many patients would be sedated or on mechanical ventilation. In clinical practice, and in epidemiologic studies, it is accepted to use proxy questionnaires to assess for pre-existing cognitive impairment (Lee et al., 2008). In the critical care setting, the Short Form Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) tool has been used to identify the magnitude of cognitive decline, using an informant (Jackson et al., 2004; Pandharipande et al., 2013). The tool consists of a series of 16 questions addressed to the patient's surrogate, usually a family caregiver, who has close knowledge of the patient. The IQCODE requires the informant to have known the patient for at least 10 years to respond to the questions. Although this 10-year timeframe has been chosen based on the reasoning that the survival

after dementia onset usually does not exceed 10 years, however, other studies have demonstrated that using a 5-year timeframe does not affect the validity of the instrument (Phung et al., 2015). In the study where the tool was translated and tested in Arabic (A-IQCODE), a period of only one year was chosen to be sufficient for the informants to have observed the patients, with the rationale that establishing a cognitive decline of one year is sufficient to diagnose dementia congruent with The International Classification of Diseases 10th revision (ICD-10) criteria (Phung et al., 2015). Each question of the Short IQCODE is rated on a 5-point scale; a score of 1 represents much improvement, a score of 3 represents not much change, and a score of 5 represents much worse performance. The total score on the 16 questions is then divided by 16 to generate a score ranging from 1 to 5, with higher scores denoting worsening cognitive function. Different cut-off thresholds have been reported in the literature, ranging from 3.3 to 3.9 to determine pre-existing cognitive impairment (Pandharipande et al., 2013). In the Life-ICUS study, patients who were suspected to have preexisting cognitive impairment on the basis of a score of 3.3 or more were excluded from the study (based on exclusion criteria) (Pandharipande et al., 2013).

4.6.7.2. During ICU stay: the following data were collected during the patient's ICU stay:

Sedation level: This was assessed by using the Richmond Agitation-Sedation Scale (RASS) (**Appendix 4.9**) used in the clinical setting. RASS was applied as it is a commonly used tool in the intensive care unit; it is a validated and reliable method to assess level of sedation in ICU patients (Ely et al., 2003). It is mostly used with mechanically ventilated patients to properly assess the patient's level of sedation and prevent complications of over or under sedation. The patient can be briefly assessed in three discrete steps that have specific criteria for levels of sedation and agitation. It is a 10-point scale, ranging from −5 to +4. A RASS score of −5 indicates deep sedation and +4 indicates combativeness (Sessler et al., 2002).

Delirium: This was assessed by the CAM-ICU tool (**Appendix 4.10a** for English version and **Appendix 4.10.b** for Arabic version) used in the clinical setting. The rationale was that several tools have been created to assess delirium in the ICU, however the American College of Critical Care Medicine guidelines for Pain, Agitation and Delirium (Barr et al., 2013), along with systematic review and meta-analysis studies (Gusmao-Flores et al., 2012), recommend the

use of CAM-ICU to diagnose and monitor delirium in critically ill patients, given its robust validity and reliability (Ely et al., 2001). The CAM-ICU uses standardized non-verbal assessments to evaluate the presence of delirium, characterized in terms of four key features: 1) acute change or fluctuating course of mental status; 2) inattention; 3) altered level of consciousness; and 4) disorganized thinking. The patient is diagnosed to have delirium if he/she scores positive in feature 1 and feature 2, and either feature 3 or feature 4. The CAM-ICU has been translated into over 25 languages, including Arabic which was tested for validity and reliability in two studies (Aljuaid et al., 2018).

4.6.8. Tools used to measure the study outcomes

The participants were assessed for physical, cognitive, and psychological status, in addition to HRQoL at discharge from ICU and at 3 months after discharge from ICU (see **Table 4.2** Summary of outcome measurement questions and interpretation).

Table 4.2. Summary of outcome measurement questions and interpretation.

Outcome Measure	Number of Questions	Interpretation
ADL[a]	6	0-33 severe dependence 34-66 moderate dependence >66 no to mild dependence
MoCA[b]	30	26-30 normal <26 referred to as MCI
HADS[c]	14	0-7 normal 8-10 borderline 11-21 case
PCL-C[d]	6	≥ 45 PTSD caseness
SF-36[e]	36	
General Health	5	50.58 (8.51)^
Physical functioning	10	48.73 (10.13)
Role limitations due to physical health	4	46.42 (9.10)
Role limitations due to emotional problems	3	43.18 (11.21)
Social functioning	2	46.18 (8.90)
Pain	2	50.09 (9.33)
Vitality	4	49.79 (9.20)
Mental Health	5	47.27 (10.15)

[a]Nasser et al., 2009; [b]Rahman et al., 2009; [c]Terkawi et al., 2017; [d]Hatch et al., 2018; [e]AboAbat et al., 2020.
MCI: Mild Cognitive Impairment
^Mean (SD)

Physical impairment: This was assessed using the ADL tool. The rationale for inclusion was that, as described above, the ADL is a short instrument that assesses physical or functional ability (Katz, 1963). Although originally designed to be used in the elderly population, its use has been well documented in critically ill patients (Hayes et al., 2000). The reliability of this tool has not been established in critical care use, but some evidence suggests for its good construct and criterion validity and responsiveness (Black et al., 2001). Similar tools have been used in the ICU setting, such as the Karnsofsky Index and Barthel Index, however, in two systematic reviews that examined the use of measures of physical functioning, the ADL Index has been found to be the most relevant (Hayes et al., 2000; Tipping et al., 2012). Another advantage of this tool, specific to the Life-ICUS study, was that it has been translated into Arabic and tested for validity and reliability in a study of elderly population conducted in Lebanon (Nasser et al., 2009).

Cognitive impairment: This was assessed by the Montreal Cognitive Assessment (MoCA) tool (**Appendix 4.11a** for English version and **Appendix 4.11b** for Arabic version). The MoCA is a screening instrument for mild cognitive dysfunction (Nasreddine et al., 2005). In comparison to the Mini-Mental State Examination, which is the most commonly used tool for diagnosing cognitive function in neurodegenerative diseases (Arevalo-Rodriguez et al., 2015), the MoCA has been found to hold better sensitivity, specificity, and suitability to measure mild cognitive impairments (Ozer et al., 2016). It has been tested for validity and reliability and used in the critical care setting in many studies (Lord et al., 2023; Stienen et al., 2019; Wergin et al., 2012). In the ICU setting, its sensitivity has been estimated to be 93-100% and specificity 98-100% (Ely et, 2001; Luetz et al., 2010). Furthermore, the tool was advocated for by SCCM in the 2020 report for the Consensus Conference on Prediction and Identification of Long-term Impairments after Critical Illness, which was developed in a three-round modified Delphi consensus approach, engaging international experts, patients/families, and other stakeholders (Mikkelsen et al., 2020). The SCCM reported that MoCA was one of the tools that was granted most favorability in screening cognitive function, and therefore was strongly recommended to be used as an assessment tool in PICS (Mikkelsen et al., 2020). The MoCA assesses the following cognitive domains: attention and concentration, executive function, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. The total possible score is 30 points; a score of 26 or above is considered normal.

The Arabic translation has been tested and validated in the elderly population (Rahman et al., 2009). Clinicians and researchers using the tool should be certified to be able to administer the tool; the researcher in this study was certified on 23/6/2020.

Anxiety and Depression: These were assessed by the Hospital Anxiety and Depression Scale (HADS) (**Appendix 4.12a** for English version and **Appendix 4.12b** for Arabic version). The HADS is an instrument developed to measure mood disorders of anxiety and depression in non-psychiatric patients (Zigmond et al., 1983). It consists of two subscales that measure the patient's symptoms of anxiety and depression. Patients are asked to indicate their emotional state over the 'past week'. Each subscale consists of 7 items scored from 0 to 3, resulting in a subscale score ranging from 0 to 21. A subscale score above 7 suggests clinically significant problems (Zigmond et al., 1983). The questionnaire has been widely used in clinical and research settings and validated among general medical patients as well as critically ill patients (Jutte et al., 2015). It is the most commonly used anxiety and depression instrument in ICU patients (Turnbull et al., 2016). In addition, the SCCM has recommended the use of this tool in post-ICU patients, after reaching an a priori consensus threshold as a recommended measure for mental health status in its 2020 consensus conference (Mikkelsen, M, et al., 2020). An important distinction between the HADS and other mood assessment scales is that it excludes items such as insomnia and loss of appetite, which although may point to anxiety and depression, but may also be prevalent in individuals suffering from physical illness (Hayes et al., 2000). Thus, this focus on psychological rather than somatic problems in mood disorders is an important factor in choosing this scale in critically ill patients. Furthermore, the Arabic version of HADS has been tested for reliability and validity in a surgically hospitalized patient population in Saudi Arabia (Terkawi et al., 2017).

Post-Traumatic Stress Syndrome (PTSD): This was assessed by the PTSD Checklist- Civilian (PCL-C) tool (**Appendix 4.13a** for English version and **Appendix 4.13b** for Arabic version). The diagnostic gold standard for PTSD is a structured interview based on predefined criteria by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) (Weathers et al., 2018). However, in post-ICU patients such an interview is not always feasible, and in this setting a self-report inventory that identifies PTSD symptomatology is accepted (Griffiths et al., 2007). In the Life-ICUS study, the PCL-C was utilized to assess PTSD symptomatology (Ruggiero et al.,

2003). PCL-C items map directly onto PTSD symptoms in the DSM-IV (Weathers et al., 2018). This civilian version of the test asks about symptoms in relation to generic "stressful experiences" and can be used in a variety of populations (Blanchard et al., 1996; Bliese et al., 2008; Freedy et al., 2010; Kimerling et al., 2010). It is a 17-item self- report measure of the 17 DSM-IV symptoms of PTSD assessing all core symptoms of intrusion, avoidance, and hyperarousal. Each of the 17 items have a response option from 1 (not at all) to 5 (extremely), to a total severity score ranging between 17 to 85. A maximum cut off point of a score of 45 or greater has been recommended in special populations such as those with Traumatic Brain Injury (TBI) (Wilkins et al., 2011). The tool has been used in studies assessing for PTSD symptoms in post-ICU patients (Hatch et al., 2018) and the Arabic version has been tested for validity and reliability in the non-critical care setting in Saudi Arabia (Alhalal et al., 2017).

Health-Related Quality of Life: This was assessed by the Short Form Health Survey (SF-36) (**Appendix 4.14a** for English version and **Appendix 4.14b** for Arabic version). In two key conferences, the Brussels roundtable conference in 2002 and the SCCM consensus conference in 2019, dedicated to the exploration of long-term outcomes of ICU care and their measurement, the SF-36 was recommended as the single most dependable tool in evaluating HRQoL outcomes in post-ICU patients (Angus et al., 2003; Mikkelsen et al., 2020). This 36-item questionnaire is a "generic" and widely used instrument to evaluate HRQoL, irrespective of disease (Angus et al., 2002). It is the most commonly used instrument in ICU patients (Turnbull et al., 2016), and it has been tested for validity and reliability in critically ill patients (Dowdy et al., 2005). It measures eight health concepts: physical functioning (10 items), bodily pain (2 items), role limitations due to physical health problems (4 items), role limitations due to emotional problems (3 items), emotional well-being (mental health) (5 items), social functioning (2 items), energy/fatigue (vitality) (4 items), and general health (5 items) (Lins et al.,, 2016; Ware et al., 1992). Scoring of the SF-36 is undertaken in two steps (Ware et al., 1992): 1) pre-coded numeric values are recoded per a scoring key given in a table. Each item is scored on a 0 to 100 range so that the lowest and highest possible scores are 0 and 100, respectively. Scores represent the percentage of total possible score achieved. 2) Items in the same scale are averaged together to create the 8 scale scores. Another table lists the items averaged together to create each scale. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Hence, scale scores represent the

average for all items in the scale that the respondent answered. A high score defines a more favorable health state. Means for normative data in Saudi Arabia for each subcategory is presented in Table 4.2 (AboAbat et al., 2020). The tool has been translated to several languages, and psychometric testing of the translated versions demonstrates that the tool is a valid and reliable general health survey across various languages and cultures (Mehraban et al., 2003). The Arabic version has been tested and validated in Saudi Arabia (Coons et al., 1998; Sheikh et al., 2015).

Table 4.3 is a summary of the psychometric properties of outcome measures.

Table 4.3. Psychometric properties of outcome measurement tools.

Outcome Measure	Content Validity	Internal consistency	Criterion validity	Construct validity	Reliability	Responsiveness	Tested in Arabic
ADL	NK	NK	+	±	NK [+]	+	✓
MoCA	NK [±]	NK [+]	NK [+]	NK [+]	+	NK	✓
HADS	+	+	+	NK	NK	NK [+]	✓
PCL-C	NK [+]	NK [+]	NK [+]	NK [+]	NK [+]	NK	✓
SF-36	+	+	+	+	+	NK [+]	✓

ADL, Activities of Daily Living; MoCA, Montreal Cognitive Assessment; HADS, Hospital Anxiety Depression Scale; PCL-C, Post-Traumatic Stress Disorder Checklist-Civilian; SF-36, Short Form Health Survey-36.
NK Not Known. In this case, when available, the property of the tool used in non-critical care studies are shown in brackets.
+ Some Evidence
± Inconsistent evidence
The psychometric properties in this table are drawn from Lord et al., 2023; Stienen et al., 2019; Haines, 2016; Ozer, 2016; Parry et al., 2015; Tipping et al., 2012; Angus et al., 2002; Black et al., 2001.

4.7. Statistical Analysis

All patients who completed assessments both at discharge from ICU and at 3-month follow-up were included in the analysis. Descriptive statistics were used to describe patient demographics, and clinical characteristics. Means (M) and standard deviations (SD) or median and interquartile range (IQR) for all continuous variables as appropriate, and frequencies (F) and percentages (%) for all categorical variables were computed. Demographic and clinical characteristics were compared between all included patients, followed-up patients, and not followed-up patients using t-test (normally distributed) and Mann-Whitney test (skewed data) when comparing continuous variables, and chi-square when comparing categorical variables. Bivariate analysis using the Wilcoxon signed-rank test was used to demonstrate the difference in outcomes scores between discharge and 3 months follow-up. This test was used as the non-parametric paired t-test.

Linear regression was used as a post-hoc analysis to demonstrate associations between demographic characteristics (model 1), clinical characteristics (model 2), and long-term outcomes at 3-months. A priori-selected variables were compared between patients at discharge and patients at 3-month follow up. Five independent demographic variables (age, gender, BMI, educational level, and household annual income) and six clinical variables (having hypertension and diabetes, admission status, length of stay in ICU, APACHEII score, IQCODE score, and ADL score at admission) were included in the final models to determine associations with the outcomes of the study [Physical (ADL), Cognitive (MoCA), Anxiety and Depression (HADS), Post traumatic stress (PCL-C), and HRQOL (SF-36)]. Variables such as days of mechanical ventilation, CAM-ICU, RASS in ICU, and use of corticosteroids were not included in the analysis because of low occurrence of mechanical ventilation, delirium, sedation, and use of corticosteroids in the sample size. Data was analysed using Stata (StataCorp. 2023. *Stata Statistical Software: Release 18*. College Station, TX: StataCorp LLC); $p<0.05$ was chosen to indicate statistical significance.

The data analysis plan was developed in consultation with a statistician to ensure the robustness and appropriateness of the statistical methods. The inclusion of both parametric and non-parametric tests aimed to accurately capture the data characteristics and address

the research questions comprehensively.

Descriptive statistics provided a detailed overview of the patient population, while inferential statistics were used to explore relationships and differences between groups. The linear regression models were carefully constructed to control for potential confounders and identify significant predictors of long-term outcomes.

The consultation with a statistician was crucial in refining the analysis plan, particularly in selecting the appropriate tests and ensuring the correct interpretation of results. This collaboration helped enhance the validity and reliability of the findings, providing a strong foundation for the subsequent discussion and implications.

4.8. Conclusion

This chapter presented the conceptual model underpinning this study and presented the methods adopted for the conduction of the prospective cohort study of long-term outcomes and HRQOL of ICU patients in Saudi Arabia. The following chapter will outline the results and a discussion of the key findings from this study.

5. Chapter 5: Results and Discussion of Phase II study

Long-term outcomes and Health related Quality of **Life** in **I**ntensive **C**are **U**nit Patients: a prospective cohort study in **S**audi Arabia (**Life-ICUS study**)

5.1. Chapter Overview:

The previous chapter described the methods and the justification for the methodological choices of the prospective cohort study, Life-ICUS, which set out to examine the long-term outcomes (physical, cognitive, and psychological) and HRQoL of a Saudi ICU cohort. In this chapter the findings of this study will be presented highlighting the characteristics of the study population and focusing on the study outcomes. To have a thorough understanding of the outcomes of the ICU patients, first their outcomes at the time of ICU discharge will be presented, followed by the changes in their outcomes between the time of discharge and at long term (3 months after discharge). Finally, to understand the determinants of the long-term outcomes, a thorough investigation of the predictors of long-term outcomes will be presented. A discussion section will follow, highlighting main findings, making comparisons to exiting literature, and identifying the contributions of the study. The strengths and limitations of this phase of the research will be elaborated at the end. Overall contributions, recommendations, and conclusions of the study will be further elaborated in the integrated discussion chapter (Chapter 7), after the presentation of the Phase III, qualitative study of this research.

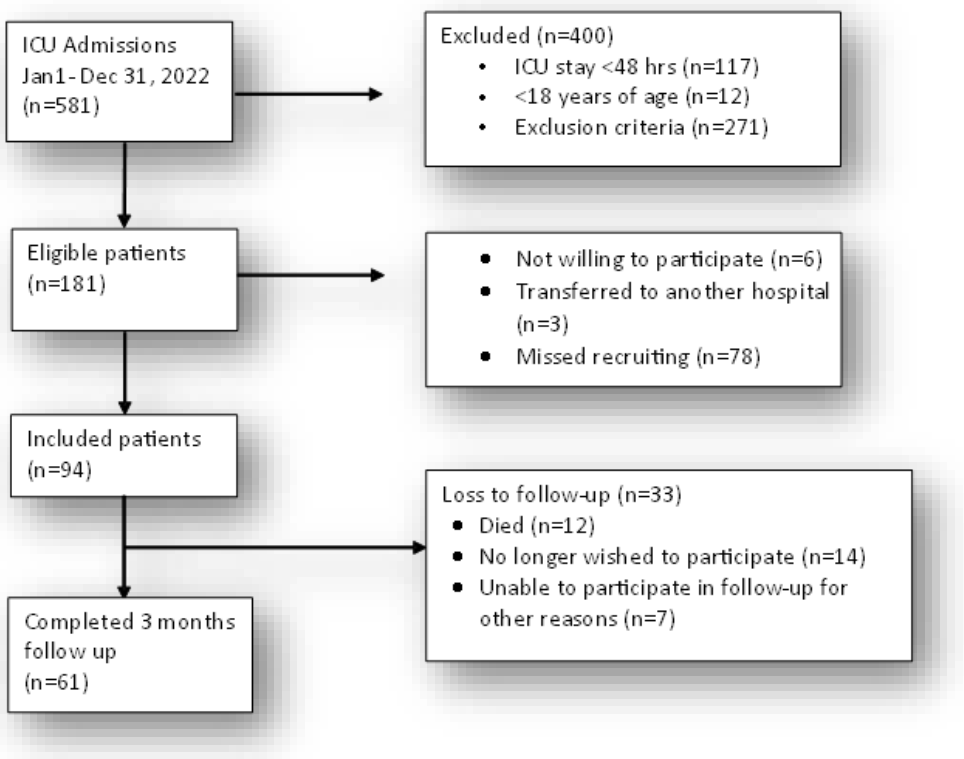
5.2. Results

5.2.1. Study population

In 2022, from January 21 to December 31st, the ICU in the study site admitted 581 patients. Out of these, 400 (69%) patients were excluded because they did not meet the inclusion criteria. Out of the remaining 181 eligible patients, 94 (52%) patients were recruited to the study. All patients completed physical, cognitive, psychological, and HRQoL assessments at discharge and were followed up for a three-month assessment. A total of 61 patients (65%)

completed the 3 months follow-up (**Figure 5.1.** Flow diagram).

Figure 5.1 Flow Diagram



5.2.2. Patient demographic and clinical characteristics:

Table 5.1 contains demographic and clinical data comparing all participants, followed-up patients, and not followed-up patients.

Participants in the followed-up group did not differ significantly in their demographic characteristics from the patients in the not followed-up group in terms of gender, BMI, educational level, and income. There was, however, a significant difference in age ($p<0.001$) and work status ($p<0.001$). The followed-up group was younger and held jobs compared to the not followed-up group. In terms of their clinical characteristics, followed-up patients did not differ significantly from not followed up patients in their admission status, comorbidities, disease severity (APACHE II score), and ADL score at admission. However, there was a

statistical difference in the two groups in admission diagnosis (p=0.005) with more respiratory failure patients in the not followed-up group. Also, the average length of ICU stay was longer in the not followed up group (p=0.001), and the IQCODE was slightly lower (p=0.013).

In the followed-up group, the mean age was 50 (SD ± 15) years, ranging between 22 to 80 years; 29 (48%) patients were males and 32 (52%) were females. The mean BMI was 30 (SD ± 9.4). Respiratory failure was the most common presentation (n=12, 20%) followed by acute kidney injury (n=10, 16%) and septic shock (n=8, 13%).

Table 5.1: Comparison of demographic and clinical characteristics between all, followed-up, and not followed-up patients.

Demographic and Clinical Data	All (n=94)	Followed-up (n=61)	Not followed up (n=33)	p-value follow-up/not followed-up
Age	53 ±17	50 ±15	61 ±18	<0.001*
Age groups				0.007*
< 50	42 (45%)	33 (54%)	9 (27%)	
50 – 70	33 (35%)	21 (34%)	12 (36%)	
> 70	19 (20%)	7 (12%)	12 (36%)	
Gender				0.847
Male	44 (47%)	29 (48%)	18 (55%)	
Female	50 (53%)	32 (53%)	15 (45%)	
BMI	30.1 ±9.6	30.0 ±9.4	30.3 ±10.1	0.880
BMI groups				0.973
< 25	31 (33%)	20 (33%)	11 (33%)	
25 – 29.9	27 (29%)	18 (30%)	9 (27%)	
≥30	36 (38%)	23 (38%)	13 (39%)	
Education level				0.839
Never + elementary to middle school	26 (28%)	16 (26%)	10 (30%)	
Middle to secondary school + secondary	42 (45%)	27 (44%)	15 (46%)	
Undergraduate + vocational + graduate	26 (28%)	18 (30%)	8 (24%)	
Current occupation				<0.001*
Does not work	66 (70%)	35 (57%)	31 (94%)	
Work	28 (30%)	26 (43%)	2 (6%)	
Household annual income				0.307
Less than $10K	24 (26%)	15 (25%)	9 (27%)	
$10-19K	44 (47%)	26 (43%)	18 (55%)	
More than $19K	26 (28%)	20 (33%)	6 (18%)	
Admission diagnosis				0.005*
Respiratory failure	31 (33%)	12 (20%)	19 (58%)	
Acute kidney failure	13 (14%)	10 (17%)	3 (9%)	
Septic shock	10 (11%)	8 (13%)	2 (6%)	
Diabetic Ketoacidosis	5 (5%)	5 (8%)	0	
Sickle Cell Disease crisis	5 (5%)	5 (8%)	0	
Others	30 (32%)	21 (34%)	9 (27%)	
Admission status				0.152
Non-surgical	82 (87%)	51 (84%)	31 (94%)	
Surgical (emergent & elective)	12 (13%)	10 (16%)	2 (6%)	
Comorbidities				
Diabetes mellitus	40 (43%)	28 (46%)	12 (36%)	0.372
Hypertension	38 (40%)	24 (39%)	14 (42%)	0.771
HTN & DM	27 (29%)	18 (30%)	9 (27%)	0.819
None	18 (19%)	11 (18%)	7 (21%)	0.708
ICU – Length of stay (days)	7.6 ±5.7	6 ±3	10.7 ±7.8	<0.003*
ICU stay				0.001*
≤ 7 days	63 (67%)	48 (79%)	15 (45%)	
> 7 days	31 (33%)	13 (21%)	18 (55%)	
APACHE II – Total Score	14% ±7	13% ±7	16% ±7	0.065
ADL at admission	5 ±1.8	5 ±1.9	4.9 ±1.7	0.565
ADL groups at admission				0.434
None to mild	77 (82%)	51 (84%)	26 (79%)	
Moderate	7 (8%)	3 (50%)	4 (12%)	
Severe	10 (11%)	7 (12%)	3 (9%)	
IQCODE SCORE at admission	54 ±9	52 ±9	57 ±9	0.013*

5.2.3. Study Outcomes:

5.2.3.1. Study outcomes at discharge:

Table 5.2 shows comparison of outcome data at discharge in all and followed-up groups with no significant differences between the two groups. At discharge, the outcomes of the follow-up group were as follows: 40 (65%) of patients scored in the none to mild ADL category, 39 (75%) in the mild cognitive impairment (MCI) category for MoCA, 48 (79%) in the normal PCL-C category, 40 (66%) in the normal HADS-Depression category, 44 (72%) in the normal HADS-Anxiety category, and a mean total SF-36 score of 48.7 (SD±18.8).

Table 5.2. Discharge assessments in all and follow-up groups.

Discharge Assessments	All (n=68)	Followed-up (n=61)
ADL at Discharge	4.1 ±2.2	4.4 ±2.0
ADL categories: None to mild	41 (60%)	40 (65%)
Moderate	13 (19%)	12 (20%)
Severe	14 (21%)	9 (15%)
MoCA at discharge	N= 55	N= 52
Mean ±SD	20 ±6	20 ±6
MoCA categories: Normal	13 (24%)	13 (25%)
MCI	42 (76%)	39 (75%)
PCL-C at discharge	33 ±14	32 ±14
PCL-C categories: Normal	53 (78%)	48 (79%)
PCL-C case	15 (22%)	13 (21%)
HADS at discharge		
HADS total score - Depression	6.4 ±4.6	6.3 ±4.5
HADS-Depression categories: Normal	43 (63%)	40 (66%)
Borderline	8 (12%)	7 (11%)
Case	17 (25%)	14 (23%)
HADS total score - Anxiety	5 ±5	5 ±5
HADS-Anxiety categories: Normal	47 (69%)	44 (72%)
Borderline	9 (13%)	7 (12%)
Case	12 (18%)	10 (16%)
SF-36 Total at Discharge	46.9 ±18.9	48.7 ±18.8
General health	52.8 ±15.8	53.6 ±15.2
Physical functioning	35.2 ±33.6	38.4 ±33.5
Role limitations due to physical health	23.5 ±41.2	26.2 ±42.7
Role limitations due to emotional problems	46.6 ±49.9	50.3 ±50
Social functioning	61.9 ±26.3	63.1 ±25.7
Pain	50.8 ±26.6	50.4 ±26.1
Vitality	50.1 ±20.1	52.6 ±19.9
Mental health	71.8 ±19.3	72.8 ±19.2

5.2.3.2. Study outcomes between discharge and 3 months follow-up:

Table 5.3 shows the difference in outcome scores between discharge and at 3 months follow-up.

There was a statistically significant increase in the ADL score from discharge to follow-up from a mean of 4.4 (SD±2.0) to 5.3 (SD ±1.5) (p<0.001). An increase in the score in ADL meant an improvement. Similarly, there was a statistically significant increase in the MoCA score from a mean of 20 (SD±6) to 21 (SD ±7) (p=0.047). An increase in the score in MoCA meant an improvement. Also, the decrease in the PCL-C score from a mean of 32 (SD±14) to 29 (SD ±13) was statistically significant (p=0.015) and it signified an improvement. In the psychological domain, there was a statistically significant decrease in the HADS-depression score from a mean of 6.3 (SD±4.5) to 4 (SD ±3.5) (p<0.001). The HADS-anxiety score also decreased significantly from a mean of 5 (SD±5) to 3.1 (SD ±3.9) (p<0.001). A decrease in the HADS scores meant an improvement. In the measurement of HRQoL, the total SF-36 score significantly increased at 3 months from a mean of 48.7 (SD±18.8) to 66.7 (SD ±20.0) (p<0.001) showing improved HRQoL. All the scores for the subcategories of SF-36 significantly increased at follow-up.

Table 5.3: Comparison of scores at discharge and at 3 months

Assessments	At discharge (n=61)	At 3 months (n=61)	P value
ADL score	4.4 ±2.0	5.3 ±1.5	<0.001
MoCA score	20 ±6	21 ±7	0.047
PCL-C score	32 ±14	29 ±13	0.015
HADS- Depression score	6.3 ±4.5	4.0 ±3.5	<0.001
HADS- Anxiety score	5 ±5	3.1 ± 3.9	<0.001
SF-36 total score	48.7 ±18.8	66.7 ±20.0	<0.001
General health	53.6 ±15.2	61.6 ±14.3	<0.001
Physical functioning	38.4 ±33.5	60.8 ±36.1	<0.001
Role limitations due to physical health	26.2 ±42.7	66.4 ±46.3	<0.001
Role limitations due to emotional problems	50.3 ±50	77.6 ±41.2	<0.001
Social functioning	63.1 ±25.7	78.1 ±22.2	<0.001
Pain	50.4 ±26.1	69.1 ±28.5	<0.001
Vitality	52.6 ±19.9	61.6 ±16.7	<0.001
Mental health	72.8 ±19.2	76.8±13.6	0.135

5.2.3.3. Factors associated with post-ICU outcomes:

Table 5.4 demonstrates the single and multiple regression analyses for the difference in outcome scores between discharge and 3 months follow-up. The difference in outcomes scores refers to the score of a specific outcome at 3 months follow up minus the score of the same outcome at discharge. As described in the previous chapter's statistical methods section, Model 1 demonstrated associations between demographic characteristics and long-term outcomes at 3 months follow up, and Model 2 demonstrated associations between clinical characteristics and long-term outcomes at 3-months.

In the adjusted models, having middle school to secondary school education and having higher education (undergraduate, vocational, or graduate) increased ADL score difference after 3 months follow-up significantly by 24.6 (CI 3.5: 45.8) and 31.7 (CI 3.2: 60.2) respectively. Being admitted with a surgical diagnosis increased ADL difference after 3 months follow-up significantly by 24.8 (CI 5.7: 44.0).

Being between 50 to 70 years of age decreased MOCA score difference at 3 months follow-up significantly by 4.8 (CI -7.9: -1.6). Having a lower IQCODE decreased MOCA score difference after 3 months follow-up by significantly by 0.2 (CI -0.3: -0.003).

None of the demographic or clinical characteristics were statistically associated with PCL-C score differences from discharge to 3 months follow up.

Being in the 50 to 70 age range and being above the age of 70 increased HADS-Depression score difference after 3 months follow-up significantly by 2.8 (CI 0.3: 5.3) and 3.8 (CI 0.1: 7.5) respectively.

Being in the 50 to 70 age range increased HADS-Anxiety score difference after 3 months follow-up significantly by 2.6 (0.2: 5.1). Being admitted with a surgical diagnosis decreased HADS - Anxiety score difference after 3 months follow-up significantly by 2.5 (-5.0: -0.02).
Being a male increased SF-36 total score difference after 3 months follow-up significantly by 11.8 (CI 1.7-21.8).

Table 5.4. Single and multiple regression analysis for the differences in outcome scores between discharge and 3 months follow-up. * refers to statistical significance.

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
ADL Score				
Age (years)				
<50	1	1		
50 – 70	0.3 (-15.3 : 15.8)	7.6 (-11.2 : 26.5)		
> 70	13.0 (-10.2 : 36.2)	31.4 (3.6 : 59.1)		
Gender				
Female	1	1		
Male	-2.5 (-16.8 : 11.8)	-2.4 (-19.0 : 14.1)		
BMI				
Normal weight	1	1		
Overweight	-3.0 (-21.1 : 15.2)	-4.9 (-24.0 : 14.2)		
Obese	4.9 (-12.2 – 22.0)	16.9 (-3.6 : 37.4)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	8.7 (-8.9 : 26.4)	24.6 (3.5 : 45.8)*		
Undergraduate + vocational + graduate	5.8 (-13.4 : 25.0)	31.7 (3.2 : 60.2)*		
Household annual income				
Less than $10K	1	1		
$10 – 19K	9.6 (-8.4 : 27.7)	16.1 (-3.2 : 35.5)		
More than $19K	4.0 (-15.0 : 23.1)	4.2 (-17.5 : 25.9)		
Having hypertension & diabetes			8.2 (-7.3 : 23.7)	12.4 (-3.8 : 28.6)
Admission status				
Non-surgical			1	1
Surgical			25.7 (7.6 : 43.9)*	24.8 (5.7 : 44.0)*
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			9.8 (-7.4 : 27.1)	7.2 (-10.4 : 24.8)
IQCODE score			-0.1 (-0.9 : 0.7)	-0.2 (-1.0 : 0.7)
APACHE total score			0.1 (-1.0 : 1.1)	-0.1 (-1.1 : 1.0)
ADL Score at admission				
None to mild			1	1
Moderate/severe			4.8 (-14.5 : 24.1)	2.5 (-17.0 : 22.0)

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
MOCA score				
Age (years)				
<50	1	1		
50 – 70	-3.9 (-6.5 : -1.3)*	-4.8 (-7.9 : -1.6)*		
> 70	4.7 (-1.6 : 10.9)	3.6 (-3.0 : 10.2)		
Gender				
Female	1	1		
Male	-0.5 (-3.2 : 2.2)	-0.6 (-3.4 : 2.1)		
BMI				
Normal weight	1	1		
Overweight	-1.5 (-4.8 : 1.8)	0.1 (-3.1 : 3.3)		
Obese	-1.5 (-4.8 : 1.8)	-1.4 (-4.8 :2.0)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	-0.9 (-5.3 : 3.4)	-3.4 (-7.8 : 1.0)		
Undergraduate + vocational + graduate	0.04 (-4.5 : 4.6)	-5.1 (-10.5 : 0.3)		
Household annual income				
Less than $10K	1	1		
$10 – 19K	-0.7 (-4.2 : 2.8)	-1.3 (-4.7 : 2.1)		
More than $19K	2.0 (-1.5 : 5.5)	2.1 (-1.5 : 5.7)		
Having hypertension & diabetes			-3.3 (-6.2 : -0.3)*	-2.5 (-5.6 : 0.7)
Admission status				
Non-surgical			1	1
Surgical			0.5 (-3.2 : 4.2)	-0.05 (-3.6 : 3.5)
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			2.4 (-0.7 : 5.6)	2.2 (-1.0 : 5.5)
IQCODE score			-0.2 (-0.3 : -0.01)*	-0.2 (-0.3 :-0.003)*
APACHE total score			0.04 (-0.2 : 0.2)	0.1 (-0.1 :0.3)
ADL Score at admission				
None to mild			1	1
Moderate/severe			-0.4 (-4.1 : 3.3)	-0.6 (-4.3 :3.0)
PCL-C Score				
Age (years)				
<50	1	1		
50 – 70	1.4 (-4.6 : 7.3)	2.9 (-4.5 : 10.4)		
> 70	7.5 (-1.4 : 16.4)	10.0 (-0.9 : 20.9)		

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
Gender				
Female	1	1		
Male	-5.7 (-11.1 : -0.4)*	-5.7 (-12.2 : 0.8)		
BMI				
Normal weight	1	1		
Overweight	-2.5 (-9.6 : 4.5)	-3.1 (-10.6 : 4.4)		
Obese	1.7 (-4.9 : 8.3)	-0.3 (-8.3 : 7.8)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	-3.4 (-10.2 : 3.4)	0.4 (-7.9 : 8.8)		
Undergraduate + vocational + graduate	-2.6 (-10.1 : 4.8)	3.1 (-8.1 : 14.3)		
Household annual income				
Less than $10K	1	1		
$10 – 19K	-2.4 (-9.5 : 4.6)	-0.2 (-7.8 : 7.4)		
More than $19K	-0.5 (-8.0 : 6.9)	2.7 (-5.8 : 11.3)		
Having hypertension & diabetes			1.5 (-4.5 : 7.6)	1.0 (-5.3 : 7.3)
Admission status				
Non-surgical			1	1
Surgical			-7.8 (-15.0 : -0.6)*	-7.7 (-15.2 : -0.3)
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			-4.6 (-11.2 : 2.1)	-4.4 (-11.2 : 2.5)
IQCODE score			0.1 (-0.2 : 0.5)	0.1 (-0.2 : 0.4)
APACHE total score			0.1 (-0.3 : 0.5)	0.05 (-0.4 : 0.5)
ADL Score at admission				
None to mild			1	1
Moderate/severe			4.9 (-2.5 : 12.2)	7.1 (0.5 : 14.7)
HADS score – Depression				
Age (years)				
<50	1	1		
50 – 70	2.2 (0.1 : 4.3)*	2.8 (0.3 : 5.3)*		
> 70	2.4 (-0.8 : 5.5)	3.8 (0.1 : 7.5)*		
Gender				
Female	1	1		
Male	-2.1 (-4.1 : -0.2)	-1.7 (-3.9 : 0.6)		
BMI				
Normal weight	1	1		

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
Overweight	-1.0 (-3.5 : 1.5)	-1.9 (-4.5 : 0.6)		
Obese	1.4 (-1.0 : 3.7)	0.2 (-2.5 : 3.0)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	-0.2 (-2.6 : 2.3)	1.3 (-1.5 : 4.1)		
Undergraduate + vocational + graduate	-1.5 (-4.2 : 1.2)	1.1 (-2.7 : 4.9)		
Household annual income				
Less than $10K	1	1		
$10 – 19K	-1.6 (-4.2 : 0.9)	-0.5 (-3.1 : 2.1)		
More than $19K	-0.3 (-2.9 : 2.4)	1.4 (-1.5 : 4.3)		
Having hypertension & diabetes			0.6 (-1.6 : 2.8)	-0.04 (-2.4 : 2.3)
Admission status				
Non-surgical			1	1
Surgical			-0.9 (-3.6 : 1.8)	-0.5 (-3.3 : 2.2)
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			-1.9 (-4.3 : 0.5)	-2.3 (-4.8 : 0.2)
IQCODE score			0.1 (-0.03 : 0.2)	0.1 (-0.1 : 0.2)
APACHE total score			0.1 (-0.04 : 0.3)	0.1 (-0.1 : 0.2)
ADL Score at admission				
None to mild			1	1
Moderate/severe			1.3 (-1.3 : 4.0)	1.7 (-1.1 : 4.5)
HADS score – Anxiety				
Age (years)				
<50	1	1		
50 – 70	1.7 (-0.3 : 3.8)	2.6 (0.2 : 5.1)*		
> 70	1.5 (-1.6 : 4.5)	2.3 (-1.3 : 5.6)		
Gender				
Female	1	1		
Male	-0.2 (-2.1 : 1.7)	-0.7 (-2.8 : 1.4)		
BMI				
Normal weight	1	1		
Overweight	-0.2 (-2.6 : 2.2)	-1.1 (-3.6 : 1.3)		
Obese	-0.8 (-3.1 : 1.5)	-2.2 (-4.8 : 0.4)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	0.1 (-2.2 : 2.5)	-0.2 (-3.0 : 2.5)		

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
Undergraduate + vocational + graduate	0.1 (-2.5 : 2.7)	-0.1 (-3.7 : 3.6)		
Household annual income				
Less than $10K	1	1		
$10 – 19K	-1.5 (-3.8 : 0.8)	-1.8 (-4.3 : 0.7)		
More than $19K	1.2 (-1.3 : 3.6)	1.5 (-1.3 : 4.3)		
Having hypertension & diabetes			1.2 (-0.9 : 3.2)	1.0 (-1.1 : 3.1)
Admission status				
Non-surgical			1	1
Surgical			-2.6 (-5.1 : -0.1)*	-2.5 (-5.0 : -0.02)*
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			-1.8 (-4.1 : 0.5)	-1.7 (-4.1 : 0.5)
IQCODE score			0.1 (-0.04 : 0.2)	0.03 (-0.1 : 0.1)
APACHE total score			0.04 (-0.1 : 0.2)	0.02 (-0.1 : 0.2)
ADL Score at admission				
None to mild			1	1
Moderate/severe			1.9 (-0.6 : 4.5)	2.9 (0.3 : 5.4)
SF-36 score				
Total Score	N= 61	N= 61	N= 61	N= 61
Age (years)				
<50	1	1		
50 – 70	-14.2 (-24.1 : -4.3)*	-10.9 (-22.3 : 0.6)		
> 70	-7.8 (-22.6 : 7.0)	-1.9 (-18.7 : 14.9)		
Gender				
Female	1	1		
Male	14.4 (5.5 : 23.3)*	11.8 (1.7 : 21.8)*		
BMI				
Normal weight	1	1		
Overweight	1.1 (-11.1 : 13.2)	4.6 (-7.0 : 16.1)		
Obese	-7.3 (-18.7 : 4.1)	8.3 (-4.1 : 20.7)		
Education level				
Never + elementary to middle school	1	1		
Middle to secondary school + secondary	9.4 (-2.0 : 20.7)	8.6 (-4.2 : 21.4)		
Undergraduate + vocational + graduate	16.6 (4.3 : 28.9)*	13.4 (-3.8 : 30.7)		
Household annual income				
Less than $10K	1	1		
$10 – 19K	13.7 (1.8 : 25.5)*	10.4 (-1.3 : 22.1)		

Outcome measure	Model 1 (demographic characteristics)		Model 2 (clinical characteristics)	
	Unadjusted (95% CI)	Adjusted (95% CI)	Unadjusted (95% CI)	Adjusted (95% CI)
More than $19K	8.8 (-3.7 : 21.2)	-2.0 (-15.2 : 11.1)		
Having hypertension & diabetes			-5.2 (-15.7 : 5.3)	-2.1 (-13.2 : 9.1)
Admission status				
Non-surgical			1	1
Surgical			8.7 (-4.1 :21.6)	8.4 (-4.9 : 21.6)
Length of stay in ICU				
≤ 7 days			1	1
> 7 days			7.5 (-4.1 : 19.1)	7.5 (-4.4 : 19.4)
IQCODE score			-0.7 (-1.2 : -0.1)*	-0.5 (-1.1 : 0.07)
APACHE total score			-0.5 (-1.2 : 0.2)	-0.3 (-1.0 : 0.4)
ADL Score at admission				
None to mild			1	1
Moderate/severe			-2.8 (-15.8 : 10.3)	-4.1 (-17.3 : 9.1)

5.3. Discussion

In this prospective cohort study, a significant proportion of the patients experienced PICS symptoms in at least one domain. Only 5 (7%) patients at discharge and 10 (16%) patients at follow up did not demonstrate PICS in any of its domains. Cognitive problems were the most frequently reported, with most patients demonstrating serious cognitive impairments similar to Mild Cognitive Impairment (MCI). The followed-up and not-followed-up groups were similar in terms of their demographic and clinical characteristics. None of the predictors for PICS in this cohort were found to be modifiable. Each domain of PICS and HRQoL findings will be discussed now in detail.

5.3.1. Physical domain

In the Life-ICUS cohort, 32% of patients at discharge and 10% at follow-up demonstrated moderate to severe physical impairments. The ADL score improved significantly from partially independent (moderate) to almost independent (no to mild) at follow up. Predictors for improved physical function were higher education and having a surgical diagnosis at the time of the ICU admission.

Compared to other studies, the study's findings in terms of occurrence of long-term physical impairments were better than the reported 50-80% rates in the literature (Harvey et al., 2016; Ohtake et al., 2018). This could be explained in light of the systematic review conducted by the researcher in Chapter 3. In the latter, factors that led to physical dysfunctionality were found to include ICU delirium, prior depression, prolonged bed rest, and prolonged ICU length of stay. In the Life-ICUS cohort, 89% of patients did not experience delirium, were excluded if they had documented premorbid mental health diseases and had a relatively short stay (6 days) in the ICU. However, the difference in these ICU related factors and patient characteristics between the literature and Life-ICUS study is not the only explanation for the findings of lower occurrences of physical impairments. Having a systematic assessment and management protocol for ICU delirium (Mart et al., 2021) and exercising via a robust early ambulation program (Paton et al., 2021) in this research site could have ameliorated the possibility of developing delirium and acquiring muscle weakness and atrophy in this cohort.

Also, as almost 80% of patients of this cohort stayed less than seven days in the ICU, possibly due to a less critically ill patient population and diligent triaging and discharge planning in the study site, muscle wasting that has been attributed to longer stays (Fazzini et al., 2023) might have been prevented. In addition, long mechanical ventilation which has also been linked to ICUAW (Stevens et al., 2007), also did not occur in this cohort as most patients were ventilated for three days, and this could be attributed to the early awakening and spontaneous breathing trials practiced in the ICU. It is evident that critical illness myopathy, a form of ICUAW, improves over time (Koch et al., 2014), a finding which substantiates our cohort's experience of progression to independence in ADLs at the follow-up period.

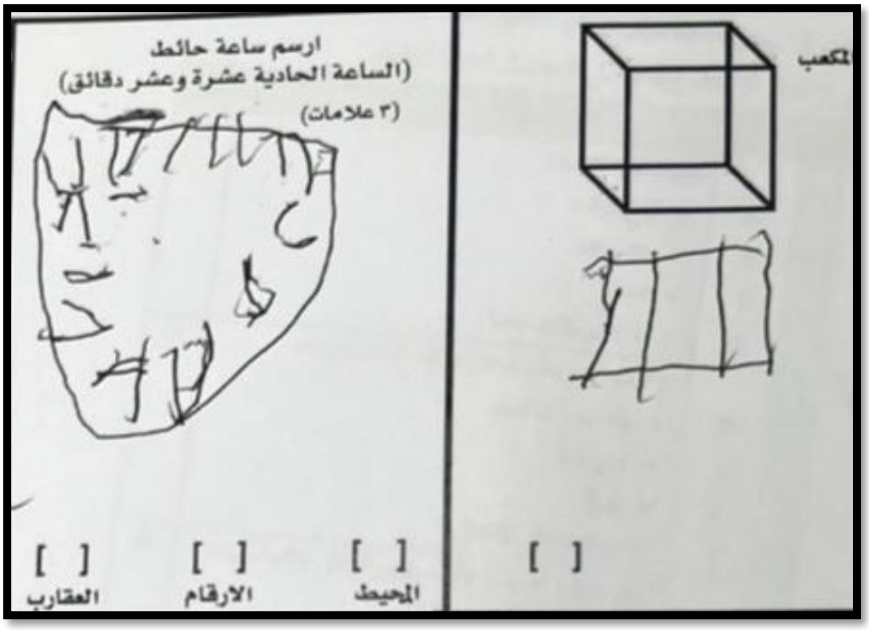
Higher levels of education being a protective factor of long-term physical impairments is a relatively novel finding in our study. Education is proven to mitigate frailty and psychological aspects of PICS in mechanisms which are not yet established in the literature (Geense et al., 2021; Marra et al., 2017). It could be hypothesized that those with higher education are more apt to assimilate the education provided by ICU healthcare providers and therefore comply with early mobilization after critical illness. Also, compared to their medical counterparts, surgically admitted ICU patients had a higher likelihood of avoiding physical impairments of PICS, and this may be due to the possibility of the elective nature of their ICU admission, relatively shorter stay, and earlier and more aggressive rehabilitative measures in the ICU, elements that have been associated with better PICS outcomes (Geense et al., 2021; Mart et al., 2021).

5.3.2. Cognitive domain

In this cohort, 74% of patients at discharge and 72% at follow-up demonstrated cognitive dysfunction with a significant improvement between the two timepoints. Predictors for poor cognitive outcomes were older age and pre-existing cognitive disabilities. A large proportion of the patients experienced profound cognitive impairments suggestive of MCI. The latter is described as "*an intermediate clinical state between normal cognitive aging and dementia, and it precedes and leads to dementia in many cases*" (Nasreddine et al., 2005 p. 695). The most common and severe clinical manifestation of Life-ICUS patients completing the MoCA test was in visuo-constructional and visuo-spatial skills (clock and cube drawing) (see **Figure**

5.2). Poor visuo-spatial planning, coordination, and perception during cube drawing are cognitive mechanisms identified in Alzheimer disease patients (Julayanont et al., 2013). Drawing a clock also requires planning, conceptualizing, and figurative illustration (Julayanont et al., 2013). Both clock and cube drawing difficulties point to diminished executive function (Nasreddine et al., 2005).

Figure 5.2. Clock and cube drawing by one of the study patients. The clock lacks contour, numbers, and hands. The cube demonstrates a two-dimensional shape and misses some lines.



In the MoCA test, the cube drawing is evaluated by looking if patients illustrated a 3-dimentioal cube with all its lines present. The clock drawing is evaluated if the clock had a well-contoured circular form, with all its numbers aligned in the correct placements, and if the clock hands pointed to the time 11:10 (Nasreddine et al., 2005). It was worthwhile asking at this point whether the educational level of the Life-ICUS patients affected their ability to draw three-dimensional cubes and a well-constructed clock. More than one quarter of the sample in this study had never attended school or reached elementary levels of education. Studies have shown that literacy and education play a role in the patient's ability to draw and copy, more so in older patients (Rossetti et al., 2011), probably due to challenged ability to employ compensatory neural networks (old age) in a state of low cognitive reserve (low education) (Nasreddine et al., 2011). Although in the regression models of this study education was not

found to be significantly associated with cognitive outcomes, this finding should be interpreted cautiously and investigated further.

The finding that older patients and those with prior cognitive impairment were at highest risk in this cohort seemed to be in accordance with previous studies (Bruck et al., 2018; Estrup et al., 2018). One of the modifiable risk factors on the other hand, delirium, could not be correlated with cognitive impairments, possibly because of too few delirious occurrences in this cohort to show an association (Estrup et al., 2018).

One unexpected finding was the presence of low total scores on the MoCA, in light of the low occurrence of ICU delirium in this cohort. Delirium in other studies, when assessed by the same tool used in this study (CAM-ICU), has been systematically evaluated as a predominant factor associated with long-term cognitive morbidity (Girard et al., 2010; Wolters et al., 2013). To explain this finding, two possibilities emerged. Either MoCA was misinterpreted, or delirium was not assessed properly. The former seemed unlikely because the MoCA test was administered by the trained and certified researcher (described in the previous chapter, methods section). Whether CAM-ICU, as a measure of delirium, was assessed accurately and appropriately in the study site, was found questionable. Although CAM-ICU was practiced both in English and Arabic forms in the clinical setting, having predominantly Arabic speaking patients and primarily non-Arabic speaking nurses raised concerns about correct methods applied, language used, and interpretations of the tests done. The tool has been translated to Arabic and tested for reliability and validity, however it was done in a study in Cairo, where most healthcare providers and patients speak the same dialect of Arabic (Selim et al., 2018). This was not the case in the Life-ICUS study site. Only one study using CAM-ICU in Saudi Arabia was published in the Annals of Saudi Medicine (Alamri et al., 2018). In this study, “trained” providers, who most likely were Arabic speakers, administered the tool, giving little insight to how language barriers were assessed. As no studies investigating this caregiver-patient language variation and its effects on the use of CAM-ICU were found, it is highly recommended that the practice of delirium assessment be critically re-evaluated in the study site. It is noteworthy to mention that in a study assessing delirium knowledge in an ICU in Saudi Arabia, it was found that more than half of the nurses and physicians self-appraised their knowledge

as fair to poor (Aljuaid M, 2019), attracting considerable attention for education and evaluation of delirium practices in the country.

The Life-ICUS study patients improved significantly in their cognitive skills over time. Whether or not cognitive function improves over time is studied in various studies with inconsistent findings. In Denmark, a similar study protocol, in a comparable size ICU, and similar sample characteristics of general ICU patients, found no improvement in cognition over time (Estrup et al., 2018), and large studies have confirmed persistent, long term (one to three years) impairments (Hopkins et al., 2004; Jackson et al., 2004). However, these studies were considerably different in terms of presence of long sedation days and prevalence of delirium.

The finding that most of the patients demonstrated MCI in this cohort was of paramount importance since many measures were taken in the design of the study to control overestimation. Patients with pre-existing neurodegenerative conditions and patients with other diseases associated with long-term disturbances in cognition (e.g., cardiac surgery, neuro and neurosurgical patients) were excluded from enrollment in the study, which signals to genuine representation of cognitive outcomes in this cohort.

5.3.3. Psychological domain

In the Life-ICUS cohort, the most commonly reported mental health problems were depression (14%), followed by PTSD (11%) and anxiety (7%) at follow up. However, all these areas improved significantly from the time of discharge to follow-up. Younger age was a predictor for anxiety and depression. Having a surgical diagnosis at ICU admission was another predictor for depression. None of the patient-characteristics or clinical factors were found to be a predictor of PTSD.

First, it was determined that symptoms of depression were more common mental health manifestations in this cohort than symptoms of anxiety and PTSD. Evidence from a longitudinal study (BRAIN-ICU), which is methodologically similar to the current Life-ICUS study but with a larger cohort and a longer duration of study, implied the same trend of more prevalence of depression (Jackson et al., 2014). It also suggested that depression, although

diminishing over time, persisted for almost one year after critical illness (Jackson et al., 2014). Similar to the results of the systematic review described in Chapter 3, younger patients performed poorly with anxiety and depression, a finding that may indicate deleterious consequences on those with young families, on their careers, and social and financial opportunities (Jackson et al., 2014).

Although less common in its occurrence, the manifestation of PTSD was clinically very important in this cohort since it may potentially have had an impact on the overall quality of the patients' lives (Righy et al., 2019). It was imperative that PTSD was discovered early, which may have indicated acute stress symptoms generated by the ICU experience and memories associated with it (Righy et al., 2019). These patients were referred to their primary physicians for assessment and management of their symptoms, however further follow-up by the researcher was not pursued for ethical and privacy reasons. None of the study variables could predict PTSD, possibly because factors associated with it in previous literature, such as prior depression, ICU length of stay, and alcohol use (Bienvenu et al., 2013) were not relevant to this study. That is because pre-existing mental health problems were an exclusion to study enrollment, patients in this cohort had short ICU stays, and alcohol use by patients was not questioned due to its cultural sensitivity (during routine patient assessments and history taking, the use of alcohol is not questioned in Saudi Arabia for religious purposes).

The relatively low occurrence and significant improvement in mental health outcomes over time shed a positive outlook for this cohort. It was interesting to learn more about the reasons behind this phenomenon, which was explored further in the qualitative study described in the next chapter of this thesis.

5.3.4. HRQoL

All subcategories of the HRQoL measurements in SF-36 significantly improved in the follow up group and were higher than the normative data (AboAbat et al., 2020). The highest scores were attributed to social functioning. The participants in this study did not perceive limitations in their general health, physical, mental, and social life. This could be attributed to the improvements in ADLs, cognitive, and psychological wellbeing described earlier. The only

factor statistically associated with better reporting of HRQoL in the adjusted model was male gender.

It was interesting that the high BMI in the cohort, and the fact that more than a third of the cohort were in the obese category, did not affect the perceptions of physical wellbeing of the patients. In a study conducted in Riyadh, Saudi Arabia (El-Sobkey, S, 2014), exploring physical inactivity in Saudi and its effect on quality of life, it was found that those in lower levels of activity perceived poorer quality of life. One would hypothesize that inactivity would be one of the reasons for obesity and therefore obesity would also be associated with lower quality of life perceptions, however this was not the case in this cohort. In the Riyadh study, it was also reported that males recorded higher levels of activity than females and this could be due to the culturally driven better opportunities for males to exercise and participate in sports events (El-Sobkey, S, 2014). This could be one of the reasons why male gender was found to be a predictor of better HRQoL in the Life-ICUS study. Comorbid diseases, on the other hand, have also been found to be associated with poorer HRQoL (Orwelius et al., 2010). In the Life-ICUS cohort, a third of the patients had comorbid hypertension and diabetes, however these were not found to be predictors for poorer HRQoL.

The significant improvement in all subcategories of SF-36 in the follow-up period in this cohort was a novel finding. Most recent studies of similar sample sizes evaluating the quality of life of ICU patients have not shown this trend; either no improvements or further deteriorations in HRQoL were reported (Estrup et al., 2021; Rai et al., 2020). Considerable differences exist in the clinical course of the patients between the Life-ICUS cohort and these previous studies however, where patients were more acutely ill, stayed longer in the ICU, and experienced more days of mechanical ventilation than those in the Life-ICUS study patients.

Through the SF-36, patients reported social functioning to be the least affected in their life. This could be due to the family structure and social ambiance in Al-Ahsa, the Eastern province of Saudi Arabia, where the study was conducted. In fact, in the systematic review described in Chapter 3, social integration after hospitalization was reported to affect HRQoL to a larger extent than demographic and ICU related factors (Orwelius et al., 2011). Family and social structure are central in the Saudi culture in general and in Ahsa in specific, where family is

regarded as a pillar for social, financial, and economic support (Britannica, 2023). The qualitative study described in the next chapter will shed light on the role of family and friends in the recovery of the patients in this cohort.

These findings suggested that patients perceived their quality of life in a generally positive manner, regardless of the difficulties they encountered in the individual domains of PICS. Hofhuis describes a "response shift" phenomenon by which patients, over time, alter their internal measures and beliefs about their limitations, which in turn affect their perceptions and reporting of HRQoL (Hofhuis, 2014). Inevitably there are other factors such as resilience and adaptation which are key to perceptions of quality of life in ICU patients (Fok et al., 2005; Pauley et al., 2022), however the systematic measurements for these components were not within the scope of the quantitative Life-ICUS study. In the qualitative interviews of the patients, these elements will be explored and described further.

The inclusion of the measurement of HRQoL, in addition to the other domains of PICS, in this cohort was beneficial. It brought a multidimensional perspective to the PICS picture. In line with literature promoting HRQoL to be a "central outcome for ICU survivors" (Teixeira et al., 2021) and as critical care clinicians and researchers learned from the latest reports of Covid-19 ICU patients (Heesakkers et al., 2022), integrating HRQoL aspects in studies is now highly needed and beneficial for the overall understanding of long-term outcomes of ICU survivors.

5.3.5. Clinical and Research implications

This study confirmed that the Saudi sample in this study experienced significant PICS problems in all its domains. It suggested that changes in micro and macro health system in Saudi Arabia ought to integrate PICS in its practice, evaluations, and financial structures of governmental and third-party payers. The information gained from this study was important in order to gain deeper understanding of the problem and assist in the generation of evidence-based interventions, sensitive to Saudi cultural variances. In regard to research, the results may create an opportunity for more interest and research at the national level. Further PICS studies might be encouraged to be conducted in Arabic, which, if undertaken utilizing sound methodology and applying standardized tests and timelines, would enhance

comparability of studies. More on the clinical and research recommendations of this research will be presented in Chapter 7.

5.3.6. Strengths, Limitations, and Challenges

This was the first cohort study of ICU long-term outcomes in Saudi Arabia and the Arab region. With 94 patients assessed at baseline and, after rigorous follow-up, with 61 (65%) patients who completed follow-up, meaningful correlation tests could be performed between independent variables and outcomes in this cohort. The three-month period of follow up was adequate; it was close enough to detect consequences of ICU experience and yet not so distant to have had other factors interfere with the findings.

Another strength was that a thorough set of risk factors and confounding variables were examined, guided by a comprehensive conceptual framework. Pre-ICU physical and cognitive disabilities were assessed by questioning proxies, and this helped in eliminating over or under reporting of these impairments. Pre-morbid quality of life was not assessed in the study. This decision was taken because challenges in assessment of pre-morbid QOL in critically ill patients have been well documented (Angus, 2002). Critical illness may have influenced the patients' recollection and perceptions of pre-illness health status, and thus introduced recall bias (Angus, 2002). On the other hand, assessments by proxies may not have closely reflected the perceptions of patients (Gifford et al., 2010). To find a balanced alternative, having two timepoints of assessment for HRQoL was considered as a good solution, as it served as an optimal indicator of the status and evolution of heath perceptions of the patients. In addition, normative data regarding HRQoL were considered and referrals to normative SF-36 data in Saudi Arabia were made in the discussion section.

A full set of assessment tools were utilized to address all three domains of PICS, in addition to HRQoL, as the latter was deemed a natural consequence if impairments were discovered in the former three. To date, only a small number of studies have incorporated all the elements of PICS in one cohort study.

This study had some limitations and challenges as follows. In this prospective cohort study investigating the long-term outcomes of ICU patients, an initial cohort of 581 patients was considered. However, due to stringent exclusion criteria, 400 patients (approximately 69%) were deemed ineligible for inclusion in the study. The main reason for these exclusions was the initial ICU admission diagnosis of cardiac and neurological diagnoses, which fell outside the scope of our study's focus. Such a significant proportion of exclusions is noteworthy and can substantially impact the findings of the study. The exclusion of a large number of patients can introduce selection bias, potentially limiting the generalizability of the results to the broader ICU patient population. However, it is important to note that the study remains highly valuable, as it specifically targets a more homogeneous group of ICU patients, enhancing the precision and relevance of the findings for those without cardiac or neurological diagnoses. The stringent statistical methods applied further ensure the reliability and robustness of the findings, making them valuable contributions to the understanding of long-term ICU outcomes.

Moreover, the resulting study population was relatively small, which affected the quality and robustness of the data. A smaller sample size reduces the statistical power of the study, increasing the likelihood of Type II errors (failing to detect a true effect). It also limits the ability to conduct comprehensive modeling analyses, as fewer data points restrict the complexity and reliability of the models. Additionally, a smaller sample size can increase the risk of Type I errors (false positives), as random variations have a more pronounced effect on the results. Despite these challenges, the exclusion criteria ensure that our study is highly generalizable to the general ICU patient population without initial cardiac or neurological diagnoses. This targeted approach provides valuable insights into this specific group, reinforcing the importance and applicability of the study findings. Transparency in the reporting of the exclusion process and its implications on the study results was ensured to safeguard the integrity and credibility of this research.

Due to a small sample and limited number of participants in the follow-up group, associations could not be made with some important variables such as mechanical ventilation and sedation in the ICU. In addition, some patients (n=11) found the MoCA cognitive screening tool arduous and did not want to complete it, making cognitive outcomes measurement

limited. In the future, reasons behind patients' apprehension could be explored and alternative methods of cognitive screening tools could be considered.

Attrition and drop out were also limitations in this study. Attrition was mainly ascribed to the mortality rate in the sample, which was 13%. This mortality was however found reasonable due to the nature of the disease process of critically ill patients and their progression (Desai et al, 2011). Drop out from the study for reasons other than mortality during the months following discharge was 22%. The reasons for drop out were explained in Figure 5.1. This might have posed a potential source of bias.

Another limitation was that the present study was not exhaustive in assessing all long-term outcomes of PICS identified in the conceptual framework of the study; it could have integrated outcomes such as pain, fatigue, sexual dysfunction, consumption of healthcare costs, and return to work. Another potential area of assessment that could have been well integrated in the current study was the measurement of frailty and its association with PICS. In a study conducted by Marra, et al. 2018, frailty was found to be an independent predictor of the development of all domains of PICS (Marra et al., 2018). The understanding of PICS is evolving, and these factors will hopefully be assessed by the researcher in future studies.

The protracted data collection period was challenging as it took a full year to gather all study data. However, close communication with the ICU physicians and the ICU manager helped address this challenge as day-to-day communication was maintained for the potential recruitment of patients. It was initially anticipated to recruit 15 patients per month to reach a good number of participants for follow-up. This goal was not fully reached; however, ultimately an adequate sample of patients were recruited, and all data were gathered by the end of the data collection year.

5.4. Conclusion

Most patients in the Life-ICUS study experienced PICS in all its domains. Improvements in physical, cognitive, psychological, and HRQoL status were significant over time. Although the findings of this study concluded that none of the PICS domains were modifiable, clinicians

should exercise diligent identification of those at risk (older age, male, prior cognitive disabilities, surgical diagnosis) during ICU stay and thereafter. Many of the elements of the conceptual framework of PICS were addressed in this study, however further research is needed to explore the effect of personal and social characteristics of participants on post-ICU outcomes. The following chapter will describe the perspectives and experiences of the post-ICU patients from a qualitative point-of-view. In the next chapter the complete qualitative study, Life-ICU-Q, will be presented.

6. Chapter 6: Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia (Life-ICUS-Q)

6.1. Chapter overview

The previous chapter quantitatively explored the long-term post-ICU outcomes and HRQoL in a Saudi Arabian cohort. Long-term PICS outcomes showed impairments in all physical, cognitive, and psychological domains but significant improvements of PICS and HRQoL over time were noted. This chapter will describe the Phase III of the study exploring the lived experiences of ICU patients at least 3 months after ICU discharge in a qualitative method. The chapter will introduce previous literature and the background of the study. It will then describe the methodological approaches taken to qualitatively examine the patients' experiences. Four themes, each with three subthemes will be presented then findings will be thoroughly discussed, while drawing similarities with previous literature and showcasing novelties of the study. Finally, strengths, limitations, recommendations, and a conclusion will be described at the end of the chapter.

6.2. Introduction

As described in the previous chapter, admission to the ICU with a critical illness produced negative long-term consequences in a sample of patients in Saudi Arabia, ranging from limitations in physical functionality, altered cognition, and mental health issues. It is likely that in quantitative descriptions of the post-ICU experience, there may have been several aspects of the patients' journey which were not captured. In previous qualitative studies exploring the perspectives of patients regarding their post-ICU recovery and elements that contributed to it, patients reported a range of challenges and personal and social factors that contributed to their overall experience (Alexandersen et al., 2021; Hashem et al., 2016; Henao-Castaño, Rivera-Romero et al., 2022). A qualitative study was conducted as part of this research to gain a deeper understanding of the lived experiences of ICU patients post ICU discharge. This was called Life-ICUS-Q study.

6.3. Literature Review and Background

Experiences of patients in their post-ICU recovery phase have been studied across the globe. Several studies have documented reports of patients suffering from physical, cognitive, and psychological problems. In the physical aspect, immobility and fatigue after the ICU discharge were reported by many (Adamson et al., 2004; Agard et al., 2012; Czerwonka et al., 2015; Deacon et al., 2012; Maddox et al., 2001). Physical changes such as voice, weight, and appearance were also reported and perceived as 'bothersome' by patients (Henao-Castaño et al., 2022). In a recent study in Columbia, qualitative interviews were conducted at the homes of patients after 3 months of ICU discharge, which revealed alterations in cognition, mood, and sleep (Henao-Castaño et al., 2022). These physical and psychological changes were perceived as significant by the patients as they left them in a sense of exhaustion, necessitated dependence on family members in daily activities, and resulted in avoidance of social interactions (Agard et al., 2012; Henao-Castaño et al., 2022).

Earlier literature of the 2000's reported extreme post-traumatic stress reactions and "peculiar" stories from patients; such experiences were described as being in a different time and space zone (on a ferry, a wheelbarrow, a boat) (Storli et al., 2007), images of flying or falling, bodies taking a different shape, feeling a sense of emptiness and nothingness (Papathanassoglou et al., 2003), and preoccupation with ICU-related thoughts, intrusions, flashbacks, and panic attacks (Papathanassoglou et al., 2003; Storli et al., 2007). These experiences exerted a transformational power on patients' lives, sometimes leading to feelings of numbness, emotional distance, and isolation (Corrigan et al., 2007).

Post traumatic stress disorder has been identified in several more recent studies as well, but in less graphic forms (Abdalrahim et al., 2014; Chahraoui et al., 2015; Ewens et al., 2014). These were described as disturbing dreams and flashbacks, which in turn triggered depression, anxiety and created a state of paralysis for patients, accompanied by inability to look forward and find meaning in life (Hashem et al., 2016).

Memories of ICU after 3 months of ICU discharge were addressed in a study in France; patients recalled disturbing events such as being in physical restraint, upsetting noises, confusion

about time, not understanding their care in the ICU, feelings of impending death, and abandonment (Chahraoui et al., 2015). In the UK, a focus group-based study revealed that patients suffered from social withdrawal, feelings of abandonment, and a significant sense of vulnerability due to lack of information and uncertainty about the future (Walker et al., 2015). In Norway, a recent study interviewed patients after a longer period, six to twenty months after ICU discharge, examining "salutogenic resources", the person's willpower and motivation to return to good health, and how it affected patients' recovery (Alexandersen et al., 2021). Although patients carried a heavy physical and psychological burden, most faced their new life with willpower, and found going back to home and work as uplifting and motivating (Alexandersen et al., 2021).

The emergence of new health problems after critical illness has been shown to elicit an existential crisis for some patients (Vester et al., 2022). Two studies in Denmark, conducted with both patients and caregivers, found that patients were struggling with resumption of their pre-ICU self-image and identity (Agard et al., 2012; Vester et al., 2022). Critical illness had affected almost all aspects of their lives, including return to work, relationships with family and friends, and perceptions of life. The extent of dependency on others also created a sense of bitterness and a pessimistic view of their future health (Agard et al., 2012; Vester et al., 2022). Similarly, changes in relationships, feeling like a burden, and feeling "not needed" were common findings in many other studies (Abdalrahim et al., 2014; Corrigan et al., 2007).

Finally, to understand what matters most to patients, in a qualitative study exploring patient priorities after ICU, it was noted that firstly, priorities changed over time, and then, very similarly to Maslow's hierarchy of needs, they evolved from basic to complex needs (Scheunemann et al., 2020). Initial needs of comfort, mobility, and self-care, evolved to more complex needs of fulfilling roles, relationships, maintaining self-respect, and dignity, reaching to "self-actualization" needs which were fulfilled by pursuing new experiences, participating in ICU support groups, and other activities (Scheunemann et al., 2020). This signified the complex and dynamic process of patients' recovery after ICU.

To date, no qualitative studies of ICU survivors' experiences in Saudi Arabia exist to our

knowledge. In the previous chapter, quantitative data of a patient cohort showed disruptions in all areas of PICS but improvements over time were noted in long-term outcomes and HRQoL. Through a deeper understanding of the patients' perceptions of their recovery trajectory, a more holistic and meaningful picture would be drawn to their post-ICU experiences. This picture will enhance the awareness of critical care healthcare providers in Saudi Arabia and potentially improve practices, research, and education throughout the trajectories of care for critically ill patients. Therefore, a sequential qualitative study was conducted, named Life-ICUS-Q (Q referring to Qualitative), to gain an in-depth understanding of the patients' lived experiences after their ICU stay.

6.4. Aim and Objectives

The main aim of this study was to explore the experiences of ICU patients at least 3 months after ICU discharge.

The objectives were:

- To understand the perceptions of patients of their overall health and recovery after discharge from ICU.
- To explore the physical, emotional, and social challenges faced by patients after discharge from the ICU.
- To gain insight from patient' perceptions on the factors that contributed to their overall wellbeing and recovery.
- To identify patients' coping strategies following ICU discharge.
- To generate recommendations for healthcare providers and policy makers to enhance the experience of patients following their ICU admission.

6.5. Research Design and Methods

This was an exploratory, qualitative study, that followed the prospective cohort study described in Chapters 4 and 5. The subjective experiences of patients who had been

discharged from the ICU for at least 3 months were explored by using semi-structured interviews.

6.5.1. Ethics approval

Ethics approval was granted from King's College London Ethics Committee (HR/DP-22/23-34875) (**Appendix 6.1**) and AlMoosa Specialist Hospital Institutional Review Board (ARC-23.02.05) (**Appendix 6.2**). In the process, both consent forms and information sheets were prepared (**Appendix 6.3a** and **Appendix 6.3b**).

6.5.2. Participants

A purposive sample of patients, part of the quantitative prospective cohort study (Life-ICUS), were approached to participate in qualitative interviews. For context, the Life-ICUS study recruited patients from Almoosa Specialist Hospital's ICU and were followed up for evaluations of ICU-acquired physical, cognitive, psychological dysfunctions, and HRQoL at the time of ICU discharge and at three months after discharge. Since Life-ICUS-Q was a subsequent nested study to the Life-ICUS study, enrolment did not start before 16 months of initiation of data collection of initial study (considering the time needed to receive ethics approvals), hence patients' enrolment time in this qualitative study varied between 8 to 16 months after initial discharge from the ICU. For this qualitative study, purposive sampling was considered in order to maximize diversity of participants with respect to age, gender, ICU length of stay, and admitting diagnoses.

Purposive sampling criteria were as follows:

- Participants who, during the three month follow up of the quantitative Life-ICUS study, were voluntarily elaborating on their post-ICU experience rather than only responding to survey questions.
- Participants who had a MoCA score of 22 or higher during their 3-months follow up. This criterion was included to ensure that participants could engage in an interview for at least 30 minutes and major cognitive impairments would not interfere with

communication and expression.

6.5.3. Data collection

Semi-structured interviews were conducted using an interview question guide. For a description of the guide's components, questions, and prompts please refer to **Table 6.1.** The full guide is in **Appendix 6.4.** This guide was based on Eakin et al.'s study that investigated the outcomes of patients after acute respiratory failure utilizing the PROMIS framework (Patient-Reported Outcomes Measurement Information System) (Eakin et al., 2017). In this study, the guide was developed and revised based on feedback from five individuals who were experts clinically and in the field of patient-reported outcome measurements (PROMs) (Eakin et al., 2017). In the Life-ICUS-Q study, this guide was utilized as a starting point and follow-up questions were asked to fully explore participants' experience in each component of recovery.

Using Eakin's PROMIS framework for this qualitative study provided several compelling advantages. The PROMIS framework offered a robust structure for assessing patient outcomes across multiple domains of health. This framework ensured a comprehensive evaluation of physical, mental, and social health, which were crucial for understanding the multifaceted impacts of ICU experiences on patients' long-term wellbeing. This framework also provided a set of measures that have been utilized in similar patient populations, which were found important to enhance the credibility and comparability of the Life-ICUS-Q findings. By adopting this framework, the study benefited from a well-defined and consistent methodology, which was crucial for producing replicable and generalizable results. In addition, using Eakin's interview guide allowed building on existing research and directly compare study findings with others. This comparison was valuable for identifying common themes and divergences in patient experiences, thereby contributing to a more comprehensive understanding of the long-term outcomes after ICU care. The ability to align the study findings with established literature was found important to strengthen the rigor of the study and situate it within a broader context of patient outcomes research. Moreover, the PROMIS framework covered a comprehensive range of health domains, including physical functioning, emotional distress, social participation, and cognitive functioning. This holistic approach was particularly suited for exploring the long-term impacts of ICU stays, as patients

often experience complex and interrelated health challenges. An inductive approach, while flexible and exploratory, may have lacked the structured comprehensiveness needed to capture the full spectrum of patient experiences in a systematic and comparable manner. Utilizing Eakin's PROMIS framework offered a sound approach to the Life-ICUIS-Q study. It ensured thorough coverage of relevant health domains, facilitated meaningful comparisons with existing research, and enhanced the rigor of the study findings.

The first segment of the interview consisted of open-ended questions about the survivor's baseline functioning prior to ICU and overall health and recovery following ICU. Some examples from this segment were: "How have you been doing since you came home from the hospital?" and "How would you describe your health now?". In the second part of the interview, open-ended questions about perceptions in the areas of physical, mental, and social health were asked. Some examples from this segment were: "How do you feel physically?" and "How would you describe your mood now?".

Table 6.1. Interview questions

Topic	Question number	General question	Prompts
Introduction		I would like to learn more about how your health has been since you were in the ICU. Do you have any questions before I get started?	
Baseline functioning prior to ICU	One	Can you tell me a little bit about what your life was like before you were in the ICU?	If not discussed: probe physical, emotional/psychological health and social status, fatigue, cognitive abilities, day to day activities and employment situation prior to the onset of the acute illness.
Overall recovery following ICU	Two	How have you been doing since you came home from the hospital? Walk me through the timeline of your recovery after the hospital. What, if anything, do you think helped you the most since you have been home from the hospital?	*If needed:* What was it like when you were first discharged from the hospital? *If needed:* What is it like now?
	Three	Is there anything that you miss a lot from your life before you were in the hospital? Is there anything you would like to change about your health or well-being currently?	If yes, what?
	Four	Do you have any worries or concerns about your recovery? Did you have any worries when you first came home from the hospital?	If yes, what?
	Five	How would you describe your health now? How, if at all, has your health changed since you have been home? What do you do to help cope with problems experienced after being home?	
Physical Health	Six	How do you feel physically now? How, if at all, has your physical functioning changed since you came home from the hospital?	
	Seven	How would you describe your energy level now? How has that changed since you came home from the hospital? How would you describe your ability to finish tasks? What if anything stops you from finishing your tasks?	*If needed:* Do you feel like you get tired easily or have fatigue?
	Eight	Are you having any pain now? If yes, can you describe it?	*If yes:* Is pain interfering with your life? How?
	Nine	Tell me about how you sleep on a typical night now.	
Social Health	Ten	How would you describe a typical day now? How, if at all, have you changed your daily routines since you came home	*If needed*: What types of things do you do day-to-day?

		from the hospital?	Probe: if they have started doing new activities, changed how they do activities, or stopped doing activities they used to do.
	Eleven	What things do you do for fun now? What changes have you made to how you spend your time since you came home from the hospital?	*If needed:* How do you spend your leisure time now? *If needed:* How do you fill your time now?
	Twelve	How have you been getting along with your friends and/or family now? Are there any people you don't talk to or see as much anymore? How, if at all, have your relationships changed with your friends and/or family since you came home from the hospital?	*If yes*: Tell me more about that.
	Thirteen	How have you been spending time with your friends and/or family? Are there things you no longer do, or do less often, with your friends and/or family now? How if at all has this changed since you came home from the hospital?	*If yes*: Tell me more about that.
	Fourteen	How if at all have your goals or life plans changed since being in the hospital?	Probe career changes, financial changes, family planning, etc.
Mental Health & Cognition	Fifteen	How would you describe your mood now? Have you felt sad or worried? How is this different from before you were in the ICU? How, if at all, has that changed since you have been home from the hospital? What do you think contributes to you feeling that way?	*If patient is worried:* What types of things do you worry about? *If patient reports negative affect (e.g. anger, depression, anxiety, and stress):* Can you tell me more about those times?
	Sixteen	Have you had any trouble with your thinking or memory? Have you had any difficulties with organizing and planning things? Have you had any difficulties with paying attention or focusing? How, if at all, have these thinking or memory issues changed since you have been home from the hospital?	*If yes:* Tell me more about that.
PTSD	Seventeen	What memories or feelings do you have NOW about being in the ICU? Do you have any unwanted thoughts or memories? Do you ever avoid certain things because it reminds you of the ICU? How if at all has this changed since you have been home from the hospital?	*If yes*: Tell me more about that.
Overall, Health Recap	Eighteen	How would you describe "being healthy"? What areas would you include?	*If needed:* What does it mean to "be healthy"? *If needed:* Tell me what a healthy person would look like.

6.5.4. Procedures

Based on the purposive sampling criteria described above, the researcher contacted potential participants from the Life-ICUS study cohort by phone. She enquired, since the participant had consented to be approached for future studies on the Life-ICUS consent form, if the participant would be willing to receive information regarding a follow up study to Life-ICUS. It was briefly explained that this would be a qualitative study and its purpose would be to explore their experiences after ICU discharge. Participants were then given a minimum of 24 hours to decide if they would like to hear more about the study. If a patient communicated back and expressed interest and willingness to serve as a research participant, then the researcher initiated the process of providing further information via the study information sheet and obtaining informed consent. Each participant was seen in person at home or at the clinic, based on the patient's preference. A family member was welcome to attend the interview session. The patient was provided with written information about the objectives, benefits, and risks of the study in clear and simple language, both in Arabic and English. The participant was given ample time to ask questions, inquire further information and decide whether to participate or not. Two original consent forms were completed, dated, and signed by the participant and researcher. Once a participant consented to the study, he/she was assigned a study identification (ID) number which was the only number linked to the interview. After signing the consent form, an appointment was made to conduct the interview at the patient's convenience.

The interviews were conducted for 30-45 minutes, in the presence of two members: the primary researcher HT and the nurse FA. The nurse FA is an ICU nurse with three years of experience at the study site. She is a local Saudi nurse, who speaks the dialect of "Hasawi" (belonging to Al-Ahsa) Arabic. The decision to include FA during the interviews was based on her contributions to the study, which were described in the Patient and Public Involvement section of the methodology chapter (Chapter 2), her critical care expertise, and her native Arabic fluency and understanding of the local dialect. While HT, the primary researcher, had resided in Saudi Arabia for the past three years and possessed proficiency in Arabic, her Lebanese upbringing resulted in a distinct dialect, different than the prevalent dialect in Al-Ahsa, Saudi Arabia. Recognizing the importance of linguistic precision and cultural nuance in

data collection, the nurse FA was invited to participate in the interviews. The collaborative effort aimed to address potential language barriers and ensure the accuracy of participants' narratives. The interview process was primarily conducted and led by the primary researcher, HT, with additional support from nurse FA, who clarified some terms and expressions that might have otherwise been challenging for the primary researcher. After each interview, HT and FA engaged in a brief discussion to further elucidate specific aspects of the conversations, ensuring a comprehensive understanding of the participants' experience. This methodological choice aligned with established research principles, emphasizing the significance of linguistic and cultural competence to enhance the rigor and authenticity of qualitative findings within the context of this research.

The interviews were done in a private setting, either at the patients' home or at the clinic. They were all audiotaped using an external recorder. During the interviews, participants were given the space to lead the conversation. Some prompts were given. Participants were asked to inform the interviewer if they felt uncomfortable during the interview. After finishing the interview, the participants were given the option to listen to the recording. Each recording was labelled with the study ID number. The patient's name or other identifiers were not labelled on the recordings. A sheet was devised containing links of study ID and recordings; this sheet was stored separately from the recordings, was password-protected, and was only accessible to the researcher. During and after the study, all hard copies of consent forms that contained the participants' names and contact information were saved in the researcher's office, in a locked cabinet accessible only to her. Recordings were transcribed verbatim by a professional transcriber and translated also by a professional translator. Data files were saved on the KCL OneDrive, which was accessed by username and password known only to the researcher.

6.5.5. Data Analysis

Using an inductive approach, thematic analysis was performed based on the steps outlined in the publication by Braun and Clarke, 2006. Thematic analysis is a method by which patterns are identified inside and across a set of data, then they are examined, and then conveyed as themes (Braun and Clarke, 2006). This type of analysis was chosen to be able to explore the

current state of the research participants' perceptions about their health and examine their experiences and the meanings behind them (Braun and Clarke, 2006). First, the researcher read the transcripts and familiarized herself with the data, taking notes and writing initial impressions (**Appendix 6.5.** Initial Draft Code Sample). Then, looking at the most basic information or elements in the data, line by line coding of transcripts was performed. Another member of the research team (HM) also read and coded all the transcripts independently, after which a discussion was held regarding the potential set of codes that would go into analysis. The transcripts were read again by the researcher several more times, organizing data for each code. Categories of codes were then identified as patterns emerged and "units of meaning" from the participants' experiences arose (Braun and Clarke, 2006). Categories were then collated, and as they started to appear to be capturing an important aspect of the research aim, they were formed under potential themes (Braun and Clarke, 2006) (**Appendix 6.6.** Sample theme collation). Throughout this stage, themes were formed not only by the explicit meanings of participants' statements, but also by some interpretation of underlying thoughts, feelings, and values. The themes were then discussed among the team members (HT, GL, AMR) and consensus was established. The specifics of each theme were refined and revised, and the names of the themes were changed in the context of the overall information and stories that the analysis of the data generated. No new themes were identified after the sixth interview. Interviews were stopped when saturation of themes was achieved. **Table 6.2.** shows the six phases undertaken in the Thematic Analysis. These phases were successive in sequence, however a "process of moving back and forth" between the steps occurred throughout the data analysis phase (Braun and Clarke, 2006).

Table 6.2. Phases of Thematic Analysis (Braun & Clarke, 2006; Braun & Clarke, 2022)

Phase	Title	Steps
1	**Familiarizing yourself with the dataset**	Read and re-read (immerse in the data). Take notes.
2	**Coding**	Generate codes. Collate codes. (2 or more rounds)
3	**Generating initial themes**	Examine steps in 2. Develop patterns. Identify potential subthemes and themes.
4	**Developing and reviewing themes**	Check the themes against the codes. Further develop themes.
5	**Refining, defining and naming themes**	Develop details of each theme. Determine the "essence" and "story" of each. Name each.
6	**Writing up**	Narrate and contextualize.

6.5.6. Trustworthiness and rigor

Trustworthiness was established in the study by adhering to criteria described by Nowell et al., 2017. Throughout the study, standardized approaches were adopted to enhance these criteria which relate to credibility, transferability, dependability, and confirmability (Nowell, et al.,2017). Credibility was enhanced when an expert panel of ICU clinicians (HM, FA) and researchers (GL, AMR, AM, AS) were invited to serve as advisors to the researcher and reviewed the research process and preliminary findings in a peer-review approach. In addition, as described above, the interviews were conducted by two individuals, one of which was a native Saudi nurse, proficient in speaking the Arabic dialect of the Eastern Region of Saudi Arabia. Furthermore, initial coding was performed by two members of the research team (HT and HM) and then shared with other members of the team (GL and AMR); and finally, codes, sub-themes, and themes were discussed with all team members. These steps were conducted to enhance the credibility of the study. Data was transcribed and translated professionally and checked for accuracy by an expert researcher native to Saudi Arabia (AM). Abundant descriptions of data were included in the writing phase so that those who read the findings could judge their usefulness in different settings. These were performed to improve the transferability of the findings. The research process was described in detail (methods section) so that reliability can be achieved, and field notes and an audit trail were consistently

maintained to ensure dependability. And finally, reporting the methodological choices, as well as the research process in a systematic and transparent manner was maintained to establish truthfulness and thus promote confirmability of the study.

6.6. Results

Between May and July 2023, semi-structured interviews were conducted with six patients who were in the Life-ICUS cohort study, 8-16 months after ICU discharge (see **Table 6.3** for a description of the patient characteristics).

Table 6.3. Patient characteristics

Patient	Age	Gender	ICU Diagnosis	Length of Stay	Time of interview after ICU discharge	Place of interview
PA	49	Male	Septic Shock	3 Days	233 Days/8 months	Clinic
PB	33	Female	Diabetic Ketoacidosis	6 Days	479 Days/16 months	Home
PC	36	Male	Sickle Cell Disease	9 Days	488 Days/16 months	Clinic
PD	55	Male	Acute Kidney Failure	6 Days	361 Days/12 months	Clinic
PE	48	Female	Crohn's Disease	7 Days	326 Days/11 months	Home
PF	33	Female	Diabetic Ketoacidosis	7 Days	314 Days/10 months	Clinic

The lived experiences of patients were represented in four themes and three sub-themes for each theme (Table 6.4). It is important here to highlight how thematic analysis was employed to distill core themes from patient quotations. The analysis began with the systematic collection of raw data through in-depth interviews, during which patients shared their experiences and perceptions. These interviews yielded direct quotations, which were then carefully coded to capture the key elements of each statement. For example, a quotation such as "I couldn’t move from the pain…I needed pain killers" was coded as "Pain," reflecting the physical distress reported by the patient.

Following the initial coding, these codes were grouped into subthemes that represented broader categories of related experiences. For instance, codes like "Pain" and "Limitations in movement" were categorized under the subtheme of "Physical distress." This subtheme captured the various facets of physical challenges experienced by patients, including pain, immobility, and other physical limitations. Similarly, codes related to psychological

challenges, such as "It was more of a mental exhaustion. It was psychological fatigue," were grouped under the subtheme "Psychological distress."

In addition to these subthemes, other significant categories emerged, such as "Memories of ICU," which included codes like "Cold" and "Sounds," reflecting sensory memories associated with the ICU environment. Quotations such as "The air conditioner was like a refrigerator...the room was cold" and "I heard loud noises…" illustrated these sensory experiences. Another category, "Associations," included codes like "Smell," highlighting how certain scents, such as "the smell of perfume or these wipes," evoked strong memories of the ICU.

The final step involved synthesizing these subthemes into overarching themes that encapsulated the central aspects of the patients' post-ICU experiences. For instance, subthemes like "Physical distress in the ICU" and "Psychological distress in the ICU" were integrated into the theme "My ICU experience," providing a holistic view of the multifaceted challenges faced by patients during their ICU stay. This theme encompassed both the physical and psychological dimensions of their experiences, highlighting the complex interplay between these factors.

Overall, this comprehensive thematic analysis ensured that the derived themes accurately reflected the patients' experiences and provided a robust framework for understanding the long-term impacts of ICU admission on their lives. By meticulously coding and categorizing the data, the analysis preserved the richness of the patients' narratives while distilling them into meaningful themes that could inform future research and interventions.

Table 6.4. Themes and Sub-themes of study

Study Themes	Study Sub-themes
Theme 1: My ICU experience	Physical and psychological distress Memories of ICU Lasting associations with ICU
Theme 2: I move towards health	Body and mind in the immediate post-ICU phase Body and mind in the long-term post-ICU phase Restoration of health
Theme 3: My Inner strength, Gratitude, and Faith	Resilience Thanks to ICU team and family/friends. My religion, my faith
Theme 4: I Survived and Learned	I beat it Lessons learned Re-defining meaning of health

6.6.1. Theme 1: My ICU experience

The patients remembered the ICU and described their reflections of the ICU experience as one which was physically and psychologically challenging. They also had memories of certain events and associations of ICU that persisted in affecting them.

6.1.1.1. Subtheme 1.1: Physical and psychological distress

The patients reported limitations in movement in the ICU because of long stays in bed and muscle weakness.

> *When I remember my experience, for almost 8 or 9 days I was in bed, my feet did not reach the ground, literally.* ***PB***

> *What bothered me were the devices. I mean, the devices were the ones hindering me from movement…* ***PC***

> *My body muscles were not the same…* ***PC***

The patients also reported pain, which for some caused additional limitations in movement.

> *…I couldn't tolerate the least pain, I would need pain killers, things like that, it affected me a lot…* ***PB***

> *I couldn't move from the pain…I needed pain killers.* ***PA***

They also referred to feeling dependent in performing their basic activities, which caused them psychological distress.

> *I couldn't do the minimum for myself, I mean going to the bathroom, that was very very hard, it affected me a lot…That you are in need, that you need someone's help, you feel, I mean, it's very difficult.* ***PB***

The patients expressed that their overall challenge in the ICU was psychological in nature, and that when they started improving physically, their psychological wellness followed.

> *It was more of a mental exhaustion. It was psychological fatigue.* ***PC***

> *The difficulty in the first three days in ICU, the situation that I was in and the events that followed me, there were some things that bothered me psychologically…but after these three days, I can tell you that the situation changed by one hundred and eighty degrees, of course for the better…And I started getting better and this started to lift my spirits, especially when the fever stopped…* ***PF***

6.1.1.2. Subtheme 1.2: Memories of ICU

Patients had vivid recollections of their physical experiences in the ICU such as feeling cold and hearing loud voices.

> *The air conditioner was like a refrigerator...the room was cold.* ***PA***

> *The first feeling that comes to my mind is that I was cold, the ICU was cold…**PE***

> *I told my father I would rest. I slept; I woke up as if I was sitting in an imaginary house that they were building. I mean they were hitting, takh, takh, I heard loud noises…**PA***

Patients remembered having their blood drawn and this experience caused them a significant amount of distress.

> *I was very affected…They came to take blood from me, they nibbled my hands, that was the day I had the most bleeding, and they came to clean it, and that was worse…**PC***

> *They were not able to take blood, I mean, the blood was not coming out. They used to bring me nurses, as you say, specialists, in drawing blood or something like that, maybe an "IV team". It was very difficult to take my blood….I frankly suffered psychologically, and I had feared and awed when they said that if my veins did not work, they would put it (medication)*

through a vein in the neck…Real horror…My hands were stained blue and green…That was suffering I can't forget honestly… ***PF***

6.1.1.3. Subtheme 1.3: Lasting associations with ICU

The stay in the ICU left persistent associations in the minds of the patients, especially relating to the smells of the ICU.

The smell of perfume or these wipes…I started smelling the ICU everywhere I saw a wet wipe. I intentionally bought it so that I try the bad thing that I experienced because of this smell, so oh, I have it in the office, in the car, at home, everywhere, to get rid of this bad feeling. I mean, a strong memory is present with these fragrant wipes... ***PE***

…There are some smells that remind me of the hospital, not that I hate them, but they are associated with the hospital…The smell of sterilizers, this disinfectant… ***PF***

6.6.2. Theme 2: I move towards health

This theme was characterized by two phases: the "immediate post-ICU phase", which was referred to as the transition from the time of ICU discharge to the general ward and then to the first few days at home. The "long-term post-ICU phase", which was referred to several weeks to months after the discharge from ICU.

Patients continued to experience persistent physical and psychological changes in the immediate post-ICU phase. However, as patients progressed to their long-term post-ICU phase, they signalled their readiness to find health and they were active in identifying and executing healthy behaviours and coping strategies.

6.6.2.1. Subtheme 2.1. Body and mind in the immediate post-ICU phase

Most patients referred to the immediate post-ICU phase as one with difficulties in doing their usual physical activities, accompanied by pain, fatigue, and difficulties in sleep. Many

expressed psychological disturbances ranging from sadness to frustration, and resentment.

> *In the first week I was suffering from difficulty in movement and walking and I had difficulty in sleeping.* ***PF***

> *In the beginning, when I got out of ICU, there was still fatigue, there was still, oh, pain. There was no energy at all, there were days, oh, I would cry, not from pain, I would cry because enough, I couldn't take it anymore, I couldn't bear it…****PB***

> *I went through a situation with a bit of chest tightness, I went through a state of a little frustration, because I resented myself… I resented the events that came to me after what happened to me…I was worried, scared, frustrated.* ***PF***

Patients expressed fear of the consequences of their critical illness and its recurrence.

> *I felt tight and upset…I didn't know what would be, God forbid, the consequences…One does not know the unseen; however, one can sit and think whether this situation will continue in the future. Will it have bad consequences, God forbid? Does it mean that I will enter other matters, God forbid?* ***PF***

> *When I first left the ICU, I was a bit concerned that I might return to this situation, I had fears…****PE***

A patient was profoundly disturbed by not being able to fulfil religious acts and obligations (praying and fasting) due to the bleeding she was having after a few days of discharge from the ICU.

> *…because of the bleeding, it was difficult to do religious matters, to pray. I mean, how do you deal with it? Sometimes it (bleeding) was profuse and sometimes not, I mean sometimes I doubted whether it was bleeding or it was my period, and by God, this situation makes you tired…I was concerned about fasting, so it was difficult, because it's forbidden…especially that I must pray, it is considered istihaadah*..these things distract you; for example, you need to wash twice a day or do ablution twice, how do you deal with this? So, this is what confused me more…****PC***

*In Islam, Istihaddah (Arabic: اِسْتِحَاضَةٌ) represents a disturbance of the menstrual cycle which prevents a woman from performing religious rituals.

6.6.2.2. Subtheme 2.2: Body and mind in the long-term post-ICU phase

When describing their current state, after several months of ICU discharge, patients spoke of generally marked improvements and progress in health, especially in the physical and psychological components. Almost all patients reported no change in their cognition and in their social health.

*There is no pain now…there is nothing except health…**PA***

*My mood was so-so (after ICU) …now it's okay…**PA***

*Mentally, I am better (says the year, the month, and the day) …I mean, I don't feel there is a change in my mind before and after…**PA***

*I can do the activities that I used to do before ICU… **PC***

*Psychologically I am better than before…The improvement is clear, in the beginning (legs) were swollen and then by God, everything changed to the better in my body…Sleep... is better than before…I found wellness and health, better than before…I changed more than 100%, even my body changed…**PD***

*…I don't suffer from anything now, it (health) is good. I returned to good, my cognitive and physical health, thank God, my life is comfortable…my sleep became better. I remember there was a time when it used to take me two hours to sleep, but now... the moment I want to sleep, I sleep…I think this is a good sign…**PE***

6.6.2.3. Subtheme 2.3: Restoration of health

Patients elaborated on what they did to achieve restoration of health. They actively sought physical rehabilitation and healthy behaviours. All patients returned to work and active coping and distraction techniques were reported by most.

Patients were engaged in physical activity, whether by attending physiotherapy sessions or simply “going out”, “moving”, and “walking”.

> *…until now I work two days a week intensive physical rehab, three hours a day every time.* ***PA***

> *I am going out and walking now…**PA***

> *…At night I would go out... I would move…I would walk for half an hour, 45 minutes, I would take a break or two…I would walk in the farm close to the house…**PD***

Patients took the initiative to adopt healthy habits. Two patients (PA and PD) had quit smoking, and one patient expressed a strong wish to enter a smoking cessation program (PE). Exercise and healthy eating were on their agenda even if at times it meant doing the “simple things”.

> *One month ago, I started diet and gym, without anyone’s recommendations, I mean on my own. And when you go to the gym, you must eat well. I stopped the soft drinks, and I stopped the sweet things, simple things I mean…* ***PE***

Some patients were dissatisfied with their weight and were seeking help.

> *I just need help to lose weight…I saw a snap (snapchat) of a person, before and after, he changed…now I am 95 (kg), I want to reach 70-75 (kg).* ***PA***

> *…My weight. I went back several times to the doctor, I mean, I lost control (over food) over the past months, and I have to go back again.* ***PE***

Patients reported following up with their primary physicians.

> *What helped me most is the follow up… follow up and the advice from the doctor…* ***PE***

Patients engaged in leisure activities with their friends and families. “Changing scenery” and

being in nature were reported to bring solace.

> *…in the evening, I would go out and walk in the farm, and one of our guys has opened his diwaniyah**, I would sit with them… I take the family to the city, sometimes to Bahrain and Emirates..I mean I want to go out and change scenery for me and for them.* ***PD***

> *I got into my cousin's car, I told him to take me out, I mean to just change scenery…I went to the sea, I have friends who go to the sea…I talked to the sea (laughing) and said… O sea, take as much as you want from me…****PA***

> ***Diwaniyah is a traditional gathering where people come to discuss various social issues.*

Many patients engaged in recreational activities for distraction.

> *I would distract myself…For example, I would do housework, watch the news, use social media for example, for recreation…Search for news, information, Twitter. I would read, I would want to cook…****PF***

> *I like to read, I like to re-organize, change in décor, I like to draw, and sometimes I draw for my family…****PC***

Some patients were active in learning about different coping strategies.

> *…I read about it (health situation), I searched on how to cope.* ***PC***

And finally, many patients opted to just forget their ICU experience as a coping mechanism.

> *I don't remember and I don't want to remember (laughing)…* ***PA***

6.6.3. Theme 3: My inner strength, gratitude, and faith

6.6.3.1. Subtheme 3.1: Resilience

Patients found adaptative mechanisms within themselves to withstand their difficulties and regain their health.

Some approached their experience with determination and found it a "requirement" for moving on from the adversities of their journey of recovery.

> *Because determination is necessary…Determination is required… the psychological factor is the strongest one…I put in my head to rely on myself…No, my determination is strong, my will is strong…I had determination... and I did not despair…**PA***
> *I tried to move and not to succumb to the bed or the situation I am in…**PF***

Perseverance, stated several times in expressions as "I am trying", was evident in the patients' constant efforts to try to endure, despite some setbacks. Some patients used their fears and anxieties as motivators to persevere.

> *My health is good now, but am I satisfied with it? No, because I feel there are things I still need to work on…until now I am fighting the fears, until now I need physical fitness…there are things I am working on…I am following a physical trainer at the gym, I am trying, and he is trying with me, and I am trying with myself…Psychologically, I am trying as much as I can, to distract myself from thinking…**PB***

> *I tried to support myself psychologically…I tried not to surrender to the situation I am in, because in my normal life I am not like this… I am active in my daily life, I love movement…Perhaps this was a motive for me... I am trying not to give in to the health condition I was in, and I am trying to return to my normal life….**PF***

> *...to go back to my previous era…I am trying to go back again to the same previous conditions and the same stable mental, health, and physical state, and normal life in the house…This anxiety exists, but this is a reason for me to be somewhat careful with any condition that may*

*be similar, or with any health symptom that would require me to contact the hospital directly. I mean on one hand I reassure myself, and on the other hand, God forbid, I don't want to go through similar events. I am following with the hospital in Dammam, and I am still going to my appointment and X-ray and medical follow ups…**PF***

Patients expressed optimism and confidence in themselves to regain independence.

*I like to, as much as I can, to have a good day. **PB***

*…I get up and walk normally and try as much as I can not to use a walker…I would bring the cane just in case, but I wouldn't lean on it. **PA***

Patients found motivation by going back to work and looked forward to having a social life again.

*I enjoy when I meet people, I like to interact with them, this is what changes my mood…**PB***

*…This (work) is the thing that distracts me from thinking…I enjoy it a lot…This thing that I feel, sends me energy, to go, to go to work, to see friends, to meet reviewers, this is what I love. **PB***

My mood is fine, psychologically stable, and I am ready, God willing, for the atmosphere of Eid and the gathering of Eid… **PF***

** Eid is the holiday after the holy month of Ramadan in Islam.*

6.6.3.2. Subtheme 3.2: Thanks to ICU team and family/friends

Patients remembered the nurses and doctors who were engaged in their care and expressed immense gratitude towards them. They also shared their appreciation for the role their families and friends played in their recovery.

Thanks were expressed to the doctors and nurses for giving explanations and looking after them.

Of course, the doctor was the best doctor, doctor MY, he took the initiative and explained to me. ***PA***

*I had fears but when the doctor explained to me, it was enough…****PE***

And all the doctors and nurses, God bless, they did not fall short, God be my witness…every hour they would check on me… ***PD***

Nurses were appreciated for giving reassurance and showing empathy. At times they were a source of strength to the patients.

It's a word…God bless you…at times, when one is in the peak of sickness, when the world is over in his eyes, one word from you, makes a difference. ***PB***

*I reached exhaustion, I was tired; a nurse came by, may God remember her well…I don't even think she was Muslim; she saw me broken down in cries, she was drying my tears, and said, it's okay, it's okay, you are strong. I felt her back, I felt I was strong. If she said I am strong, it means I am strong. Her words affected me a lot…****PB***

Patients showed their gratitude towards healthcare team by asking for God's rewards and blessings.

…and the group in the hospital, may God reward them well, they played a role for which they should be thanked. ***PA***

Thanks be to God and then to you. He who does not thank people does not thank God. ***PF***

I remember her (nurse), and I pray for her that God makes her happy. ***PB***

A duaa (a prayer) was said towards a nurse:

I say to the nurse, thanks to you first and last…Your presence, my beloved, morally facilitated my affairs and made me obedient to my affairs. By God, I will never forget this favour of yours. May God reward you well and make it in the balance of your good deeds, and make it an

opening for goodness and progress, professionally, even for your personal life and family, God willing. ***PF***

Gratitude was also shown towards family and friends for their support during the ICU journey.

Of course, my husband and mother were the ones who supported me the most… ***PB***

*My family and my wife... everyone did their part…****PD***

…a close friend, a female colleague, she is the one I used to communicate with the most, and she knew my news, and of course she contained me a lot, and she communicated with me and wanted to check on me frequently, yes, and we are still, by God, continuing to do that. ***PF***

Prayers were also made to family and friends.

…those who took care of us, those who were present, may God reward them, day and night they took care of us in dignity…I remember them. He who does good should not be denied. ***PD***

*…May God reward him (husband) well, and honestly, I pray for him these days, he supported me mentally, physically, and morally, and he tried to ease the difficult days that I went through, during the days I was in the hospital and even after I was discharged from the hospital…****PF***

6.6.3.3. Subtheme 3.3: My religion, my faith

Throughout the interviews, praise to God (Hamdullilah) and by the will of God (In sha Allah) were repeatedly introjected between statements and narratives.

*Every day I say my God, praise be to you…When I went out of the ICU and I'm healthy, this is in itself blessing from God, thank God…****PB***

Patients were thankful to God for the experience.

I say thank God, it's an experience… ***PB***

Patients were hopeful by God.

But, In sha Allah (God willing), it (health) will come back with days…Now, I am in recovery period, slowly I will get there, in God's will... ***PB***

*God does not return evil, and God willing, no one will enter evil…****PF***

Patients were trusting in God.

Glory be to God; God does not burden a soul beyond its capacity. ***PB***

*…by the grace of God, that it (ICU) went well…****PF***

Patients relied on God and objected to resisting negative aspects of their experience because it was "written" by God.

*What God has written for us will be. We depended on God; God be my witness…****PD***

*This is written (by God), alas, after God's wisdom, we can't say anything about it…****PD***
I depended on God...everything is written. ***PD***

When they told me that (dialysis was needed), I said, this is something written (by God), and we don't object to our God…we do not think and we do not obsess… ***PD***

I told them, nothing will happen to you except what God has destined for you. ***PA***

*I surrendered myself to God…****PD***

6.6.4. Theme 4: I Survived and Learned

6.6.4.1. Subtheme 4.1: I beat it

In single sentences, patients referred to a sense of survival out of the ICU.

> *…the ICU is when one either comes out to be buried or comes out reborn…* ***PA***
>
> *…there were days of difficulty, but I came out alive.* ***PA***
>
> *…it's an experience I got out of.* ***PB***
>
> *I entered the ICU and came out…**PD***
>
> *I made it out of the ICU; I found in it care and attention, God be my witness.* ***PD***
>
> *..I was able to overcome the crisis…I recovered and returned to what I was…**PF***
>
> *I feel that I beat it…**PB***

6.6.4.2. Subtheme 4.2: Lessons learned

Patients drew life lessons from their experience in the ICU. They spoke about how health is important.

> *I say, how sweet it is to be healthy, I mean, I swear, one should be in good health, so we say thank God for it. This ICU experience taught me to take care of myself more, that I should pay attention to myself more, like they say, nothing will benefit you except for your health…**PB***

They spoke about finding meaning in friendship and in the value of people in life.

> *During the time of sickness, you know who is a close friend and who is not…**PB***

*…these relationships became stronger after the ICU; I felt the blessing of being connected…**PB***

*I knew the value of life during these 9 days, I knew the value of people, I say nothing in life lasts…**PB***

Patients spoke of the preciousness of time and aspired for new experiences.

*I feel that there is no time for being upset…I feel that when I get ideas, I try to block them because they will not benefit me. The fatigue, the upset, that's what affected me psychologically, so now I feel that I don't have time for that, enough. **PB***

*I feel that time has come to live one day at a time…things that I didn't do before, I want to do now, I want to achieve, I want to experience the feeling, even if simple things, I want to have this feeling. **PB***

*Before (ICU) things were simple, but now no... I aspire more…I mean this experience changed me... there are things I used to postpone, like studying, ohh, even work, but after (ICU), no. **PB***

*If I have something to do, it is not like before that I postpone doing them; if they (family) said we want to go somewhere, before I would say leave it to later…but now when they say let's go, I say, by God, let's go…Time changed…**PD***

*…confronting these things makes you think, makes you plan more, for the family and the kids…I started thinking about my future affairs…**PE***

*I don't want to say "what if", I want to see what happens if I experienced things. **PB***

The ICU experience nurtured the patients' spirituality.

*In terms of spirituality…I went deeper into it, because this, thank God, makes me stronger, in some ways psychologically and some physically. **PB***

One patient showed a strong desire to help others through her experience, and to share her stories and strength with others.

*..The experience of ICU made a difference in my life. It taught me things... there are things to share, and that the most important thing in life is health...I want people to see the simplest thing, that you are in a blessing every day, that others are not …**PB***

*I feel alive, I want to be inspirational…I want to try this thing (being an influencer) … I would like to speak to ICU patients…I know that ICU patients don't ask for much, a visit, a word, it brings back the soul; it's not the medical treatment, it's the word that returns the soul, not the treatment. **PB***

6.6.4.3. Subtheme 4.3: Re-defining the meaning of health

Patients reported to be re-thinking the meaning of health after the ICU experience, in terms of independence and physical and psychological wellness.

*That I can do things for myself, I depend on myself…if one can take care of himself and his children, praise be to God, this is health, that is sufficient. **PC***

*To sleep well, to eat well, all the vital signs to be good…so all these signs make me feel good. **PE***

*If my health states are stable, there is no setback or signs of a setback… If I practice my daily life normally, my psychological condition is stable…that's health. **PF***

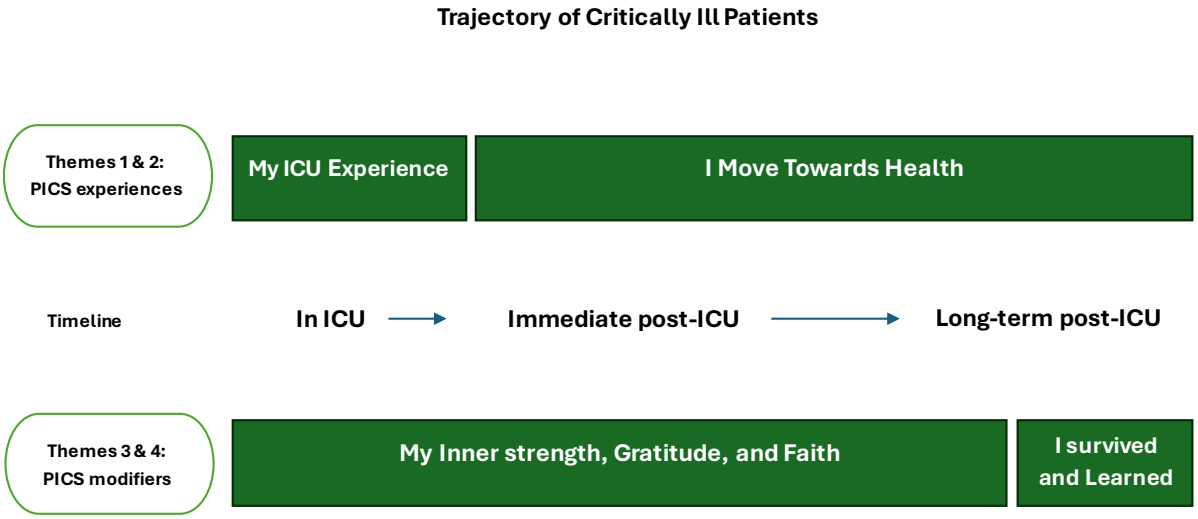
*Health is the body, health is psychology, health is all life. **PA***

6.7. Discussion

This study aimed at exploring the post-ICU experiences of patients using a qualitative approach. It revealed critically ill patients' lived experiences following ICU discharge that included aspects of PICS, such as physical and psychological, as well as their personal, social, religious, and cultural attributes of recovery. The detailed accounts of the patients however did not focus only on the post-ICU phase but covered the trajectory of critical illness from ICU stay through several months after discharge. The following diagrammatical presentation

(**Figure 6.1**) illustrates the timeline of the critically ill patients' trajectory in this study, from the time of ICU to immediate post-ICU and long-term post-ICU phases. It also demonstrates the alignment of the themes of this study along this timeline, with theme 1 and theme 2 primarily uncovering the patients' PICS experiences, and thus termed as themes of "PICS experiences"; and themes 3 and 4 referring to the personal and cultural attributes that helped the patients navigate their recovery, and hence they were named as themes of "PICS modifiers".

Figure 6.1. The trajectory of critically ill patients



In their accounts, patients had certain reflections to share about their time in the ICU (My ICU Experience: a PICS experience theme). The prolonged bed rest, muscle weakness, pain, and the presence of medical devices caused physical discomfort and a sense of confinement. The psychological distress in the ICU was mainly caused by fatigue, physical limitations, and the perception of loss of independence. Patients were also able to remember specific events and they had fragmented recollections of the temperature, smells, and noises of the environment, interactions with the ICU team, and some medical interventions. From the ICU experience, the physical variables of immobility, pain, and fatigue have been recalled by ICU patients in many studies (Adamson et al, 2004; Czerwonka et al., 2015). Patients in the ICU would like to

avoid the pain and discomfort caused by procedures, such as the ones described by the Life-ICUS-Q patients regarding blood withdrawal (Scheunemann et al., 2020). At the mental health level, patients reported some emotional distress from the ICU experience itself, but unlike other studies (Chahraoui et al., 2015), severe negative recollections such as feelings of entrapment, withdrawal, isolation, and a sense of abandonment were not described. Similarly, patients did not seem to have experienced distorted perceptions of self, time, and place, neither did they report hyper-sensory or delusional stories of transformations of body and space, which are commonly reported in many ICU qualitative studies in the past (Papathanassoglou et al., 2003; Storli et al., 2007). Compared to the existing literature, the primary difference here was that specific recollections of severe negative memories were not recalled by the Life-ICUS-Q patients. It is possible that some memories had faded by the long lag of time between ICU discharge and the time interviews were conducted (up to 16 months in this case). It is also possible that memories were replaced by mere perceptions, which was a finding in a study illustrating that even as early as 6-12 weeks after ICU, memories of ICU diminish (Maddox et al., 2001). It is also probable that patients tended to evade memories, which has been found to be a positive coping mechanism as it could be protective for overall mental health over a longer time (Jones et al., 2001). The PICS related themes of this study did not reveal an intense traumatic and emotional experience by the patients while in the ICU, and unlike previous literature, such experiences were not revealed to have been rooted in their memory and reflected in their recollections (Arntz et al., 2005; Storil et al., 2008). Unlike ordinary memories, traumatic memories have been found not to dissipate with the passage of time (Van der Kolk et al., 1996). Whether the patients in the Life-ICUS-Q study did not exhibit debilitating or overwhelming psychological effects of the ICU unlike findings from other studies or they did not report them because of cultural or social reasons was considered possible but could not be confirmed in this study.

In the immediate post-ICU phase, the psychological burden was evident in most accounts in this study. During this immediate post-ICU recovery phase, patients manifested symptoms of anxiety and depression, and these were related to frustrations with the pace of recovery, lack of energy, difficulties in performing daily activities, maintaining good sleep, and exercising religious duties such as praying. The fear of relapse was present, and this has been reported in other studies (Scheunemann et al., 2020); however, it was not as debilitating as other

reports where such distress was associated with suicidal ideations, stemming from a sense of escape from the possibility of the critical illness happening again (Corrigan et al., 2007). The mental health burdens after ICU have been described previously in qualitative studies (Corrigan et al., 2007; Maddox et al., 2001), however, as described above, the Life-ICUS-Q patients did not experience severe forms of PTSD. In the immediate post-ICU phase, nightmares, hallucinations, and other intrusive ideas did not occur in these patients. This is unlike other studies that have shown a high incidence of such events (Corrigan et al., 2007; Rundshagen et al., 2002; Strahan et al., 2003). Consequently, Life-ICUS-Q patients did not report effects of PTSD such as impairments in social interactions, withdrawal, and isolation (Corrigan et al., 2007).

The presence of new, ongoing, and substantial physical and psychological disturbances in the immediate-post ICU phase for this cohort was congruent with the definition of PICS (Needham et al., 2012). The cognitive aspect of PICS was not revealed in this group as all patients reported unchanged levels of focus, and abilities in planning and organizing. Furthermore, the disturbances in the physical aspect of recovery seemed to be the main source of psychological distress in this group. In a qualitative study of post-ICU patients' priorities, mobility was considered a high priority for patients in the immediate post-ICU phase as it meant to serve as a mechanism to build strength to accomplish other priorities, such as resuming daily routines and normalcy (Scheunemann et al., 2020). Given this picture of PICS in this study, rehabilitative measures in the ICU and in the post-ICU should be instituted early, to mitigate the negative consequences of PICS both at the physical and psychological levels.

As patients progressed through their recovery at home in the long-term post-ICU phase, a shift in perception was observed, with considerable reports of substantial improvements in health and wellness, physically and mentally (I Move Towards Health: a PICS experience theme). Patients expressed a sense of accomplishment as they actively engaged in walking, moving, and other physical activities. For many patients, it seemed that physically moving also meant moving on and away from the difficulties of the past towards a more positive present. Patients found getting back home and working to be uplifting and motivating. Returning to work was found to be of significant meaning since it symbolized being functional again, not burdening the family, and finding meaning in daily life. They activated a various set of coping

mechanisms, from letting go, to distraction, and active problem-solving. Many did not look back and re-visit their ICU experience and focused on the present. They found solace in activities in nature and engaging in hobbies that promoted relaxation and emotional healing. Most of the time patients took active steps, often incrementally, to take matters in their own hands. They adopted healthy behaviours, followed up on their health, and learned coping skills. The importance of activating coping mechanisms in response to serious health events has been long recognized in literature (Pearlin et al., 1978), and has shown a strong impact on quality of life in non-ICU populations (Schou et al., 2004; Schou et al., 2005). Hence, recognizing, nurturing, and promoting coping strategies by post-ICU clinicians is of paramount importance in this phase.

Perhaps the notion of "moving on" happened in this sample, because their post-ICU period was not dominated by PTSD and negative memories of ICU (Corrigan et al., 2007). Most importantly what is outstanding in the Life-ICUS-Q study patients, is that a conscious shift in perspective and a positive forward-thinking was evident among all participants. This could be described by the Shifting Perspective Model of Chronic Illness by Paterson, 2001. This model was the result of a meta-study performed in the qualitative constructivist approach which hypothesized that individuals with chronic illnesses go through a dynamic and evolving process of shifting perspectives as they try to normalize their condition over the trajectory of their recovery (Paterson, 2001). Two perspectives were described to be on the spectrum of this process. The "wellness in the foreground" and the "illness in the foreground" perspectives. Both are influenced by personal, social, and environmental factors. According to this model, the "wellness in the foreground" approach exerts a focus on promotion of wellbeing and quality of life, despite challenges that individuals face. It is predominantly adopted by those who engage in self-management, self-care, have a positive mindset, and are surrounded by a positive environment. The "illness in the foreground" approach, on the contrary, is characterized by a focus on being unwell, suffering, and loss (Paterson, 2001). Each perspective has its psychological function- attempting to reach balance and equilibrium in the former, and self-protection in the latter (Paterson, 2001). In the Life-ICUS-Q patients, it is obvious that patients adopted the "wellness in the foreground" approach when they demonstrated a "bounce-back" from their illness, by effectively utilizing their internal and environmental resources. This positive regard towards their health journey after critical

illness has not been documented in literature and it is a novel finding in this study. It would be interesting to study this model in a cultural context such as one in Saudi Arabia, and further delineate the cultural understandings of health and illness on the perspectives of recovery of post-ICU patients.

Perhaps what mattered most in the adoption of this positive outlook for the outcomes in this study, was the activation of the third theme, Inner Strength, Gratitude, and Faith. This theme was termed as a "PICS modifier" in the above diagram of trajectory of critically ill patients. Throughout the trajectory of their illness, patients in this study showed the strong desire to get back to their former life and demonstrated a "fighting spirit". This spirit seemed to be drawn from their inherent strength and resilience. Resilience in this context was characterized as the culmination of a bundle of elements in this study- determination, willpower, perseverance, optimism, confidence, and motivation. All these characteristics were present in this group of patients, although varying with individual differences, but in significantly high levels in most patients. In Norway, a recent study interviewing patients after a long period of time, six to twenty months after ICU discharge, examined "salutogenic resources", the person's willpower and motivation to return to good health, and how it affected critically ill patients' recovery (Alexandersen et al., 2021). Setting personal goals and using personal resources and coping skills were found to be key in the promotion of the patients' willpower, a finding which was congruent with the Life-ICUS-Q study findings. These ideas could suggest that nurses and ICU clinicians should identify and utilize patients' personal resources and coping skills from the time of inpatient ICU admissions to long-term post-ICU follow-ups (Alexandersen et al., 2021).

The immense sense and the expression of gratitude towards those who helped them, including the healthcare providers in the ICU, family, and friends, seemed to exert a therapeutic effect on the patients and helped deal with the adversities of post-ICU experience. Remembrance of compassionate care, moments of human connection, and support they received from the ICU staff were well celebrated by the patients. Family and friends were considered essential resources in supporting their strive towards independence and coping. These findings correspond with previous literature that shows that personal willpower paired with a strong social support system facilitate ICU survivors' integration back

to usual life (Alexandersen et al., 2021). Similar to other studies, finding gratitude towards these groups of people, meant not only to show appreciation towards their deeds, but also show value in the role they played in the endurance of the overall ICU and post-ICU experience (Hashem et al., 2016; Walker et al., 2015).

As all patients in the study were of Islamic faith, Islamic religious teachings were found to be of constant and paramount presence in the journey of the patients. Patients were humbled and found humility in their ICU experience, attributes that seemed to have grown from the philosophies of Islam towards illness and suffering. Muslim attitudes towards suffering come from the premise that God is cognizant of all types of suffering endured by humans, and permits it to happen, for reasons incomprehensible to humans (Siddiqui, 2020). Believers face their sufferings with prayer, repentance, and good deeds (Siddiqui, 2020). In fact, "suffering" was not a term used by the patients. On the contrary, they seemed to be pushing back the adversities of post-ICU recovery, mostly due to obligations and teachings of the Islamic faith. One of the patients versed a section from the Holy Quran, dedicated to the expression of finding strength in difficult times. It says: "*Allah never burdens anyone beyond their capacity. If you are in a state of difficulty or hardship, know that Allah has made you powerful enough to endure that pain*" (Al Baqarah, p. 286). Also, depression and sadness have been taught to be faced with an obligation to believe that in the Hereafter all the pains will be gone: "*There is no grief or fear if one remains steadfast and that the Hereafter is free of all those negative and overwhelming feelings and situations*" (Quran 43:68, 46:13) (Quranic, 2021). Islam also teaches not to dwell on the past about things that cannot be changed; instead, redirect focus, and get through the situation by holding on to faith and having confidence in Allah: "*So do not weaken and do not grieve, and you will be superior if you are (true) believers*" (Quran 3:139) (Quranic, 2021). Therefore, with a motivation and consolation that any sorrows of this world will not follow into the next, and with the conviction that Allah has a plan for everything for their good, the patients in this study were fully equipped to strongly endure the trying times of their recovery as if almost being heard exclaiming: "By God, I won't break". This manner of spirituality and the role of religious faith was not found in previous literature and was a novel finding in this first study of post-ICU patients in Saudi Arabia.

Finally in the last segment of the findings of this study, the expressions of survival from the

ICU experience, and the meanings drawn from that experience, were crafted. It appeared that with progressive attainment of functionality and independence, patients expressed a sense of appreciation and deeper understanding of the value of life. With expressions such as "*I beat it*", they effused a sense of accomplishment and victory, arising from their ability to overcome adversity. Finding gratitude and a global satisfaction to have survived the ICU experience was described in many studies (Papathanassoglou et al., 2003; Storli et al., 2008; Walker et al., 2015) and in one study conducted in Jordan, survival from ICU was seen as a "gift from God" (Abdalrahim et al., 2014). Patients adopted on an existential approach in approaching their post-ICU experience and extrapolated lessons from this milestone in their lives. They learned about the fragility of health and gained fresh insights into the value of time and experiences. This experience made one person in the study (PB) extend greater recognition and empathy towards those who face similar challenges, and vowed to dedicate time to help, educate, and infuse hope in others in the ICU. Patients in general were found to also re-think their conventional notions of health as merely the absence of disease, and assumed a more holistic definition, integrating all aspects of physical, mental, psychological, and social wellness. These expressions of survival and extrapolations of life-lessons have been found in previous studies (Scheunemann et al., 2020), and had a great impact on the recovery journey of patients, and thus contributed as a "PICS modifier" theme in the Life-ICUS-Q study.

Strengths and Limitations

The overall rigorous study design and the enrolment of patients from a longitudinal cohort study were a strength in this study. The follow up from ICU discharge to home minimized the plausibility that other occurrences interfered with the findings. Variation of the sample in terms of demographic and clinical characteristics were also strengths as these enabled the researcher to provide perspectives from different walks of life. The strongest aspect of this study was its ability to capture critically ill patients' trajectory from ICU to many months after discharge from ICU. Throughout this journey, many aspects of the patients' experiences and perspectives were obtained, including their descriptions of PICS starting from the ICU to immediate post-ICU to long-term post-ICU period, and the personal, social and cultural attributes that played a role along that trajectory. This study was able to capture a comprehensive and yet detailed snapshot of the complete critical illness journey.

There were limitations to this study. The participants in this study represented one research site in Saudi Arabia and a limited number of patients were interviewed, therefore limiting generalizability of findings; however, a heterogenous group of patients was selected purposively in this cohort in order to add heterogeneity to the experiences and perspectives of the interview findings. This limited sample size was primarily due to the specific focus on detailed, in-depth understanding of individual experiences, which is often more achievable with smaller groups in qualitative research. Although a larger sample could potentially offer broader insights, the decision was influenced by the concept of information power, where fewer participants are required if the study aim is narrow, the specificity of the sample is high, and the dialogue quality is strong. The rich, detailed data obtained from these participants provided significant insights into their recovery experiences. However, the small sample size may limit the generalizability of the findings. This limitation was anticipated, and efforts were made to ensure the robustness of the data and analysis through rigorous methodological approaches, including comprehensive thematic analysis and triangulation. Future research with larger and more diverse samples is recommended to validate and extend these findings.

Another limitation was that the patients in this study were interviewed several months after their ICU discharge; patients in the shorter post-ICU term might have had different perceptions. Similarly, memories of ICU might have been affected by this long lag of time; however, the patients' accounts were found to be resourceful and detailed, possibly because these experiences were deeply grounded in ICU survivors and easily surfaced when asked about, even after a long time. While the researcher made every effort to relay experiences of the participants in a truthful manner, the identification of themes could have carried some bias. Other researchers were asked to read this account, partly to mitigate this limitation.

Recommendations

Although the findings of this study cannot be generalized throughout Saudi Arabia, however ICU nurses in the country can draw insightful lessons and appreciate the unique position their patients hold. Rooted in faith and personal strength, with proper education and preparation before discharge, there is an enormous opportunity to create a constructive experience for the ICU patients. Further research is needed to understand how faith plays a role in accessing

rehabilitative and other post-ICU services in Saudi Arabia. In addition to measuring biopsychological elements of PICS, it would be interesting to integrate personal strength, beliefs, and values in research investigations of PICS. Moreover, research is highly needed to understand the complete spectrum of ICU nurses' knowledge and experiences with critically ill patients' post-ICU recovery, as well as caregivers' journeys and resilience with PICS-Family. More recommendations drawn from the findings of this study will be fully described in the next chapter.

6.8. Conclusion

In conclusion, this study provided a comprehensive and holistic understanding of the lived experiences of critically ill patients. It helped understand the perceptions of patients of their overall health and recovery after discharge from ICU. It also provided valuable insights into the physical, psychological, social, and cultural journeys that patients took. The distinguished features of this cohort were their outstanding inner strength and Islamic faith to overcome and endure this challenging experience. In the next chapter, findings from both the quantitative and qualitative studies of post-ICU long-term outcomes will be integrated and discussed.

7. Chapter 7: Integration and Discussion

7.1. Introduction

This chapter will present an integrated discussion of the key findings derived from this PhD thesis and contextualization in relation to existing literature. Within each phase of the study an overview of the findings and relevance to previous literature has been presented in each phase of the thesis in previous chapters. This will not be repeated; instead, wider issues captured by the phases of the research will be addressed here. The chapter will include a section on mixed methods data integration demonstrating interpretations derived from both the quantitative and qualitative studies. Contributions of this study to the wider literature and clinical practice will be described. The impact that the study has had up to date on the local organizational and Saudi level will be presented. The key methodological strengths and limitations will be presented and recommendations for clinical practice and future research will be made. The chapter revisits the case study presented in Chapter 1 highlighting the care needed by this patient after his discharge from the ICU.

Revisiting the Case Presentation

Patient HK was a 68-year-old male who was admitted to the adult medical-surgical ICU in a hospital in Saudi Arabia. He was diagnosed with septic shock due to pneumonia. His shock was immediately treated by sedation, mechanical ventilation and hydration. Throughout his 5-day stay in the ICU he received supportive treatments such as hydration and nutrition, and adverse events such as ICU-acquired infections or pressure injuries did not occur. He was cared for by the multidisciplinary members of the ICU team in a single-bed private room and his family was present at his bedside almost every day. Although he showed signs of delirium on one of the days in ICU, this condition did not persist for more than 24 hours. He was assisted to start early ambulation in the ICU and was transferred to the general ward before being discharged.

The patient followed up with his primary care doctor after one week of hospital discharge. His pneumonia had been largely resolved and his vital signs and x-ray were normal. He

complained of muscle weakness and irregularities in sleep because of fear, flashbacks, and intrusive memories of ICU. He was re-assured by the physician by saying that these symptoms are transient, and he was asked to follow up after a month for a physical check-up and a follow-up x-ray.

It is assumed that the patient recovered at home, but no information exists if this patient accessed any rehabilitative services. Reflecting on the findings of this research, had he been formally assessed for the presence of PICS, there would have been better opportunities to assess the needs of the patient and therefore offer physical rehabilitation or psychological therapy as needed.

There is a need to understand the trajectory of critical illness for patients like HK. This would ensure that patients have access to targeted assessments and rehabilitative interventions during and after their care in the critical care unit.

7.2. Summary of the thesis

The overall purpose of this thesis was to investigate the long-term outcomes and HRQoL of post-ICU patients in Saudi Arabia. The research aims of this thesis were:

- To establish what is already known regarding the nature of ICUs and the post-ICU long-term outcomes (Chapter 1: Introduction and Background).
- To determine the predictors of long-term outcomes and HRQoL by conducting a systematic review of the literature (Chapter 3: Systematic review of long-term outcomes and HRQOL in adult ICU survivors).
- To add to existing evidence by conducting a high-quality prospective cohort study in a sample of ICU patients in Saudi Arabia, investigating long-term outcomes and HRQoL, and to identify the most important risk factors in this cohort (Chapters 4: Methodology of Phase II study Long-term outcomes and Health related Quality of Life in Intensive Care Unit Patients: a prospective cohort study in Saudi Arabia (Life-ICUS study) and Chapter 5: Results and Discussion of Phase II study).

- To explore ICU survivors' lived experience after their ICU discharge by conducting a qualitative study (Chapter 6: Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia (Life-ICUS-Q).
- To develop an overall understanding of the post-ICU journey in a cohort in Saudi Arabia by integrating findings of all phases of the thesis (Chapter 7: Integration and Discussion).

The research questions of this thesis were:

- What is already known about the nature of critical illness and the long-term outcomes of post-ICU patients? (Chapter 1)
- What is already known about long-term outcomes in Saudi Arabia? (Chapter 1)
- What are the predictors of long-term outcomes and HRQoL of post-ICU patients? (Chapter 3)
- What are the concepts underpinning PICS and what are the elements of a framework that captures all aspects of PICS? (Chapter 4).
- What are the long-term outcomes and HRQoL in post-ICU patients in Saudi Arabia? (Chapters 4 and 5).
- How do patients perceive their experiences after discharge from the ICU in Saudi Arabia? (Chapter 6).
- What could be learned from integrating quantitative and qualitative findings about long-term outcomes of post-ICU patients in Saudi Arabia? (Chapter 7).

A series of studies were designed to fulfil the above aims and to answer the research questions. A comprehensive PICS conceptual framework was proposed during the thesis process (Chapter 4) composed of the multidimensional factors attributed to the complexities of care of critically ill patients, and the multifaceted nature of long-term outcomes in these patients. The study was conducted in a three-phase approach. First, a systematic review (Chapter 3) explored the long-term outcomes of ICU patients focusing on the predictors of physical, cognitive, psychological and HRQoL outcomes. Then in a mixed methods approach the long-term outcomes and HRQoL of Saudi patients was designed to be investigated. The second phase of the thesis (Chapter 4 and 5) was conducted through a prospective cohort

design investigating the long-term outcomes of post-ICU patients and the predictors of these outcomes (Life-ICUS study). Third, a qualitative approach was taken (Chapter 6) to explore the lived experiences of post-ICU patients (Life-ICUS-Q study). The sequential manner of undertaking this thesis provided a robust and comprehensive approach to understanding the complex experiences and outcomes of post-ICU patients.

In the development of the conceptual framework for this study, two previous PICS frameworks and findings from the systematic review of the thesis were utilized as foundations for the PICS phenomena. A new conceptual framework of PICS was presented in an integrated and a comprehensive structure (**Figure 4.4**). The proposed framework has the patient in the centre of care and is composed of three main components of determinants for long-term outcomes of post-ICU patients. The first component was related to ICU factors, and these included structures and processes of care in the ICU that influence critically ill patients and their outcomes. The second component was premorbid characteristics and these included patient-related demographic and clinical characteristics that affect the critical illness of a patient. And the third component was related to post-ICU factors which were the aspects of care that happen after a patient is discharged from the care of an ICU. It was proposed that these three components affect the long-term outcomes of critically ill patients. The outcomes on the other hand were divided into four domains and these included physical, cognitive, and psychological domains, in addition to HRQoL. This conceptual framework informed the subsequent phases of the study in this thesis. Most of the premorbid patient characteristics and determinants related to ICU factors were integrated and applied in the data collection and analysis phases of the mixed methods study, and all four areas of outcomes were explored in both phases of the mixed method study.

The findings of this thesis provide a unique understanding of the long-term outcomes of post-ICU patients in the Saudi context. In Phase I (Chapter 3), the systematic review of 13 studies identified key predictors of physical, cognitive, psychological, and HRQoL outcomes of post-ICU patients. Two main categories of factors influenced PICS. The first category was ICU factors such as the occurrence of ICU delirium, ICU length of stay, mechanical ventilation, and certain diagnostic groups such as sepsis; the second category were certain patient characteristics such as younger age, female gender, unemployment, lower education, and

pre-existing diseases. In Phase II (Chapter 4 and 5), the majority of patients experienced at least one domain of PICS in the immediate post-ICU period (at discharge from ICU) and in the long-term period (3-months following discharge). The trajectory of recovery from the time of discharge to the 3-month follow-up demonstrated significant improvements, however persistent deficits remained in most domains, largely in the cognitive domain. The predictors of PICS that were identified in this phase of the study were age (younger age for depression and anxiety and older age for cognitive impairments), female gender, lower education, non-surgical ICU diagnosis, and pre-existing cognitive dysfunction. In Phase III of the study (Chapter 6), in qualitative interviews, patients described their challenges throughout the trajectory of critical illness, which extended from the time of ICU to immediate post discharge and until long-term post discharge. Four themes emerged from the accounts of the patients about their trajectory of recovery, two of which denoted PICS-related experiences (My ICU Experience and I Move Towards Health), and two themes signified factors that helped the patients endure their recovery journey (My Inner Strength, Gratitude, and Faith, and I Survived and Learned).

In summary, the empirical studies in this thesis demonstrated that:

- A large proportion of ICU patients (n=63, 93%), demonstrated PICS at the time of ICU discharge.
- Physical impairments improved significantly from partially independent at discharge to almost independent levels at 3-month follow up. However, 10% of patients sustained disabilities of ADL at 3-months.
- Although cognitive function improved significantly at 3-months, a large proportion of patients (n=44, 72%) sustained mild cognitive impairments at 3-months.
- All areas of mental health (anxiety, depression, and PTSD) improved significantly from the time of discharge and returned to normal status at 3-months.
- HRQoL improved significantly from the time of discharge and returned to normal status at 3-months. Within the domain of HRQoL, physical functioning was the most affected, and social functioning was the least problematic for patients.
- Several factors in the ICU caused PICS in post-ICU patients, all of them being identified as non-modifiable. These non-modifiable factors were younger age, female gender,

education (with higher levels having a protective effect), ICU diagnosis, and pre-existing cognitive impairments.

- In qualitative investigations, improving physical functioning over time was found to have a positive impact on psychological wellness.
- Several personal and social attributes played a role in the recovery of the patients, including resilience, gratitude, faith, and the presence of healthcare providers and family.

7.3. Integrated discussion of findings

Data from phases of the mixed method study were integrated using triangulation (see Chapter 2, section 2.5.4). Within this model, findings from the systematic review and each component of the mixed method study were listed (**Table 7.1**) and comparisons were made to find agreements (convergence), complementarity, or contradictions (O'Cathain et al., 2010). In the following section, after the table, these findings will be discussed and relevance to previous literature will be highlighted.

Table 7.1. Summary of findings from the three phases of thesis

Long-term outcomes	What was learned from Systematic Review	What was learned from Life-ICUS	What was learned from Life-ICUS-Q
Physical	**Description of long-term outcomes**		
	Poor functional ability Impaired physical function Chronic pain Muscle weakness	35% of patients with moderate to severe ADL impairments at discharge. ADL improved at 3 months.	At discharge: limitations in movement, muscle weakness, ADL impairments, pain After discharge: fatigue, pain. Long term: marked improvements, no pain. What helped: walking, movement, physiotherapy, healthy behaviours (smoking cessation, exercise), follow-up care, resilience.
	Predictors of long-term outcomes		
	Delirium Prior depression Duration of MV ICU LOS Long bed rest Use of corticosteroids and neuromuscular blockers	Lower Education ICU diagnosis (non-surgical)	
Cognitive	**Description of long-term outcomes**		
	Cognitive dysfunction Sleep disturbances	75% of patients had MCI at discharge. MoCA improved at 3 months.	After discharge: Memories and associations with ICU stay; Difficulties sleeping. Long-term: no changes in cognition.
	Predictors of long-term outcomes		
	Delerium Sepsis Concurrent psychological symptoms Age Pre-existing depression	Older Age Pre-existing cognitive impairments.	
Psychological	**Description of long-term outcomes**		
	Depressive symptoms PTSD symptoms Anxiety symptoms	34% had depressive symptoms at discharge. 21% had PTSD symptoms at discharge. 28% had anxiety symptoms at discharge. All three areas improved at 3 months.	After discharge: Fear, distress. Long-term: marked improvements, better mood. What helped: improvements in physical health, return to work, leisure and recreational activities, coping strategies, resilience, gratitude, presence and communication of HCP, family and friends, religiosity and faith
	Predictors of long-term outcomes		
	Predictors for depressive symptoms: Female gender	*Depression*: Younger Age *PTSD*: none	

	Education 12 years or less Alcohol misuse Baseline disability or unemployment Higher baseline medical comorbidity Opioid use *Predictors for PTSD:* Female gender Younger age Alcohol misuse Unemployment Prior depression ICU LOS Sepsis High opiate doses Days on corticosteroids *Predictors for anxiety:* Female gender Younger age Alcohol misuse Unemployment Opioid use	*Anxiety*: Younger Age; ICU diagnosis (non-surgical)	
	Description of long-term outcomes		
HRQoL	Reduced QoL Difficulties in mobility, self-care, usual activities, and cognition.	Impaired physical functioning, and role limitations due to physical health at discharge. All categories of SF-36 improved at 3 months.	Long-term: marked improvements. What helped: health seeking behaviours, return to work, coping and distraction strategies, follow-up care, leisure and recreational activities, resilience, gratitude, family and friends, religiosity and faith, lessons learned from experience and re-defining health
	Predictors of long-term outcomes		
	Pre-existing diseases Vascular surgery and Trauma	Female gender	

7.3.1. Physical function of post-ICU patients

In the Life-ICUS cohort, as outlined in Chapter 5, more than one third of the patients (35%) suffered from moderate to severe impairments in ADLs at the time of discharge from ICU. However, at 3 months follow up, these impairments significantly improved to mild, meaning that patients regained almost all areas of independence in conducting their ADLs. Only one patient who had mild impairments at discharge deteriorated to moderate to severe impairments in ADL at 3 months follow-up. Participants with higher education (middle to graduate) and the group of surgical patients did significantly better in their ADL improvement than those with a lower education level and non-surgical diagnoses; therefore, lower education and medical diagnosis were identified as predictors for poor ADL outcomes in this study.

In the qualitative study (Chapter 4), patients depicted a complimentary scenario to the quantitative study in terms of the progression of their physical state. In the immediate post-ICU phase, patients had perceptions of fatigue, muscle weakness, and pain, but at the long-term post-ICU phase these symptoms dissipated. During interviews, patients attributed a series of self-initiated interventions such as walking, moving, undergoing physiotherapy, adopting healthy behaviours, and follow-up, to their successes in physical recovery.

On the long-term issues, factors that contributed to the overall improvement of patients' physical difficulties were perceived to include self-care and health seeking behaviours, such as walking, moving, following physiotherapy sessions, and quitting smoking. Personal strength and resilience, such as having a positive outlook, determination, motivation, and perseverance seemed to have a substantial impact on patients' physical recovery, as one patient explained:

I tried to move and not to succumb to the bed or the situation I am in …PF

To better understand the improvement trend observed in the Life-ICUS and Life-ICUS-Q cohorts regarding physical outcomes, it is important to reflect on the practices implemented in the ICU where the study took place. This unit had historically established early mobility and physiotherapy services while patients were still in the ICU. These services were initiated and formal consultations to physiotherapy, occupational therapy and other services were made

during the multidisciplinary rounds that occurred every morning. In-bed cycling and the use of lifters to facilitate mobility and muscle strength were incorporated in the plan of care. Through a series of robust research studies, these interventions have been shown to be safe, low-risk, and feasible to be conducted in the ICU clinical setting (Bailey et al., 2007; Dammeyer et al., 2013), and to be effective in regaining independent functional status at hospital discharge (Bailey et al., 2007; Kress et al., 2014). While longer-term effects of these ICU interventions remain unstudied, it is plausible that they contributed to the positive function trajectory observed in Life-ICUS and Life-ICUS-Q patients.

It is noteworthy that, with reference to existing literature, patients in this study did not discuss their sexual functioning post-critical illness. This could be due to the Islamic religious and Saudi cultural norms of non-disclosure of one's personal and sexual issues to others. Sexual dysfunction after critical illness is common; one study demonstrated that almost 40% of patients had sexual dysfunction after ICU discharge (Griffiths et al, 2006). This problem can potentially have a negative impact on patients' quality of life, psychological wellbeing, and relationships. This under-researched area should be explored in investigations pertaining to ICU survivors in general, and in Saudi Arabia in specific, by employing culturally sensitive and receptive methods.

7.3.2. Cognitive function of post-ICU patients

Three-quarters of the patients in the Life-ICUS cohort (Chapter 5), when assessed by the screening MoCA tool, exhibited mild cognitive impairments (MCI), particularly in executive functioning skills. Although MoCA scores significantly improved at 3-months follow-up of the patients with MCI at discharge, only half (n=22, 50%) showed improvement to normal cognitive function at follow-up. Furthermore, six patients (17%) who demonstrated normal MoCA at discharge deteriorated to MCI at follow-up. In the qualitative study (Chapter 6), the findings regarding cognitive function were contradictory to the quantitative findings. Unlike substantial cognitive deterioration in the quantitative results, the interviewed patients in the qualitative study did not report cognitive difficulties in the long-term post-ICU phase. Instead, they regarded their memory, focus, organizing, and planning skills as unchanged and at a good

level at the long-term phase. This difference in qualitative reports from the quantitative findings could be explained by the possibility that qualitative study participants may have been among those in the cohort who did not experience delirium in the ICU. It is also possible that patients affected by cognitive disabilities may not be aware of their own disabilities in the post-ICU phase, and the likelihood of this happening in the life-ICUS-Q cohort should also be considered.

In relation to existing literature, the trend of high prevalence of cognitive impairments in post-ICU patients, especially in the executive functions, was congruent with the systematic review and existing evidence (Chapter 3) (Hopkins et al., 2005; Sukantarat et al., 2005). Problems with executive decision making, planning, and organizing interfere with an individual's behaviours and daily functioning. For post-ICU patients, these may mean difficulties in adhering to discharge instructions, compliance with medication and dietary regimens, and following up with physicians' appointments. These issues in turn may further impair or delay the overall recovery of patients (Hopkins et al., 2005; Sukantarat et al., 2005). In one study, patients with cognitive impairments who received more than five medications as part of their home medication regimen, were at higher risk of developing adverse drug events due to inability to follow instructions (Hume et al., 2012) and subsequently were more prone to be readmitted to the hospital (Jencks et al., 2009). As cognitive dysfunction after critical illness may have detrimental effects on the patient, family, and healthcare utilization in general, specific neurocognitive rehabilitative strategies should be the focus of future clinical practices. To date, there is no clear evidence regarding which patients will benefit from cognitive rehabilitation programs, when should they start, and what interventions should they contain. As cognitive rehabilitation is a growing and evolving field, it is important to draw insights from populations such as TBI or stroke survivors. Lessons learned from interventions to improve memory, executive function, and functionality in these populations, which focus on activities that enhance environmental awareness and compensatory mechanisms, can significantly inform the design of rehabilitation strategies of ICU survivors (Cicerone et al., 2011; Wergin et al., 2012). A few efforts of combining physical and cognitive therapy have been studied in critically ill patients, such as the RETURN study (Jackson et al., 2012) and ACT-ICU study (Brummel et al., 2014), with limited evidence for the benefit of these therapies on overall patient outcomes. Serious efforts should be exerted in defining post-ICU cognitive

rehab scope, timing, and interventions.

In the Life-ICUS study, predictors of cognitive dysfunction were consistent with findings from existing literature and the systematic review described in Chapter 3. The elderly and those who had been identified as having pre-existing cognitive impairments prior to their admission to ICU (reported by proxies), were at the greatest risk of cognitive impairment. The difference in the Life-ICUS study compared to the systematic review findings, was that delirium in the Life-ICUS cohort was not determined to be a predictor of cognitive deterioration. This was an intriguing finding as literature has consistently shown that delirium has a paramount role on the continuum of cognitive injury of critically ill patients (Davydow et al, 2013). Several interpretations were suggested to this finding. One explanation could be that most patients in the cohort were not identified to have experienced delirium in the ICU to begin with. This was explored in the discussion of the findings of the Life-ICUS study (Chapter 5), attributing the causes to several factors. These factors could include patient attrition in the follow-up period, challenges in administering the delirium assessment tool in a proficient manner due to nurses' language barriers, or the patients' educational capacity to perform the MoCA test. Alternatively, there is a possibility that patients in fact did not experience lengthy and debilitating episodes of delirium in the ICU. This, in turn, could be attributed to the environment of the ICU where the study was conducted, characterized by the implementation of evidence-based practices in the care of its patients. For example, in this study ICU, non-pharmacological interventions were integrated in routine nursing care plans, such as promoting healthy sleep-wake cycles, introducing daylight, reducing noise, early mobility, and family integration. As the ABCDEF bundle (described in Chapter 2) was well exercised in this ICU, with its components of light sedation, early awakening and weaning off the ventilator, early ambulation, re-orientation and non-pharmacological delirium management, it is plausible that the occurrence of delirium might well have been prevented and managed in this cohort.

As contrasting possibilities are discussed here (the likelihood of delirium not being captured versus delirium actually not being prevalent in this study), the findings of the cognitive domain need to be interpreted carefully and further studies, enrolling larger cohorts and a more diverse group of patients in qualitative interviews, should be considered.

7.3.3. Psychological function of post-ICU patients

In the quantitative findings presented in Chapter 5, all three areas of the mental health component of PICS (depression, general anxiety, and PTSD) were prevalent in the Life-ICUS patients, more prominently with depressive symptoms. The psychological burden was significantly reduced in the 3-month long-term follow up phase, with improvements in all areas of anxiety, depression, and PTSD. Younger age was the only predictor of depression and anxiety in the Life-ICUS cohort, and no significant associations were found between demographic and clinical characteristics and PTSD.

Consistent with the Life-ICUS quantitative findings, the qualitative accounts of the Life-ICUS-Q study (Chapter 6) demonstrated that patients perceived substantial improvements in their mental health from the time of immediate-post ICU phase to the time of the long-term post-ICU phase. Qualitative findings were also in agreement with quantitative findings in terms of PTSD not being the predominant psychological issue at long-term phase. Additionally, in their interviews, patients reported that as they gradually regained their physical strength and daily functioning, they noted improvements in their psychological wellbeing.

The marked improvements in patients' psychological wellbeing in the long-term post-ICU phase was a unique finding in the quantitative part of this study, which was different from most literature that has shown persistence of clinically significant psychological morbidity at long-term. For example, depression has been previously reported to persist up to a year after ICU discharge both in young and older patients (Jackson et al., 2014; Marra et al., 2018). In addition, PTSD symptoms have been found to be prevalent, and more so than depression, in existing evidence (Jackson et al., 2014; Marra et al., 2018) with detrimental effects on patients and their social functioning (Corrigan et al., 2007). A notably different and novel outcome was found in this thesis relating to the psychological domain of PICS with relatively lower occurrence of PTSD in quantitative records and almost nil reports of extremely disturbing experiences of negative recollections, flashbacks, hallucinations, and other distorted perceptions of the ICU experience, in qualitative reports. Unlike some literature (Griffiths et al, 2007), Life-ICUS-Q patients did not seem to have developed false memories of ICU, and subsequent issues of paranoia, phobias, and delusional memories did not occur. These issues

have been reported to effect one's perceptions of quality of life and lead to inability to follow medical care and efforts of recovery (Jones et al, 2010). Not developing delirium, impaired memories, and distorted perceptions of the ICU seemed to have protected the study's patients from severed psychological morbidity at long-term. In addition, avoidance of memories, as one patient described "*I don't remember, and I don't want to remember*", as a coping mechanism, might also have played a role in overcoming disturbed psychological wellbeing.

The literature of critical illness survivorship is focused on addressing PTSD, yet the findings of this study, substantiated by others (Jackson et al, 2014), suggest that depression is more of an issue than PTSD in these patients. Though at times these conditions may overlap and cannot be managed in isolation, given depressive symptoms can be more pervasive in the immediate post-ICU phase, it is best to screen for psychological distress early, while the patient in ICU, to prevent further psychological deteriorations.

Younger age was the only predictor of depression and anxiety in the Life-ICUS cohort, in contrast to a myriad of predictors in the systematic review, including female gender, unemployment, alcohol and opioid use (Huang et al, 2016). These have been discussed in Chapter 5. It is worth explaining that younger patients may be more vulnerable to depression and anxiety following critical illness and ICU stays, because of issues of changes in daily routine, alterations in life goals, diminished decision-making and self-determination, and existential fears of death. Younger patients may also experience psychological challenges as a result of their inability to balance their aspirations of freedom and health with the reality of their sickness.

Many factors were perceived to have played an instrumental role in the mental wellbeing of the Life-ICUS-Q cohort. These included intrinsic factors such as resilience, practicing gratitude, faith, and coping strategies, as well as extrinsic factors such as return to work and support from family and friends. It is worth to briefly discuss these factors here, especially resilience, which was not discussed in previous chapters. Resilience in post-ICU patients is relatively under-studied. With the limited literature found in this area, it was noted that the Life-ICUS-Q discoveries were in congruence with previous literature. For instance, optimism and having

a positive outlook for the future are some elements of resilience which were evident in Life-ICUS-Q patients. Research in fact has shown that pessimism is associated with anxiety, depression, and PTSD during and after critical illness and ICU stay (Myhren et al, 2010). Thus, Life-ICUS-Q patients' intrinsic motivation to staying positive regarding their health and recovery assisted them in their overall psychological recovery.

In a mixed methods study investigating resilience in survivors of critical illness, patients reported that information and reassurance provided by ICU healthcare team, family support, spirituality, and a strong positive outlook on recovery facilitated their post-ICU journey (Maley et al., 2016). Resilience, measured by a standardized test, Connor–Davidson Resilience Scale, was inversely associated with physical, cognitive, and psychological difficulties in these patients (Maley et al., 2016). Despite substantial impairments in all domains of PICS, resilience in critical illness survivors was found to be normal to high in more than 70% of patients in this study. This aligns with the experiences of Life-ICUS-Q patients, who, despite facing physical and mental health challenges post-ICU, demonstrated a strong determination to regain health. This notion of resilience mirrors the concepts of thriving and personal growth established in studies in post-trauma patients (Nugent et al., 2014), suggesting their relevance to post-ICU settings as well. Furthermore, the Life-ICUS-Q patients demonstrated the psychosocial characteristics of resilience identified in trauma patients by Iacoviello and colleagues (Iacoviello et al., 2014). These included optimism, self-care, active coping strategies, maintaining a family and social network of support, and cognitive reframing and agility. However, the process by which patients develop resilience skills such as adaptation, reframing, and cognitive flexibility, remains underexplored. Understanding these processes could greatly benefit the critical care community in comprehending patients' experiences and trajectories. Several research questions should be asked in this area ranging from- what is resiliency after critical illness? how is it manifested along the trajectory of recovery? who is most resilient and what attributes make them so? what could be learned from such individuals? and how can resilience be nurtured throughout the ICU and post-ICU experience? These questions will not have simple answers, especially that a multi-component approach should be taken in answering them including personal, family, cultural, religious, and other factors. However, exerting an effort to explore these ideas will prepare clinicians in an optimal manner to identify determinants of resilience, and help patients employ resiliency-related

behaviours and strategies. It will be important for critical care community to acknowledge the characteristics of resilience and integrate plans of care that would foster these adaptive elements and promote wellbeing for post-ICU patients after adversity. Designing treatment plans and training programs that would enhance resilience-promoting behaviours represent a promising future direction in the care of post-ICU patients.

7.3.4. HRQoL of post-ICU patients

In the domain of HRQoL, the findings of the Life-ICUS cohort (Chapter 5) were strikingly in contrast with those of the systematic review (Chapter 3). The latter had indicated sustained perceptions of reduced HRQoL over time after ICU discharge; in Life-ICUS study, statistically significant improvements occurred from the time of discharge to 3-months follow up. At the time of ICU discharge, Life-ICUS patients considered their "physical functioning" and their "role limitations due to physical health" (as measured by SF-36) as the main reasons for impairments in HRQoL. However, as previously highlighted in other studies (Rai et al., 2020), perceptions of low quality of life in the immediate post-ICU phase are expected, as patients are still in the early stage of their recovery from critical illness. When followed up at 3-months, "social functioning" was perceived as the best aspect of quality of Life-ICUS patients' lives, which could largely be due to the social and family context of Saudi culture. The social aspect of HRQoL aligns with the systematic review finding that described social integration after ICU discharge to affect HRQoL to a larger extent than any other factor, such as those related to patient demographics and ICU-related factors (Orwelius et al., 2011). In general, all HRQoL ratings at 3-months were improved and as shown in chapter 5, levels were higher than those reported in normative studies. It is imperative to note that, unlike the findings from the systematic review (Chapter 3), chronic pain, one that extended beyond the immediate post-ICU phase, was not identified in this cohort, which probably had an effect on patient's positive perceptions of quality of life.

The Life-ICUS-Q reports of overall positive perceptions of health and functioning were consistent with the Life-ICUS findings. In the qualitative reports, patients attributed their successes of their recovery journey to having family, friends, and a social ambiance in their environment. In addition, preserving their physical and psycho-cognitive integrity played an

important role in the maintenance of their high quality of life perceptions. Patients pursued health-promoting lifestyle changes and sustained minimal disruptions in their compliance to medical regimens and follow-up to medical care. In addition, patients reported success in returning to work and maintaining pre-illness employment status. In fact, some reported renewed motivation to accomplish and be productive, financially and socially. These behaviours and aspirations did, undoubtedly, have an impact on the perceptions of a high performing, high quality approach to life. Although return to work and healthcare cost and utilization were not directly measured as they were not among the objectives of this thesis, a subset of this cohort demonstrated good outcomes in this regard during the interviews as all had returned to work and none had been re-admitted to the hospital. Future research would be beneficial to discern employment, productivity, and resource utilization outcomes in similar cohorts.

In Life-ICUS study, none of the patient demographic and clinical characteristics could be statistically associated to long-term HRQoL outcomes. Previous evidence has established the predictive models for poor quality of life after ICU and these have confirmed that pre-ICU frailty and poor quality of life are the most significant predictors for long-term outcomes (Wubben et al., 2021). Those coming in the ICU with a relatively better state of functionality and perceptions of quality of life will fare better than those with poorer pre-ICU states. As such, conversations with patients and families about expectations, plans of care, triage to ICU admission decisions, and opportunities to enhancing post-ICU recovery should be incorporated in routine medical approaches to care.

Finally, it is important to highlight that the domains of PICS may be interrelated as previously identified in the literature (Marra et al., 2018). Those with physical limitations may in turn develop concurrent mental health concerns, such as depression (Marra et al., 2018). Furthermore, health perception, as measured by HRQoL, is complex and encompasses not only physiological and psychological factors of PICS, but also personal, family, social, and environmental factors (Marra et al., 2019). Two individuals may perform similarly on objective tests of physical functioning, and yet perceive their health differently (Marra et al., 2019). Therefore, it is imperative that PICS domains be measured separately and objectively, as is the case in this thesis, to gain an in-depth knowledge of the underlying mechanisms of PICS.

It is equally important to understand the interrelatedness of these problems so that effective preventive measures can be taken, and interventions can be designed, as previously recommended in post-ICU studies (Proffitt, et al., 2019). Although exploring the interrelatedness of PICS outcomes was not one of the objectives of the Life-ICUS study, it was evident in the qualitative phase of this study that, indeed, patients related a deficiency in one domain to an implication in another, and vice versa, an improvement in one area to a promotion in another (e.g. improvements in physical domain enhanced perceptions of emotional wellbeing). This relationship among domains of PICS has not been established in a systematic manner in previous literature (Proffitt, et al., 2019) but may have considerable implications in practice and in the trajectory of recovery of critically ill patients.

7.4. Contributions of this thesis

7.4.1. Overall contributions

This thesis had several contributions to the body of knowledge regarding long-term outcomes of post-ICU patents in general, and to the generation of evidence in Saudi Arabia in specific. Many of the findings in this thesis could be transferrable to other ICU settings. The findings from the three phases of the thesis have provided a deeper understanding of the challenges that critically ill patients face across their trajectory of recovery. There is sufficient evidence generated by this thesis that describes the PICS outcomes and their determinants at long-term, and the patients' journeys from the time of ICU to long-term post-ICU period.

To date, there have been few attempts to explore all three domains of PICS along with HRQoL of post-ICU patients in one comprehensive prospective study, such as the one reported in this thesis. Having a robust research design and the reporting of the study methods and procedures in a detailed and transparent manner will enable others to replicate this study in other settings. Having all domains of PICS and HRQoL measured simultaneously and systematically throughout the ICU patients' recovery journey will decrease the fragmentation of data and evidence which currently characterizes the current literature and will enable a focus on the holistic approach to the investigation of critically ill patients' outcomes. Throughout the research process, an integrated conceptual framework, described in Chapter

3, was formulated which will serve as a solid foundation in the design of future epidemiological studies. This framework can also be used for educational purposes, both for health care provider groups and patients and family groups.

The systematic selection of the optimal assessment tools used in the evaluation of PICS (ADLs, MoCA, PCL-C, HADS, and SF-36), which have been tested for validity and reliability and recommended by critical care communities such as the SCCM, will encourage future studies to adopt these tools and propel the conduction of outcomes studies in this population. Standardizing the assessment tools across studies will ensure a uniform approach to evaluating patient outcomes, reducing variability in measurement techniques, and, in the process, enhance the reliability of the results. Utilizing consistent tools for assessing long-term outcomes of ICU patients in future studies holds the potential to significantly enhance the consistency and generalizability of research findings. Furthermore, employing consistent tools will facilitate the replication of studies, allowing researchers to validate and build upon existing findings and allow meta-analysis to be performed. This approach will promote a more cohesive and cumulative body of knowledge, fostering a deeper understanding of the factors influencing long-term outcomes in ICU patients.

The identification of predictors for PICS uncovered in this study has the potential to significantly advance the knowledge of critical care clinicians, thereby promoting the adoption of evidence-based practices within the ICU setting. By incorporating these predictors into clinical decision-making, clinicians can enhance their ability to assess patients early in their ICU stay, enabling proactive and tailored interventions based on individual risk profiles. This personalized approach will facilitate targeted allocation of resources and interventions, optimizing patient care. Furthermore, the knowledge gained from the study will aid in the development of standardized protocols for the proper follow-up of patients identified to be at risk, ensuring continuity of care beyond the ICU. This integration of evidence-based practices not only will enhance the quality of patient care but will also contribute to a culture of continuous improvement within critical care settings, fostering better patient outcomes and overall healthcare system efficiency.

The qualitative aspect of this study brought a distinctive dimension to the investigation of

post-ICU patients' outcomes by offering a new understanding of their experiences. It revealed that patients don't perceive their recovery journey as solely confined to a distinct long-term phase; instead, their experiences unfold linearly, encompassing the time spent in the ICU, transitioning through the immediate post-discharge period, and eventually extending into the long-term phase of recovery. This holistic perspective captures the dynamic nature of the patient's trajectory, acknowledging the interconnectedness of these phases and the evolving nature of their challenges and successes. By recognizing this continuum, healthcare practitioners can tailor interventions to address the unique needs of patients at different stages, fostering a more comprehensive and patient-centred approach to post-ICU care. The qualitative insights derived from this study contribute valuable depth to the understanding of patient experiences, enriching the overall comprehension of post-ICU outcomes.

As the inaugural post-ICU study conducted in Saudi Arabia, this research marked a pivotal milestone in the history of critical care medicine in the country. In terms of clinical practice, the study's findings offered a localized perspective on post-ICU outcomes, enabling healthcare professionals in the region to tailor interventions to the unique needs of Saudi Arabian patients. In the realm of education, the study provides a valuable resource for training healthcare practitioners, fostering a deep understanding of post-ICU care within the Saudi context. From a research standpoint, this pioneering effort opens the door for further investigations into post-ICU outcomes, setting a foundation for a growing body of knowledge specific to the Saudi population. To enhance the applicability of future studies, employing the tools used in Arabic in this study will facilitate broader participation and improving the validity of research outcomes in the Saudi healthcare context. There is a great opportunity now to utilize the findings from both quantitative and qualitative phases of the study, and lead a consensus meeting nationally, engaging different stakeholders, to form a cohesive and representative agenda for the development of Core Outcome Sets (COS) or PROMs for the assessment of post-ICU patients. Additionally, the study's insights may inform healthcare policies in the country, shaping guidelines and frameworks that address the care of post-ICU patients. This pioneering effort is hoped to catalyse positive changes in practice, education, research, and policy, ultimately advancing the quality of post-ICU care in Saudi Arabia. The next section will describe what this study has contributed so far in real life.

7.4.2. Real-time impact

Throughout the phases of the study, the Life-ICUS made a real-time impact both organizationally and at a local and national Saudi level. To contextualize the impact that this thesis has had at the organizational level, it is important to reflect on the organizational environment where this study was conducted. This was an organization that was accredited by Planetree® and Magnet®. Planetree® is a healthcare accreditation that advocates for person-centred care (PCC), promoting individualized care that is guided by patients' preferences and values, within an environment of caring, quality improvement, and partnership (Planetree®, 2023). The study organization has been accredited and re-accredited since 2019, due to strong foundations for PCC, partnership with patients and families, staff empowerment, and a culture of quality and caring. The Magnet® journey commenced in 2020 and the recognition was achieved in 2023. Magnet® is a recognition bestowed upon organizations that demonstrate excellence in nursing. Organizations which thrive on the Magnet® model put emphasis on the generation of positive patient outcomes through excellence in nursing leadership, structural empowerment, exemplary professional practice, and generation of new knowledge, innovations, and improvement (ANCC, 2023). The ICU where the study was conducted, rooted in the principles of these two accreditations, had made substantial transformations in the structural design of the unit, evidence-based practices and quality improvement, and caregiver education and wellness. The positive outcomes of such transformation were evident in the outperformance of benchmarked outcomes data. For example, the ICU in this organization reduced the use of restraints significantly, and consistently scored better compared to all Magnet units enrolled in the National Database of Nursing Quality Indicators (NDNQI). This environment was not only conducive to the conduct of the study but was fundamental due to the curiosity and motivation demonstrated by healthcare providers to make changes in the structure and processes of the ICU as the study progressed and PICS was better understood.

The impact of the study at the hospital, local, and national level has been tabulated in **Appendix 7.1** with evidence that illustrates the changes that have occurred. During the study period, the organization opened its new, PCC-centred, and technologically enabled North Tower, that hosted the ICU as one of its units. During the planning phase of the new ICU,

recommendation from the literature described in Chapter 1 regarding evidence-based design features were welcomed and readily integrated, including the use of single-bed rooms, noise reducing and daylight features, family zones and other elements that were considered to play a role in the patient's recovery and healing (please see pictures of ICU design in Appendix 7.1). During this time also, as part of the Magnet® journey, advanced practice nurses were employed for the first time in the organization, who were instrumental in introducing new standards of care such as pain and delirium assessment. The presence of family, especially in the post-Covid period, gradually returned to previous norms, and education of family on PICS was integrated in the hospital education portals and the health app inspired from the knowledge generated from the research process of this study. A multidisciplinary grand round on the topic of PICS presented by the researcher was very well received and an enthusiasm and curiosity were evident amongst the physicians and nurses, who often expressed how they changed their mindset and behaviours in the ICU after they attended the grand round. The topic was also promoted in the regional conferences such as the Emirates and Saudi Critical Care Society (SCCS) meetings, further expanding the scope of the study's influence. These will hopefully raise the knowledge and appreciation of PICS and encourage more clinicians to engage in research activities at the Kingdom's and regional level. Since the presentation of the grand round to the SCCS, two requests have been received from semi-governmental academic hospitals to brainstorm collaborative projects, one of which was specific to the interest in replicating the methodology of Life-ICUS study in a paediatric population.

The most prominent impact that this thesis has had was in the establishment of the first PICS clinic in Saudi Arabia and the region. In the month of March 2024, the first PICS clinic will be opened. The overall aim of this clinic is to improve the long-term care and outcomes of ICU patients and to serve as a role model in the country for future clinics to be established. Multidisciplinary post-ICU clinics, have, in recent years, gained support in the US and Europe, and have been formed for the purpose of evaluating long-term health status and functionality of post-ICU patients, integrating rehabilitative and support systems for patients and families (Bloom et al., 2019; Hanifa et al., 2018; Huggins et al., 2016). The research site for this thesis, being perceived as a leading private healthcare organization in the country in its value-based vision, has engaged in many pioneering activities through its leaders in the Eastern Region and in the country. Having a prominent role and responsibility in the realization of the 2030

Saudi vision referred to in Chapter 1, the organization's leaders have a great opportunity to pioneer the establishment of post-ICU services and promote health and wellness in this group of patients. The foundations of the healthcare system in the country are very promising to support the establishment of PICS clinics in the care of post-ICU patients in terms of accessibility, funding, and policymaking. The Kingdom is on its transformational journey of healthcare, focusing on primary health and prevention, and value-based provisions of care (Vision 2030, Health Sector Transformation program). Disparities in access to care have been largely eliminated in the country, due to solid regulations and policies so that all people, citizens and expats, can access care equally (Saudi Ministry of Health, 2023). There is a timely opportunity to introduce the PICS clinics with the premise to exert consistent efforts to demonstrate efficacy in terms of patient improvements, cost reductions, and hence, value generation. Thus, towards the end of the preparation for this thesis, the researcher presented a proposal to the administration of Almoosa Health Group to clinicians, researchers, and administrators, for the first PICS clinic to be established. The proposal was approved for the clinic to be instituted in the newly constructed rehabilitation hospital in the Eastern Province of Saudi Arabia. This is a facility that provides rehabilitative services to post-trauma, stroke, cardiac, orthopaedic and other surgery patients. The clinic will be led by an advanced practice nurse or one of the experienced critical care nurses who has a master's degree and a certification in critical care nursing. The clinic will be opened 2 days a week, 7:30am to 5pm. The evaluation of PICS will be conducted within the conceptual framework proposed in Chapter 4, focusing on physical, cognitive, psychological, and quality of life domains. As repeated and dynamic assessments are recommended to capture the trajectories of PICS, self-reported patient reported outcomes will be measured for patients at 2-4 weeks after ICU discharge, two months afterwards, and as needed thereon, based on individual patient needs.

One of the challenging aspects of the clinic will be the integration of PROM tools to examine each domain of PICS, as research is not yet conclusive on the optimal tools to be used. Taking a best-evidence approach, a battery of tests recommended by the latest SCCM guidelines will be used in each domain as follows. In the physical domain, patients will be evaluated for both physiologic and functional parameters. The physiologic parameters will be evaluated by the 6-minute walk test and the functional parameters will be assessed by the ADL and IADL tools. The cognitive domain will be evaluated by the MoCA or MoCA-blind. The mental health

assessments will be done utilizing the HADS for both depression and anxiety assessments, and the PCL-C for PTSD. The HRQoL domain will be evaluated by the SF-36. The scorings and thresholds of all these tests will also follow the SCCM guidelines.

After assessments are done by the nurse in the clinic, and based on the cutoffs established for each tool, a plan of care will be established for each patient in a multidisciplinary team meeting. This plan will include, based on the team's assessment, sessions of physiotherapy, hydrotherapy, occupational therapy, speech therapy, psychological counselling, cognitive therapy, art therapy, and other services as needed by the patient. Evidence regarding rehabilitative treatment protocols is currently lacking in post-ICU literature, therefore the multidisciplinary team will exercise their best clinical judgement in designing a rehabilitative program that fits best the patient needs and progress.

Data on outcomes and incurred costs will be gathered for each patient throughout the visits in the PICS clinic. **Table 7.2** describes the elements of this data. On a quarterly basis value-based reports will be generated by the advanced practice nurse, demonstrating patient outcomes and cost figures of the PICS-clinic cohort for the quarter. These reports will be shared with organization's leadership, clinicians, and all stakeholders.

The electronic health record will be utilized to record referrals to PICS clinic, all outcome data, and financial data. The organization's health application will be used for patients and families to access PICS educational information and to schedule further appointments.

After one year, the clinic will be evaluated in terms of overall patient outcomes, costs, patient/family experience, and caregivers' experience. This data will earmark the decision whether to escalate the conversation for PICS clinics at the national level, engaging stakeholders from the Ministry of Health, the Council of Health Insurance, Vision Realization Office, and professional societies such as the Saudi Critical Care Society and Saudi Nursing Association. A stakeholders' meeting will be proposed including multidisciplinary society leaders and clinicians, payers, patients, families, and volunteers.

Table 7.2. Data for PICS clinics

Value Data	Data	Responsibility
Outcomes	Demographic information Medication reconciliation; Functional reconciliation Return to work	Nurse
	6-minute walk test	Nurse
	PROMs (Arabic versions) ADL, IADL MoCA HADS IES-6 EuroQol-5D-5L	Self-report, facilitated by nurse
	PREMs	Patient experience department
	Social history	Social worker
Costs	Services in PICS clinic Physiotherapy Hydrotherapy Occupational theory Speech therapy Psychotherapy Cognitive therapy Art therapy	Finance office
	Readmission costs: Total number of hospital readmissions Total number of days spent in hospital Total costs of hospital care (Lone et al., 2016)	Finance office

7.5. Strengths and limitations of the study

As described in the previous section, this research contributed to the general knowledge base of PICS in Saudi Arabia, confirming that PICS is a universal phenomenon, affecting patients in different settings and cultural contexts; something that was not conventionally explored as PICS literature was predominantly conducted in USA and Europe. The mixed method design enriched the knowledge regarding the patients' experiences and the factors related to their recovery. The results have a significant potential to raise awareness among critical care communities, patients, and families, and a role in shaping practices inside and after the ICU.

The specific areas of strengths and limitations of each phase of the study have been detailed in each corresponding chapter in this thesis. The following is a wider perspective of the strengths and limitations of the three phases of the studies.

7.5.1. Strengths and limitations of Phase I

The key strength in Phase I was the comprehensive review of all domains of PICS, in addition to HRQoL. This was a unique intervention, designed to include all domains of PICS in one

review. The study spanned over a long period of time (24 years). This ensured that major studies relating to long-term outcomes of ICU patients were captured during the review process, including studies that were conducted before the SCCM definition of PICS was formulated and published in 2012. The protocol of the study was published in PROSPERO and followed established guidelines to promote transparency and reproducibility. The methods applied in this study were rigorous in the formulation of the inclusion and exclusion criteria, the search strategy, and its application in five major databases. The search was applied in 2019 and updated in 2023. The extraction of selected articles was conducted in a systematic manner using the Covidence software, and the quality of the studies were examined in a rigorous manner. The results were reported in a transparent fashion, and they informed the conduction of the next phases of the thesis.

The main limitation in phase 1 of the study was the inability to conduct a meta-analysis due to the heterogeneity of the studies included in the systematic review. Consequently, effect sizes could not be calculated and therefore statistical power could not be optimally achieved. However, a robust method, as described above, was adopted to identify risks, predictors, and outcomes of intensive care therapy. Overall, this review is a valuable resource for informing clinical practice and informing future research.

7.5.2. Strengths and limitations of Phase II

The second phase of this thesis was a unique contribution to PICS studies, as it included all domains of physical, cognitive, and psychological outcomes, in addition to HRQoL, making it one of the rarest comprehensive attempts in literature. Furthermore, it provided unique insights into the Saudi experience, and served as the groundbreaking study in the Middle Eastern region.

The longitudinal approach of the Phase II study with the employment of a solid set of inclusion and exclusion criteria, study procedures, and the timeline of outcome measurements were the strongest areas of the methodological aspect of this study. The prospective design allowed for the collection of data over time, minimizing recall bias and providing an accurate representation of the patients' trajectory from the time of ICU discharge to 3 months follow

up. The 3-month time period of follow up was a strength; a systematic review has shown that only around 18% of ICU outcome studies have followed patients after 30 days of ICU discharge (Gaudrey et al., 2017). In the absence of consensus regarding PROMs and tools to be used in the evaluation of long-term outcomes of ICU patients, best practices were employed, and the best tools recommended by the SCCM were applied. This promoted reliability and comparability of results. In addition, tools which were translated and tested for reliability and validity were used in the study. For example, the ADL tool was tested in a study for the elderly in Lebanon, the MoCA for the elderly in Egypt, HADS in the surgical in-hospital population in Saudi Arabia, and SF-36 in the general population in Saudi Arabia. Another strength of this study was in the analysis of the data gathered, where a thorough set of risk factors and confounding variables were examined. To have pre-illness ADL and cognitive functions be reported by proxies at the time of ICU admission was a great decision in the study, since these confounding factors could have had the potential of overreporting of physical and cognitive disabilities.

The key limitation in this study was the limited number of participants (n=94), which made the assessment of important associations, such as the use of mechanical ventilation and sedation and their effect on outcomes of patients, challenging. Although data collection was expanded over a one-year period, a larger number of patients could not be enrolled in the study. This is an inherent problem in prospective cohort studies of critically ill patients. However, the use of several time points in the study and adopting a full set of assessment tools enabled the researcher to draw meaningful recommendations and conclusions from the study. A potential area of improvement of the study could have been the employment of a longer time period of outcome measurements (such as 6 months and 12 months) as PICS impairments have been noted to persist for a long time, however, due to practical reasons and time constraints of the PhD studies, this was not realistic.

7.5.3. Strengths and limitations of Phase III

The strength of the third phase of this thesis was its unique contribution to the exploration of patients' experiences along their critical illness trajectory. As described previously, the qualitative perspectives of the patients demonstrated the linearity and interconnectedness

of the different elements of the trajectory of patients' recovery, starting from the ICU and extending several months after discharge from the ICU. This holistic approach added an important dimension to the understanding of the critically ill patients' experiences; this knowledge would be helpful in the design of care pathways for ICU patients and would aid in the promotion of future studies.

The main limitation of this phase was the limited number of participants in qualitative interviews, which made the generalizability of the findings challenging. Alternatively, a focus group approach could have been employed. Nevertheless, with the engagement of a heterogenous cohort of patients, a distinctive perspective of the patients' experiences could be extrapolated, and new insights could be drawn about the experiences of post-ICU patients, specific to the Saudi Arabian culture and context of care.

7.6. Recommendations of the thesis

Derived from the synthesis of findings of the three phases of this study (Chapters 3, 5, 6, and 7), important implications for practice and research will now be described. Recommendations from this thesis will focus on improving the continuum of care of critically ill patients. As such, recommendations will be presented in three phases of the critically ill patients' trajectory identified in Chapter 6 (see Figure 6.1): 1) ICU phase, 2) immediate post-ICU phase, and 3) long-term post-ICU phase. For each phase, the PICS related recommendations for clinical practice and research will be discussed thoroughly; these recommendations are summarized in **Table 7.3.**

Table 7.3. Recommendations of the study

Recommendations	Clinical practices	Research
ICU phase	Implementation of ABCDEF bundle	Non-pharmacological strategies for prevention of delirium, including ICU diaries, on long-term outcomes.
	Environmental re-design (noise, daylight, family area)	Pre-post studies of ICU design transformation on long-term outcomes.
	Assessment of patients at risk for PICS	Larger cohort in Saudi Arabia to detect prevalence and predictors of PICS
	Screening for PICS	Best tools to screen for PICS
	Integration of early physio, psycho, and cognitive therapy	Effect of early rehabilitation on PICS

	Healthcare provider education	
	Patient and family education	
Immediate post-ICU phase	Follow-up team	Impact of transitional practices on PICS
	Functional reconciliation	
	Medication reconciliation	
	Formal handover	
	Healthcare provider education	
	Patient and family education	
Long-term post-ICU phase	PICS clinic	Conceptual framework revisions
		Best tools to screen for PICS
		PROMs
		Trajectory of PICS
		Value based studies (outcomes over cost)
	Support group	Hospital re-admission, return to work and PICS-related costs
		Caregiver burden
	Healthcare provider education	
	Patient and family education	

As described in Chapter 1, the overall philosophy and direction for contemporary ICU practices should move towards improvement of care and prevention of adverse outcomes of ICU survivors. As modern critical care is evolving, it is important now to "re-define success" (Angus, 2003) and re-evaluate excellence in ICU care. It is clear that optimal long-term outcomes should be included within this refined definition, and excellence should be addressed not only in mortality indexes, but in value-based approaches, where evaluation of ICU care is not ceased when the patient leaves the ICU, but rather continues to measure overall health and functionality outcomes over the trajectory of the critically ill patient. As critical care strives for excellence and provision of outcome-based practices, a culture of change is needed, where structures and processes of care should be evidence-based, systematically monitored, and continuously improving. A leadership which is dynamic and responsive to the needs of patients and families should be quick, flexible, data-driven, and visionary to lead their teams towards improvements.

7.6.1. ICU phase

Recommendation 1: Implement the ICU Liberation bundle, also known as ABCDEF bundle.

As outlined in Chapter 1, the implementation of the ABCDEF bundle is recommended to incorporate evidence-based practices for the assessment and management of pain, sedation,

delirium, mobility, and family engagement (Devlin et al, 2018; Davidson et al, 2017). When deployed in hospitals in a multidisciplinary approach, it has proven to decrease occurrence of delirium, duration of mechanical ventilation, and ICU stay (Kram et al, 2015; Marra et al, 2017). As these factors have been strongly associated with PICS in phase I and phase II of this thesis, the recommendation is to use the ABCDEF bundle effectively as a key intervention that can alter modifiable risk factors of PICS. An extensive elaboration of the evidence behind each item of the bundle is demonstrated in Chapter 1 so that knowledge can be shared and actions for change in practice can be encouraged. The long-term effects of the ABCDEF bundle on PICS have not been investigated (Marra et al, 2019). Therefore, a specific research recommendation in this regard would be to identify the effect of the bundle, specifically through its non-pharmacological delirium strategies, on long-term outcomes of PICS.

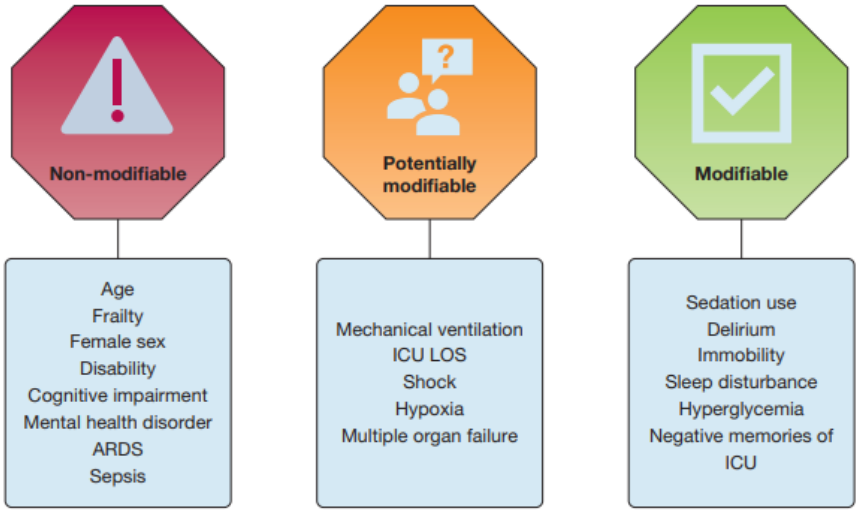
Recommendation 2: Redesign the physical structure of ICU

In the systematic review phase of this study, delirium was found to be a strong predictor of cognitive impairments of PICS, and in the qualitative interviews of this thesis, patients recalled disturbing noises and irregularities in sleep during their stay in the ICU. They also identified the role of their families throughout their ICU journey. Therefore, this recommendation relates to the physical structure and environment of care and advocates for the redesign of ICUs in evidence-based and patient-centred care approaches as they impact the processes of care and patient outcomes (Ferri et al., 2015). Materials and floor plans that reduce noise levels, incorporate daylight and other features that promote wake-sleep cycles should be adopted in the design of ICUs (Ulrich et al., 2008, Ulrich et al., 1992, Donchin et al., 1995). Families should be given enough space inside the room and near the unit to facilitate their engagement in care discussions and thus partner with the team to enhance recovery (Bay et al., 1998). ICU leaders and clinicians should be aware and exert mindful efforts to transform the ICU environment. Although all of the above measures have been demonstrated, to some degree, to enhance the experience of patients and families, however due to difficult methodological reasons, none of these have been proven to ameliorate PICS symptoms. Pre and post studies are recommended to be undertaken when healthcare organizations venture into a transformation of an ICU design, to demonstrate the long-term effects of such interventions on patient and family outcomes.

Recommendation 3: Assess and screen patients at risk for PICS

This recommendation pertains to the specific measures taken to assess patients at risk for PICS and thus screening for it while patients are still in ICU. Clinicians need to have a general knowledge of the modifiable, potentially modifiable, and non-modifiable risk factors for PICS identified in this study and others, and hence heighten their sense of suspicion that patients subjected to those risks may suffer from PICS on the long run. Patients who have prior psychological and cognitive problems, could be flagged and screened before discharge from ICU. A simple diagram, such as the one below (**Figure 7.1**), integrated in the care plans of the multidisciplinary team, can facilitate assessment and discussion of patients at risk (Schwitzer et al., 2023). Self-reporting of patient-reported outcomes (PROMs) can be promoted by using a tablet or a digital pad. Inherent to this recommendation, lies the need for research in the establishment of the right strategies to perform PROMs (right tool, right time, right person). More on PROMs will be discussed later in this chapter.

Figure 7.1. Risk factors associated with PICS. Adopted from Schwitzer et al., 2023.



Recommendation 4: Integrate early rehabilitation in plan of care

As patients were found to experience at least one aspect of PICS along the trajectory of their ICU journey, integration of early physiotherapy, psychotherapy, and cognitive therapy needs to be considered as part of the standards of care for ICU patients, specifically for those staying

for longer periods of time (Kress et al, 2014). Rehabilitation of the patient in the ICU should begin as soon as possible and continue after discharge and at long-term (Kress et al, 2014).

Recommendation 5: Patient/family and healthcare provider education

Recommendations for ICU phase cannot be complete without strong advocacy for education of patient and family members about PICS, its risk factors, and the family's role in mitigating the consequences of PICS. In this regard, the SCCM has developed a comprehensive program, The Thrive Initiative, which includes educational and informational resources about PICS. One of the methods in this initiative, the Patient Communicator app, has been designed to facilitate communication between patients, families, and healthcare providers (SCCM, 2023). Implementing this app in clinical practice will help in promoting communication with patients about their needs, feelings, and requests. It will also provide access to a diary and educational booklets on PICS for patients and families.

Regarding healthcare providers, periodic information, educational programs, and continuing education should be provided to physicians, nurses, physiotherapists, social workers, and other members of the ICU team about PICS, its risk factors, preventive measures, and long-term effects. Teams should be empowered to engage in quality improvement and research activities in this area with strong support and guidance from nursing and medical leadership.

7.6.2. Immediate post ICU phase

Recommendation 6: Follow-up of ICU patient during transitions of care

Modern critical care teams should consider innovations regarding the care needed for patients in care-transitions between ICU and general wards, and between hospital and home. Traditionally, ICU providers do not follow up patients when discharged from the ICU and do not get engaged in care transitions, which, in the case of patients at risk for PICS, may pose a gap in continuity of care, and hence missed opportunities for promotion of PICS management. Innovative approaches in these transitions could be facilitated by nurses and by integration of health information systems. A liaison nurse would be beneficial for this

model (Eliott et al., 2012; Mellinghoff et al., 2012, Chaboyer et al., 2006; Endacott et al., 2010; Priestley, 2004). Although this role has not been exercised and researched for the purposes of PICS in the mentioned countries, it could potentially be instrumental in following up of patients who have demonstrated risk for PICS. It is recommended that such a role be instituted in healthcare organizations in Saudi Arabia. It is also proposed that the scope of the liaison nurse be revised to include follow up, communication to ward staff, continuation of rehabilitative efforts started in ICU, identification of opportunities for further evaluations of PICS, and education of patients and families. Additionally, this person could be a key contact and resource for patients and families after discharge and for accessing post-ICU services.

Recommendation 7: "Functional reconciliation" and medication reconciliation

As recommended by the second stakeholders meeting of SCCM regarding PICS, a "functional reconciliation" and medication reconciliation should be performed at the care transition phase (Elliott et al, 2014). Similar to the idea of comparing the patient's current medication list to previous medications taken by patient for the purpose of safety and prevention of medication errors (The Joint Commission, 2022), functional reconciliation would compare the patient's current functional ability to that prior to hospitalization (Elliott et al, 2014). This approach is recommended to be followed throughout the transitions of care. Further research is needed for clinically applicable, valid, and reliable tools to conduct functional assessments in the ICU, in the hospital ward, and after hospital discharge (Elliott et al, 2014).

Recommendation 8: Formal handover

A proper handover between the ICU team and primary health team members is important to ensure continuity of care. The SCCM Thrive Initiative referral strategy could be applied where ICU physicians would communicate patient information, ICU course of treatment, and recommendations for PICS follow-up to the primary care physician (SCCM, 2023). A form that could be utilized in the organizations' health information systems has been drafted for this purpose (Please refer to **Appendix 7.2**).

It would be important to engage in robust research to explore the impact of the care-transition recommendations (liaison nurse, functional reconciliation, medication reconciliation, and referrals) on patient outcomes after hospital discharge.

7.6.3. Long-term Post-ICU phase

Recommendation 9: Adopt a structured follow-up program for post-ICU patients

As demonstrated in the three phases of the Life-ICUS study, the post-ICU phase of a critically ill patient is challenging, and the features of PICS are complex and multifaceted. Hence, it would be optimal to adopt a wholistic, structured, and evidence-based approach in caring for patients in this vulnerable phase of recovery. It is the recommendation of the Life-ICUS studies, for organizations to adopt a structured post-ICU program that integrates post-ICU clinics, patient and family education, support groups, opportunities for patient activation and community service, and other elements as needed.

- PICS clinics: These clinics are formed with the purpose of assessing long-term outcomes and quality of life of ICU survivors, followed with integrated rehabilitation services and support systems for the patients and their families. Full information has been disclosed in the above section 7.4.2, specifically in relation to the Saudi healthcare context and significance.

- Development of PICS PROMs

It is recommended that the tools used for the measurement of PICS outcomes be systematically evaluated and, in collaboration with the International Consortium for Health Outcomes Measurement (ICHOM), be translated into standardized sets of orders and outcome measurements. Grounded in the theoretical framework developed by the Harvard School of Business (Porter and Teisberg, 2006), ICHOM is an organization which is charged to create sets of standards for major health conditions, their measurement methods, and mechanisms for comparisons. There are currently around 45 sets of PROMs published by

ICHOM, along with the tools, time points for measurement, and mechanism for benchmarking (ICHOM, 2023). PROMs related to ICU or PICS have not been established by ICHOM yet. As a certified ICHOM member, the researcher of this thesis, has the opportunity to collaborate with the multidisciplinary team of experts, and to engage in the development of PICS PROMs and standardized sets. This will greatly assist critical care communities to measure, monitor, and compare PICS outcomes across the world.

- Establish PICS support groups

This recommendation, within the long-term post-ICU phase, advocates for the establishment of PICS patient and family support groups in Saudi Arabia, an initiative that has shown to be beneficial to ICU patients and families. These benefits have been perceived by patients in terms of validating their experiences with other survivors and hence reducing anxiety and social isolation and enhancing hope and motivation (McPeake et al., 2021). Patients also have expressed a sense of reassurance in terms of managing their expectations and understanding their recovery (McPeake et al., 2021). A strong sense of purpose has also been expressed in the context of helping others and being useful to peers (McPeake et al., 2021). On the other hand, peer support groups for ICU patients have also helped patients understand PICS and manage its symptoms better, that has led to the perception of improved quality of life (Lassen-Greene et al., 2021). As demonstrated in the Life-ICUS-Q study, patients in Saudi Arabia may be ready for such engagements, and studies are needed to document their utility and benefits.

Recommendation 10: Revise the conceptual model for PICS

Finally, driven by the findings of this thesis, especially from the qualitative phase, it is timely now, that the SCCM conceptual model for PICS be more integrated and engage elements such as religiosity, spirituality, and the role of personal strength and resilience in their impact of outcomes. The conceptual model proposed in Chapter 4 is an important step towards the transformation of the PICS conceptualization. In the future, studies will be needed to further explore communities where religion is pivotal in peoples' understating and values of life, and their approaches in enduring suffering, adversities of disease, and recovery.

Research recommendations in this section refer to the need to continue conducting long-term follow-up outcomes, extending to several months or years after the critical illness, in order to assess the trajectory of recovery and identify potential late complications in post-ICU patients. These studies can provide insights into the chronic health conditions and functional impairments that may persist beyond the initial recovery period. There is a need to form an international consensus within the critical care community to define PICS in a comprehensive manner, and to determine the best PICS assessment tools or PROMs at the best measurement time-points across the continuum of critical illness trajectory. Patients, families, and healthcare providers should be involved in these initiatives and outcomes which are identified as important by all should be addressed. This consensus would enhance the quality of future observational and interventional studies. Research should also examine heath system factors that influence post-ICU outcomes, such as those related to organizational structures, staffing models, and healthcare policies. Understanding these system-level factors can guide quality improvement initiatives and enhance the delivery of post-ICU care. Further investigation is needed to evaluate the effectiveness of different intervention strategies in post-ICU care. This includes exploring the impact of multidisciplinary care teams, peer support programs, and telemedicine interventions on patient outcomes. Additionally, studies should examine the cost-effectiveness of these interventions to inform healthcare policy and resource allocation. Finally, the exploration of PICS by using mixed methods designs has an increasingly important place in critical care research. As critical care research has evolved from mortality indexes to patient-centred outcomes, research methodology should also evolve in this setting, to allow the exploration of the complex phenomena behind PICS, and ultimately assist in improving the outcomes for patients. Similarly, study efforts should also increase in the assessment of family outcomes of PICS.

7.7. Reflections on the personal journey of the PhD thesis

I started my career in nursing almost thirty years ago. Most of these years I spent in clinical practice caring for ICU patients in my different roles as clinical nurse, then charge nurse, then clinical nurse specialist. Throughout those years I passionately learned and cared for ICU patients along with remarkably talented clinicians; we cared, we treated, and we celebrated if we got our patients out of the ICU. We didn’t think of what happens to them when they

leave the ICU. The idea of this study came from my interaction with a post-ICU patient. He was an around 45-year-old, male, cancer patient that I happened to see on the oncology ward when rounding with my students. When spoken to, this patient seemed aloof and isolated to me. When I questioned about his past medical history, it came apparent to me that he had been in the ICU for the treatment of septic shock, and he had just returned to the oncology ward and getting prepared to be discharged. At first, he was hesitant to speak to me, but when I approached him gently and caringly, he disclosed to me about the sleeping difficulties he was having, and the recurrent dreams that he'd been having that awakened him with fear. He was having flashbacks from the time he was in the ICU, and he had nightmares that he'd been taken mistakenly to the operating room for an operation. He spoke to me about his fears, his out-of-body experiences, and he seemed lost and confused about his state and his prospects for the future. I was saddened to see him that way but was intrigued by his memories and stories of ICU. Upon coming out of the room, I immediately got on my computer, and googled, "what happens to patients when they come out of the ICU?". I guess that was my first attempt to formulate my PhD research question.

I enrolled in my PhD studies at King's College London in October 2018. I used to live in Beirut, Lebanon at that time and I was a faculty member at American University of Beirut (AUB), School of Nursing. By June 2019, I completed the required modules at King's by attending face-to-face classes (I travelled 5 times to and from Beirut and London during that period). By July 2019, my initial research proposal was ready, and I applied for funding and ethics approvals both at my university (AUB) and at King's; funding and all ethics approvals were received successfully. My study had the same research questions, aims, and methods as the ones presented in this thesis report. I started the preparation of three hospitals in Beirut to serve as clinical sites for the study by meeting with the administrators, clinicians, and research team members. All agreements were completed, and non-disclosure agreements (NDAs) signed among all parties. In July 2019 I also published our systematic review protocol and started working on it with a team of a librarian and a colleague. The progress was on track.

In October 2019 however, a revolution started in Lebanon. This was followed by a quick downturn in the economy and a sharp devaluation of the currency. We all lost our years' savings. The money that I had diligently saved for years to self-fund my studies was lost. Being

an international, part-time student, I did not have opportunities for external funding. At this time, I could not pay tuition fees and complete my financial obligations towards King's, hence, with the support of my supervisors, I made a decision to interrupt my studies. In the beginning of 2020, the Covid-19 pandemic started growing, and the situation in Lebanon, compounded by the pandemic and the economic crisis, severely deteriorated. What made it worse was the Beirut explosion that happened on August 4, which caused mass destruction, destroyed our city, and crushed our streets, our homes, and our spirits (my friends and I wrote an article about this (Jabbour et al., 2021)). The three hospitals that were our research sites were completely destroyed. This was an extremely difficult time for me and my family. Towards the end of 2020, after realizing that I was unable to provide for my family, support my children's education, and continue my studies, I made the difficult decision to leave my family in Lebanon and relocate to Saudi Arabia for a better opportunity. I accepted a Chief Nursing Officer (CNO) job at Almoosa Specialist Hospital in Al Ahsa, Saudi Arabia, and relocated in February 2021.

These circumstances had a major effect on the progress of my studies, as my focus was shifted, priorities reshuffled, and the research could not be conducted in Lebanon anymore. However, with the support of my supervisors, family, and colleagues, I was able to bring this process back on track. In July 2021, we received ethics approval at Almoosa Specialist Hospital; we prepared the teams, and we re-started the work on the systematic review. In July 2022, I had my upgrade meeting which I passed at first attempt; it was a moment that ignited my motivation. There was no turning back. In parallel, in my capacity as CNO, I was able to set a visionary strategic plan for my department and was able to lead my team towards the first Magnet® accreditation for private hospitals in Saudi Arabia. This was a monumental achievement for my team, which we are celebrating until today. I was also promoted as Group CNO as our organization grew from one to three hospitals within the time period that I was here. The demands of my job and my responsibilities for the PhD studies kept me away from going home to see my children and family; they often left me fatigued and at times lonely. The financial challenges to balance between supporting my family and continuing my studies was daunting. However, with the support of my family and my supervisors, I was able to continue my journey.

In my assessments of the patients during this study, I had the privilege to have a glimpse of some aspects of peoples' lives that I hadn't imagined I would be able to. For them, at times the sessions were overwhelming with emotions. Nevertheless, I sensed that as though they explored different aspects of themselves too. The magnitude of how I affected our patients is unpredictable, but I hope that it led them to a place that is better than before. I too explored qualities of myself that I was not fully aware of. That course was unexpectedly enjoyable. I know that it has made me a better person. I am genuinely excited about where this study will take ICUs in Saudi Arabia. As I write this, we are planning to see our first patient in the first PICS clinic in Saudi Arabia. I plan to respond back to people who have reached to me to explore possibilities of doing research in this area. I know that from here, ICUs will be better in Saudi Arabia. I only hope that, in the future, I could make the same difference for patients in my hometown, in beautiful Beirut, and enhance the lives of people who first inspired me and supported me to pursue this study.

7.8. Conclusion

This three-phased thesis of post-ICU patients generated important findings for the long-term care of critically ill patients in general, and for Saudi patients in specific. The critical illness trajectory depicted by patients in the quantitative and qualitative reports clearly demonstrated that critical illness does not subside at the time of discharge from the ICU. It starts from the time of critical illness and extends to the phases of immediate post-ICU and long-term post-ICU. The magnitude of PICS in the long-term period of post-ICU patients is significant in terms of functionality, emotional and cognitive burden, and can be detrimental for these vulnerable patients as they strive to find a better quality of life. Patients admitted to general ICUs may inadvertently be exposed to any of the risk factors or predictors of PICS identified in this study, hence preventive and adequate management measures should be taken by all caregivers in the ICU team. As this study has shown the impact of family and personal strength in the trajectory of critical illness recovery, ICU teams should be continuously striving for engaging family and amplifying the patients' positive personal attributes and values in the journey of recovery.

To our knowledge, this was the first report on long-term outcomes and quality of life in ICU survivors in Saudi Arabia. This study has made significant contributions to the understanding

of the challenges faced by patients after critical illness. By identifying risk factors and PICS impairments in both quantitative and qualitative methods, the study has a promising potential to enhance knowledge, practice, and research locally and globally. The knowledge generated will hopefully be important for the promotion of evidence-based interventions in Saudi ICUs and creation of opportunities for further research, attuning to local and cultural variances. This study hopefully will also have an impact on policy making locally in terms of establishing post-ICU services. The proposed post-ICU clinic will be the first initiative in the kingdom and would hopefully serve as a role model for the rest of the country. It will also help in the advancement of the nursing image and leadership, and the role of nursing in mitigation of risks and provision of value-based healthcare.

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Appendix 1.1 History of Critical Care Medicine

Written by Hera Tashjian

"When I want to understand what is happening today
Or try to decide what will happen tomorrow, I look back."
Omar Khayyam

When one wants to look at the history of critical care and how it became the independent field of medicine we now know, one cannot dismiss the impact of how human crises, the drive for the human being to respond in most creative means, and the determination of some pioneer and visionary minds come to play.

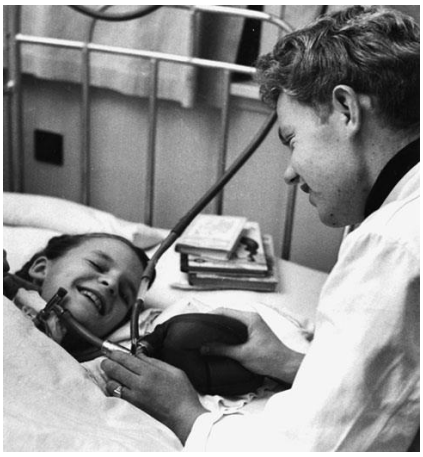
Wars

Most historical inferences made to the origins of critical care point to times of war. Many believe that the work of Florence Nightingale in the Crimean War was the precedent of what we know of intensive care today. Situating patients in segregates of the most severely injured under close nursing observation is traced back to the conception of "intensive care nursing" (Weil & Tang, 2011). In World War I intensive care was practiced when identifying shock states and resuscitating with intravenous fluid, and in World War II the techniques of blood transfusion and nursing for the severely injured in specialized shock wards was established (M. R. Rosengart, 2006; Weil & Tang, 2011). The creation of recovery units in World War II was modelled after the first postop care unit for neurosurgery patients initiated by Dr Walter Dandy in 1923 at Johns Hopkins Hospital, Baltimore (Grenvik & Pinsky, 2009).

The 1950's

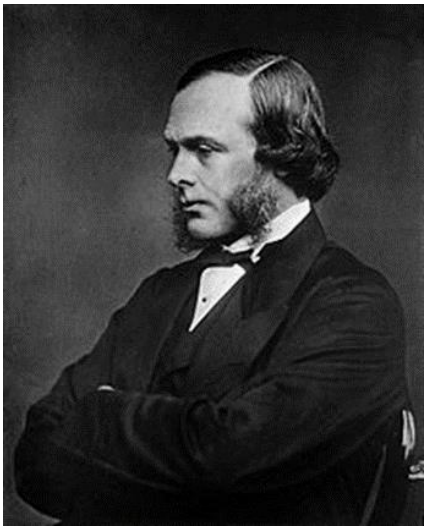
The 1950's witnessed the mushrooming of postop recovery units across the US, and the idea of obtaining real-time objective measurements of the patients started to be thought of optimal to survival. During these times, the poliomyelitis epidemic in North America and Europe advanced the use of what is known today as positive pressure ventilation, when Dr

Bjorn Ibsen recruited medical students to provide manual ventilation to hundreds of patients at risk for respiratory paralysis in Copenhagen, Denmark (Grenvik & Pinsky, 2009). The iron lung, created in 1929 by Dr Cecil Drinker, a Harvard medical researcher, started to be used widely outside of the operating room setting.



A young patient with poliomyelitis being manually ventilated by a medical student during the poliomyelitis epidemic in Copenhagen, 1953. Source: (Reisner-Senelar, 2011)

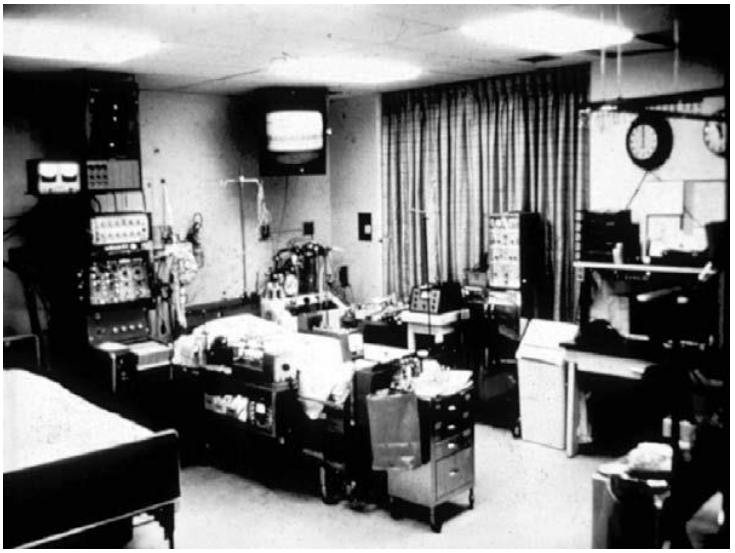
Another invention, which had been introduced much earlier by Dr Joseph Lister, was instrumental in post op patient care- this was antisepsis. Lester, who had initially failed to prove improvements in sepsis-related mortality with his work on "germ theory" (M. R. Rosengart, 2006), successfully introduced antisepsis to surgery at King's College, London. Being a stern critique of his own work, Lister continued challenging his wound care techniques, and at times recruiting himself as his own "research subject", he advanced newer methods of bandaging with antisepsis, and went on to finding steam and chemical techniques of equipment sterilization. The importance he placed on hand hygiene in preventing wound infections and thus mortality related to it, is still precious and essential in today's critical care practice.



Joseph Lister (1827-1912) reprinted from https://en.wikipedia.org/wiki/Joseph_Lister

Lister's carbolic steam spray apparatus, Hunterian Museum, Glasgo

The 1950's also brought the establishment of two critical care units in the US which are considered pivotal to the maturation of critical care as a defined clinical service. The first is the unit at University of Southern California (USC) by Dr Herbert Shubin and Dr Max Herry Weil, and the second is the medical/surgical ICU in Baltimore City Hospital by Peter Safar. The 4-bed "shock ward" at USC served as a prototype for the early ICUs, as continuous measurements of vital signs through monitors was believed to enhance the opportunity for proactive interventions in circulatory failure and shock states. Within a few years, the university expanded the service to a 42-bed "Center for the Critically Ill" where practice, education, and research evolved in the care of the medical-surgical and cardiac patients. It is here where bedside monitors and computers were created in order to obtain real-time arrhythmia monitoring and hemodynamic measurements, including arterial and central venous pressures and cardiac output measures. Devices such as infusion pumps were also designed in order to intervene with fluid and drug therapies.



The “shock ward”, University of Southern California, LA, 1958. Source: (Ristagno, 2009)

Peter Safar on the other hand, first in Baltimore and then in University of Pittsburgh, put the stepping stones of what we know of cardiopulmonary resuscitation (CPR), which until then was widely known by the acronym VIP- ventilation, perfusion, pump. Safar emphasized airway management and breathing techniques, the A and the B in ABC’s of CPR. Along with chest compressions, the “C” in ABC’s, he was an advocator for preserving cerebral perfusion, thus his initial proposition was to name it Cardiopulmonary Cerebral Resuscitation (CPCR) (Ristagno, 2009). Training of CPR was enabled when he joined efforts with a Norwegian company to create the first CPR mannequin, “ResusciAnne”. Several American and European companies have developed many simulators since, including high-fidelity ones, making simulation an important aspect of critical care training. Safar’s contribution to critical care medicine extend to the development of US’s first critical care medicine program and prehospital emergency ambulance services (M. R. Rosengart, 2006), accompanied by guidelines for the designs and standards for the training of the paramedics (Grenvik & Pinsky, 2009).

Peter Safar

Source: https://www.anesthesiology.pitt.edu/news/profiles-diversity-peter-safar-md

Both of these pioneering Intensive care units shared a common notion of providing resuscitative medical care in a setting of close monitoring, delivered by trained physicians, nurses and technicians, engulfed in an environment of teaching, innovation, and research. The 1950's ended with a legacy of an array of sophisticated inventions in critical care, such as vascular pressure and cardiac output measuring, cardiac pacing, defibrillation, cardioversion, and blood gas analysis (Weil and Tang, 2011). The tanks used for mechanical ventilation evolved with the employment of basic airway management principles such as humidification, prevention of increased oxygen tension, and careful chest physiotherapy. The concepts behind positive pressure ventilation led many companies in the UK, Germany and Scandinavia to test and put in place several volume-cycled and time-cycled ventilators (Rosengart, 2006). On the nursing front, although initially restricted to practice under direct supervision of physicians, nurses started developing their own practice and procedures (Grenvik, 2009). The "intensive care" idea stretched beyond the locale of the unit itself, to many discoveries in the field, embracing the training and specialization of the professionals inside.

The 1960's

The professional movement towards specialization in critical care gave birth to the specialty associations in medicine and nursing in the 1960's. By a joint effort by Drs Max Harry Weil, a cardiologist, Peter Safar, an anesthesiologist, and William Shoemaker, a trauma surgeon, 28

medical leaders from different specialties met in 1967 discussing common goals and conceptions in the care of the critically ill; a step which led to the formation of the Society of Critical Care Medicine (SCCM) in 1969. In the same year, the American Association of Critical Care Nurses (AACN) was founded (Grenvik, 2009). In 1973 SCCM published the first issue of its official journal, Critical Care Medicine (CCM). In the past 50 years, SCCM has grown from its initial 28 members to 16,000 members today, representing various critical care professionals from more than 100 countries. Its journal, CCM, is considered a leading publication of critical care medicine. On the other hand, AACN, has grown its membership on a large scale, and has proven to be a proactive organization in the care of the critically ill, developing evidence-based guidelines and standards, establishing autonomous critical care nursing practices, and ensuring appropriate qualification of critical care nurses through the Critical Care Registered Nurse (CCRN) certification.

In the 1960s, the idea of ICU spread to Europe. In the UK, the first ICU caring for patients with neuromuscular diseases was established in Kettering in 1962 (Crocker, 2007). The respiratory care units, which were closed after the polio epidemics of the 1950's, re-opened as general medical/surgical intensive care units, to care for patients needing ventilation and close monitoring. This movement was augmented with other changes in healthcare, such as the National Health Service's "golden age of technology" and the drive to reorganize care based on specialization. Diagnostic tools, such as radiography, and therapy, such as antibacterial agents and blood transfusion, started to be widely utilized. Surgeons, especially those operating on cardiac patients, began to value the presence of a skilled nurse and its relation to their patients' prognosis (Crocker, 2007).

Based on previous discoveries, innovations in critical care technology continued in the 1960's. Although today the name "Swan Ganz" is commonly referred to the pulmonary artery catheter (PAC), the inception goes to R.D Bradley in 1964. Using a thermistor at the tip of a catheter, principles of thermal dilution were used to obtain cardiac output measurements. The discovery was advanced by HJC Swan and William Ganz by adapting a balloon at the tip of the catheter. With the support of Edwards Laboratory (well known for their heart valves and embolectomy catheters at the time), Swan and Ganz piloted their flow-directed pulmonary artery catheter on a dog. Upon inflation, the balloon floated from the right side of

the heart to the pulmonary artery, “wedged” itself there, and produced waveforms on the computer that represented distal pulmonary artery pressures. This groundbreaking discovery was disseminated in New England Journal of Medicine in 1970 and soon became the “gold standard” in advanced hemodynamic monitoring in the clinical setting. Although in recent years, after careful examination of its benefits, the use of the PAC has been less employed in the clinical setting, its impact on the critical care practice remains invaluable (M. R. Rosengart, 2006; Matthew R. Rosengart & Pinsky, 2014).

The 1970’s

The development of specialty associations of critical care of the US echoed in other countries. Australia and New Zealand founded the Australia–New Zealand Intensive Care Society (ANZICS) in 1975. The Canadian Critical Care Society was founded in 1977. In the same year, the World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM) was established in Europe, engaging national and regional societies as its members. In 1982, eight European countries formed the European Society for Intensive Care Medicine (ESICM), which now hosts more than 9000 members. Asia Pacific Association of Critical Care Medicine (APACCM) followed (Grenvik & Pinsky, 2009; Matthew R. Rosengart & Pinsky, 2014). The common thread among all these societies have been a strong voice in patient advocacy, development and dissemination of clinical practice standards, continuing education of critical care professionals, and qualification through certification.

The 1980’s

By the end of 1970’s and following through the 1980’s, the critical care field distinguished itself as a specialty, by getting organized, setting standards, and streamlining practices. Almost every major medical center or hospital had established a “closed unit” known as either Intensive Care Unit (ICU) or Intensive Therapy Unit (ITU) (Ristagno, 2009). The motto of this decade was that a “well-organized approach, not merely individual excellence, could save the lives of the very sick” (Lewis et al., 2016). In order to perfect the art and science of life support and hence the timely and accurate intervention in a failing organ or organ system, further advances were made in understanding pathophysiology, severity of illnesses, technology, and

aggressive invasive interventions. Teams got organized in a multidisciplinary fashion (medical and surgical specialists, clinical nurse specialists, clinical pharmacists, respiratory therapists, nutritionists, and other allied personnel). Training focused around intubation techniques and mechanical ventilation for respiratory failure, pharmacological, electrical, and mechanical interventions for cardiac failures, fluid resuscitation and vasoactive drugs.

One of the icons of intensive care medicine in the 1980's was the assessment of severity of illness and prediction of outcomes. Knaus and colleagues developed the Acute Physiology and Chronic Health Evaluation (APACHE) model (Knaus WA, 1985), and Le Gall and colleagues proposed the Simplified Acute Physiology Score (SAPS) (Le Gall J-R, 1983). These instruments were utilized both at the individual patient level and at the ICU/organizational level. At the individual level, the tools are mainly used to describe the severity of the patient's illness, identify those who are at high risk to develop complications, and those who are too sick to benefit from an ICU (futility of care). The scoring systems are also useful to ensure comparability of the individual's illness to those reported in epidemiological studies. At the ICU or organizational level, the instruments are mainly used for internal and external benchmarking, and to understand patterns of practice related to end-of-life decision-making, patient outcomes, and resource utilization. Worldwide, they have been used to describe differences in risk-adjusted mortality across different countries and have served as the basis for large registries and benchmarking entities. Following the early APACHE studies, on behalf of the Intensive Care Society, Professor Kathy Rowan addressed the Department of Health in the UK with a proposal to set up a national center for comparative audit and evaluative research in intensive care. Intensive Care National Audit & Research Centre (ICNARC) in the UK was established. Others followed, such as, the Austrian Center for Documentation and Quality Assurance in Intensive Care Medicine (ASDI) in Austria, and the Gruppo Italiano per la Valutazione degli interventi in Terapia Intensiva (GiViTI) in Italy (Moreno, 2009).

The 1990's

The specialty grew rapidly into the 1990's with a focus on evidence-based practice and further application of peer-reviewed standards of care. However, patient-centeredness also surfaced as highly regarded as standardization. Following a decade of advances in life support

education, technology, and interventions, the specialty came to a realization that the goal of intensive care is not prolonging life solely but providing a dignified death to those who did not survive. The motto here was that a "well-organized approach can provide a good death (or a good dying process) to those we cannot save" (Lewis et al., 2016). Excellence in patient care started to be defined by concepts of patient preferences, symptom palliation, and engagement of patient and family in a fashion that supported shared decision-making. Researchers started looking at patient preferences, family meetings, and family presence during resuscitation. The care approach favoring patient-centeredness effected how ICUs were designed and technology was used. Bedside patient monitoring (rather than remote or central monitoring) with the nurse typically situated between two beds was becoming the norm. Use of mobile devices (such as dialysis and x-ray machines) were more often employed to ease access and avoid mobilization of the critically ill patient. Nevertheless, concerns started surfacing regarding optimal patient to nurse ratios and cost effectiveness of aggressive interventions.

The 2000's

The 2000's brought a notion of simplification to the care provided in critical care. The shift focused on less invasive, when possible, less interventional, and more humane care. Critical questions were raised regarding the effectiveness of invasive diagnostic and interventional methods. These questions translated into well-designed Randomized Control Trials, and hence solid, high-level evidence was generated, more and more favoring less invasive means of assessments. The widely used Swan Ganz catheter was deemed necessary in high-risk patients in circulatory shock yet found to be a source of high-risk complications itself. Cardiac output monitoring and large vessel catheterization, in addition to being labor-intensive and expensive, was found unnecessary and misleading in hypo-perfused states (Ristagno, 2009). Old practices were refuted and a "less is more" approach was adopted. For example, triggers to start blood transfusion was lowered (Hebert PC, 1999), use of high tidal volumes was proven to be harmful (Network, 2000), the use of low-dose dopamine in renal failure was shown to be not beneficial (Bellomo R, 2000), and over-sedation was linked to worse outcomes (Girard TD, 2008). Most of these studies had mortality as an end point.

In addition, healthcare in general started realizing that advances in complex technology have improved patient prognosis at times, however they have led to the risk of medical errors (MEs) and adverse events AEs). This era started to be characterized by optimization of limited resources and patient safety. The Institute of Medicine had just released its “To Err is Human” report in 1999 in the US. Quality improvement (QI) started becoming the central tenet in healthcare. Clinical Governance had been introduced in 1998 by the National Health Services in the UK as a new approach to QI (Lumb, 2009). These two monumental movements started setting a stage for healthcare in general, and for critical care in specific, to recognize errors, to scrutinize structures and processes, and to lead improvements in outcomes in an evidence-based, holistic, and compassionate manner. A diverse structure of ICU management existed, with a “closed unit” model primarily in Europe and Australia, and a “team model” in the US (Lumb, 2009). The Leapfrog Group, which was formed in 1998 by several large US purchasers of healthcare, for the aim of improving overall safety and value of healthcare, had published the standards for ICU structure and had advocated for a “closed unit”, managed exclusively by board-certified intensivists. This type of a model was shown to decrease mortality rates, length of ICU stay, and hospital costs (Lumb, 2009). In the US there were many barriers for not abiding by this standard, mainly shortage of intensivists, and reluctance from non-intensivists to accept such a model due to fears of lack of control and financial income loss. To overcome these barriers, more reliance was put on the employment of non-physicians, mainly nurse practitioners, and alternative methods of monitoring such as telemedicine, and structuring such as regionalization, were explored.

Multidisciplinary care structures were also emphasized in order to improve quality of care and safety. For example, having a clinical pharmacist during morning rounds were shown to reduce avoidable drug errors by 65% (MacLaren R, 2008). In order to improve care processes, standardized care pathways and protocols, order sets, and checklists were integrated into clinical practice. The Institute of Health Improvement (IHI) had been established, which helped implementation of evidence-based practices through “bundles” of care. These are sets of preventive steps or interventions that, when used together, significantly improve patient outcomes.

However, how well was critical care doing when it came to patient safety and resource

utilization? Not so well. In 2005 and 2006, the Safety Study in the US and the Sentinel Event Study in Europe were published respectively. In summary, the first study found that a patient staying in the ICU for only 3 days would likely suffer from at least one adverse event or medical error. The second study listed the most common sentinel events: medication errors, airway mismanagement, mishandling of catheters and drains, failure of equipment, and issues with clinical alarms. In a study exploring the magnitude of resources allocated to AEs and MEs (Kaushal R, 2007), it was revealed that critical patients paid very high costs due to these events with significant increase in expenditure and prolonged length of stay.

There was at this time a significant amount of evidence that intra-hospital transfers pose a great risk to patient safety. Hand-offs were linked to medication errors, breaks in communication, loss of important information, and delays and interruptions in patient care (Barach, 2009). These threats are pronounced for the intensive care patient, since the need to transport patients to and from diagnostic or interventional procedures outside the ICU is frequent, and eventually patents transfer to a step-down unit or a general ward after recovery from ICU. Until today, more studies are needed to achieve a better understanding of patient outcomes and costs associated with transport of ICU patients.

In this era, the critical care community once again attempted to face the problem of patient safety and quality with attempts to improve the quality structure in the service by introducing multidisciplinary improvement committees, audit tools, key performance indicators, and a feedback-looped process. All staff members were encouraged to report in a voluntary and anonymous manner, emphasizing a non-punitive approach. This step was undoubtedly a transformational one on the culture of safety and team performance in ICUs as safety and quality became everyone's business.

Despite the enormous efforts of healthcare institutions, professional organizations, and various consumer groups to incorporate evidence-based practices in healthcare, there seemed to be a great gap between practice and quality. This was highlighted by the Institute of Medicine's report titled "Crossing the Quality Chasm: A new Health system for the 21st Century" in 2001 (IOM, 2001). Far too many healthcare-associated infections occurred, many of them in the form of deadly central line blood stream infections, ventilator-associated

pneumonias, and catheter associated urinary tract infections. Johns Hopkins University championed a multidisciplinary program, including three main aspects: a system to measure and report outcomes, a Comprehensive Unit-based Safety Program (CUSP), and a model for Translating Evidence into Practice (TRiP). This initiative was adapted and implemented in many other ICUs worldwide, aiming to reach the drastic decreases in infections that Johns Hopkins experienced (Lareau & Mealer, 2012).

Sepsis was targeted at a large scale because of its incidence and significance. Sepsis represents one third of patient admissions and its incidence increased from 82.7 to 240.4 per 100,000 population between 1979 and 2000. It is the leading cause of death in medical/surgical ICUs, with a mortality rate ranging between 30 to 50%. It accounts for more than 40% of total ICU expenditure, costing around 6-16 billions of dollars in the US and across Europe (Hurtado, 2009). Male gender and chronic conditions such as diabetes and cancers, increase the risk for it. Increasing age, progressive number of organ failures, and hospital-acquired infections are linked with higher risk of death. The Surviving Sepsis Campaign was launched in 2002, spearheaded by the European Society of Intensive Care Medicine, International Sepsis Forum, and International Society of Critical Care Medicine, with a primary goal of increasing awareness and improving outcomes. In its second phase, the campaign resulted in an evidence-based guideline (Dellinger, 2004), developed by a consensus committee of international experts and societies. The guidelines included screening tools, blood culture standards, resuscitation and antibiotic use guidelines, and training. The guidelines went through a series of updates in subsequent years, integrating the GRADE methodology for evaluating evidence (Vincent, 2009). In its last phase, the campaign focused on translating the guidelines into practice through the development of Sepsis Bundles (Severe Sepsis Resuscitation Bundle and Sepsis Management Bundle) in collaboration with the Institute for Health Care Improvement. More than 160 ICUs in 18 countries provided data on how PDSA (Plan-Do-study-Act) cycles of bundle adaptation have affected the care for their septic patients (Vincent, 2009). However, studies have shown that compliance with the bundles are still not optimal. Hospitals continue working on means to increase their compliance with the guidelines by more education and standard sets of orders; nevertheless, there remains considerable ground to improve awareness. Research continues in this area to dissipate uncertainties- when is an optimum time to intervene, which IV fluid should be used,

which vasoactive drug should be employed, when to use steroids, and how tight should glucose be controlled.

Difficult questions such as how to maximize quality while minimizing cost remained to be addressed. The financial cost of critical care was closely scrutinized. Cost-effectiveness studies and cost-containment efforts started affecting policy and practice. At this time, it was estimated that more than 1/5th of the hospital budget is spent on intensive care patients in the US, and around 2% of hospital expenditures are spent on around 100,000 critically ill patients in the UK (Gallesio, 2009). A large project called the RECOVER program was started in 2007 by the Canadian Critical Care Trials group to re-look at the composition of ICU patients (Herridge et al., 2016), and understand to whom do we deliver this expensive service- in times of precious ICU bed availability, what is happening to those who neither thrive nor die in the ICU? Not surprisingly, older patients and those staying more than 2 weeks in the ICU were shown to do worse. Almost 41% of those who survived the ICU were readmitted to the hospital within a year. Around two thirds of the survivors were alive in a year, and those oldest and long stayers were likely to die within 6 months.

It is during this time that challenging ethical concerns were also discussed in relation to aggressive care to a population of potentially terminal outcomes. Allocation of resources and futility of management were questioned for the chronically critically ill. Thus, the true mission of critical care was re-examined. The American Thoracic Society Bioethics taskforce set out the objectives of an intensive care unit in 3 statements (ATS, 1997): 1) resuscitation and preservation of human life, measured by actual mortality against expected mortality; 2) to provide suitable rehabilitation as soon as the patient begins to recover from his critical condition, measured by morbidity and quality of life after discharge; and 3) To provide palliative care and affective support to the non-recoverable patient and his family, measured by futility (however, the taskforce clearly indicated that there is no valid instrument to measure futility so far).

Better communication and family engagement continued to be trumpeted. Less restricted visiting policies were advocated, family conferences were becoming part of daily practice, and abandoning our paternal approaches to end-of-life decision making were welcomed (Curtis

JR, 2001).

Resources are an integral part of the structure and processes of ICUs. The allocation of these resources is influenced by the characteristics and case mix of the admitted patients, human resources and care processes, and accessibility. It is estimated that between 45 to 60% of ICU costs are attributed to human resources, and another 30 to 35% to supplies and medications.

At this time, critical nursing shortage, especially in specialty areas, added pressures in healthcare. It is now estimated that turnover rates of 26% exist in intensive care units (Lareau & Mealer, 2012) and the shortage of nurses will grow to 260,000 by 2025 in the US. Some even have reported estimates of 800,000 of nursing shortage by 2020 (Gallesio, 2009). A study of 23 countries in 2001 reported two priorities and concerns facing critical care: staffing levels and working conditions (C. W. Williams G, Thornsteindottir R, 2001). A few years later the study was repeated in 51 countries, and revealed that staffing levels and working conditions remain among the most important issues critical care nursing is facing (C. W. Williams G, Alberto L, 2007). Many other studies have shown similar results (Albarran J, 2005; Scribante J, 2004; Stechmiller, 2002; Williams, 1997; S. S. Williams G, Alberto L, 2006). Only a few countries, such as the UK (Pilcher T, 2001) and Australia (Australian College of Critical Care Nurses, 2003) have adopted staffing guidelines.

Many factors are the basis for this nursing crisis in critical care: high stress level and burnout due to the challenging work environment; high incidence of PTSD and secondary traumatic stress; and organizational factors. In order to quantify the workload of an ICU nurse based on tasks performed on the patients, the simplified Therapeutic Intervention System (TISS), which was originally created in 1974 (Cullen DJ, 1974), was revised and modified by Miranda and colleagues (Miranda, 1996; Moreno R, 1997). It has been reported that a TISS score of more than 40-50 points would be unrealistic for a nurse to carry out. Miranda and colleagues continued this line of work with a proposed new tool, the Nursing Activities Score (Miranda DR, 2003), with the argument that workload of nurses should not necessarily be related only to complexity of care but actual time spent in also simple care. These two tools, TISS and NAS, are currently widely used in ICU studies linking staffing to patient outcomes. ICU nurses have expressed distress due to daily exposure to patient mortality, ethical issues at end-of-life,

moral distress related to withholding/withdrawing and supporting families in decision-making. Mealer and colleagues (Mealer M, 2011) explored the concept of resilience in critical care and found it detrimental in preventing PTSD and burnout syndrome (BOS) in ICU nurses. The authors continued with a qualitative study exploring characteristics of resilience in those working in these challenging workplaces and proposed strategies that would potentially help nurses in targeting resilience (Mealer M, 2011).

Studies relating nurse-patient ratios and skill mix to patient outcomes have been numerous. The following are some select studies that relate specifically to critical care nursing. Decreased numbers of licensed nurses providing direct patient care has been associated with:

- Increased risk of central line infections, pressure ulcers, falls, and increased use of restraints (Whitman G, 2002)
- Medication errors, patient injuries, and death (Aiken LH, 2003)
- Drastic increases in time to wean off the patient from mechanical ventilation (Endacott, 1996), hence, increased length of stay and complications (Thorens JB, 1995)
- Postoperative complications (Dang D, 2002)

Severity scores and staging systems are still the subject of research studies, in order to better characterize patients, reduce heterogeneity in ICU population, and predict outcomes. Accurately predicting outcomes is instrumental in showing efficacy and improving decision-making, especially when the stakes are so high. Hundreds of studies have been published since the inception of the previously described severity tools in ICU (APACHE and SAPS), and the critical care community has learned a lot. Recently, however, it is getting clear that we are apt to commit the mistake of what is called the “paradox of outcome evaluation” (Garland, 2009): first, at the individual level, we depend on the scoring systems completed at admission or during the first 24 hours, at a time patient’s severity of illness evolves and should be assessed daily; and second, at the organizational level, we use these individual patient scoring systems to evaluate the performance of our ICUs, without considering other organizational characteristics that play a role. Recently, attempts have been made to, slowly but steadily, ameliorate these mistakes by replacing the general scoring systems by organ

dysfunction/failure scores. The premise behind this shift is that, collectively with other patient characteristics, incorporating biologic parameters in the scores will render better capabilities for prognosis and for evaluation of effectiveness of care. Looking into the future, one must remember, that regardless of the scoring model used, accuracy should be periodically tested and the models modified; clinical evaluation should stay core to the prognostic predictions, and only complemented with these models (Moreno, 2009).

The 2010's and 2020's

Evolving from an enormous move to control and improve quality in critical care, there was a time when we started realizing that while most of the efforts quantified success in terms of hospital mortality rate and ICU length of stay, what's most important to people is long-term survival and quality of life. Today's decade is characterized by a tone of dissatisfaction with critical care services in terms of preserving long-term outcomes of ICU survivors. We are no longer content with representing critical care outcomes with only 2 poles: dead or alive. Building on our experience in resuscitation since the 1970's and 1980's, to determining "good death" and best end-of life practices in the 1990's, to increased efforts in decreasing ICU mortality and enhancing quality of care in the 2000's, we are now ambitious in improving the lives of those surviving the critical illness, beyond our ICU walls. The motto here is: "a well-organized approach can help those who survive critical illness live full new lives; lives not the same as they were before necessarily, but also not necessarily less" (Lewis et al., 2016).
Although intensive care has grown and changed over time, our ICU designs still do not address the core elements of the ICU patient experience: little privacy, lack of control, little sleep, a lot of disorientation, noise, immobility, and a predominant sense of dehumanization. Although we have mastered the skills of taking care of the acute physiologic needs of the patient, a significant portion of ICU survivors suffer long-term, permanent and devastating physical, psychological, and cognitive damage that impact their quality of life.

Patient outcomes can be influenced by patient demographics, comorbidities, the organ system most responsible for ICU admission, and severity of illness (Garland, 2009). The RECOVER program that started in 2007, continued through 2017, and provided critical care with a wealth of data. Patient-reported outcomes in physical ability, psychological health, and

cognitive function pose a great concern. Given the high number of one-year survivorship of ICU, the disabilities in the above-mentioned areas of functionality form a critical medium for improvement in the recovery and rehabilitation of ICU survivors.

It is refreshing to see that progressive humanization is on its way in critical care. We have come to full realization that besides the overwhelming physiologic stress of disease process that targets our patients, many features of our care structures and processes, such as bed rest, immobilization, continuous and excessive sedation, poor sleep, and gaps in communication impact our patient's long-term outcomes. We therefore have ceased to ignore what happens to our patients after they leave our units. We have thus chosen to explore these long-term outcomes and quality of life as our current priority in critical care.

We have learned from the critical care history, that when posed with a challenge, we tend to take action, most times in organized but yet sophisticated and expensive ways; then we dig and understand the causes well; then we simplify our practices and improve our care. When it comes to long-term outcomes of ICU patients, we now know that we have a challenge, and we are still searching for the causes and predictors of bad outcomes. We are yet to be bombarded with innovative epidemiologic and biologic data that would explain the mechanisms of deterioration versus successful recovery. If history holds true, we should expect that very soon we will be able to reorganize again and simplify and coordinate the post-ICU care in ways that would improve recovery and add value to life.

Fortunately, the 2020's are ending with a wealth of information on the status of the ICU survivor post ICU. A review of the literature on this topic will be the subject of this chapter and a systematic review will be presented in Chapter 3.

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Appendix 1.2 Guidelines- Family Centered Care Gap Analysis Tool

To access the instructional video on using this tool visit:
https://youtu.be/gpxvGnTgm-I

Identification of Your ICU's Practice Differences From the 2017 SCCM Guidelines for Family-Centered Care in the ICU

Hospital Name:

Name or Type of ICU:

Society of Critical Care Medicine
The Intensive Care Professionals

How often does your ICU follow each of these recommendations?

* Use the drop-down menus in the "Frequency" column to indicate how frequently your unit currently implements each family-centered care recommendation. A detailed explanation of each recommendation can be found in the full guidelines manuscript, available on the SCCM website and in the journal *Critical Care Medicine* .
* This spreadsheet will automatically calculate a numerical score from zero to 50 for each recommendation based on your responses. Higher scores suggest more opportunities for change.
* Once you complete the scoring on this worksheet, move to the Step 2 worksheet to find your top 5 opportunities for change.

Note: The recommendations are grouped into the same topical categories as they are presented in the guidelines.

Item	Recommendation	Outcome Points	Frequency	Item Score	Item Rank
Category 1: Family Presence					
1	Family members of patients are offered open, flexible presence at the bedside.	3		0	1
2	Family members of patients are offered the option of participating in interdisciplinary team rounds.	3		0	1
3	Family members of patients are offered the option of being present during resuscitation efforts, with a staff member assigned to support the family.	5		0	1
Category 2: Family Support					
4	Family members of critically ill neonates are offered the option to learn how to assist with the care of their loved ones.	5		0	1
5	Family education programs are included as part of clinical care.	5		0	1
6	Peer-to-peer support in the neonatal ICU has been implemented.	5		0	1
7	Family members are provided information leaflets about the ICU setting.	5		0	1
8	ICU diaries for family members are available and are encouraged.	5		0	1
9	Validated decision support tools for family members are used when relevant validated tools exist.	4		0	1
10	Clinicians use a communication approach, such as the "VALUE" mnemonic, during family conferences for patients who have a poor prognosis.	4		0	1
Category 3: Family Communication					
11	Routine interdisciplinary family conferences are used in the ICU to improve family satisfaction with communication and trust in clinicians, reduce conflict between clinicians and family members.	4		0	1
12	During family conferences for dying patients, clinicians use structured approaches to communication, such as the "VALUE" mnemonic, and offer families a written brochure regarding bereavement.	5		0	1
13	Clinicians receive family-centered communication training as one element of ongoing education.	4		0	1
Category 4: Consultations					
14	Proactive palliative care consultations are provided among selected critically ill patients.	1		0	1
15	Ethics consultation are obtained for selected critically ill patients when there is conflict regarding goals of care.	1		0	1
16	Consultation with a psychologist for a multimodal approach based on cognitive behavioral technique is provided for mothers of pre-term babies admitted to the neonatal ICU. Furthermore, targeted video and reading materials are provided for psychological support to mothers of pre-term babies.	5		0	1
17	Social workers participate in interdisciplinary family meetings.	3		0	1
18	Family navigators are assigned to families throughout their ICU stays to facilitate communication.	5		0	1
19	Spiritual support with a spiritual advisor or chaplain is offered to families.	3		0	1
Category 5: Operational and Environmental Issues					
20	Protocols have been implemented to ensure adequate and standardized use of sedation and analgesia during withdrawal of life support.	2		0	1
21	Nurses are involved in decision-making about goals of care and are trained to provide support for family members.	4		0	1
22	The hospital has implemented specific policies and programs to promote family-centered care in the ICU.	3		0	1
23	Noise reduction and environmental hygiene practices have been implemented, and private rooms are used.	3		0	1
24	Families are given a place to sleep.	3		0	1

Creation of Organizationlal Strategy for Improvement

Hospital Name

Name or Type of ICU:

Society of Critical Care Medicine
The Intensive Care Professionals

The table below has been auto-populated with recommended priorities for change based on your gap analysis responses in Step 1 of this tool. Please print out this worksheet and use it to facilitate discussion among members of your ICU family-centered care improvement group to determine your own ICU's priorities for quality improvement projects.

Item Rank	Item Score	Recommendation that are in potential need for attention, prioritized by Item Score	How does your ICU differ from the guidline recommendation?	What are the barriers to implementing the guideline recommendation?	Please re-rank the listed recommendations in order of priority for pursuing change
1	0	Family members of patients are offered open, flexible presence at the bedside.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Family members of patients are offered the option of participating in interdisciplinary team rounds.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Family members of patinets are offered the option of being present during resuscitation efforts, with a staff member assigned to support the family.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Family members of critically ill neonates are offered the option to learn how to assisit with the care of their loved ones.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Family education programs are included as part of clinical care.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Peer-to-peer support in the neonatal ICU has beed implemented.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Family members are provided information leaflets about the ICU setting.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	ICU diaries for family members are avilable and are encourged.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Validated decision support tools for family members are used when relevant validated tools exits.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	
1	0	Clinicians use a communication approach, such as the "VALUE" mnemonic, during family conferences for patients who have a poor prognosis.		[ ] High cost [ ] Lack of staff time [ ] Lack of staff knowledge [ ] Staff resistance to change [ ] Lack of authority to change practice	

Appendix 3.1 Data extraction form

Data Extraction Form

Reviewer: _____ Date: _____

General Information

Study ID (Surname of Lead Author, Year)	
Reference Citation	
Publication type *(e.g. full report, abstract, letter)*	

Study Eligibility

Study Characteristics	Eligibility criteria	Eligibility criteria met?			Location in text (page)
		Yes	No	Unclear	
Type of Study	Randomized Controlled Trial	☐	☐	☐	
	Quasi-randomized Controlled Trial	☐	☐	☐	
	Non-randomized Controlled Trial *(An experimental study with non-random allocation)*	☐	☐	☐	
	Interrupted Time Series *(observations at multiple points before and after an intervention)*	☐	☐	☐	
	Cohort study	☐	☐	☐	
	Case-control study	☐	☐	☐	
	Cross-sectional study	☐	☐	☐	
	Other design (specify):	☐	☐	☐	
Participants	Adults (age ≥ 18 years)	☐	☐	☐	
	Intensive/ critical care patients	☐	☐	☐	
Types of Intervention					
Types of Comparison					
Types of outcome measures	Long-term outcomes (Physical, Cognitive, Psychological, QOL, others)	☐	☐	☐	
	Outcomes measured at ≥ 3 months	☐	☐	☐	

INCLUDE	EXCLUDE

Reason for exclusion	

Notes:

DO NOT PROCEED IF STUDY EXCLUDED FROM REVIEW

Characteristics of included studies

Methods

	Descriptions as stated		Location in text
Aim of study *(e.g. efficacy, equivalence, pragmatic)*			
Design *(e.g. parallel, crossover, non-RCT)*			
Start date			
End date			
Duration of participation *(from recruitment to last follow-up)*			
Ethical approval needed/ obtained for study	Yes No Unclear		
Notes:			

Participants

	Description		Location in text
Population description *(from which study participants are drawn)*			
Setting *(including location and social context)*			
Inclusion criteria			
Exclusion criteria			
Method of recruitment of participants *(e.g. phone, mail, clinic patients)*			
Informed consent obtained	Yes No Unclear		
Total no. randomized *(or total pop. at start of study for NRCTs)a*			
Clusters *(if applicable, no., type, no. people per cluster)*			
Withdrawals and exclusions			
Age (years)			
Sex			
Race/Ethnicity			
BMI			
Socioeconomic status			

Severity of Illness on admission	APACHE II, III, IV		
	SAPS II, III		
	SOFA		
	MODS		
	GCS		
	ISS		
	Other:		
Charlson comorbidity index			
Main causes/type of admissions			
ICUlength of stay (days)			
Hospital length of stay (days)			
Mechanical ventilation, N (%)			
Duration of mechanical ventilation (days)			
Delirium in hospital, N (%)			
Duration of delirium (days)			
Coma, N (%)			
Duration of coma (days)			
Sepsis in the ICU, N (%)			
Duration of sepsis			
Sedative use, N (%)			
Duration of sedative use (days)			
Type of sedative			
Analgesic use, N (%)			
Duration of analgesic use (days)			
Type of analgesic			
In-hospital mortality, N (%)			
One-year mortality, N (%)			
Physical function at baseline	ADL		
	Katz ADL		
	FAQ		
	PFIT		
	Barthel Index		
	Other:		
Cognitive status at baseline	MoCA		
	IQCODE		
	Other:		
Psychological status at baseline	IES		
	HADS		
	Other:		
Pre-admission QOL score	Physiologic functions subscale score		

	Normal daily activities subscale score		
	Emotional state subscale score		
Notes:			

Interventions

Intervention:	Group 1	Group 2	Group 3
No. randomised to group *(specify whether no. people or clusters)*			
Duration of intervention			
Timing *(e.g. frequency, duration of each episode)*			
Delivery			
Co-interventions			
Integrity of delivery			
Compliance			

Outcomes

Outcome 1:

	Description as stated in report/paper		Location in text
Outcome name			
Time points measured *(specify whether from start or end of intervention)*			
Time points reported			
Outcome definition *(with diagnostic criteria if relevant)*			
Person measuring/ reporting			
Unit of measurement *(if relevant)*			
Scales: upper and lower limits *(indicate whether high or low score is good)*			
Is outcome/tool validated?	**Yes No Unclear**		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*			
Assumed risk estimate *(e.g. baseline or population risk noted in Background)*			

Power *(e.g. power & sample size calculation, level of power achieved)*		
Notes:		

Outcome 2:

	Description as stated in report/paper		Location in text
Outcome name			
Time points measured *(specify whether from start or end of intervention)*			
Time points reported			
Outcome definition *(with diagnostic criteria if relevant)*			
Person measuring/ reporting			
Unit of measurement *(if relevant)*			
Scales: upper and lower limits *(indicate whether high or low score is good)*			
Is outcome/tool validated?	**Yes No Unclear**		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*			
Assumed risk estimate *(e.g. baseline or population risk noted in Background)*			
Power *(e.g. power & sample size calculation, level of power achieved)*			
Notes:			

Outcome 3:

	Description as stated in report/paper	Location in text
Outcome name		
Time points measured *(specify whether from start or end of intervention)*		
Time points reported		
Outcome definition *(with diagnostic criteria if relevant)*		
Person measuring/ reporting		

Unit of measurement *(if relevant)*			
Scales: upper and lower limits *(indicate whether high or low score is good)*			
Is outcome/tool validated?	**Yes No Unclear**		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*			
Assumed risk estimate *(e.g. baseline or population risk noted in Background)*			
Power *(e.g. power & sample size calculation, level of power achieved)*			
Notes:			

Outcome 4:

	Description as stated in report/paper		Location in text
Outcome name			
Time points measured *(specify whether from start or end of intervention)*			
Time points reported			
Outcome definition *(with diagnostic criteria if relevant)*			
Person measuring/ reporting			
Unit of measurement *(if relevant)*			
Scales: upper and lower limits *(indicate whether high or low score is good)*			
Is outcome/tool validated?	**Yes No Unclear**		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*			
Assumed risk estimate *(e.g. baseline or population risk noted in Background)*			
Power *(e.g. power & sample size calculation, level of power achieved)*			
Notes:			

Other

Study funding sources (including role of funders)		
Possible conflicts of interest (for study authors)		
	Notes:	

Data and analysis

For RCT/CCT Dichotomous outcome

	Description as stated in report/paper				Location in text
Comparison					
Outcome					
Subgroup					
Time point *(specify from start or end of intervention)*					
Results	Intervention		Comparison		
	No. with event	Total in group	No. with event	Total in group	
Any other results reported *(e.g. odds ratio, risk difference, CI or P value)*					
No. missing participants					
Reasons missing					
No. participants moved from other group					
Reasons moved					
Unit of analysis *(by individuals, cluster/groups or body parts)*					
Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*					
Reanalysis required? *(specify, e.g. correlation adjustment)*	**Yes No Unclear**				
Reanalysis possible?	**Yes No Unclear**				
Reanalysed results					

Notes:

For RCT/CCT ***Continuous outcome***

	Description as stated in report/paper						Location in text
Comparison							
Outcome							
Subgroup							
Time point *(specify from start or end of intervention)*							
Post-intervention or change from baseline?							
Results	Intervention			Comparison			
	Mean	SD *(or other variance, specify)*	No. participant	Mean	SD *(or other variance, specify)*	No. participants	
Any other results reported *(e.g. mean difference, CI, P value)*							
No. missing participants							
Reasons missing							
No. participants moved from other group							
Reasons moved							
Unit of analysis *(individuals, cluster/ groups or body parts)*							
Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*							
Reanalysis required? *(specify)*	**Yes No Unclear**						
Reanalysis possible?	**Yes No Unclear**						
Reanalysed results							
Notes:							

For Controlled Before-and-After study (CBA)

	Description as stated in report/paper				Location in text
Comparison					
Outcome					
Subgroup					
Time point *(specify from start or end of intervention)*					
Post-intervention or change from baseline?					
No. participants	Intervention		Control		
Results	Intervention result	SE *(or other variance, specify)*	Control result	SE *(or other variance, specify)*	
	Overall results		SE *(or other variance, specify)*		
Any other results reported					
No. missing participants					
Reasons missing					
No. participants moved from other group					
Reasons moved					
Unit of analysis *(individuals, cluster/ groups or body parts)*					
Statistical methods used and appropriateness of these					
Reanalysis required? *(specify)*	**Yes No Unclear**				
Reanalysis possible?	**Yes No Unclear**				
Reanalysed results					
Notes:					

Appendix 4.1. Almoosa IRB Approval_ARC_21.07.03

ALMOOSA ACADEMIC AFFAIRS

مستشفى الموسى التخصصي
Almoosa Specialist Hospital

Date:	IRB log No:	Category of Approval:	Affiliation:
08/07/2021	ARC-21.07.03	Expedite	Almoosa Specialist Hospital

Study Title:
Assessing Prevalence and Predictors of Long-term Outcomes and HealthRelated Quality of Life in post-ICU patients in Saudi Arabia (PrevaILS study).

PI
Hera Tashjian
Co-PI
Dr. Samer Qarah **Anne Marie Rafferty** **Dr. Abbas Al Mutair**

Dear Hera Tashjian,

This is to clarify that the IRB has reviewed and approved the study titled in this letter.
Terms and conditions of approval:

- Abide by the rules and regulations of the Government of Saudi Arabia, NCBE.
- The approval of the study is valid for ***One Year***.
- To conduct research as per the approved documents and no amendments maybe made prior to further approval by the IRB.
- The principle investigator is responsible for the document retention and storage for a period of ***3 years*** from study completion.
- The Principle Investigator is expected to submit a Progress Report every ***6 months***.
- At the end of the study, the Principle Investigator must submit Final Report including a conclusion abstract and the manuscript intended for publication.

On behalf of the IRB members, we thank you for submitting your study and wish you the best of luck as you move forward with your research.

Sincerely Yours,

Dr. Abbas S. Al Mutair # 10682
Al Mocsa Research Director
IRB Chairperson

Dr Abbas Al Mutair, Ph.D
Chairman of IRB

National Registration Number with NCBE-KACST, KSA: (H-05-HS-100)

Appendix 4.2. King's ethics approval_HR.1920.14821

Research Ethics
Office

Franklin Wilkins Building
5.9 Waterloo Bridge Wing
Waterloo Road
London SE1 9NH
Telephone 020 7848 4020/4070/4077
reo@kcl.ac.uk

KING'S College LONDON

Hera Tashjian

4 December 2019

Dear Hera,

Study Title: Assessing Prevalence and Predictors of Long-term Outcomes and Health-Related Quality of Life in post-ICU patients in Lebanon (PrevalL study)

Study Reference:HR-19/20-14821

I am pleased to inform you that full approval for your project has been granted by the PNM Research Ethics Subcommittee .

For your information, ethical approval has been granted for 3 years from 4 December 2019. If you need approval beyond this point, you will need to apply for an extension at least two weeks before this. You will be required to explain the reasons for the extension. However, you will not need to submit a full re-application unless the protocol has changed.

Ethical approval is required to cover the data-collection phase of the study. This will be until the date specified in this letter. However, you do not need ethical approval to cover subsequent data analysis or publication of the results. For secondary data-analysis, ethical approval is applicable to the data that is sensitive or identifies participants.

Please ensure that you follow the guidelines for good research practice as laid out in UKRIO's Code of Practice for research: https://www.kcl.ac.uk/research/support/integrity-good-conduct/index.aspx

Please note you are required to adhere to all research data/records management and storage procedures agreed to as part of your application. This will be expected even after the completion of the study.

If you do not start the project within three months of this letter, please contact the Research Ethics Office.

Please note that you will be required to obtain approval to modify the study. This also encompasses extensions to periods of approval. Please refer to the URL below for further guidance about the process:

https://internal.kcl.ac.uk/innovation/research/ethics/applications/modifications.aspx

Please would you also note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

If you have any query about any aspect of this ethical approval, please contact the Research Ethics Office:

(https://internal.kcl.ac.uk/innovation/research/ethics/contact.aspx)

We wish you every success with this work.

Yours sincerely,

Mr James Patterson
Senior Research Ethics Officer

For and on behalf of the PNM Research Ethics Subcommittee

Appendix 4.3 Informed Consent and Information Sheet

Informed Consent Form to Participate in a Clinical Research Study	
نموذج موافقة للمشاركة في دراسة بحثية سريرية	
Study Title: Assessing Prevalence and Predictors of Long-term Outcomes and Health-Related Quality of Life in post-ICU patients in Saudi Arabia.	
عنوان الدراسة : تقييم انتشار ومتنبآت النتائج الطويلة الأمد وجودة الحياة المتعلقة بالصحة في الناجين من وحدة العناية المركزة في السعودية (PrevalS Study)	
Study Sponsor: AlMoosa Specialist Hospital	**راعي الدراسة:** مستشفى الموسى التخصصي
Chief Investigator: Hera Tashjian	**الباحث الرئيسي:** هيرا طاشجيان
You are invited to participate in the study because you: are intensive care unit (ICU) patient, or admitted in ICU before, and this study is to explore long term outcomes of ICU patients.	**أنت مدعو للمشاركة في الدراسة لأنك:** مريض في العناية المركزة ، أو كنت ترقد فيها من قبل ، وهذه الدراسة لاكتشاف النتائج الطويلة الأمد لمرضى العناية المركزة.
Aims of the study: This research study aims to assess the long-term outcomes and quality of life of intensive care unit (ICU) patients in Saudi Arabia by following them up and using some questionnaires.	**أهداف الدراسة:** هذه الدراسة البحثية تهدف لتقييم النتائج الطويلة الأمد وجودة الحياة المتعلقة بالصحة في المرضى الناجين من وحدة العناية المركزة من خلال متابعتهم واستخدام بعض الاستبيانات.
Number of expected participants: 140	**عدد الأشخاص المتوقع مشاركتهم في الدراسة: ١٤٠**
Participation is voluntary: Your participation is voluntary. Please take time to read the information carefully before you decide whether you want to take part in this study or not. Feel free to ask any questions that you may have or need clarification about what is stated in this form and the study as a whole.	**المشاركة في الدراسة مشاركة تطوعية/اختيارية:** مشاركتك طوعية. يرجى أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بعناية قبل أن تقرر(ي) ما إذا كنت تريد(ين) المشاركة في الدراسة أم لا. بإمكانك السؤال ، طلب المزيد من المعلومات أو طلب التوضيح عن أي شيء مذكور في هذه الاستمارة أو عن الدراسة ككُل .
Study Procedures: To ensure your privacy, your recruitment will be done through a two-step approach. First, your treating physician or another member of the medical team responsible for your care will ask you about taking part in the study. If you are interested in participating in the study, the research team will then approach you with further information about the study and to obtain your consent. In some instances, you might be in a position, where you are on a medication that make you asleep and have a breathing tube at the time of recruitment. In this situation, written informed consent will be obtained from your next-of-kin or your legal guardian. If there is more than one next-of-kin or legal guardian, we will ensure that all agree to your participation.	**إجراءات الدراسة:** للحفاظ على خصوصيتك، سيتم طلب المشاركة من خلال خطوتين. الخطوة الأولى: سيتم سؤالك للمشاركة في الدراسة من خلال طبيبك المعالج أو أحد أعضاء الفريق المسؤول عن علاجك. الخطوة الثانية: إن كنت مهتم(ة) في المشاركة بالدراسة، سيتواصل معك فريق البحث لتقديم معلومات البحث المفصلة ولأخذ الموافقة. في بعض الأحيان، قد تكون تحت تأثير أدوية مهدّئة أوعلى أنبوبة تنفس اصطناعي مِما قد يمنعك من الإمضاء على استمارة الموافقة. في هذه الحالة، سيتم الطلب على موافقة إشتراكك من قبل أقرب أقربائك أو وكيلك القانوني. إن كان هناك أكثر من قريب أو وكيل قانوني واحد، سيتم الطلب على موافقة إشتراكك من جميع المعنيين بالإجماع والحصول على إمضائهم. ما إن تصبح/ين قادر/ة على مراجعة الاستمارة ، ستُؤخذ مُوافقتك.

Once you are able to review the form, your consent will also be obtained.

Adult patients (18 years of age or more) who have spent 48 hours or more in the ICUs at the hospital are eligible to participate.

You will be followed up over six months. While in the hospital, some information will be collected from your medical records. At discharge from the ICU, you will be assessed by five questionnaires, described below. After you are discharged from the hospital, you will receive a phone call from our team in order to set up a suitable time for a follow up assessment. There will be two home/place of residence visits. Each visit may last for an hour approximately. You will be given time to rest in between completing questionnaires and for any questions you might have.

By signing this consent form, you agree to the following research procedures. If you do not wish to answer any of the questions that are sensitive or private, this will be considered and noted.

The following assessment tools will be used:

- **Activities of Daily Living, Arabic version (ADL – 2 minutes):** This is a short questionnaire that assesses your physical or functional ability in 6 areas: bathing, dressing, going to the toilet, transferring, ability to control movements of the bowels and bladder and feeding. Your physical function will be assessed at baseline, ICU discharge and at 3 and 6 months follow up.
- **Arabic Version of the Informant Questionnaire on Cognitive Decline for the Elderly (A-IQCODE – 10 minutes):** This questionnaire is used to assess any psychological conditions such as dementia.
- **Montreal Cognitive Assessment, Arabic version (MoCA – 11 minutes):** This is a questionnaire that focuses on your memory and attention. It will be used at ICU discharge, and at 3 and 6 months follow up.
- **Hospital Anxiety and Depression Scale, Arabic version (HADS – 6 minutes):** This is a self-rating scale used to ask if you have any depression or anxiety symptoms and will be used at ICU discharge, and at 3 and 6 months follow up.

المرضى البالغين (١٨ سنة أو أكثر) الذين أمضوا ٤٨ ساعة أو أكثر في أحد أقسام العناية المركزة الثلاثة في المستشفى مؤهلون للمشاركة في الدراسة.

سيتم متابعتك على مدى ٦ أشهر. خلال فترة بقائك في المستشفى، سيتم جمع بعض المعلومات من السجل الطبي الخاص بك. عند خروجك من العناية المركزة، سيتم تقييمك من خلال ٥ استبيانات موصوفة أدناه. بعد مغادرتك المستشفى، سوف يتصّل بك فريقنا من أجل تحديد موعد مناسب لفحص المتابعة. المتابعة ستكون من خلال زيارتين إلى منزلك/مكان سكنك. كل زيارة قد تدوم ساعة تقريباً. سوف تحصل على وقت للراحة ما بين إتمام الاستبيانات ولأية أسئلة قد تكون لديك.

عند توقيع استمارة الموافقة ، إنك توافق(ين) على الإجراءات البحثية التالية. إن لم ترغب/ي بالإجابة على بعض الأسئلة التي تُعتبر حساسة أو خاصة ، سيتم أخذ ذلك بعين الاعتبار وتدوينه.

سيتم استخدام أدوات التقييم (الاستبيانات) التالية:

- **نشاطات الحياة اليومية، النسخة العربية (ADL – دقيقتين):** هذه أداة قصيرة لتقييم قدرتك الجسدية أو الوظيفية في ٦ مجالات: الاستحمام، ارتداء الملابس، الذهاب إلى الحمام، إمكانية التنقل، القدرة على التحكم بعملية التبول والتغوط ، و التغذية. سيتم تقييم وظيفتك الجسدية في بداية الدراسة ، عند خروجك من العناية المركزة، وأثناء أشهر المتابعة (خلال ٣ إلى ٦ أشهر).
- **استبيان مخبر عن التدهور الإدراكي لدى المسنين، النسخة العربية (A-IQCODE – ١٠ دقائق):** هذا الاستبيان يُستخدم لتقييم أي مشاكل نفسية مثل التدهور العقلي أو الخرف .
- **التقييم المعرفي المتبع في مونتريال، النسخة العربية (MoCA – ١١ دقائق):** هذا الاستبيان يُركز على الذاكرة والانتباه. سوف يُستخدم عند خروجك من العناية المركزة ، وأثناء أشهر المتابعة (خلال ٣ إلى ٦ أشهر).
- **مقياس القلق والاكتآب في المستشفى، النسخة العربية (HADS – ٦ دقائق):** هذا مقياس تقييم ذاتي للسؤال عن وجود أي أعراض قلق أو اكتئاب لدى المريض. سوف يُستخدم عند خروجك من العناية المركزة ، وأثناء أشهر المتابعة (خلال ٣ إلى ٦ أشهر).
- **قائمة اضطراب ما بعد الصدمة، النسخة المدنية ، النسخة العربية (PCL-C – ٥ دقائق):** هذا مقياس تقييم

• **PTSD Checklist – Civilian Version, Arabic version (PCL-C – 5 minutes):** This is a self-report rating scale for Post-Traumatic Stress Disorder, which you will be assessed for at ICU discharge, and at 3 and 6 months follow up. • **Short Form 36-Item Health Survey, Arabic version (SF-36 – 12 minutes):** This is a questionnaire asking about your quality of life and will be assessed at ICU discharge, and at 3 and 6 months follow up.	ذاتي لكشف اضطراب ما بعد الصدمة. سوف يُستخدم عند خروجك من العناية المركزة ، وأثناء أشهر المتابعة (خلال ٣ إلى ٦ أشهر). • **استبيان االصحة ذو 36 عنصر ، النسخة العربية (SF-36 – ١٢ دقائق):** هذا الاستبيان يهدف للسؤال عن جودة الحياة . سوف يُستخدم عند خروجك من العناية المركزة ، وأثناء أشهر المتابعة (خلال ٣ إلى ٦ أشهر).
Which part of the study is experimental: None	**ما هو الإجراء التجريبي في الدراسة: لا يوجد**
Expected benefits: If there are any findings that we think are important to your health, we will let you know. In the case where we think you have depression or anxiety or distress, with your permission, a referral will be made to your treating physician. You will be asked to sign a referral form. The referral will be on your own expense. In addition, information gained from your participation in this study may be important in determining the long-term outcomes of ICU patients in the Saudi Arabia population. Results of this study may also help future ICU patients and families be better prepared for the care needed after discharge from ICU by gaining pre-discharge information and support.	**الفوائد المتوقعة:** سيتم إخبار جميع المشاركين بالنتائج السريرية المهمة. اذا كنت تريد معرفة نتائج تقييماتك. في حال اكتشاف اكتئاب ، قلق ، أو اضطراب ، ستتم إحالتك الى الطبيب المعالج الخاص بك، وسيُطلب منك توقيع نموذج الإحالة. ستكون الإحالة على نفقتك الخاصة. بالاضافة ، قد تكون المعلومات المكتسبة من مشاركتك في هذه الدراسة مهمة في تحديد النتائج الطويلة الأمد لمرضى العناية المركزة في السعودية. نتائج هذه الدراسة قد تساعد مرضى العناية المركزة وعائلاتهم على الاستعداد بشكل أفضل لمرحلة الرعاية بعد مغادرة العناية المركزة من خلال الحصول على المعلومات والدعم قبل الخروج.
Expected risks: There are no more than minimal risks to participating in this study. Minor distress or fatigue might be caused by some of the tests. These tests are widely used in clinical practice. If you do not wish to complete the tests, ample time for rest will be provided. In case you experience tiredness or distress, you are unable to continue and you would like to end the session, please inform the researcher. We will stop immediately and you will be allowed to have time to rest and given the option to resume the session or not.	**المخاطر المتوقعة:** ليس هناك أكثر من الحد الأدنى من المخاطر الناجمة عن المشاركة في الدراسة. قد تتسبب بعض الاختبارات بتعب ذهني أو ضيق نفسي طفيف. هذه الاختبارات تُستخدم على نطاق واسع في الممارسة السريرية. إن لم ترغب بإكمال الاختبار ، ستُعطى الوقت الكافي للاستراحة. في حال أحسست بإجهاد أو تعب ولم تعد لديك القدرة على إكمال الجلسة ، يرجى إبلاغ الباحث. سنتوقف على الفور وسيسمح لك ببعض الوقت للراحة إلى حانب تخييرك بين متابعة الجلسة أو التوقّف.
Freedom of withdrawal: You have the right to withdraw your consent or discontinue participation at any time for any reason. Your decision to withdraw will not involve any penalty or loss of benefits to which you are entitled. The investigator might also choose to end your participation at any time. Discontinuing participation in no way affects your relationship with AlMoosa Specialist Hospital.	**حرية الانسحاب:** لديك الحق في سحب موافقتك أو وقف مشاركتك في أي وقت ولأي سبب. لن يتضمن قرارك بالانسحاب أي عقوبة أو خسارة في الفوائد التي أنت مؤهل لها. قد يختار المحقق أيضًا إنهاء مشاركتك في أي وقت. الرفض أو الانسحاب من الدراسة لن يؤثر بأي شكل من الأشكال على علاقتك مع مستشفى الموسى التخصصي.
Study revision and approval:	**مراجعة الدراسة واعتمادها:**

This study was revised and approved by Almoosa IRB (ARC-21.07.03) And submitted to SFDA (if any)	لقد تمت مراجعة واعتماد هذه الدراسة من قبل لجنة الأخلاقيات التابعة لمجموعة الموسى (ARC-21.07.03) وتمت تقديمها إلى الهيئة السعودية للغذاء والدواء (قرار الهيئة ان وجد)
How information and results will be used: The result of this study will be published in a scientific journal to enable post-ICU patients to benefit from these results.	**كيفية استخدام نتائج ومعلومات الدراسة؟** سيتم نشر نتائج هذه الدراسة في مجلة علمية لإتاحة الفرصة لجميع مرضى العناية المركزة السابقين للاستفادة من هذه النتائج.
Confidentiality: If you give consent to participate in this research study, you will be giving us permission to access your medical records. All information will be kept confidential. We will not have any documented data of any participant who does not meet the study inclusion criteria and/or refuses to take part in the study. Only participants who meet the inclusion criteria and agree to participate in the study will be assigned an identification number when they are enrolled. The patient names will be documented on all consent forms. All documents with patient names will be stored in the Principal Investigator's office in a locked cabinet. The key will only be available to the Principal Investigator. All other data collection forms, including the above-mentioned questionnaires, will be made anonymous and only have the participant identification number. To secure the confidentiality of your responses, your name and other identifying information will never be attached to your answers. All research data will be kept in a password protected computer that is kept secure. Data access is limited to the Principal Investigator and researchers working directly on this project. Study records will be monitored and may be audited by the Institutional Review Board without violating confidentiality. All data will be destroyed responsibly after 10 years. Your privacy will be maintained in all published and written data resulting from this study. Your name or other identifying information will not be used in our reports or published papers.	**سرية المعلومات**: في حال موافقتك على المشاركة في هذه الدراسة البحثية، سوف نحصل على إذنك للاطلاع على سجلاتك الطبية. سيتم الحفاظ على سرية كل المعلومات. لن يكون لدينا اي اسم موثق لأي مشارك(ة) لا يستوفي(تستوفي) معايير المشاركة و/أو يرفض(ترفض) المشاركة في الدراسة. سيتم تعيين رقم تعريف خاص فقط للمشاركين الذين يستوفون معايير المشاركة ويوافقون على المشاركة في الدراسة. سيتم وضع أسماء جميع المرضى على استمارة الموافقة . ستبقى جميع المستندات التي تحمل أسماء المشاركين في مكتب الباحثة أو المحققة الرئيسية في خزانة مغلقة. سيبقى مفتاح الخزانة مع الباحث الرئيسي فقط. جميع المستندات لجمع البيانات، بما في ذلك أدوات التقييم أو الاستبيانات المذكورة أعلاه، ستكون مجهولة الاسم وسيكون عليها رقم التعريف الخاص بالمشاركين فقط. لحفظ خصوصية اجاباتك ، لن يتم إرفاق اسمك أو معلومات التعريفية معها. سيتم حفظ البينات على حاسوب المحققة الرئيسية الذي يتم حمايته باسم مستخدم وكلمة مرور محمية. يقتصر الوصول إلى البيانات على الباحث الرئيسي والباحثين الذين يعملون مباشرة على هذا المشروع. سيتم مراقبة سجلات الدراسة وقد يتم تدقيقها من قبل مجلس المراجعة المؤسسية دون انتهاك السرية. سيتم تدمير جميع البيانات بمسؤولية بعد ١٠ سنوات. سيتم الحفاظ على خصوصيتك في جميع البيانات المنشورة والمكتوبة الناتجة عن هذه الدراسة. لن يتم استخدام اسمك أو معلومات التعريف الأخرى في تقاريرنا أو أوراقنا المنشورة.
What to do if a side effect or something wrong happens: There are no anticipated adverse events associated with this research study. In case of any medical issue that arises during the study period, there will be no	**الإجراء المتخذ عند حدوث أي مكروه أو عرض جانبي**: لا توجد أحداث سلبية متوقعة مرتبطة بهذه الدراسة البحثية .في حال وجود أي مشكلة طبية تنشأ خلال فترة الدراسة ، لن يكون هناك تعويض لتغطية نفقاتها.

compensation to cover its expenses.	
For further information, you can contact: Hera Tashjian at +966559296154	**لمزيد من المعلومات يمكنك التواصل مع** : هيرا طاشجيان ، على الرقم التالي: 966559296154+

A Statement of Consent and Acknowledgement I hereby confirm that all aspects related to the study have been explained to me including aims and procedures and that the study (does/does not) include any experimental therapies and that my participation is voluntary with no extra-expenses and there (is/is no) payment offered to me for participation. I have been given a copy of data related to the study and a copy from this statement**.**	**بيان موافقة و إقرار** أقر أنا الموقع أدناه أنه قد تم شرح كل ما يتعلق بالدراسة لي شاملا أهدافها و إجراءاتها وأنها(تتضمن/ لا تتضمن) أي علاجات تجريبية وأن مشاركتي تطوعية/اختيارية وأنه لن تترتب على المشاركة أية نفقات إضافية علي كما أنه (يوجد/ لا يوجد) مقابل مادي للمشاركة. وقد تم إعطائي نسخة من المعلومات المتعلقة بالدراسة ونسخة من هذا الإقرار.
Signature of the participant:	**توقيع المشارك:**
Date of The Consent *(To be personally dated by the participant):*	**تاريخ الموافقة** (يكتب المشلرك التاريخ بنفسه) :
Name of the participant's legal guardian and relation (if applicable):	**اسم الولي القانوني علي المريض و صلة القرابة** (إن وجد)*:*
Signature of the participant's legal guardian (if applicable):	**توقيع الوصي القانوني علي المريض** (إن وجد):
Date of the Consent *(personally dated by the participant's guardian if applicable):*	**تاريخ الموافقة** (يكتب بواسطة الوصي القانوني على المريض إن وجد):
Name of the Principal Investigator *(or delegate):*	**اسم الباحث الرئيسي** (أو من ينوب عنه)*:*
Signature of the Principal Investigator *(or delegate):*	**توقيع الباحث الرئيسي** (أو من ينوب عنه)*:*
Date of the Consent *(To be personally dated by the Principal Investigator or delegate):*	**تاريخ الموافقة** (يكتب التاريخ بمعرفة الباحث الرئيسي أومن ينوب عنه)*:*
Name of the Witness *(if applicable):*	**اسم الشاهد** (إن وجد)*:*
Signature of the Witness *(if applicable):*	**توقيع الشاهد** (إن وجد)*:*
Date of the Consent *(To be personally dated by the Witness):*	**تاريخ الموافقة** (يكتب التاريخ بواسطة الشاهد)*:*

Appendix 4.4 Information Sheet for Family

INFORMATION SHEET FOR PARTICIPANTS

Version Number
10/11/2019

Ethical Clearance Reference Number: HR-19/20-14821

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of study

Assessing Prevalence and Predictors of Long-Term Outcomes and Health-Related Quality of Life in Post-ICU Patients in Saudi Arabia

Invitation Paragraph

I would like to invite you to participate in this research project which forms part of my doctoral studies in nursing research at King's College London. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. You have time until your discharge to decide if you would wish to participate. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

This is a research study about the long-term outcomes and quality of life of intensive care unit (ICU) patients in Saudi Arabia. Some patients who have been cared for in an ICU may experience long-lasting consequences that affect their quality of life, such as physical, mental, and psychological disabilities. Physically, problems may happen in mobility, ability to take care of self, and falls. In addition, problems effecting memory, problem solving abilities, and attention might occur. Problems effecting the mental well-being of patients may appear in the form of anxiety, depression, nightmares, and difficulty falling asleep.
The purpose of this study is to assess the above-mentioned long-term outcomes at 3 months after discharge from hospital by using some questionnaires.

Why have I been invited to take part?

You are being invited to participate in this study because you are an adult patient who has spent 48 hours or more in a general ICU at Almoosa Specialist Hospital.

What will happen if I take part?

If you agree to take part, some information will be collected from your medical records while you are still in the ICU. At discharge from the ICU, you will be assessed by questionnaires, described below. After you are discharged from the hospital, you will receive a phone call from our team in order to set up a suitable time for a follow up assessment. This will be done at 3 months after your discharge from the ICU. There will be one visit to your home or place of residence after 3 months of your discharge from the ICU. The visit may take approximately one hour. You will be given time to rest in between completing questionnaires and for any questions you may have.

During your ICU stay:

The following information will be gathered while you are still in the ICU:

1. *Demographic information*: age; gender; height and weight; educational level; socio-economic status; admission diagnosis; previous illnesses; medications used before admission; type of admission; length of stay in ICU and hospital. This information will be gathered from your medical file.

2. *Severity of illness, using the APACHE II*: this tool measures the severity of your illness when you were admitted to the ICU. This information will be gathered from your medical file.

3. *Pre-existing mental difficulties, using the Arabic Version of the Informant Questionnaire on Cognitive Decline for the Elderly (A-IQCODE):* This is a questionnaire that will be used to assess for any mental conditions, such as memory problems, that existed before you were admitted to the ICU. This questionnaire will take around 10 minutes. In the case where you are on a medication that makes you sleep and/or you have a breathing tube, this information will be gathered from your next-of-kin or legal guardian.

4. *Activities of Daily Living (ADL), using the Arabic version of ADL:* This is a short questionnaire that assesses your physical ability in 6 areas: bathing, dressing, going to the toilet, transferring, ability to control movements of the bowels and bladder, and feeding. This questionnaire will take around 2 minutes. In the case where you are on a medication that makes you sleep and/or you have a breathing tube, this information will be gathered from your next-of-kin or legal guardian.

5. *Sedation level, using the Richmond Agitation-Sedation Scale (RASS):* this is a commonly used tool to assess the level of sedation in ICU patients. This test will be done as part of your routine care and no questioning or time is needed from you.

6. *Confusion, using the Confusion Assessment Method for ICU (CAM-ICU):* this is also a commonly used tool in the ICU to assess presence of confusion. This test will also be done as part of your routine care.

Follow-up at ICU discharge and 3 months:

The following information will be gathered at discharge and during our visit to you at 3 months after ICU discharge:

1. *Activities of Daily Living (ADL), Arabic version:* as described above.

2. *Mental abilities, using the Montreal Cognitive Assessment, Arabic version (MoCA):* This questionnaire asks about your memory and attention. It will take around 11 minutes.

3. *Psychological status, using Hospital Anxiety and Depression Scale, Arabic version (HADS):* This is a self-rating scale used to ask if you have any depression or anxiety symptoms and will take around 6 minutes.

4. *Post-traumatic stress symptoms, using PTSD Checklist – Civilian, Arabic version (PCL-C):* This is a self-report rating scale for Post-Traumatic Stress Disorder, which will take around 5 minutes.

5. *Quality of life, using the 36-Item Short Form Health Survey, Arabic version (SF-36):* This is a questionnaire asking about your health-related quality of life and will take around 12 minutes.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing

not to take part will not disadvantage you in anyway. If you choose to take part you will be asked to provide your consent. To do this you will be asked to indicate that you have read and understand the information provided and that you consent to your anonymous data being used for the purposes explained.

You are free to withdraw at any point during completion of the survey, without having to give a reason. Withdrawing from the study will not affect you in any way. Once you submit the survey, it will no longer be possible to withdraw from the study because the data will be fully anonymous. Please do not include any personal identifiable information in your responses.

Your decision to withdraw will not involve any penalty or loss of benefits to which you are entitled. Discontinuing participation in no way affects your relationship with Almoosa Specialist Hospital.

What are the possible risks of taking part?

There are no more than minimal risks to participating in this study. Minor distress or fatigue might be caused by some of the tests. If you get tired during assessments, ample time for rest will be provided.
In case you experience tiredness or distress, and you are unable to continue, and you would like to end the session, please inform the researcher. We will stop immediately, and you will be allowed time to rest and given the option to resume the session at a later time.
You are not required to pay for any of the tests or assessments that will be performed.

What are the possible benefits of taking part?

If there are any findings that we think are important to your health, we will let you know. In the case where we think you have depression, anxiety, or distress, with your permission, a referral will be made to your treating physician so you can get the proper help. You will be asked to sign the referral form. The referral will be on your own expense.

In addition, information gained from your participation in this study may be important in determining the long-term outcomes of ICU patients in the Saudi population. Results of this study may help ICU physicians and nurses better understand what happens to patients on the long run. Therefore, the study might help future ICU patients and families be better prepared for the care needed after discharge from ICU by receiving pre-discharge information and support.

Data handling and confidentiality

If you give consent to participate in this research study, you will be giving us permission to access your medical records. All information will be kept confidential. We will not have any documented data of any participant who does not meet the study inclusion criteria and/or refuses to take part in the study. Only participants who meet the inclusion criteria and agree to participate in the study will be assigned an identification number when they are enrolled.

The patients' names will be documented on all consent forms. All documents with patient names will be stored in the Principal Investigator's office in a locked cabinet. The key will only be available to the Principal Investigator.

All other data collection forms, including the above-mentioned questionnaires, will be made anonymous and only have the participant identification number. To secure the confidentiality of your responses, your name and other identifying information will never be attached to your answers.

All research data will be kept in a password protected computer that is kept secure. Data access is limited to the Principal Investigator and researchers working directly on this project.

Study records will be monitored and may be audited by the Institutional Review Board without violating confidentiality.

All data will be destroyed responsibly after 10 years. Your privacy will be maintained in all published and written data resulting from this study. Your name or other identifying information will not be used in our reports or published papers.

The data controller for this project will be King's College London (KCL). Research is a task that the University carries out in the public interest. Your data will be processed in accordance with the standards set by the General Data Protection Regulation 2016 (GDPR).

What will happen to the results of the study?

The results of the study will be summarised in the principal investigator's research dissertation in her doctoral studies in nursing research. The research findings will be published in a professional journal. Your privacy will be maintained in all published and written data resulting from this study. Your name or other identifying information will not be used in our reports or published papers.

Who should I contact for further information?

If you have any questions or require more information about this study, please contact me using the following contact details:

Hera Tashjian,
Almoosa Specialist Hospital, Dhahran Rd, Al Mubarraz 36342; Tel: 966559296154; Email: CNO@almoosahospital.com.sa
Or
King's College London, Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care, Tel: 0207 848 3201, Email: hera.tashjian@kcl.ac.uk

What if I have further questions, or if something goes wrong?

If this study has harmed you in any way or if you wish to make a complaint about the conduct of the study you can contact:

Almoosa Specialist Hospital
Dhahran Rd, Al Mubarraz 36342
Saudi Arabia
Tel: 013 536 9999
Email: research.center@almoosahospital.com.sa

- King's College London, Dr Geraldine Lee
  Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care,
  King's College London, Room 2.16, James Clerk Maxwell Building,
  57 Waterloo Road,
  LONDON
  SE1 8WA
  Tel: 0207 848 3201

Email: gerry.lee@kcl.ac.uk

Thank you for reading this information sheet and for considering taking part in this research.

Appendix 4.5 Demographic data sheet

Demographic data

Study ID number: ----------

Date: ----------

1. Date of birth: DD/MM/YYYY
2. Gender: □ Male □ Female
3. BMI [weight (kg)]:---------- Height: ---------- Weight: ----------
   [Height (m)]²
4. Educational level:
   □ Never attended school or only went to preschool
   □ Elementary to middle school education (1st grade to 8th grade)
   □ Middle school to secondary school education (9th grade to 11th grade)
   □ Secondary school education (12th grade or Baccalaureate II)
   □ One to three years vocational education
   □ Undergraduate education (BA, BS, DEA)
   □ Graduate education (MA, MS, MD)
   □ Doctoral education (PhD, physician)
5. Current Occupation: ----------
   □ Does not work
6. Annual income:
   (from all sources)
   □ < $6000
   □ $6000 to < 10,000
   □ 10,000 to < 15,000
   □ 15,000 to < 20,000
   □ 20,000 to < 25,000
   □ 25,000 to < 30,000
   □ 30,000 to < 35,000
   □ 35,000 to < 50,000
   □ 50,000 to < 75,000
   □ 75,000 or more
   □ Don't know/not sure
   □ No answer
7. Admission diagnosis: ----------
8. Admission status: □ non-surgical □ surgical, elective □ surgical, emergent
9. Comorbidities: ----------

   ----

10. Medications used before admission: ----------
    ----
11. Hospital admission date: DD/MM/YYYY
12. ICU admission date: DD/MM/YYYY

Appendix 4.6 APACHE II

APACHE II scoring system

A - Physiology Score (APS)

Parameter	+4	+3	+2	+1	0	+1	+2	+3	+4
Rectal temperature [°C]	>= 41	39 - 40,9		38,5 - 38,9	36 - 38,4	34 - 35,9	32 - 33,9	30 - 31,9	<= 29,9
MAP [mmHg]	>= 160	130 - 159	110 - 129		70 - 109		50 - 69		<= 49
Heart rate [min-1]	>= 180	140 - 179	110 - 139		70 - 109		55 - 69	40 - 54	<= 39
Ventilation rate [min-1]*	>= 50	35 - 49		25 - 34	12 - 24	10 - 11	6 - 9		<= 5
Oxygenation [mmHg]									
FiO_2 >= 0,5 $A\text{-}aDO_2$	>= 500	350 - 499	200 - 349		< 200				
FiO_2 < 0,5 PaO_2					> 70	61 - 70		55 - 60	< 55
Arterial pH	>= 7,7	7,6 - 7,69		7,5 - 7,59	7,33 - 7,49		7,25 - 7,32	7,15 - 7,24	< 7,15
Serum Sodium [mmol/l]	>= 180	160 - 179	155 - 159	150 - 154	130 - 149		120 - 129	111 - 119	<= 110
Serum Potassium [mmol/l]	>= 7	6 - 6,9		5,5 - 5,9	3,5 - 5,4	3 - 3,4	2,5 - 2,9		< 2,5
Serum Creatinine [mg/dl]**	>= 3,5	2 - 3,4	1,5 - 1,9		0,6 - 1,4		< 0,6		
Hematocrit [%]	>= 60		50 - 59,9	46 - 49,9	30 - 45,9		20 - 29,9		< 20
WBC [t/mm^3]	>= 40		20 - 39,9	15 - 19,9	3 - 14,9		1 - 2,9		< 1
HCO_3-venous [mmol/l]***	>= 52	41 - 51,9		32 - 40,9	22 - 31,9		18 - 21,9	15 - 17,9	< 15
Glasgow-Coma-Scale	Score = 15 minus actuel Glasgow-Coma-Scale								

* non-ventilated or ventilated

** score points doubled for acute renal failure

*** missing blood gas analysis

B - Age points

age	points
<= 44	0
45 - 54	2
55 - 64	3
65 - 74	5
>= 75	6

C - Chronic Health points

If the patient has a history of severe organ system insufficiency or is immuno-commpromised assign points as follows

a) non-operative or emergency postoperative patients	5 points
b) elective postoperative patients	2 points

Definition of severe organic and immune deficiency

Liver	- Biopsy proven cirrhosis and documented portal hypertension
	- Episodes of past upper GI bleeding at attributed to portal hypertension
	- Proir episodes of hepatic failure / encephalopathy / hepatic coma
Cardiovascular	- Chronic heart failure NYHA IV
Respiratory	- Chronic restrictive, obstructive or vascular disease
	- Documented chronic hypoxia, hypercapnia, secondary polycythemia
	- Severe pulmonary hypertension (> 40 mmHg)
	- Respirator dependency
Kidney	- Receiving chronic dialysis
Immuno-compromised	- Therapeutic immune suppression
	- Chemotherapy, radiation
	- Long-term or recent high dose steroids
	- Leukemia, lymphoma, AIDS

APACHE II Score

Sum of A + B + C

APS-Score	A
Age points	B
Chronic points	C
Total APACHE II	

Appendix 4.7a ADL in English

ACTIVITIES POINTS (1 or 0)	**INDEPENDENCE:** (1 POINTS) *No* supervision, direction or personal assistance	**DEPENDENCE:** (0 POINTS) *With* supervision, direction, personal assistance or total care
BATHING POINTS: _____	**(1 POINT)** Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity	**(0 POINTS)** Needs help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing.
DRESSING POINTS: _____	**(1 POINT)** Gets clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes	**(0 POINTS)** Needs help with dressing self or needs to be completely dressed
TOILETING POINTS: _____	**(1 POINT)** Goes to toilet, gets on and off, arranges clothes, cleans genital area without help	**(0 POINTS)** Needs help transferring to the toilet, cleaning self or uses bedpan or commode
TRANSFERRING POINTS: _____	**(1 POINT)** Moves in and out of bed or chair unassisted. Mechanical transferring aides are acceptable	**(0 POINTS)** Needs help in moving from bed to chair or requires a complete transfer
CONTINENCE POINTS: _____	**(1 POINT)** Exercises complete self control over urination and defecation	**(0 POINTS)** Is partially or totally incontinent of bowel or bladder
FEEDING POINTS: _____	**(1 POINT)** Gets food from plate into mouth without help. Preparation of food may be done by another person	**(0 POINTS)** Needs partial or total help with feeding or requires parenteral feeding
TOTAL POINTS = _____ 6= High (*patient independent)* 0= Low (*patient very dependent)*		

Appendix 4.7b ADL in Arabic

نشاطات الحياة اليومية Activities of Daily living (ADL)

ضع دائرة حول العلامة المناسبة

ADL01 - النظافة الجسدية

– استقلالية تامة	1
– مساعدة جزئية	1/2
– معتمد على الآخرين	0

ADL02 -إرتداء الملابس

– استقلالية تامة في إنتقاء الملابس وإرتدائها	1
– مثل أول جواب ولكن مع حاجة للمساعدة في إنتعال الحذاء	1/2
– معتمد على الآخرين	0

ADL03 -الذهاب الى المرحاض

– استقلالية تامة للذهاب الى المرحاض، خلع الملابس وإعادة إرتدائها	1
– وجوب مرافقته أو حاجته للمساعدة في خلع وإعادة إرتداء الملابس	½
– لا يستطيع الذهاب بمفرده	0

ADL04 -إمكانية التنقل

– استقلالية تامة	1
– بحاجة للمساعدة	½
– طريح الفراش	0

ADL05 -إحتباس البول والبراز

– القدرة على التحكم	1
– سلس في بعض الأحيان	½
– سلس كامل	0

ADL06 -وجبات الطعام

– تناول الطعام بمفرده	1
– بحاجة للمساعدة لتقطيع اللحم أو تقشير الفاكهة	½
– مساعدة تامة	0

Appendix 4.8a IQCODE in English

Backward translation:

The Informant Questionnaire on Cognitive Decline in the Elderly (Short form)

Now we want you to remember how your friend or relative was 10 years ago, compare this wilth how he/ she became now. It was the year of 19— 10 years ago. Below there are situations where thr person uses his/her memory or intelligence to perform, we need you to refer whether the patient has improved , remained the same, or got worse in each situation over the last 10 years. It is important to compare his/ her current performance to the performance 10 years ago. For example, if the person used to forget where he / she placed things 10 years ago, and he/ she still does. This is considered as "did not change much". Please refer to your observed changes by circling the appropriate answer.

Compared with 10 years ago how is this person at:

	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
1. Remembering things related to family or friends e.g. occupation, birthdays, addresses	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
2. Remembering recent events	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
3. Recalling conversations occurred few days ago	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
4. Remembering own address / telephone number	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
5. Remembering the day and the month	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
6. Remembering the usual place for keeping	Major	Minor	Did not	Minor	Major deterioration

things	improvement 1	improvement 2	change much 3	deterioration 4	5
7. Remembering where things are if placed in an unusual place	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
8. Knowing how to use familiar house appliances	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
9. Learning how to use a new house appliances	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
10. Learning new things in general	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
11. Following a story in a book or on TV	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
12. Making decisions on every day matters	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
13. Handling shopping finances	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
14. Handling financial matters e.g. pension, Bank accounts	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
15. Dealing with other arithmetic problems e.g. knowing the amount of food to buy, knowing the duration between visits from family or friends	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5
16. Using his/her intelligence to understand what's happening and to rationalize things	Major improvement 1	Minor improvement 2	Did not change much 3	Minor deterioration 4	Major deterioration 5

Appendix 4.8b A-IQCODE in Arabic

استبيان مخبر (راوى) عن التدهور الإدراكي لدى المسنين (النسخة المصغرة)

الان نريد منك ان تتذكر كيف كان صديقك او قريبك منذ 10 اعوام و ان تقارن ذلك بما اصبح/ اصبحت عليه الآن. منذ 10 سنوات كان العام –19. يوجد بالاسفل مواقف حيث يستخدم الشخص ذاكرته/ها او ذكاؤه /ها ونريد منك ان تشير اذا كان المريض تحسن او ظل على حاله أو تدهور فى هذا الموقف خلال اخر 10 سنوات. يجب ا تلاحظ اهمية مقارنة اداؤه/ها الحالى بادائه منذ 10 سنواتز فمثلا اذا كان الشخص منذ 10 سنوات ينسى اين وضع/ت الاشياء و مازال /ت يفعل ذلك يحسب ذلك (لم يحدث تغيير كبير). من فضلك اشر الى التغيرات التى لاحظتها بعمل دائرة حول الاجابة المناسبة

مقارنة بالسنوات العشرة السابقة: كيف يكون أداء هذا الشخص فى:

1. تذكر اشياء متعلقة بعائلته و اصدقائه مثلاً (وظائفهم ,تاريخ الميلاد, عناوينهم)	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
2. تذكر أشياء حدثت مؤخراً	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
3. اعادة تذكر المحادثات من ايام قليلة مضت	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
4. تذكر عنوانه / رقم تليفونه	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
5. تذكر اليوم الحالى والشهر	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
6. تذكر مكان الحفظ المعتاد للأشياء	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
7. تذكر مكان أشياء وضعت فى غير مكانها المعتاد	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
8. معرفة كيفية تشغيل الاجهزة المنزلية المألوفة	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
9. تعلم استخدام اجهزة جديدة بالمنزل	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
10. تعلم أشياء جديدة بصورة عامة	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
11. متابعة قصة فى كتاب أو فى التليفزيون	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
12. اتخاذ قرارات بخصوص الشئون اليومية	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
13. المعاملات المالية للتسوق	تحسن ملحوظ	تحسن طفيف	لم يحدث تغيير	تدهور طفيف	تدهور بشدة

	(1)	(٢)	كبير (٣)	(٤)	(٥)
14. المعاملات المادية مثل المعاش أو التعاملات البنكية	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
15. التعامل مع المشكلات الحسابية الاخرى مثل (معرفة كمية الطعام اللازم شرائها او المدة بين زيارات الاهل او الأصدقاء)	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)
16. استخدام ذكاؤه لفهم ما يحدث و ليعقل (يدرك) الاشياء	تحسن ملحوظ (1)	تحسن طفيف (٢)	لم يحدث تغيير كبير (٣)	تدهور طفيف (٤)	تدهور بشدة (٥)

Appendix 4.9 RASS

Richmond Agitation Sedation Scale (RASS) *

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* (≥10 seconds)	Verbal Stimulation
-2	Light sedation	Briefly awakens with eye contact to *voice* (<10 seconds)	
-3	Moderate sedation	Movement or eye opening to *voice* **(but no eye contact)**	
-4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation	Physical Stimulation
-5	Unarousable	No response to *voice or physical* stimulation	

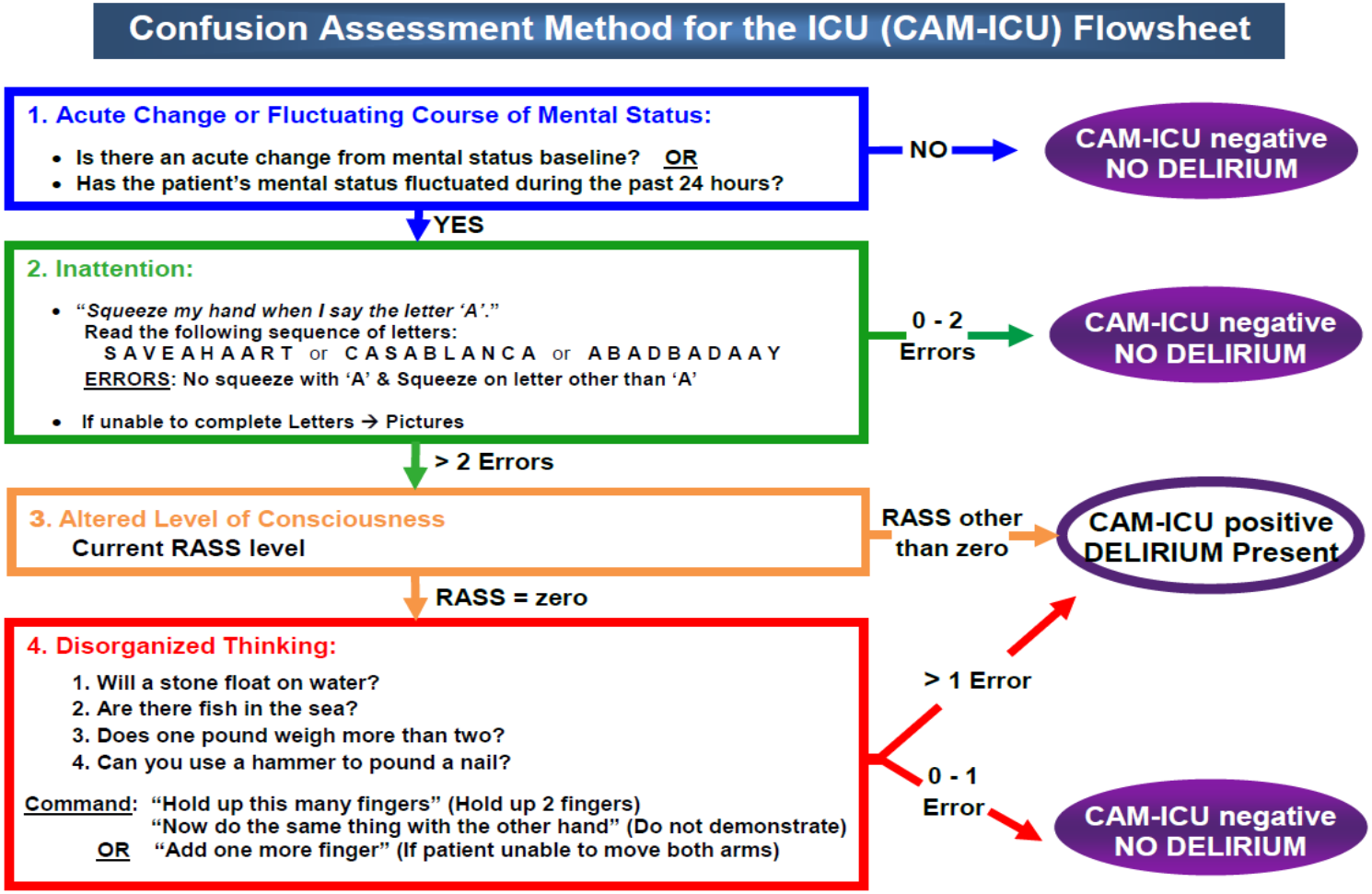
Procedure for RASS Assessment

1. Observe patient
   a. Patient is alert, restless, or agitated. **(score 0 to +4)**
2. If not alert, state patient's name and *say* to open eyes and look at speaker.
   b. Patient awakens with sustained eye opening and eye contact. **(score –1)**
   c. Patient awakens with eye opening and eye contact, but not sustained. **(score –2)**
   d. Patient has any movement in response to voice but no eye contact. **(score –3)**
3. When no response to verbal stimulation, physically stimulate patient by shaking shoulder and/or rubbing sternum.
   e. Patient has any movement to physical stimulation. **(score –4)**
   f. Patient has no response to any stimulation. **(score –5)**

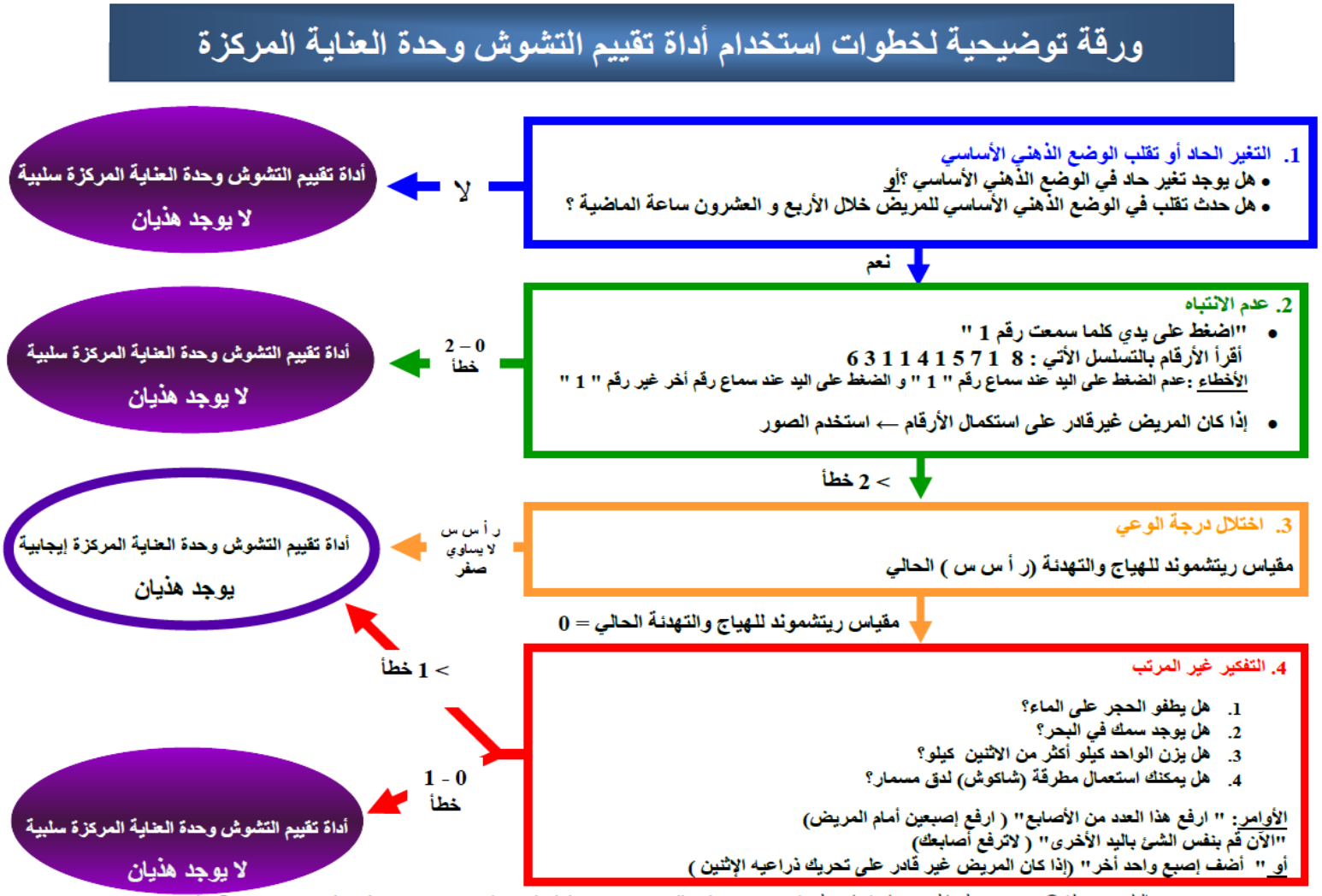
* Sessler CN, Gosnell M, Grap MJ, Brophy GT, O'Neal PV, Keane KA et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care patients. Am J Respir Crit Care Med 2002; 166:1338-1344.

* Ely EW, Truman B, Shintani A, Thomason JWW, Wheeler AP, Gordon S et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation Sedation Scale (RASS). JAMA 2003; 289:2983-2991.

Appendix 4.10a CAM-ICU in English



Appendix 4.10b CAM-ICU in Arabic

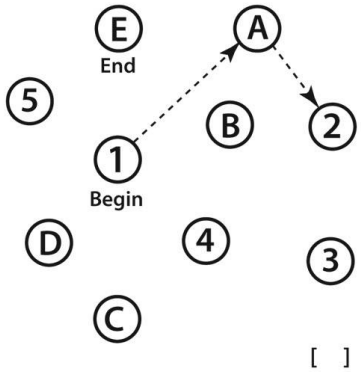


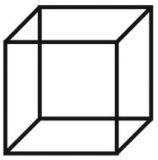
Appendix 4.11a MoCA in English

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE





Copy cube

[ ] [ ]

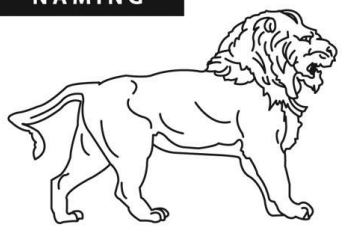
Draw CLOCK (Ten past eleven)
(3 points)

[ ] Contour [ ] Numbers [ ] Hands

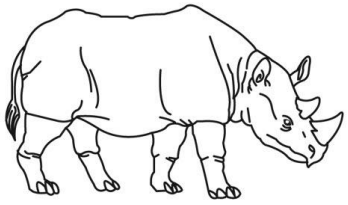
POINTS

__/5

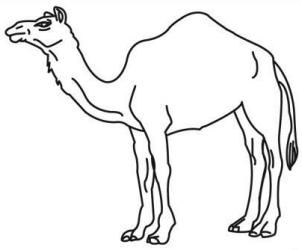
NAMING



[ ]



[ ]



[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words **WITH NO CUE**	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

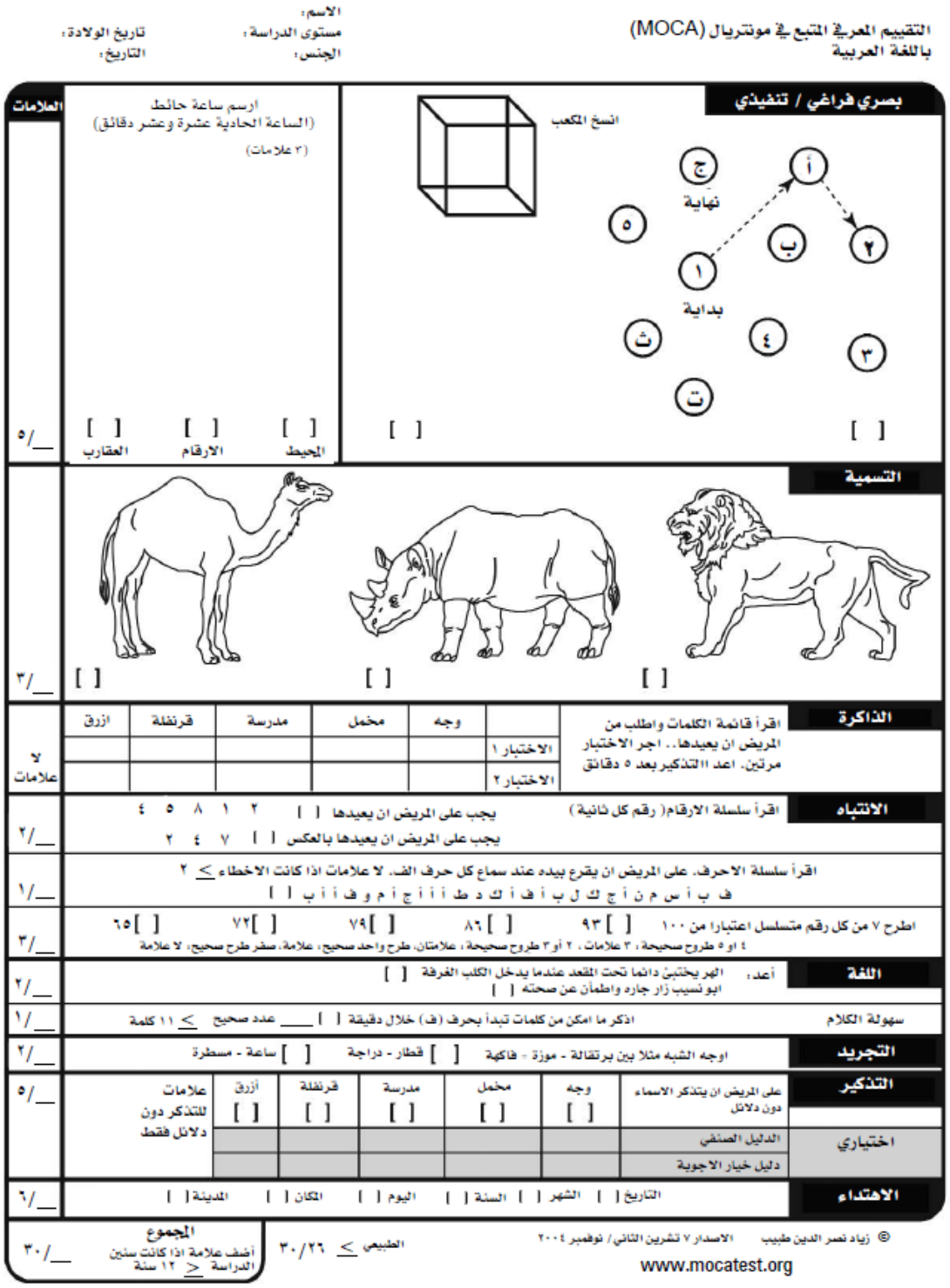
© Z.Nasreddine MD **www.mocatest.org** Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

Appendix 4.11b MoCA in Arabic



Appendix 4.12a HADS in English

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

Scoring:
Total score: Depression (D) _____ Anxiety (A) _____
0-7 = Normal
8-10 = Borderline abnormal (borderline case)
11-21 = Abnormal (case)

Appendix 4.12b HADS in Arabic

هذا الاستبيان يساعد الطبيب لمعرفة مشاعرك وقراءة أحاسيسك ، لذا يرجى إحاطة الرقم الموازي لأفضل اختيار يصف حالتك خلال الأسبوع الماضي. ليس من المطلوب الاستغراق في التفكير لإختيار الإجابة، وإنما تفضل الإجابات العفوية التلقائية.

من فضلك، قم بإختيار الإجابة المناسبة بوضع دائرة عليها:			Hospital Anxiety Depression Scale (HADS):	
	أحس بأنني هامد (فاقد للطاقة) :	D	أشعر بالتوتر الشديد:	A
3	• تقريباً في كل وقت		3 • أكثر الوقت	
2	• في كثير من الأحيان		2 • عدة مرات	
1	• في بعض الأوقات		1 • أحياناً	
0	• لا أشعر بذلك مطلقاً		0 • لا أشعر بذلك مطلقاً	
	ينتابني شعور بالخوف:	A	أنا لازلت أتمتع بالأشياء التي اعتدت أن أستمتع بها:	D
0	• لا، على الإطلاق		0 • بالتأكيد، كما كنت	
1	• أحياناً		1 • ليس تماماً	
2	• كثيراً		2 • قليلاً	
3	• في أغلب الأوقات		3 • بالكاد، على الإطلاق	
	لقد فقدت الإهتمام بمظهري:	D	أشعر بنوع من الخوف, وكأن شيئا مروعا على وشك الحدوث:	A
3	• بالتأكيد فقدت كل الاهتمام		3 • بالتأكيد، وبشكل مزعج	
2	• أنا لا أهتم بمظهري كما يجب أن أهتم		2 • نعم، ولكن أقل سوءاً	
1	• قد لا أعتني بمظهري كما يجب		1 • قليلاً، لكنه لا يقلقني	
0	• أعتني بمظهري بشكل جيد كما كنت سابقا		0 • لا أشعر بذلك على الاطلاق	
	الإحساس بضيقة الصدر دون مجهود جسدي:	A	أستطيع الضحك و رؤية الجوانب الممتعة في الاشياء:	D
3	• في الواقع، كثيراً جداً		0 • كما كنت سابقا	
2	• كثيراً، لابأس به		1 • اقل مما كنت سابقا	
1	• أشعر بذلك قليلاً		2 • بالتأكيد، ليس كثيراً الآن	
0	• لا أشعر بذلك على الإطلاق		3 • لا أشعر بذلك على الإطلاق	
	أنا أتطلع للأشياء من حولي باستمتاع:	D	تأتيني دائما افكار مقلقة:	A
0	• بقدر ما يمكنني فعله		3 • أغلب الأوقات	
1	• نوعا ما أقل مما اعتدت على فعله		2 • معظم الأوقات	
2	• بالتأكيد أقل مما اعتدت على فعلة		1 • من وقت لآخر، ولكن ليس كثيراً	
3	• لا، على الإطلاق		0 • أحيانا	
	ينتابني إحساس مفاجئ بالفزع:	A	أشعر بالبهجة:	D
3	• في الواقع، في كثير من الأحيان		3 • لا، على الإطلاق	
2	• غالباً		2 • ليس كثيراً	
1	• ليس كثيراً		1 • في بعض الأحيان	
0	• لا أشعر بذلك على الإطلاق		0 • في أغلب الأوقات	
	يمكنني الإستمتاع بقراءة كتاب جيد أو مشاهدة البرامج التلفزيونية أو الإستماع إلى الإذاعة:	D	يمكنني الجلوس براحة و الشعور بالاسترخاء:	A
0	• غالباً		0 • بكل التأكيد	
1	• في بعض الأحيان		1 • عادة ما	
2	• ليس كثيراً		2 • ليس كثيراً	
3	• نادراً جداً		3 • لا يمكنني ذلك على الإطلاق	

Appendix 4.13a PCL-C in English

PTSD CheckList – Civilian Version (PCL-C)

Client's Name: _____

Instruction to patient: Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*.

No.	Response	Not at all (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1.	Repeated, disturbing *memories, thoughts, or images* of a stressful experience from the past?					
2.	Repeated, disturbing *dreams* of a stressful experience from the past?					
3.	Suddenly *acting* or *feeling* as if a stressful experience *were happening* again (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful experience from the past?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful experience from the past?					
6.	Avoid *thinking about* or *talking about* a stressful experience from the past or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because they *remind you* of a stressful experience from the past?					
8.	Trouble *remembering important parts* of a stressful experience from the past?					
9.	Loss of *interest in things that you used to enjoy?*					
10.	Feeling *distant* or *cut* off from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being *"super alert"* or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

PCL-M for DSM-IV (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD - Behavioral Science Division

PTSD CheckList – Civilian Version (PCL-C)

The PCL is a standardized self-report rating scale for PTSD comprising 17 items that correspond to the key symptoms of PTSD. Two versions of the PCL exist: 1) PCL-M is specific to PTSD caused by military experiences and 2) PCL-C is applied generally to any traumatic event.

The PCL can be easily modified to fit specific time frames or events. For example, instead of asking about "the past month," questions may ask about "the past week" or be modified to focus on events specific to a deployment.

How is the PCL completed?

□ The PCL is self-administered

□ Respondents indicate how much they have been bothered by a symptom over the past month using a 5-point (1–5) scale, circling their responses. Responses range from **1** *Not at All* – **5** *Extremely*

How is the PCL Scored?

1) Add up all items for a total severity score

or

2) Treat response categories **3–5** (*Moderately* or above) as symptomatic and responses **1–2** (below *Moderately*) as non-symptomatic, then use the following DSM criteria for a diagnosis:

- Symptomatic response to at least 1 "B" item (Questions 1–5),
- Symptomatic response to at least 3 "C" items (Questions 6–12), and
- Symptomatic response to at least 2 "D" items (Questions 13–17)

Are Results Valid and Reliable?

□ Two studies of both Vietnam and Persian Gulf theater veterans show that the PCL is both valid and reliable (Additional references are available from the DHCC)

What Additional Follow-up is Available?

□ All military health system beneficiaries with health concerns they believe are deployment-related are encouraged to seek medical care

□ Patients should be asked, **"Is your health concern today related to a deployment?"** during all primary care visits.

• If the patient replies "**yes**," the provider should follow the Post-Deployment Health Clinical Practice Guideline (PDH-CPG) and supporting guidelines available through the DHCC and www.PDHealth.mil

Appendix 4.13b PCL-C in Arabic

Structure interview: Arabic

هناك 3 أقسام أو مقاييس في هذه المقابلة التي تحتوي على أسئلة حول: صحتك، تجاربك خلال فترة الطفولة، ومعلومات تختص بك مثل عمرك. عادة ما تستغرق هذ المقابلة ما بين 15 الى 20 دقيقة. سأقرأ كل الأسئلة معك وسوف ادون إجاباتك. إذا كنت بحاجة إلى التوقف عن المقابلة في أي وقت، اسمحي لي أن أعرف. إذا كان هناك أسئلة لا تريد الإجابة عليها فقط اخبريني. تذكري أن كل إجاباتك سرية....

أدناه قائمة من المشاكل والشكاوى التي يعاني منها الأفراد في بعض الأحيان نتيجة لتجارب الحياة المؤلمة. يرجى قراءة كل مشكلة وشكوى بعناية ووضع علامة "X" في المربع للإشارة إلى مدى انزعاجك من هذه المشكلة في *الشهر الماضي*.

في الشهر الماضي، ما هو مدى انزعاجك من:

ت	الاستجابة	لا على الاطلاق	قليلاً	باعتدال	لا بأس	كثير جداً
1.	*ذكريات وأفكار* متكررة ومزعجة *أو صور* لتجربة مؤلمة أو صعبة نفسياً من الماضي؟					
2.	*أحلام* متكررة ومزعجة لتجربة مؤلمة أو صعبة نفسياً من الماضي؟					
3.	*تصرف أو شعور* مفاجئ كما لو كانت تجربة مؤلمة أو صعبة نفسياً *تحدث* لك مرة أخرى (كما لو كنت تعيشها مرة ثانية)؟					
4.	الشعور *بالضيق كثيراً* عندما يكون هناك *شيء يذكرك* بتجربة مؤلمة أو صعبة نفسياً من الماضي؟					
5.	حصول *ردود فعل بدنية* (مثل زيادة دقات القلب أو صعوبة في التنفس أو التعرق) عندما يكون هناك *شيء يذكرك* بتجربة مؤلمة أو صعبة نفسياً من الماضي؟					
6.	تجنب *التفكير* أو *الحديث* عن تجربة مؤلمة أو صعبة نفسياً من الماضي أو تجنب *المشاعر* المتعلقة بها؟					
7.	تجنب *الأنشطة* أو *المواقف* التي *تذكرك* بتجربة مؤلمة أو صعبة نفسياً من الماضي؟					

8.	صعوبة في تذكر *أجزاء مهمة* من تجربة مؤلمة أو صعبة نفسياً من الماضي؟					
9.	فقدان الاهتمام في الأشياء التي كنت تستمتع بها بالعادة؟					
10.	الشعور بالبعد أو العزلة عن الآخرين؟					
11.	الشعور باللامبالاة العاطفية أو عدم القدرة على البوح بمشاعر محبة للمقربين لك؟					
12.	الشعور كما لو أن مستقبلك سوف يكون قصيراً بطريقة ما ؟					
13.	صعوبة الدخول با لنوم أو البقاء نائماً؟					
14.	الشعور بتعكر المزاج أو وجود حالات غضب؟					
15.	وجود صعوبة في التركيز؟					
16.	تصبح "منتبهاً للغاية" أو يقظاً ؟					
17.	الشعور بالتقلب أو الجفل بسهولة؟					

Appendix 4.14a SF-36 in English

SF-36 QUESTIONNAIRE

Name:_____ **Ref. Dr:**_____ **Date:** _____

ID#: _____ **Age:** _____ **Gender: M / F**

Please answer the 36 questions of the **Health Survey** completely, honestly, and without interruptions.

GENERAL HEALTH:
In general, would you say your health is:
◯ Excellent ◯ Very Good ◯ Good ◯ Fair ◯ Poor

Compared to one year ago, how would you rate your health in general now?
◯ Much better now than one year ago
◯ Somewhat better now than one year ago
◯ About the same
◯ Somewhat worse now than one year ago
◯ Much worse than one year ago

LIMITATIONS OF ACTIVITIES:
The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.
◯ Yes, Limited a lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Lifting or carrying groceries
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Climbing several flights of stairs
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Climbing one flight of stairs
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Bending, kneeling, or stooping
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking more than a mile
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking several blocks
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Walking one block
◯ Yes, Limited a Lot ◯ Yes, Limited a Little ◯ No, Not Limited at all

Bathing or dressing yourself

◯Yes, Limited a Lot ◯Yes, Limited a Little ◯No, Not Limited at all

PHYSICAL HEALTH PROBLEMS:

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

Cut down the amount of time you spent on work or other activities

◯Yes ◯No

Accomplished less than you would like

◯Yes ◯No

Were limited in the kind of work or other activities

◯Yes ◯No

Had difficulty performing the work or other activities (for example, it took extra effort)

◯Yes ◯No

EMOTIONAL HEALTH PROBLEMS:

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Cut down the amount of time you spent on work or other activities

◯Yes ◯No

Accomplished less than you would like

◯Yes ◯No

Didn't do work or other activities as carefully as usual

◯Yes ◯No

SOCIAL ACTIVITIES:

Emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

◯Not at all ◯Slightly ◯Moderately ◯Severe ◯Very Severe

PAIN:

How much bodily pain have you had during the past 4 weeks?

◯None ◯Very Mild ◯Mild ◯Moderate ◯Severe ◯Very Severe

During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

◯Not at all ◯A little bit ◯Moderately ◯Quite a bit ◯Extremely

ENERGY AND EMOTIONS:
These questions are about how you feel and how things have been with you during the last 4 weeks. For each question, please give the answer that comes closest to the way you have been feeling.

Did you feel full of pep?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you been a very nervous person?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you felt so down in the dumps that nothing could cheer you up?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you felt calm and peaceful?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Did you have a lot of energy?
- ◯ All of the time
- ◯ Most of the time
- ◯ A good Bit of the Time
- ◯ Some of the time
- ◯ A little bit of the time
- ◯ None of the Time

Have you felt downhearted and blue?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Did you feel worn out?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Have you been a happy person?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

Did you feel tired?

- ○ All of the time
- ○ Most of the time
- ○ A good Bit of the Time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

SOCIAL ACTIVITIES:
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

- ○ All of the time
- ○ Most of the time
- ○ Some of the time
- ○ A little bit of the time
- ○ None of the Time

GENERAL HEALTH:
How true or false is each of the following statements for you?

I seem to get sick a little easier than other people

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

I am as healthy as anybody I know

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

I expect my health to get worse

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

My health is excellent

Definitely true | Mostly true | Don't know | Mostly false | Definitely false

Appendix 4.14b SF-36 in Arabic

استبيان صحي

الجنس☐ ذكر

☐ انثى

العمر_____سنة

المؤهل العلمي: ابتدائي ☐

اعدادي ☐

ثانوي ☐

بكالوريوس ☐

ماجستير ☐

دكتوراه ☐

من فضلك، أجب على كل الأسئلة الموجودة في هذا الاستبيان. في حالة عدم وضوح أي سؤال، أرجو اختيار أقرب اجابة لمفهومك للسؤال.

١- بصورة عامة، كيف ترى حالتك الصحية؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

☐ ممتازة

☐ جيدجدا

☐ جيدة

☐ لا بأس بها

☐ سيئة

٢- مقارنة بعام مضى، كيف تقيم حالتك الصحية الآن بصورة عامة؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

☐ أفضل بكثير مما كانت عليه قبل عام

☐ أفضل نوعا ما من العام الماضي

☐ تقريبا على ما هي عليه

☐ أسوأ نوعا ما من العام الماضي

☐ أسوأ بكثير مما كانت عليه قبل عام

٣- تتعلق البنود التالية بأنشطة يمكن ان تقوم بها خلال يومك العادي. **في الوقت الحالي**، الى اي مدى **تقيدك حالتك الصحية**:	(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)		
	نعم تقيدني كثيرا	نعم تقيدني قليلا	لا تقيدني اطلاقا
أ) من ممارسة **الأنشطة الشاقة** مثل: الجري، حمل الاشياء الثقيلة او مزاولة الأنشطة الرياضية المجهدة جدا؟	☐	☐	☐
ب) من ممارسة **الأنشطة متوسطة الجهد**، كتحريك الطاولة او التنظيف باستخدام المكنسة الكهربائية او تنظيف حديقة المنزل والعناية بها ؟	☐	☐	☐
ج) من حمل المشتريات من البقالة او السوق المركزي (السوبرماركت)؟	☐	☐	☐
د) من صعود الدرج **لعدة ادوار**؟	☐	☐	☐
هـ) من صعود الدرج **لدور واحد فقط**؟	☐	☐	☐
و) من الانحناء او الركوع او السجود ؟	☐	☐	☐
ز) من المشي لأكثر من **كيلومتر ونصف**؟	☐	☐	☐
ح) من المشي لمسافة **نصف كيلومتر**؟	☐	☐	☐
ط) من المشي لمسافة **مئة متر**؟	☐	☐	☐
ي) من الاستحمام او ارتداء الملابس بنفسك؟	☐	☐	☐

الصحة الجسمية

٤- تتعلق البنود التالية (أ ، ب ، ج ، د) بالمشاكل التي يمكن ان تواجهـــك خلال تأديتك لعملك او للأنشطة اليومية المعتادة نتيجة لحالتك الصحية الجسمية. **خلال الأسابيع الأربعة الماضية**، هل تسببت حالتك الصحية الجسمية في:	نعم	لا
أ) **التقليل من الوقت** الذي تقضيه في العمل او اي انشطة اخرى؟	☐	☐
ب) **التقليل** مما تود **انجازه** من العمل أو أي أنشطة أخرى؟	☐	☐
ج) **تقييدك في أداء نوع** معين من الأعمال أو أي أنشطة أخرى؟	☐	☐
د) **أن تجد صعوبة في** تأدية العمل أو أي أنشطة أخرى؟ (على سبيل المثال، احتجت الى جهد اضافي لتأديتها)	☐	☐

(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)

الصحة النفسية

٥- تتعلق البنود التالية (أ ، ب ، ج) بالمشاكل التي يمكن ان تواجهك خلال تأديتك لعملك او الانشطة اليومية المعتادة كنتيجة لحالتك الصحية النفسية. (مثلا الشعور بالاكتئاب او القلق) **خلال الاسابيع الأربعة الماضية**، هل تسببت حالتك الصحية النفسية في:	نعم	لا
أ) **التقليل من الوقت** الذي تقضيه في العمل او اي انشطة اخرى؟	☐	☐
ب) **التقليل** مما تود **انجازه** من العمل أو أي أنشطة أخرى؟	☐	☐
ج) **عدم انجاز** العمل او اي انشطة اخرى **بالحرص المعتاد**؟	☐	☐

(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)

الصحة الجسمية او النفسية

٦- **خلال الاسابيع الاربعة الماضية**، الى اي مدى تعارضت **صحتك الجسمية او النفسية** مع تأديتك لنشاطاتك الاجتماعية المعتادة مع عائلتك او اصدقائك او جيرانك او اي من المناسبات الاجتماعية الأخرى؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي تعارض اطلاقا
- ☐ كان هناك تعارض قليل
- ☐ كان هناك تعارض متوسط
- ☐ كان هناك تعارض كبير
- ☐ كان هناك تعارض كبير جدا

شدة الألم

٧- ما **شدة الألم الجسمي** الذي عانيت منه خلال **الاسابيع الاربعة الماضية**؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي ألم
- ☐ كان هناك ألم خفيف جدا
- ☐ كان هناك ألم خفيف
- ☐ كان هناك ألم متوسط
- ☐ كان هناك ألم شديد
- ☐ كان هناك ألم شديد جدا

٨- **خلال الاسابيع الاربعة الماضية**، الى اي مدى ادى **الالم الجسمي** الى التعارض مع تأديتك لأعمالك المعتادة (سواء داخل المنزل او خارجه)؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ لم يكن هناك أي تعارض
- ☐ كان هناك تعارض قليل جدا
- ☐ كان هناك تعارض متوسط
- ☐ كان هناك تعارض كبير
- ☐ كان هناك تعارض كبير جدا

١٠- **خلال الاسابيع الأربعة الماضية**، ما مقدار الوقت الذي تعارضت فيه **صحتك الجسمية او مشاكلك النفسية** مع نشاطاتك الاجتماعية (مثل زيارة الأصدقاء والأقارب وغير ذلك) ؟

(اختر اجابة واحدة وضع علامة ✓ أمام الاجابة المناسبة)

- ☐ كان التعارض في كل الأوقات
- ☐ كان التعارض في معظم الأوقات
- ☐ كان التعارض في بعض الأوقات
- ☐ كان التعارض في قليل من الأوقات
- ☐ لم يكن هنالك تعارض في أي وقت من الأوقات

١١- ما مدى **صحة او خطأ كل** من العبارات التالية (أ ، ب ، ج ، د) بالنسبة الى حالتك الصحية؟

(اختر اجابة واحدة وضع علامة ✓ تحت الاجابة المناسبة)

	صحيحة بلا شك	صحيحة غالبا	لا اعلم	خطأ غالبا	خطأ بلا شك
أ) يبدو أنني أصاب بالمرض أسهل من الآخرين.	☐	☐	☐	☐	☐
ب) حالتي الصحية مساوية لأي شخص أعرفه.	☐	☐	☐	☐	☐
ج) أتوقع أن تسوء حالتي الصحية.	☐	☐	☐	☐	☐
د) حالتي الصحية ممتازة.	☐	☐	☐	☐	☐

****** شكرا لتعاونكم ******

Appendix 6.1 King's ethics approval for qual_HRDP-2223-34875

Research Ethics
Office

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5.9 Waterloo Bridge Wing
Waterloo Road
London SE1 9NH
Telephone 020 7848 4020/4070/4077
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KING'S College LONDON

Hera Tashjian

5 May 2023

Dear Hera

Project Title: Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia
Project Reference: HR/DP-22/23-34875

Ethical Clearance

I am pleased to inform you that full approval for your project has been granted by the Health Faculties (Purple) Research Ethics Subcommittee.

For your information, ethical approval has been granted for **5 years** from 5 May 2023. If you need approval beyond this point, you will need to apply for an extension at least two weeks before this. You will be required to explain the reasons for the extension. However, you will not need to submit a full re-application unless the protocol has changed.

Ethical approval is required to cover the data-collection phase of the study. This will be until the date specified in this letter. However, you do not need ethical approval to cover subsequent data analysis or publication of the results.

Please ensure that you follow the guidelines for good research practice as laid out in UKRIO's Code of Practice for research: http://ukrio.org/publications/code-of-practice-for-research/.

If you do not start the project within three months of this letter, please contact the Research Ethics Office.

Please note that you will be required to obtain approval to modify the study. This also encompasses extensions to periods of approval. Please refer to the URL below for further guidance about the process:

https://internal.kcl.ac.uk/innovation/governance-ethics-integrity/research-ethics/applications/modifications

If you have any query about any aspect of this ethical approval, please contact the Research Ethics Office:

(https://internal.kcl.ac.uk/innovation/governance-ethics-integrity/research-ethics/contact)

Data Protection Registration

As you have indicated in Section E that personal data will be processed as part of this research project, this letter also confirms that you have also met your requirements for registering this processing activity with King's College London. This is required in line with the College's role as a Data Controller, in accordance with the General Data Protection Regulation (GDPR).

Please note it is the responsibility of the researcher(s) to ensure compliance with other aspects of the GDPR, more information about this can be found here: https://internal.kcl.ac.uk/innovation/governance-ethics-integrity/research-governance-office/data-protection-law-and-research/how-does-uk-dp-law-affect-research

You are required to adhere to all research data/records management and storage procedures agreed to as part of your application. This will be expected even after the completion of the study.

If there are any changes to the project that will impact on how you will you collect, manage or otherwise use your data, these must also be reflected in a modification request as outlined above.

Please note that we may, for the purposes of audit, contact you from time to time to ascertain the status of your research.

We wish you every success with this work.

Yours sincerely,

Ms Gemma Singleton

Research Ethics Facilitator

For and on behalf of

Chair of the Health Faculties (Purple) Research Ethics Subcommittee

Appendix 6.2 IRB Approval for qual_ARC-23.02.05

ALMOOSA ACADEMIC AFFAIRS

مستشفى الموسى التخصصي
Almoosa Specialist Hospital

Date:	IRB log No:	Category of Approval:	Affiliation:
02/02/2023	ARC-23.02.05	Expedite	Almoosa Specialist Hospital

Study Title:
"Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia"

Principal Investigator
Hera Tashjian

Co-Investigator
Hratch Moskofian
Fatima AlGhaith
Dr Geraldine Lee
Prof Anne Marie Rafferty

Dear Hera Tashjian,

This is to clarify that the IRB has reviewed and approved the study titled in this letter.

Terms and Conditions of Approval:

- Abide by the rules and regulations of the Government of Saudi Arabia, NCBE, GCP guidelines, the policies and procedures of Research Center at Almoosa Specialist Hospital
- The approval of the study is valid for ***One Year,*** from the approval effective date.
- To conduct research as per the approved documents and no amendments maybe made prior to further approval by the IRB.
- The Principal Investigator is responsible for the document retention and storage for a period of ***3 years*** from study completion.
- The Principal Investigator is expected to submit a Progress Report every ***6 months***.
- At the end of the study, the Principal Investigator must submit a Final Report including a conclusion abstract and the manuscript intended for publication.

On behalf of the IRB members, we thank you for submitting your study and we wish you the best of luck as you move forward with your research.

Sincerely Yours,

Dr. Abbas S. Al Mutair # 10682
Al Moosa Research Director
IRB Chairperson

Assoc. Prof. Dr. Abbas Al - Mutair
Chairman, ASH Institutional Review Board

National Registration Number with NCBE-KACST, KSA: (H-05-HS-100)

Appendix 6.3a Informed Consent_Life-ICUS-Q

CONSENT FORM FOR PARTICIPANTS IN RESEARCH PROJECTS

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research

Title of project: Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia	
Ethical review reference number:	**Version number: 31/3/23**

	Tick or initial
1. I confirm that I have read and understood the information sheet dated 31-03-2023 for the above project. I have had the opportunity to consider the information and asked questions which have been answered to my satisfaction.	
2. I consent voluntarily to be a participant in this project and understand that I can refuse to take part and can withdraw from the project at any time, without having to give a reason, up until three days after the interview.	
3. I consent to the processing of my personal information for the purposes explained to me in the Information Sheet. I understand that such information will be handled under the terms of UK data protection law, including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018.	
4. I understand that my information may be subject to review by responsible individuals from the College for monitoring and audit purposes.	
5. I understand that confidentiality and anonymity will be maintained, and it will not be possible to identify me in any research outputs	
6. I agree that the researcher/ research team may use my data for future research and understand that any such use of identifiable data would be reviewed and approved by a research ethics committee. (In such cases, as with this project, data would/ would not be identifiable in any report).	
7. I consent to my participation in the research being audio recorded.	
8. I understand that I must not take part if I fall under the exclusion criteria as detailed in the information sheet and explained to me by the researcher.	
9. I understand that the information I have submitted will be published as a report.	

Name of Participant	**Date**	**Signature**
Name of Researcher	**Date**	**Signature**

Appendix 6.3b Information Sheet_Life-ICUS-Q

Version Number 24/11/22

INFORMATION SHEET FOR PARTICIPANTS

Ethical Clearance Reference Number: HR/DP-22/23-34875

YOU WILL BE GIVEN A COPY OF THIS INFORMATION SHEET

Title of project

Lived Experiences of Intensive Care Unit Survivors: A Qualitative Study in Saudi Arabia

Invitation Paragraph

I would like to invite you to participate in this research project which forms part of my doctoral studies in nursing research at King's College London. Before you decide whether you want to take part, it is important for you to understand why the research is being done and what your participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask me if there is anything that is not clear or if you would like more information.

What is the purpose of the project?

The purpose of the project is to explore the patients' lived experiences after their ICU stay by interviewing survivors after 3 months of their ICU discharge.

In the study Assessing Predictors of Long-term Outcomes and Health-Related Quality of Life in post-ICU patients in Saudi Arabia, where you are a participant, the research team is exploring the research question of what happens to long-term outcomes and quality of life in patients after being discharged from the ICU in quantitative methods. Quantitative method is the process of collecting and analyzing numerical data.

The current study is a qualitative one, where we do not deal with numbers, but we aim to have an in-depth look at your experience as described by you. We are conducting this study in follow up to the previous study in order to gain a more complete picture of our research question, to put findings in context, and to add richer details to our conclusions.

In addition, this study will help understand how the patients' experiences of survivorship relate to the Patient Reported Outcomes Measurement Information System (PROMIS) framework.This framework is known as a "set of person-centered measures that evaluates and monitors physical, mental, and social health in adults and children." (https://www.promishealth.org/).

Why have I been invited to take part?

You are being invited to participate in this project because you were previously recruited to be part of the Assessing Predictors of Long-term Outcomes and Health-Related Quality of Life in post-ICU patients in Saudi Arabia.

In the current study, we are using a purposive sampling criteria as such:

- Participants who, during the three month follow up of the quantitative study are expressing thoughts and emotions and are elaborating on their post-ICU experience rather than only answering survey questions numerically.

- Participants who have a MoCA score of 22 or higher during their 3 months follow up. (The participants of the previousstudy undergo cognitive testing using the Montreal Cognitive Assessment (MoCA) tool at their 3 months follow-up visit by the researcher. A score of 22 and above on this cognitive testing would indicate that major cognitive impairments are not present. Participants for the current qualitative study should be able to attend to a semi-structured interview. Major cognitive impairments that may interfere with communication and expression of thoughts may hinder such interviews. Therefore, only those participants who have scored 22 and above on the MoCA at the 3 months follow up period of the previous study are being approached for the current study).

What will happen if I take part?

If you choose to take part in the project you will be asked to sit for an interview with two of our research team members at your home, at your convenience, at a time selected by both you and the PI or research assistant. With your consent, the interview will be audiotaped using a recorder. The interview will focus on assessing your lived experience after your ICU stay. You will be asked about your baseline functioning prior to the ICU admission, followed by some questions regarding your recovery post ICU in the following areas: physical, social, health, and cognition. Some questions will be asked such as: "can you tell me a little bit about what your life was like before you were in the ICU?"; "Is there anything you miss a lot about your life before you were in the hospital?", "Have you felt sad or worried?", "What memories or feelings do you have NOW about being in the ICU?".

The interview will not be conducted remotely.The interview will take around thirty minutes to complete. Only one interview will be conducted; you will not be asked for a follow up interview. After finishing the interview, you will be given the option to listen to the recording privately at home.

Do I have to take part?

Participation is completely voluntary. You should only take part if you want to and choosing not to take part will not disadvantage you in any way. Once you have read the information sheet, please contact us if you have any questions that will help you make a decision about taking part. If you decide to take part we will ask you to sign a consent form and you will be given a copy of this consent form to keep.

What are the possible risks of taking part?

There are some risks in participating in this study. Since you will be interviewed regarding your experience after surviving the intensive care unit (ICU), questions will relate to your post-ICU physical, social, mental health, and cognition. Speaking about these areas of wellbeing may pose potential for discomfort or distress to you as they may evoke feelings of loss, grief, trauma, anger, or fear related to the disclosure of personal and sensitive memories associated with the experience of being in the intensive care unit.

You will be given ample time to be comfortable during the interview. In case you experience tiredness or distress and you are unable to continue and you would like to end the session, please inform the researcher. We will stop immediately and you will be allowed time to rest and given the option to resume the session at a later time.

In the event when you become uncomfortable or distressed while discussing your cognitive, psychological, or overall health after the ICU experience, the following actions will be taken by the examiner [Principal Investigator (PI) or Research Assistant (RA)]:

- The examiner will enquire whether you wish to terminate the assessment session.
- If you wish to carry on, the assessment will be resumed.
- If you wish that the session terminates, the examiner will stop the questioning.
- The examiner will offer immediate support, within the scope of the examiner's abilities, to discuss and address your concerns and support you.
- The examiner will recommend that you speak to your treating physician or another health professional or mental health provider to discuss your concerns and seek further advice or support.
- If you permit, a referral will be made to your treating physician or another health professional or mental health provider at the research hospital. You will be asked to sign the referral form. The referral will be on your expense.
- If you consent, the examiner will make a follow-up phone call the following day to ensure that you are alright. During this call, the recommendation previously done regarding speaking the treating physician or another healthcare provider will be, once again, provided. The examiner will encourage you to call if you experience increased distress in the following hours or days.

What are the possible benefits of taking part?

If there are any findings that we think are important to your health, we will let you know. In the case where we think you have depression, anxiety, or distress, with your permission, a referral will be made to your treating physician so you can get the proper help. You will be asked to sign the referral form. The referral will be on your own expense.

In addition, information gained from your participation in this study may be important in determining the long-term outcomes of ICU patients in the Saudi population. Results of this study may help ICU physicians and nurses better understand what happens to patients on the long run. Therefore, the study might help future ICU patients and families be better prepared for the care needed after discharge from ICU by receiving pre-discharge information and support.

Data handling and confidentiality

Your data will be processed under the terms of UK data protection law (including the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018). Participants will have the option if they want to use a pseudo-name or no name during the interview. Participants will not be mentioned by their name in the final report and paper. Participants will be named as Mr or Mrs. A, B, C, etc.

After collection, data will be stored in a secure location until completion of study, after which it will be destroyed. During data storage, participants' names will not be mentioned anywhere except in the consent form. Collected data will only be shared with the research team members and the professional transcriber.

Hard documents will be stored in a locked cabinet in the primary investigator's office. The electronic data will be stored on the PI's university drive (KCL OneDrive) located inside her restricted access office; the computer has an access password. Data collection,

transcription, translation, and analysis will take place in the eastern province of Saudi Arabia.

King's College London has a responsibility to keep information collected about you safe and secure, and to ensure the integrity of research data. Specialist teams within King's College London continually assess and ensure that data is held in the most appropriate and secure way.

Data Protection Statement

If you would like more information about how your data will be processed under the terms of UK data protection laws please visit the link below:

https://www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research

What if I change my mind about taking part?

You are free to withdraw at any point of the project, without having to give a reason. Withdrawing from the project will not affect you in any way. You are able to withdraw your data from the project up until 2 weeks after the interview. After this date withdrawal of your data will no longer be possible because the data would be anonymized and transcription started. If you choose to withdraw from the project we will not retain the information you have given.

What will happen to the results of the project?

The results of the study will be summarised in the principal investigator's research dissertation in her doctoral studies in nursing research. The research findings will be published in a professional journal. Your privacy will be maintained in all published and written data resulting from this study. Your name or other identifying information will not be used in our reports or published papers.

Who should I contact for further information?

If you have any questions or require more information about this project, please contact me using the following contact details:

Hera Tashjian, King's College London, Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care, Tel: 0207 848 3201, Email: hera.tashjian@kcl.ac.uk
Or
Hera Tashjian, Dahran St. Alfaisal District, Al-Ahsa, P.O. Box 5098 Eastern Province, Saudi Arabia, Tel: 0559296154, Email: CNO@almoosahospital.com.sa

What if I have further questions, or if something goes wrong?

If this project has harmed you in any way or if you wish to make a complaint about the conduct of the project you can contact King's College London or Almoosa Specialist Hospital using the details below for further advice and information:

- King's College London, Dr Geraldine Lee
  Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care,

King's College London, Room 2.16, James Clerk Maxwell Building,
57 Waterloo Road, LONDON, SE1 8WA
Tel: 0207 848 3201
Email: gerry.lee@kcl.ac.uk

- Almoosa Specilaist Hospital, Intitutional Review Board
  Tel: 0135469666
  Email: research.center@almoosahospital.com.sa

Thank you for reading this information sheet and for considering taking part in this research.

Appendix 6.4 Interview Guide

INTERVIEW QUESTION GUIDE

If oral consent was on a different day: I would like to learn more about how your health has been since you were in the ICU around (insert date). Your participation today is completely voluntary and you may stop participating at any time or choose not to answer any questions. We are taping the session today so that we can get down all of your input and ideas,but anything you say in this discussion will be held in strict confidence. The themes that arise from interview will be summarized; however, this summary will not include any identifiable information about specific people involved with the project. Do you have any questions beforeI get started?

Baseline functioning prior to ICU

1. Can you tell me a little bit about what your life was like before you were in the ICU?
    a. If not discussed: probe physical, emotional/psychological health and social status, fatigue, cognitive abilities (e.g. memory, mental organizational abilities), day to day activities and employment situation prior to the onset of the acute illness that caused them to be admitted to the hospital.

Overall recovery following ICU

I want to ask about your recovery after the ICU. Please note that for all questions, "Hospital" refers to Almoosa Specialist Hospital, the hospital in which you were in the ICU.

2. How have you been doing since you came home from the hospital?
    a. Walk me through the timeline of your recovery after the hospital.
        i. *If needed:* What was it like when you were first discharged from the hospital?
        ii. *If needed:* What is it like now?
    b. What, if anything, do you think helped you the most since you have been home from thehospital?

3. Is there anything that you miss a lot from your life before you were in the hospital?
    a. Is there anything you would like to change about your health or well-being currently?
        i. If yes, what?

4. Do you have any your worries or concerns about your recovery? If yes, what?
    a. Did you have any worries when you first came home from the hospital? If yes, howwere they different from now?

5. How would you describe your health now?
    a. How, if at all, has your health changed since you have been home from the hospital?What do you do to help cope with problems experienced after being in the ICU?

PHYSICAL HEALTH

6. How do you feel physically now?
    a. How, if at all, has your physical functioning changed since you came home from thehospital?

7. How would you describe your energy level now?
    a. *If needed:* Do you feel like you get tired easily or have fatigue?
    b. How has that changed since you came home from the hospital?
        c. How would you describe your ability to finish tasks? What if anything stops you fromfinishing your tasks?

8. Are you having any pain now? If yes, can you describe it?
    a. If yes, Is pain interfering with your life? How?

9. Tell me about how you sleep on a typical night now.

SOCIAL HEALTH

10. How would you describe a typical day now?
    a. *If needed*: What types of things do you do day-to-day?
        b. How, if at all, have you changed your daily routines since you came home from thehospital?
        c. *Probe*: *if they have starting doing new activities, changed how they do activities, orstopped doing activities they used to do.*

11. What things do you do for fun now?
    a. *If needed:* How do you spend your leisure time now?
    b. *If needed:* How do you fill your time now? What changes has you made to how you spend your time since you came home from the hospital?

12. How have you been getting along with your friends and/or family now?
    a. Are there any people you don't talk to or see as much anymore?
        i. *If yes*: Tell me more about that.
    b. How, if at all, have your relationships changed with your friends and/or family sinceyou came home from the hospital?

13. How have you been spending time with your friends and/or family?
    a. Are there things you no longer do, or do less often, with your friends and/or family now?
        i. *If yes*: Tell me more about that.

How if at all has this changed since you came home from the hospital?

14. How if at all have your goals or life plans changed since being in the hospital?

Probe career changes, financial changes, family planning, etc.

MENTAL HEALH & COGNITION

15. How would you describe your mood now?
    a. Have you felt sad or worried?
        i. *If patient is worried:* What types of things do you worry about?
        ii. *If patient reports negative affect (e.g. anger, depression, anxiety, and stress):* Can you tell me more about those times?
    b. How is this different from before you were in the ICU starting around (insert date)?
    c. How, if at all, has that changed since you have been home from the hospital? What do you think contributes to you feeling that way?

16. Have you had any trouble with your thinking or memory?
    a. *If yes:* Tell me more about that.
    b. Have you had any difficulties with organizing and planning things?
        i. *If yes*: Tell me more about that.
    c. Have you had any difficulties with paying attention or focusing?
        i. *If yes*: Tell me more about that.
    d. How, if at all, have these thinking or memory issues changed since you have been homefrom the hospital?

PTSD

17. What memories or feelings do you have NOW about being in the ICU?
    a. Do you have any unwanted thoughts or memories?
    b. Do you ever avoid certain things because it reminds you of the ICU?
        i. *If yes*: Tell me more about that.
    c. How if at all has this changed since you have been home from the hospital?

OVERALL HEALTH RECAP

18. How would you describe "being healthy"?
    a. What areas would you include?
    b. *If needed:* What does it mean to "be healthy"?
    c. *If needed:* Tell me what a healthy person would look like.

Appendix 6.5. Initial Draft Codes- Sample Patient A

Initial Code	Quote in English	Quote in Arabic
Health seeking behaviour	I quit smoking.	تركت الدخان
Grateful to doctor	Of course, the doctor was the best doctor, doctor MY…	طبعاً الدكتور كان أفضل دكتور ، دكتور محمد ياسين
Explanation by doctor	he took the initiative and told to me and said if we had given you full anesthesia I would have entered in complete coma, but with local anesthesia, thank God, I did not enter coma, but I stayed in the ICU under monitoring...	بادرني وقال لي إذا عطيناك بنج كامل حـ تدخل في غيبوبة كاملة، بس لكن بنج ، الحمد لله عدت، ولا دخلت في غيبوبة، بس قعدت في العناية المركزة لمدة 24ساعة تحت الملاحظة، كان فيه ألم
Grateful to ICU team	the group in the hospital, may God reward them well, they played a role for which they should be thanked.	والجماعة في المستشفى الله يجزاهم خير، قاموا بدور يشـ يشكروا عليه
Pain in ICU	There was pain	كان فيه ألم
Physical Rehab	And until now I work two days a week intensive physical rehab, three hours a day every time	وإلى الآن أنا أعمل في الأسبوع يومين علاج طبيعي مكثف بكل فترة كل 3 ساعات في اليوم
Walking	After the operation I got up and walked normally,	بعد العملية قمت أطلع وأروح وأجي طبيعي
Willingness Wanting Independence	and tried as much as I can not to use a walker, to walk normally	وأحاول قدر ما أستطيع ما استخدم المشاية، أمشي طبيعي
Determination	Because determination is necessary…Determination is required. If I think that I am going to have an operation, I will not do the operation …why…the psychological factor is the strongest one	لأن لازم عزيمة العزيمة مطلوبة، إذا أنا بحط في دماغي إن أنا مسوي عملية ما باقوم من العملية ... وين؟ العامل النفسي هو اقوى واحد
Physical difficulty in the beginning	When I first went home, I had difficulty 95%	أول ما رحت البيت، كانت عندي صعوبة 95%
Determination	I put in my head to rely on myself	خلاص حطت بدماغي اتكل على حالي
Willpower Determination	No, the determination is strong, the will is strong	لأ العزيمة قوية الإرادة قوية
Determination	I had determination, I entered the operation, and I did not despair, I did not despair	كان عندي عزيمة، دخلت العملية وأنا ما يأست ما يأست
Faith (Rely on God)	I told them, nothing will happen to you except what God has destined for you I went into operation, we rely on God and the doctor, and	قل لن يصيبكم إلا ما كتب الله لكم دخلت العملية، نتكل على الله والدكتور ونتكل على الدكتور ونتكل على الله

	we rely on the doctor, and we rely on God	
Memories of ICU- Feeling cold	The air conditioner was as like a refrigerator...cold...the room was cold	التكييف كأنه ثلاجة خضره كأن ثلاجة بارده اهي باردة الغرفة
Memories of ICU- sounds	I told my father I will rest, I slept, I woke up as if I was sitting in an imaginary house that they are building. I mean they are hitting, takh, takh, I hear noises, takh, I feel…bones	قلت له أبي أريح، نمت، صحيت كأني جالس في بيت توهم يبنونه يعني يطقون طاخ طاخ اسمع أصوات، طق، أحس العظم
Talking to staff	I was chatting with the Sudanese (nurses)	قعدت أسولف مع السودانيين
Insomnia	I couldn't get sleep	ما يجيني نوم
Strong morale	He (doctor) told me, God bless, your spirits are strong	قال لي ماشاء الله عليك، معنوياتك قوية
Independence	And I would bring the cane just in case, I wouldn't lean on it	والعصا أجيبها للاحتياط ما اتكي عليها
Pain Pain killer	I couldn't move from the pain…I needed pain killer	من الألم مسكن الألم
Difficulty in walking in the beginning	On the second day, somebody from physiotherapy came, I walked as if my leg weighed one ton…I felt it heavy, I felt it as a rod of iron concrete, of course, there was no iron. The first day I walked, it was difficult	يوم ثاني جاي واحد من عندكم (....) في العلاج الطبيعي (...مو واضح)مشيت كأن ثقلي هذي وزنها طن،إي والله، كأن وزنها طن، أحسها ثقيلة، أحسها صب خرسانة حديد (...مو واضح) شباك، شبكة حديد، طبعا مو حديد كان أول يوم مشيت، صعبة
Difficulty in walking in the beginning	I stayed at home, and one week after discharge from the ICU, I went out	قعدت في البيت، أول ما طلعت من العناية بعد أسبوع طلعت، جيت
Going out Friends Nature Coping	I got into my cousin's car, I told him to take me out, I mean to just change scenery…I went to the sea, I have friends who go to the sea…I talked to the sea (laughing) and said… O sea, take as much as you want	ركبت ويا ولد عمي في السيارة، قلت له ودني البيت كأنه أغير جو بس رحت البحر ، طبعاً عندي جماعة من أرامكو يدخلون بحر أسولف أقول خذ يا بحر قد ما تبي يعني أشياء اسولف مع البح
Good health now	My health is good now	صحتي عال العال
Dissatisfaction with weight	I just need help to lose weight…I swear to God, not only it is bothering me…I saw a snap (snapchat) of a person, before and after, he changed…I don't know, now I am 95 (kg), I want to reach 70-75 (kg)	كيف أنزل وزني والله مو بس مضايقني شفت سنابراح أحد صورة، قبل وبعد، تغير، يعني كان كذا، صار هاللون، أنا ما ادري الحين (...مو واضح) 95، أبي أوصله إلى 75 -70
Physical Rehab Fear	After I returned home, I came back to you (hospital) on the second day to do physical therapy...She told me to step on my leg, I told her I am scared the rod will come out, she said no, rely on God…(these exercises) helped me a lot	بعد ما رجعت البيت، عدت لكم بعد يوم ثاني، جيت للعلاج الطبيعي قال لي ادعس على رجل قلت لها أخاف يطلع الصيخ ، قالت ما يطلع، اتكل على الله

		ساعدتني واجد إيه
Family support (Mother) Friends	I have dinner with mother every day…every day the guys (friends) come	أنا حاضر كل يوم للوالدة على الأكل كل يوم يجون الشباب
No pain now Pain killer	There is no pain now. After ICU, I had pain for 2-3 days…I needed pain killer…now, there is no pain, there is nothing except health…	لا مافي ألم مسكن يومين 3 الحين، مافي إلا العافية
Walking	I am walking now…	هداني أمشي
Work	(I enjoy) my work, certainly, my work	أنا شغلتي، طبعاً شغلتي ولا
Overthinking Worry	I swear to God, look, overthinking is there...I think of stocks…financially	والله شوفي التفكير موجود أسهم، يفكر بأسهم مالياً
Faith (Thank God)	Thank God	الحمد لله
Faith (Thank God)	Praise to God, lord of all worlds	الحمد لله رب العالمين
No financial worry	No, no it doesn't worry me	لا لا ما يقلقني
Improved cognitive function No change in cognitive function	Mentally, I am better (says the year, the month, and the day) …I mean, I don't feel there is a change in my mind before and after	ماشاء الله عليك صرت احسن من أول تمام، يعني ما تحس فيه تغيير في ذهنك قبل وبعد
Mood change in the beginning No change in mood now	My mood was so-so (after ICU), now it's okay	والله المزاج يعني شوي لأ تمام
Health definition	Health is the body, health is the psychology, health is all life	الصحة والعافية الجسد، الصحة والعافية النفسية، الصحة والعافية هي كل الحياة
Memories of ICU Thirst Pain	What I remember from ICU is pain and thirst	أتذكر وأنا في العناية قعدني الألم وعطشان،
Don't want to remember!	I don't remember and I don't want to remember	لأ، ولا اتذكر ولا ابغى اتذكر
Overcoming Tolerating	The ICU is about the ego…the ego only…they were days of difficulty.	العناية غرور، غرور بس كانت أيام صعوبة
Survivor Second Chance	The ICU, you say the ICU, the ICU is when one either comes out to be buried or comes out reborn	عناية، انتي قلتي عناية، العناية الواحد يطلع منها مقبور أواحد يطلع منها مولود

Appendix 6.6. Theme 1 collation

Theme	Subtheme	Code	Patient quotation
My ICU experience	Physical and psychological distress	Pain	*I couldn't move from the pain…I needed pain killers.* ***PA*** *I couldn't tolerate the least pain, I would need pain killers, things like that, it affected me a lot…* ***PB***
		Limitations in movement	*When I remember my experience, for almost 8 or 9 days I was in bed, my feet did not reach the ground, literally.* ***PB*** *What bothered me were the devices. I mean, the devices were the ones hindering me from movement…* ***PC*** *My body muscles were not the same…* ***PC***
		Psychological	*It was more of a mental exhaustion. It was psychological fatigue.* ***PC*** *The difficulty in the first three days in ICU, the situation that I was in and the events that followed me, there were some things that bothered me psychologically…but after these three days, I can tell you that the situation changed by one hundred and eighty degrees, of course for the better…And I started getting better and this started to lift my spirits, especially when the fever stopped…* ***PF***
	Memories of ICU	Cold	*The air conditioner was like a refrigerator...the room was cold.* ***PA*** *The first feeling that comes to my mind is that I was cold, the ICU was cold…****PE***
		Sounds	*I told my father I would rest. I slept; I woke up as if I was sitting in an imaginary house that they were building. I mean they were hitting, takh, takh, I heard loud noises…****PA*** *Yes, yes, the sounds of the devices and feeders (IV pumps) that were in my hands because they were putting two together for me…PF*

		Blood draw	*I was very affected…They came to take blood from me, they nibbled my hands, that was the day I had the most bleeding, and they came to clean it, and that was worse…**PC*** *They were not able to take blood, I mean, the blood was not coming out. They used to bring me nurses, as you say, specialists, in drawing blood or something like that, maybe an "IV team". It was very difficult to take my blood….I frankly suffered psychologically, and I had fear and awe when they said that if my veins did not work, they would put it (medication) through a vein in the neck…Real horror…My hands were stained blue and green…That was suffering I can't forget honestly… **PF***
	Associations	Smell	*The smell of perfume or these wipes…I started smelling the ICU everywhere I saw a wet wipe. I intentionally bought it so that I try the bad thing that I experienced because of this smell, so oh, I have it in the office, in the car, at home, everywhere, to get rid of this bad feeling. I mean, a strong memory is present with these fragrant wipes, and oh yeah, I got used to it now. **PE*** *…There are some smells that remind me of the hospital, not that I hate them, but they are associated with the hospital…The smell of sterilizers, this disinfectant… **PF***

Appendix 7.1 The real-time impact of thesis

Area of impact	Objective	Action	Responsibility	Status/date	Evidence
ICU experience	Enhance ICU environmental factors by introducing evidence-based ICU design.	Integration of features for reduction of noise, daylight, incorporation of family areas in the patient room and lounge area	Hospital administration and Life-ICUS researcher	Complete/December 2021	Images a, b, c
	Promote patient communication and PICS education.	Introduction of the Patient Communicator App	ICU manager	Complete/November 2023	Image d, e
	Assess and manage pain in a systematic manner	Implementation of the CPOT assessment tool	ICU clinical nurse specialist	Complete/June 2021	Image f
	Detect delirium to instigate preventive and early management strategies	Implementation of the CAM-ICU delirium screening tool	ICU clinical nurse specialist	Complete/February 2021	Image f
ICU clinicians' education	Enhance the knowledge of ICU doctors and nurses on PICS	Grand round for all medical and nursing team on PICS Presentation at Emirates Critical Care Conference	Life-ICUS researcher	Complete/May 2022	Image g
Patient and family education	Promote knowledge of PICS among patients and families	Implementation of the Patient Communicator App	ICU manager	Complete/November 2023	Image d, e
		Video about PICS	Life-ICUS researcher	Complete/May 2022	Video a
Transitions of care	Enhance communication among clinicians responsible for care of patient in ICU and after ICU	Implementation of the ICU referral form	ICU clinical nurse specialist	In process	Appendix 7.2
Post-ICU experience	Provide post-ICU care and screening of PICS symptoms	Establishment of the post-ICU or PICS clinic	ICU clinical nurse specialist and Life-ICUS researcher	In process	Section 7.4.2
		Integration of post-ICU appointments in organization's Patient App	ICU clinical nurse specialist and Life-ICUS researcher	In process	Image h
	Activate patient and community engagement	Establishment of a PICS support group	Life-ICUS researcher and senior ICU nurse	Not started	None
		Establishment of ICU volunteer program	Life-ICUS researcher and senior ICU nurse	Not started	None
Critical Care Community engagement	Engage critical care professional communicates in discussions regarding PICS	Presentation of study and information on PICS to Saudi Critical Care Society	Life-ICUS researcher	In process	Image i

Image a. ICU room- single bed, windows from ground to ceiling, noise reducing walls, lifting and mobility device imbedded in ceiling, and other features. (Almoosa Specialist Hospital, 2021)

Image b. ICU nursing monitoring; decentralized stations, safety and privacy features. (Almoosa Specialist Hospital, 2021)

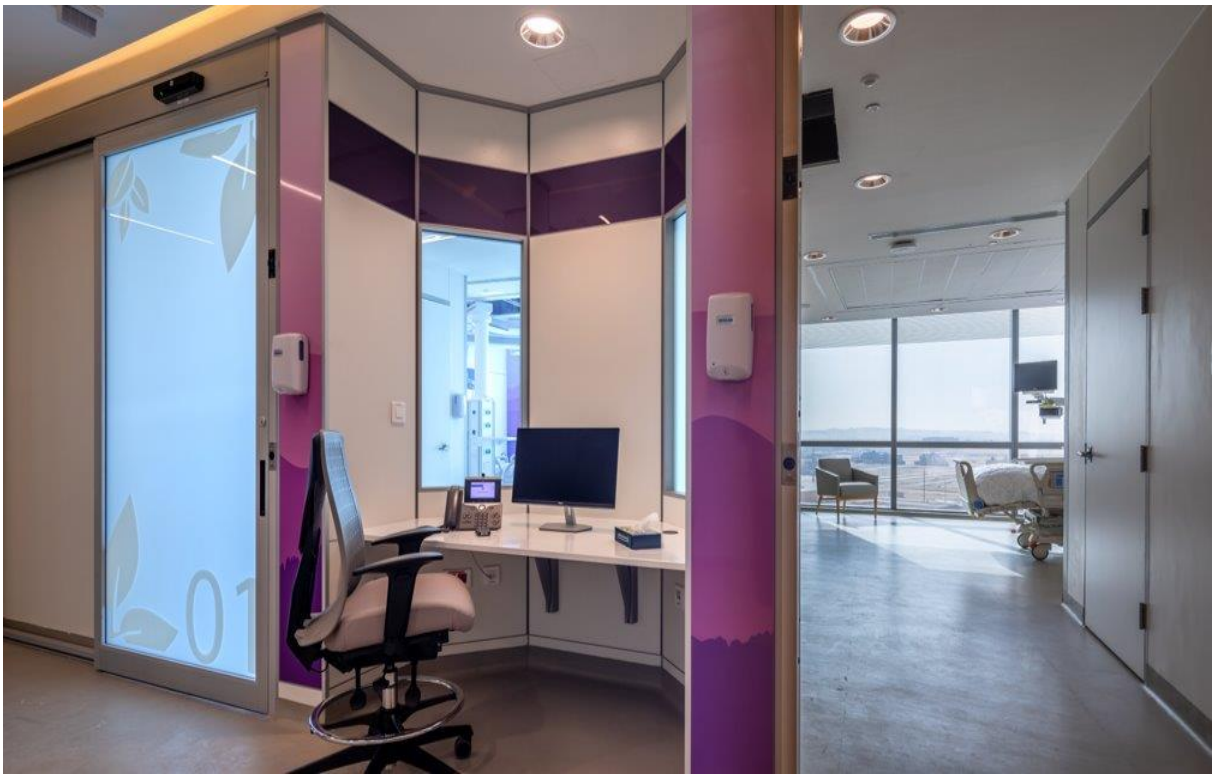


Image c. Hanging Garden for family and visitors. (Almoosa Specialist Hospital, 2021)

Image d. ICU communicator app in Arabic and English

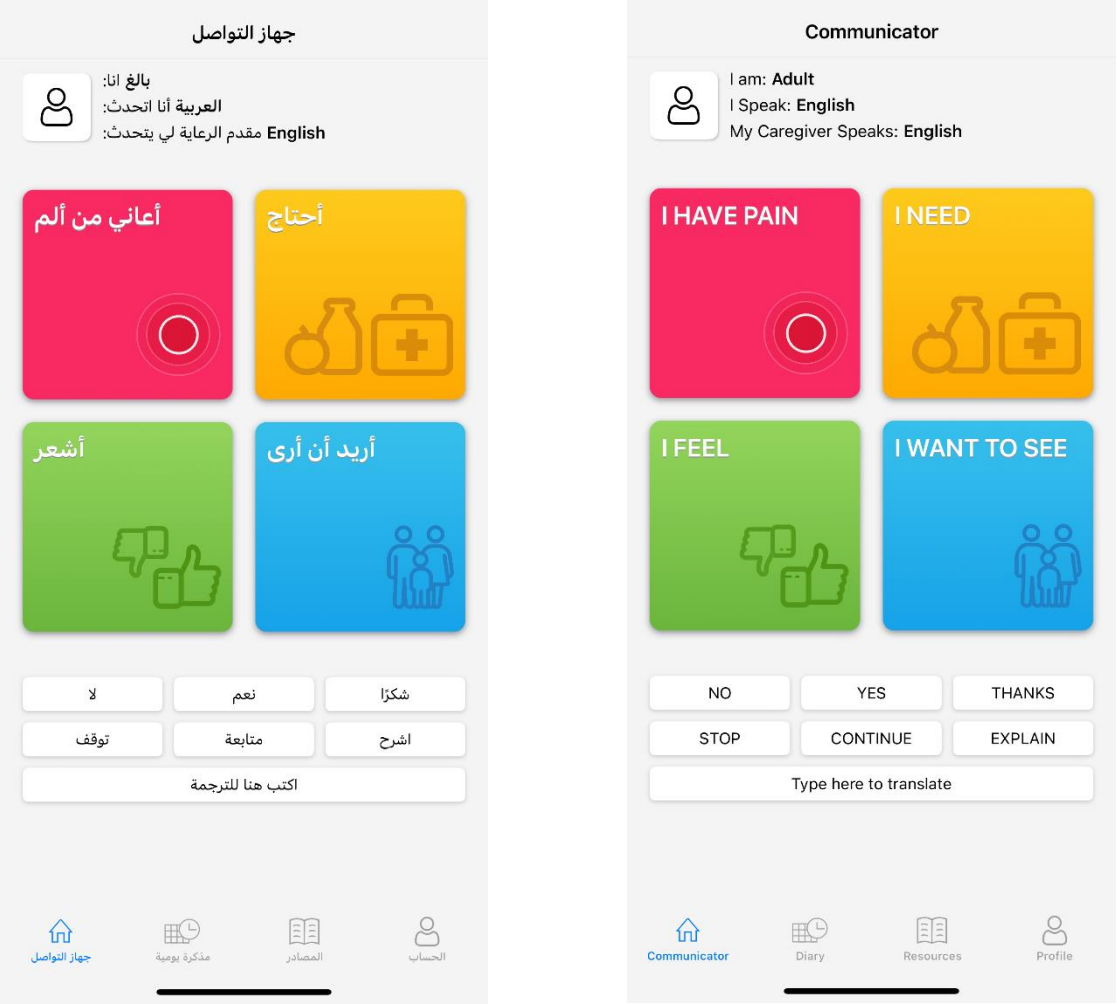
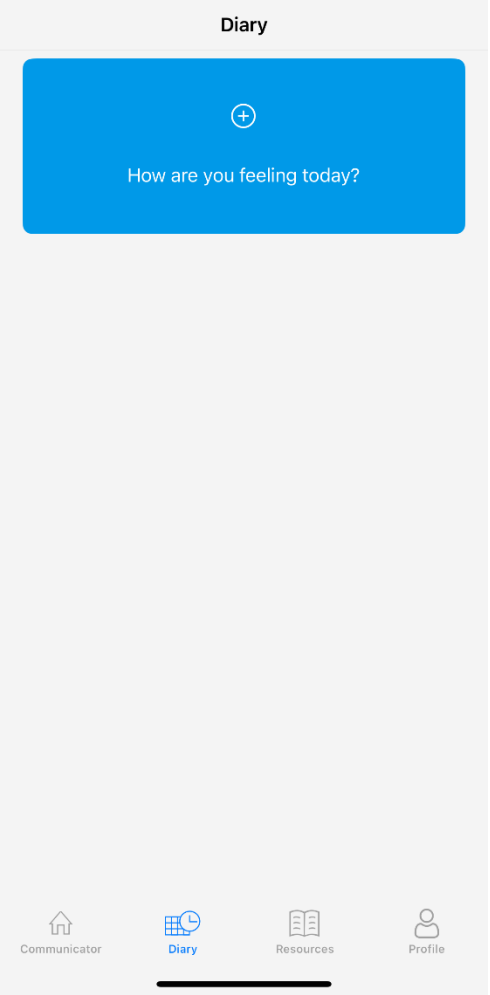


Image e. ICU communicator app- Diary feature, and PICS information



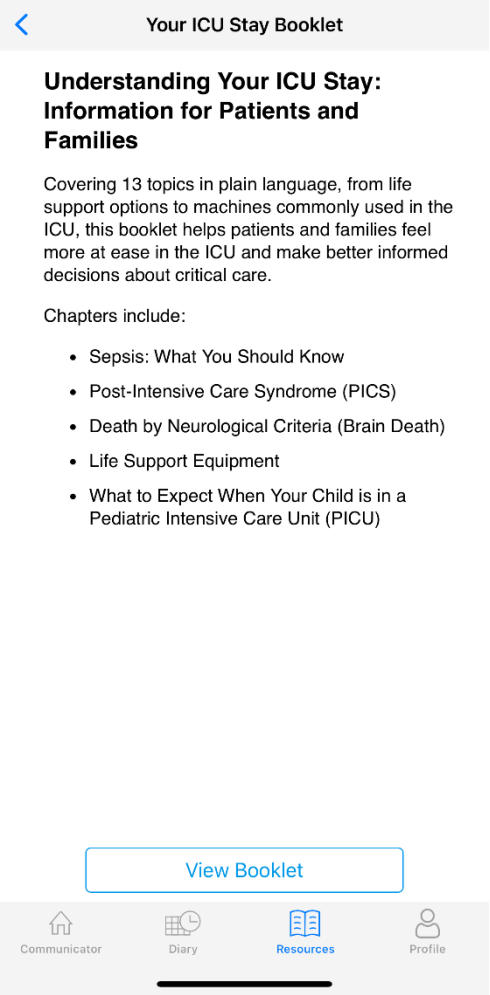


Image f: Implementation of CPOT tool

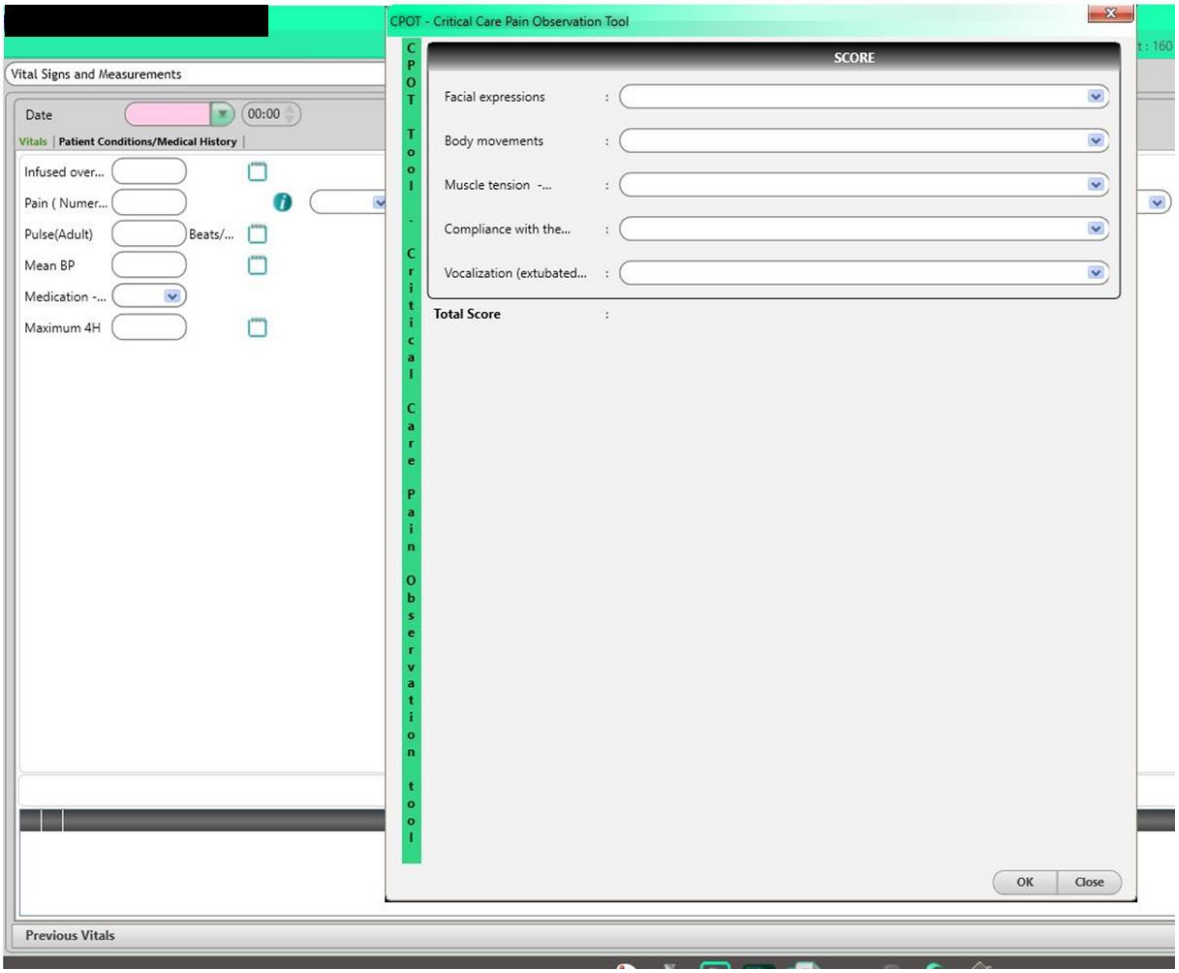


Image g: Grand round for all medical and nursing team on PICS

CLOUDY MIND - NU BONIGLIO

SURVIVING THE INTENSIVE CARE UNIT:

Post Intensive Care Syndrome

Grand Round

Hera Tashjian, RN, CCNS

May 2022

Image h Patient appointments through Almoosa App

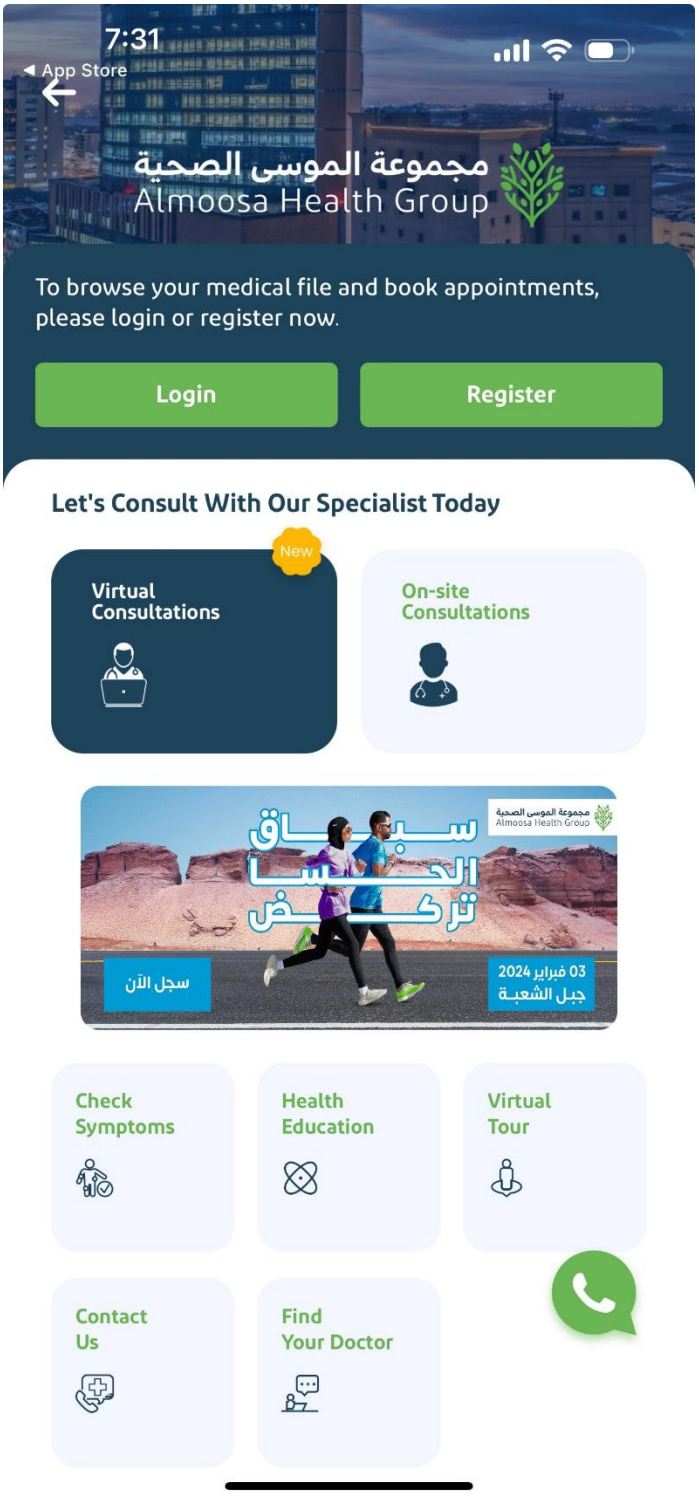


Image i: Presentation at Saudi Critical Care Society

Appendix 7.2 Referral form

Date:	
To:	
From (Name, Phone Number):	
Patient:	

I recently cared for your patient, referenced above, in our intensive care unit. This patient had the following diagnoses and hospital course

Date of Admission:	
Date of Discharge:	
Diagnoses:	
Hospital course (Insert Narrative):	
Surgeries/ Procedures:	
Discharge Medications (Mark new medications with (*) asterisks)	

I would also like to bring to your attention that the patient has been screened for suggestive symptoms of post-intensive care syndrome (PICS) upon discharge from the ICU. The following are screening test results upon discharge and recommendations for follow up:

1. Physical impairments:

- ☑ ADL Score
- ☑ IADL Score
- ☑ Consult physiotherapist
- ☐ Consult speech therapist
- ☐ Consult occupational therapist
- ☐ Follow-up patient in ____ days
- ☐ Schedule patient for follow-up in post-ICU clinic

2. Cognitive impairments:

- ☐ MoCA score _____
- ☐ Consult cognitive rehab specialist
- ☐ Follow up in ____ days
- ☐ Schedule patient for follow-up in post-ICU clinic

3. Mental health

☐ HADS Anxiety score _____

☐ HADS Depression score _____

☐ PTSD screening

☐ Consult mental health specialist

☐ Follow up in ____ days

☐ Schedule patient for follow-up in post-ICU clinic

I would be happy to speak with you if you have questions about this patient's ICU course or about what to expect after critical illness. Feel free to contact me at the phone number above.