The health and social consequences of alcohol related admissions to critical care

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Abstract

Introduction: Alcohol related admissions to critical care are increasing. However, there is uncertainty about the impact of excessive alcohol use on the intensive care stay and recovery from critical illness.

Aim: The aim of this study was to understand the impact of alcohol use disorders on the critically ill patient's journey.

Settings & participants: The setting for this study was a 20 bed mixed ICU, in a large teaching hospital in Scotland. On admission patients were allocated to one of three alcohol groups: low risk; harmful/hazardous or alcohol dependency.

Methods: This was a mixed methods study. An 18 month prospective observational cohort study was undertaken. In addition, 21 in depth, semi structured interviews were undertaken with patients with and without alcohol use disorders, three to seven months after discharge from critical care.

Results: 580 ICU patients were screened for the presence of alcohol use disorders during the study period. 34.4% of patients were admitted with a background of alcohol misuse. ICU stay was significantly different between the three study groups, with those in the alcohol dependency group having a longer stay (p=0.01). After adjustment for all lifestyle factors which were significantly different between the groups, alcohol dependence was associated with more than a twofold increased odds of ICU mortality (OR 2.28; 95% CI 1.2-4.69, *p*=0.01). Four themes which impacted on recovery from ICU were identified in this patient group: psychological resilience; impact and support for activities of daily living; social support and cohesion; and the impact of alcohol use disorders on recovery.

Conclusions: Alcohol related admissions account for a significant proportion of admissions to critical care and alcohol dependency is independently associated with ICU outcome. A more targeted rehabilitation pathway for all patients leaving critical care, with specific emphasis on alcohol misuse if appropriate, needs to be generated.

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Publications related to this programme of study

McPeake, J. (2012) Holistic Rehabilitation from intensive care: lessons from America. International Practice Development Journal; 2(2):1.

McPeake, J. O'Neill, A. Kinsella, J. (2013) Assessing alcohol related attendance at emergency departments. Emergency Nurse; 20(9):26-30.

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McPeake, J. Shaw, M. O'Neill, A. Forrest, E. Puxty, A. Quasim, T. Kinsella, J. (2015) Do alcohol use disorders impact on long term outcomes from intensive care? A prospective observational cohort study. Critical Care; 19:185.

Published Abstracts related to this programme of study

Emerson, P. **McPeake, J.** O'Neill, A. Gilmour, H. Forrest, E. Kinsella, J. (2013) The utility of scoring systems in critically ill patients with cirrhosis admitted to a general ICU. Critical Care Medicine; 41(12): Suppl. 745.

Emerson, P. **McPeake, J**. O'Neill, A. Gilmour, H. Puxty, A. Forrest, E. Kinsella, J. (2014) Organ failure, outcomes and deprivation status among critically ill cirrhosis patients – a one year cohort study. Journal of the Intensive Care Society; 15(2):178.

McPeake, J. Shaw, M. O'Neill, A. Puxty, A. Forrest, E. Quasim, T. Kinsella, J. (2014) Alcohol Related Admissions to ICU: An 18 month prospective cohort study. Critical Care Medicine; 42(12):A1459.

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Soulsby, CR, **McPeake, J.** Ashcroft, C. Kinsella, J. Shaw, M. Quasim, T. (2015) Utilisation of existing community rehabilitation services by critical care survivors. Critical Care; 19(1):P557.

McPeake, J. Soulsby, C. Quasim, T. Kinsella, J. (2015) Intensive care referral and admission: do the criteria for liver disease match? Critical Care;19(1):P384.

Millar, J. **McPeake, J.** Fulton, R. Kinsella, J. (2015) Not all cirrhotics are equal: acute on chronic liver failure in the ICU. Journal of the Intensive Care Society; 16(1): Supplement 47.

Research funding related to this PhD

Funder	Title of Project	Amount Obtained	Date
Winston Churchill Memorial Trust	Holistic Rehabilitation from critical care: lessons from America (Travelling Fellowship Award)	£4500	2011
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Medical Research Scotland Vacation Scholarship	Liver Cirrhosis and predictive scoring tools in critical care *McPeake, J. Emerson, P. Kinsella, J.*	£1400	2013

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Health Foundation (Shine Award 2014)	**In**tensive Care **S**yndrome: **P**romoting **I**ndependence and **R**eturn to **E**mployment (InS:PIRE) *McPeake, J. Devine, H. Daniel, M. Fleming, L. Crawford, R. McTavish, P. Walker, A. Kinsella, J. Quasim, T.*	£68,265	2014-2015
CSO NMAHP Clinical Academic Fellowship	The promotion of self-management in acute and critical care *McPeake, J. Quasim, T. Forrest, E. O'Neill, A. Burns, H. Kinsella, J*	£125, 869	2014-2017
Scottish Government (Sustainability Award)	**In**tensive Care **S**yndrome: **P**romoting **I**ndependence and **R**eturn to **E**mployment (InS:PIRE) *McPeake, J. Devine, H. Daniel, M. McTavish, P. Kinsella, J. Quasim, T.*	£100,000	2015-2017

Further applications for funding in submission:

Funder	Title of Project	Funding application	Outcome date
Society of Critical Care Medicine Thrive Award	Peer Support in Critical care Survivors: International Collaboration *McPeake, J. and Quasim, T.*	$5000	July 2015
Health Foundation (Scale up and Sustainability Award)	**In**tensive Care **S**yndrome: **P**romoting **I**ndependence and **R**eturn to **E**mployment (InS:PIRE) *McPeake, J. Devine, H. Daniel, M. Crawford, R. McTavish, P. Kinsella, J. Quasim, T.*	£500,000	February 2016

Author's Declaration

I declare that this thesis represents my own work except where referenced to others.

I declare that this thesis does not include work forming part of a thesis presented successfully for another degree.

Joanne McPeake

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List of Abbreviations

Acute Physiology and Chronic Health Evaluation	APACHE
Acute Respiratory Distress Syndrome	ARDS
Acute Kidney Injury Network	AKIN
Akaike's Information Criterion	AIC
Alcohol Use Disorder	AUD
Alcohol Use Disorder Identification Test	AUDIT
Alcohol Withdrawal Syndrome	AWS
Alcoholic Liver Disease	ALD
Area Under the Curve	AUC
Arterial Partial Pressure of Oxygen	Pa02
Aspartate Transaminase	AST
Bolus Titrated Group	BTG
Brief Chronic Pain Inventory	BCPI
Brief Illness Perception Questionnaire	BIPQ
Brief Michigan Alcohol Screening Test	B-MAST
British Association of Critical Care Nurses	BACCN
% Carbohydrate-Deficient Transferrins	%CDT
Catheter Related Blood Stream Infection	CRBSI
Centre for Epidemiologic Studies Depression Scale	CES-D
Child-Turcotte Pugh	CTP
Child Turcotte Pugh-Lactate	CTP-L
Child Turcotte Pugh+ Lactate	CTP+L
Chronic Liver Failure- Sequential Organ Failure Assessment	CLIF-SOFA
Chronic Pain	CP
Clinical Institute Withdrawal Assessment	CIWA
Confidence Interval	CI
Confusion Assessment Method for the Intensive Care Unit	CAM-ICU
Coronary Care Unit	CCU
Creatinine	Cr
Cut Down, Annoyed, Guilty, Eye Opener	CAGE
Delirium Tremens	DTs
Department of Health	DoH
EuroQol-5D	EQ-5
Fast Alcohol Screening Test	FAST
Fraction of Inspired Oxygen	Fi02
Gamma-aminobutyric acid	GABA
Gamma-Glutamyl-Transferase	GGT
Generic Rehabilitation Assistant	GRA
Glasgow Alcoholic Hepatitis Score	GAHS
Glasgow Centre for Population Health	GCPH
Glasgow Modified Alcohol Withdrawal Scale	GMAWS
Glutathione	GSH
Hazard Ratio	HR
Hepatorenal Syndrome	HRS
High Dependency Unit	HDU
Hospital Anxiety and Depression Score	HADS
Impact of Events Scale	IES
Information Service Division	ISD
Infusion Titrated Group	ITG
Intensive Care Delirium Screening Checklist	ICDSC

Intensive Care Society	ICS
Intensive Care Unit	ICU
Intensive Care Stress Reaction Scale	ICSRS
Intermittent Positive Pressure Ventilation	IPPV
Interpretative Phenomenological Analysis	IPA
Interquartile Range	IQR
Intravenous	IV
Length of Stay	LOS
Mean Corpuscular Volume	MCV
Medical Intensive Care Unit	MICU
Mental Health Substance Abuse	MHSA
Michigan Alcohol Screening Test	MAST
Model for End Stage Liver Disease	MELD
Mortality Rate Ratio	MMR
Multi Disciplinary Team	MDT
N-methyl-D-aspartate	NMDA
National Health Service	NHS
National Institute of Health and Care Excellence	NICE
Next of Kin	NOK
Odd Ratio	OR
Post Intensive Care Syndrome	PICS
Post Traumatic Stress Diagnostic Scale	PDS
Post Traumatic Stress Disorder	PTSD
Quality Adjusted Life Year	QALY
Quality of Life	QOL
Quintile-Quintile	Q-Q
Randomised Control Trial	RCT
Readiness to Change Questionnaire	RCQ
Receiver Operator Characteristic	ROC
Renal Replacement Therapy	RRT
Repeatable Battery for the Assessment of Neuropsychological status	RBAWS
Risk, Injury, Failure, Loss and End Stage Renal Disease	RIFLE
Royal Free Hospital	RFH
Scottish Index of Multiple Deprivation	SIMD
Self Efficacy Score	SES
Short Form Health Study 36 Item	SF-36
Short Michigan Alcohol Screening Test	SMAST
Scottish Intensive Care Society Audit Group	SICSAG
Six Minute Walk Test	6MWT
Scottish Trauma Audit Group	STAG
Sequential Organ Failure Assessment	SOFA
Simplified Acute Physiology Score	SAPS
State-Trait Anxiety Inventory	STAI
Stages of Change Readiness and Treatment Eagerness Scale	SOCRATES
UK End Stage Liver Disease	UKELD
Ventilator Associated Pneumonia	VAP
Visual Analogue Scale	VAS
White Cell Count	WCC
World Health Organisation	WHO

Chapter One: Introduction

Chapter One provides the context and rationale for this thesis. The research objectives and an overview of the subsequent thesis chapters is also provided.

1.1 Background to study

Alcoholism is a complex disorder responsible for a host of economic, social, medical and personal afflictions (Litten and Fertig 2003). Very few Western countries have felt this burden as severely as Scotland.

Deaths and alcohol related admissions have risen steeply in the UK (Scottish Government 2009, Mayor 2010). Moreover, the UK has one of the fastest growing rates of liver disease in the world (Leon and McCambridge 2006, Walsh, McCartney, McCullough et al 2013). Indeed, 40% of patients with an alcohol related admission are estimated to experience alcohol withdrawal in hospital. Therefore, alcohol misuse represents a significant public health problem (Benson, McPherson, Reid 2012).

Over the last decade, unhealthy alcohol use has impacted heavily in the Intensive Care Unit (ICU). However, there is genuine uncertainty regarding concerning the acute and chronic effects of alcohol use disorders (AUDs) and their impact in this population, despite its frequent presence in patients admitted to critical care areas (Gentilello 2007).

From the limited body of evidence available, it is clear that there are a variety of detrimental effects which can occur as a consequence of alcohol dependency in critical care. For example, alcohol dependence is independently associated with sepsis, bacterial infections such as ventilator-associated pneumonia and a prolonged duration of mechanical ventilation (de Wit, Best, Gennings et al 2007, O'Brien, Lu, Ali et al 2007, Gacouin, Legay, Camus et al 2008). Furthermore, alcohol dependency has been associated with increased ICU and hospital mortality (O'Brien et al 2007).

Despite this, the impact of AUDs, including complications and detrimental effects on all disease processes in critical care, has never been extensively

researched in the UK. Importantly, the effect of the combination of alcohol related disease and critical illness on long term outcomes has been poorly studied despite its increasing importance. Indeed, patients with AUDs have been specifically excluded from previous studies exploring critical care experience and follow up. This dearth of research, particularly from the UK, forms the main justification for this PhD.

1.2 Aim and objectives

The overall research aim of this study was to explore the health and social consequences of alcohol related admissions to critical care.

This thesis aimed to address the following research objectives:

1. Analyse the nature and complications of alcohol related admissions to critical care

2. Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis

3. Explore patterns of recovery for patients with and without alcohol use disorders

4. Determine whether alcohol use disorders are associated with survival in critically ill patients at six months post ICU discharge

5. Examine the impact of critical care on future behaviour with regards to alcohol intake.

1.3 Thesis structure

This thesis comprises nine chapters and begins by reviewing topic specific literature relevant to the thesis. Chapter two provides a context to the problem of unhealthy alcohol behaviours in Scotland and reviews the current literature on the subject of alcohol related admissions to critical care. This chapter also identifies gaps in the current body of literature.

Chapter Three explores the literature surrounding the specific research methods which were employed within this body of work.

Chapter Four details how these research methods were employed during the programme of work.

Chapter Five presents the results from the 18 month prospective observational cohort section of this study. This analysis firstly explores the issues associated with alcohol related admissions in critical care; it then details long term outcomes of this cohort.

Chapter Six presents the results of the liver cirrhosis sub study. This chapter is presented in two sections. The first phase of Chapter Six explores the outcomes of patients admitted with a background of liver cirrhosis during the first 12 months of the study period. The second phase of this chapter, which was a collaboration with another research group (St George's, London and St Thomas', London), externally validated two new prognostic scoring tools for patients admitted with a background of liver cirrhosis to a general ICU setting. Both of these studies were conducted by the PhD student supervising two undergraduate medical students undertaking an intercalated BSc.Med.Sci. They undertook this work as part of their degree programme. The PhD student's role in Chapter Six included overall design of the study, contribution with data collection, supervision of analysis, supervision and overall responsibility for the presentation of results in the form of academic reports and final publications.

Chapter Seven presents the qualitative findings from this mixed methods study. This section of the study aimed to explore recovery from ICU and the impact of alcohol on this recovery. In total, 22 in depth, semi structured interviews were undertaken, three to seven months after intensive care discharge. Interpretative Phenomenological Analysis was used as the analytical framework.

In Chapters Five and Six, individuals involved in the study are referred to as 'patients'. However, in Chapter Seven individuals taking part in the semi structured interviews are referred to as 'participants'. At three to seven months post intensive care discharge, individuals are no longer patients.

Chapter Eight discusses the results and findings from the entire thesis. The results and findings of this thesis will be presented in relation to the Salutogenic perspective of health. Salutogenesis is the theory of health proposed by the medical sociologist Aaron Antonovsky (1979). Final conclusions and key recommendations for clinical practice are presented in Chapter Nine.

Chapter Two: Literature Review

2.1 Search strategy

A literature search was undertaken to examine the content of current evidence in this area. Keywords explored included: adult; alcohol; alcohol use disorders; alcoholic; alcohol dependency; harmful; intensive care; critical care; problem drinker; withdrawals; ethanol and cirrhosis. The following databases were searched for this literature review: Medline; CINAHL; British Nursing Index; EMBASE; Cochrane Library; Web of Science and The Knowledge Network (Guidelines). Additionally, relevant books, government websites and professional association policy documents were utilised. References of retrieved articles were reviewed and additional references which were deemed to be relevant were evaluated. The literature review was limited to the most recent papers (2009 onwards), however, highly cited seminal papers were also included for review. This literature search was repeated at regular intervals throughout the research period to ensure all evolving evidence in this topic area was analysed.

It is well documented that the subject of alcohol related admissions to critical care is not discussed extensively in the literature (Gentilello 2007). Further, there are limited trials and interventional studies in this particular area. Those who study evidence based medicine methodology, place prospective randomised control trials (RCTs) at the highest echelon of evidence to judge the true benefits of an intervention. Multicentre studies are preferred to ensure the effectiveness of interventions in the real environment (external validity) (Sorensen, Lash, Rothman 2006, Ospina-Tascon, Buchele, Vincent 2008, Polit and Beck 2009). Due to the heterogeneity of critically ill patients, RCTs are not always feasible, appropriate or ethically permissible in the ICU environment (Ospina-Tascon et al 2008). Further, when they are available, RCTs do not necessarily provide all the answers and may in fact raise more questions than the researcher started with (Vincent 2004). Therefore, while the RCT provides the best evidence regarding an intervention or therapy, when none exist in the area of interest, other forms of evidence should be graded to provide the answers to the question being posed (Vincent 2004, Dellinger, Vincent, Marshall et al 2008). Therefore all available evidence, irrespective of the methodologies

employed, was examined and critically appraised throughout this review of the literature.

2.2 The cultural history of alcohol

The earliest evidence of humans preparing or fermenting alcohol comes from the chemical analysis of residues found inside pottery jars discovered in the ancient grave in Jiahu, Northern China, from around 7000-6600 BC (Gately 2008). The findings from China suggest that the local population made fermented drinks with rice, honey, grapes and hawthorn berries. However, it is impossible to know what part alcohol played in the lives of residents in Jiahu. For example, it may have merely been the best technology available for storing highly perishable items such as grapes, or it may have had the function of purposeful intoxication (Gately 2008).

Evidence from the settlement of Skara Brae in Orkney Scotland, whose stone dwellings have been preserved since 3100BC-2500 BC by virtue of having been buried beneath a sand dune for many thousands of years, provides the best evidence that the inhabitants were drinking for effect rather than to satisfy their hunger or their thirst (Dineley 2004). Pottery jars, with the capacity of up to thirty gallons have been found. The analysis of the vessels confirms that alcoholic beverages, which were made from barley and oats, were flavoured with meadowsweet and laced with deadly nightshade, henbane and hemlock (Dineley 2004, Gately 2008). Nightshade, henbane and hemlock are hallucinogenic and are deadly in certain quantities. Henbane induces blurred vision, dilated pupils, rapid heartbeat, dizziness, nausea and euphoria, as well as hallucinations in very small doses (Gately 2008). Deadly nightshade can cause the dilation of pupils, a mental state resembling mania and often pleasant or unpleasant hallucinations (Lee 2007). Hemlock on the other hand, is best known as a neurotoxin that paralyses before it kills (Gately 2008).

Over the thousands of years that have followed the era of Skara Brae, there has been an ever changing relationship with alcohol across the world, with different cultures finding a variety of roles for alcohol in society (Nicholls 2012). For the orthodox Jew, the drinking of alcohol is inherent in many types of religious

occasions. On the other hand, abstinence from alcohol is essential in the Islamic faith (Edwards 2000). Within traditional Scottish culture, however, the negative relationship could be seen to be largely static (Leon and McCambridge 2006).

2.3 Alcohol misuse and the Scottish context

Alcohol is the most frequently abused drug in the world. It is a global problem with compromises both individual and social development, with the harmful use of alcohol resulting in approximately 2.5 million deaths worldwide a year (World Health Organisation (WHO) 2011). Further, the WHO (2011) identifies alcohol as the third largest risk factor for ill health in developed countries behind only tobacco and high blood pressure.

Alcohol is an integral part of 21st century Scottish Life (Cameron, Morris, Forrest 2006). Around the globe Scotland is renowned for its whisky, as well as gin, vodka and other liqueurs. Breweries can be found the length and breadth of the country, from small croft breweries in the most remote rural areas of the country, to the large inner city plants (Scottish Government 2009). However, in recent years the negative consequence that alcohol has had on all aspects of Scottish society is easily identifiable (Scottish Government 2010a).

The impact that alcohol consumption has on the health of the Scottish Nation is startling, with one Scot dying every three hours of an alcohol attributable cause (Scottish Government 2011). Alcohol related mortality has not only doubled in the last 15 years, Scotland also has one of the fastest growing rates of liver disease and cirrhosis in the world (Leon and McCambridge 2006, Scottish Government 2009). Leon and McCambridge (2006) carried out an analysis of mortality rates across Europe from liver cirrhosis between 1955 and 2001. Mortality rates were calculated from the data in the WHO mortality database, which is one of the most detailed consolidated European data sets for cirrhosis mortality. During the periods of 1987-1991 and 1997-2001, Scottish cirrhosis mortality in men more than doubled (104% increase) and mortality in women increased by almost half (46%). These relative increases are the steepest in Western Europe and contrast with the declines apparent in most other countries, particularly those in the wine drinking regions of Southern Europe. Undoubtedly,

the rising Scottish problem of liver cirrhosis is directly linked with alcohol use (Figure 2.1).

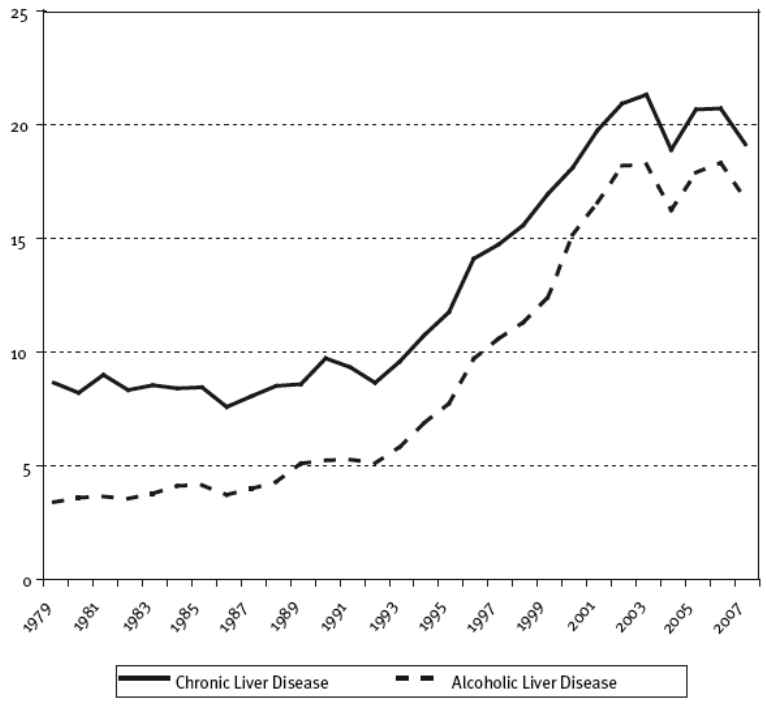

Figure 2.1: Death rates per 100,000 population in Scotland (age/sex-standardised, using European Standard Population) (Scottish Government 2008)

As consequence, the Chief Medical Officer has added alcoholic liver disease to the list of 'big killers' in Scotland, alongside heart disease, stroke and cancer (Scottish Government 2009).

2.3.1 Defining deprivation

Throughout this PhD the term deprivation will be referred to. This short section will provide a working definition. The terms deprivation and poverty are often used interchangeably (Scottish Government 2012). However, deprivation is defined more widely as the range of problems that arise due to lack of resources or opportunities in health, safety, education, employment, housing and access to services, as well as absolute income (Scottish Government 2012).

The Scottish Index of Multiple Deprivation (SIMD), which was first developed in 2004, is the Scottish Government's official tool for identifying those geographical areas in Scotland suffering from deprivation (Scottish Government 2012). It has

advantages over the previous tool utilised: the Carstairs (DEPCAT) score. The predominant criticism of the Carstairs score was the 10 year lag between updates due to its derivation from census data (McLoone 2003). In contrast, the SIMD is updated on a more frequent basis.

The SIMD incorporates different aspects of deprivation and summarises them into one score. It separates Scotland into 6505 small areas called data zones. The index then provides an overall ranking for each data zone, as well as an individual ranking for each data zone. Within a research context, the SIMD data zones are usually split into quintiles, deciles or vintiles (Scottish Government 2012). The different aspects of deprivation which are incorporated into the SIMD are: employment; income; health; education, skills and training; geographic access to services; crime and housing (Scottish Government 2012).

Within this PhD, the SIMD will be used as a measure of deprivation and the data zones presented in deciles. Furthermore, deprivation will be defined as the two lowest deciles of the SIMD.

2.3.2 The Glasgow effect

While a number of dimensions of health are no different in Glasgow to elsewhere in Scotland and other de-industrialised areas of the UK, there are many indicators which are elevated in this region (Glasgow Centre for Population Health (GCPH) 2014a). Traditional explanations of the poor health profile of Glasgow have focussed on the effects of socio economic deprivation driven by the post-industrial decline in recent decades. However, despite their importance, these explanations do not appear to fully explain the particularly poor health profile in Glasgow (Walsh, Taulbut, Hanlon 2010a).

This was exemplified in research published in 2010 which detailed the deprivation profiles of Liverpool, Manchester and Glasgow (Walsh, Bendel, Jones et al 2010b). Premature death in Glasgow was 30% higher than the two English cities, with deaths at all ages 15% higher. Furthermore, the excess mortality was shown for all adult age groups, sexes and across all neighbourhood types (deprived and non-deprived) (Walsh et al 2010b). These results and findings have resulted in researchers looking at why these differences exist and more importantly, looking to new solutions for improving health and wellbeing in deprived areas.

Initially the excess mortality in Glasgow was attributed to chronic disease conditions such as cardiovascular disease and ischemic heart disease. However, by the 1990's excess mortality in this area was replaced by deaths from alcohol, drugs, suicide and violence (McLoone 2003). Although the increase in alcohol related deaths has been seen in all areas of Glasgow, the largest rise was seen in the most deprived data zones. In the period between 1981 and 2001, alcohol related deaths increased by 177% in the most deprived areas of Glasgow compared to an 81% increase in the least deprived areas (Shipton, Whyte, Walsh 2013, GCPH 2014a).

Despite a drop in alcohol related deaths in the mid 2000's in all Scottish cities, in the last year these deaths have continued to rise again. Particularly worrying is that the young working age adult shows particular vulnerability to alcohol related deaths. Such deaths are increasing and the all-cause mortality rate in this group is the highest in Western Europe (GCPH 2014a). The differences in gender, age and deprivation demonstrate that excess mortality from alcohol in Scotland is a result of deep rooted societal level factors (GCPH 2014a). Thus, solely tackling the alcohol specific causes of poor health is unlikely to improve health and wellbeing (Shipton et al 2013).

2.3.3 A new approach to health and well being

There is now a well established research base underpinning a focus on resilience at an individual, community and city level to improve health and wellbeing. This approach moves beyond the traditional model of treating illness and disease and fosters an approach which encompasses society as a whole (GCPH 2014b). The

promotion of resilience and assets may be key in tackling the negative societal impact of poor health which is evident in Glasgow. When reviewing the literature, there are an abundance of definitions given for resilience, especially within the public health domain. An element which is key to most definitions of resilience is that it is not a property or trait possessed by an individual; it is a process which involves individuals being supported by the resources in their environment to provide positive outcomes in the face of adversity (GCPH 2014b). In terms of public health, resilience in characterised not by short term shocks or disasters, but by challenges which fundamentally change the circumstances and infrastructure in which people live, where people are not only required to bounce back but adapt and thrive in new circumstances as a community (GCPH 2014b).

Resilience works in partnership with the asset based approach to health and wellbeing. Asset based approaches are ways of working that promote and strengthen health assets (GCPH 2014b). Such assets include resources that individuals and communities have that help protect against poor health and support the maintenance of healthy communities. This approach in turn is likely to improve resilience and potentially build social capital across and within communities (GCPH 2014c).

The concept of resilience is referred to frequently throughout this thesis. For clarification, the working definition of resilience in this thesis is:

'The capacity for populations and individuals to endure, adapt and generate new ways of thinking and functioning, in the context of change, uncertainty or adversity' (GCPH 2014b).

2.4 Alcohol misuse

2.4.1 Defining Alcohol Use Disorders (AUDs)

Previously the main focus for health and social care practitioners and researchers was severe alcohol dependency or alcoholism. However, it is now recognised that a spectrum of alcohol misuse categories exist (WHO 2010) (Table 2.1).

Table 2.1: Categories of alcohol misuse (WHO 2010)

Category	Criteria
Hazardous Drinking	Alcohol intake above recommended levels with no current evidence of physical, psychological or social harm.
Harmful Drinking	Clear evidence exists that the substance was responsible for (or substantially contributed to) physical or psychological harm, including impaired judgement or dysfunctional behaviour which may lead to disability or have adverse consequences for interpersonal relationships; The nature of harm is clearly identifiable; The pattern has persisted for at least one month or has occurred repeatedly within a 12 month period; The disorder does not meet the criteria for any other mental or behavioural disorders.
Alcohol Dependence	A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some point during the previous year: A strong desire or compulsion to take alcohol; Difficulty in controlling drinking in terms of onset, termination or level of use; A physiological withdrawal state when drinking has been ceased or reduced; Evidence of tolerance, such as increased doses are required in order to achieve effects originally produced at lower doses; Progressive neglect of alternative pleasures or interests because drinking has and increased amount of time necessary to recover from its effects; Persisting with alcohol use despite awareness of overtly harmful consequences, such as harm to the liver.

Henceforth, the term AUD will be used to encompass all of the alcohol categories.

2.4.2 Health related problems associated with AUDs

The relationship between alcohol misuse and organ failure has been known for centuries (Boe, Vandivier, Burnham et al 2009). Dr Benjamin Rush in his 1785 paper- '*An inquiry into the effects of ardent spirits upon the human body and mind'*- described the impact between alcohol and disease, observing that *'ardent spirits dispose to every form of acute disease'* (Rush 1943).

When abused chronically, alcohol has been reported to alter the function of almost every organ system in the body (Boe et al 2009). The potential problems and the systemic effects of alcohol misuse and are summarised in Table 2.2.

Table 2.2: Physiological problems associated with alcohol misuse

System	Problems Associated with excessive alcohol use
Central Nervous System	• Impaired judgement and memory (Welch 2011) • Impaired balance and motor co-ordination • Alcohol Withdrawal Syndrome (Hall and Zador 1997) • Wernicke's encephalopathy and Korsakoff's psychosis (Agabio 2005) • Alcohol Induced Seizures (Samokhvalov, Irving, Mohapatra et al 2010)
Cardiovascular	• Alcoholic Cardiomyopathy (Piano 2002, Skotzko, Vrinceanu, Krueger et al 2009) • High Blood Pressure (Nicoll and Henein 2011) • Cardiac Arrhythmias (Spies, Sander, Stangl et al 2001a)
Respiratory	• Increased incidence of Acute Respiratory Distress Syndrome (Moss and Burnham 2003) • Increased risk of bacterial infections (Boe et al 2009)
Gastrointestinal	• Alcoholic Liver Disease (Rehm, Taylor, Mohappatra et al 2010) • Esophageal inflammation and varices (Al Sanouri, Dikin, Soubani 2005) • Esophageal and oropharyngeal cancer (McKinley 2005) • Acute Pancreatitis (Al-Sanouri et al 2005)
Musculoskeletal	• Low bone density (McKinley 2005) • Increased risk of bone fractures (McKinley 2005)
Metabolic and Renal	• Renal Failure (Moss and Burnham 2006) • Hypoglycemia (Al Sanouri et al 2005) • Alcohol ketoacidosis (Bilbault, Levy, Vinzio et al 2008) • Electrolyte disturbance

2.5 AUD assessment in clinical practice

2.5.1 The use of validated screening tools in clinical practice

The detection of AUDs is of great importance to healthcare professionals to ensure timely and appropriate treatment for patients (Cameron et al 2006). Accordingly, the use of appropriate screening instruments is crucial in order to identify, prevent and offer early treatment in clinical practice (Meneses-Gaya Crippa, Zuardi et al 2010, Pilling, Yesfu-Udechuku, Taylor et al 2011).

Asking patients to self-report on their drinking habits, usually leads to an estimate lower than the actual number of alcoholic drinks per day (O'Brien 2008). Further, the properties of screening tools have been shown to be superior to biomarkers such as gamma-glutamyl-transferase (GGT), mean corpuscular volume (MCV), aspartate transaminase (AST) and percent carbohydrate-deficient transferrins (%CDT) to detect patients with chronic heavy alcohol consumption in both primary care and trauma patients (Bernadt, Taylor, Mumford, et al 1982, Neumann, Gentilello, Neuner et al 2009).

This was exemplified by Neumann et al (2009), who undertook a prospective, single centre, observational cohort study in an emergency department in Germany between 2001 and 2003. The purpose of the study was to evaluate the diagnostic accuracy of the patient reported Alcohol Use Identification Test (AUDIT) as well as biomarkers for the detection of alcohol misuse (alcohol dependence or harmful use and/or at high risk) in injured patients and to determine if the combined use of the AUDIT and biomarkers was superior to the use of AUDIT alone. In Neumann's study, patients admitted to the emergency department were evaluated with the AUDIT (Appendix I) and blood sampled to determine %CDT, GGT and MCV. The final cohort consisted of 1233 patients (25% of patients approached, 787 males and 446 females). At a specificity >0.8, sensitivity for all biomarkers was <0.43, whereas sensitivity for the AUDIT was 0.76 (Area Under the Curve (AUC) 0.874, 95% Confidence Interval (CI): 0.842-0.905) for males and 0.81 (AUC 0.889, 95% CI: 0.831-0.947) for females. Further, the addition of biomarkers added little information compared to the use of AUDIT in isolation. Despite the significance of this paper, one important study limitation should be noted. Patients with obvious intoxication were

excluded as the researchers could not gain fully informed consent. This may have influenced the performance of the AUDIT and biomarkers as an important group of patients were excluded.

The use of patient reported standard screening tools have also been shown to be more cost effective, with a lower cost per true positive for all consumption outcomes, rather than obtaining biomarkers (Coulton, Drummond, James et al 2006). Indeed, preventative cost efficiency studies related to alcohol screening and counselling have found that preventative services of this type were determined to have cost effectiveness ratios similar to what is observed in screening for colorectal cancer, hypertension and influenza (Burnham 2008).

Until the mid-1980's, the four item 'Cut-down, Annoyed, Guilty, Eye-Opener' (CAGE) and the Michigan Alcohol Screening test (MAST) were the primary tools available for healthcare professionals in screening for alcohol use (Selzer 1971, Pokorny, Miller, Kaplan 1972, Mayfield, McLeod, Hall 1974). However, there are now many screening instruments available for the assessment of AUDs in health care practice (Kelly, Donovan, Chung et al 2009). Table 2.3 demonstrates the different screening tools available for AUDs in the clinical environment. Appendix I contains the contents of each of these screening tools. Furthermore, a full critique of these tools was published by our research group (McPeake, O'Neill, Kinsella 2013) (Appendix II).

2.5.2 Comparison of proxy and patient responses with alcohol screening tools

General concerns have been expressed about the reliability and validity of self-reports of alcohol intake (Donovan, Dunn, Rivara et al 2004). Despite substantial amounts of work demonstrating the reliability and validity of self-reporting tools such as the Fast Alcohol Screening Tool (FAST) and AUDIT, it has been proposed that further confirmatory information about the patient's drinking behaviours should be obtained whenever possible, as traditional models of alcoholism characterise denial as an important feature of the disorder (Donovan et al 2004). One way of obtaining further information regarding an individual's drinking behaviours is to ask a next of kin (NOK) or a proxy for further information regarding the patients' drinking habits and behaviours. Such an approach has been utilised in a small number of seminal studies, where alongside the patient

completion of a validated tool such as CAGE or MAST, the patient proxy also completes the same questionnaire. Overall, these studies have found a high degree of consistency between patients' self-reports and those of their proxies (McCrady, Paolino, Longabaugh 1978, Leonard, Dunn, Jacob 1983, Chermack, Singer, Beresford 1998, Donovan et al 2004).

The use of proxy reporting does have its own potential problems and methodological issues, for example ensuring an appropriate proxy. Further, there appears to be no study which has analysed or validated these tools with either patients or patient proxies within the UK ICU environment.

Table 2.3: Alcohol screening tools in clinical practice (adapted from McPeake et al 2013)

Alcohol Screening Tool	Acronym	Details of tool	Scoring	Reliability measures	Estimated time to complete
Michigan Alcohol Screening Test (Selzer 1971,	MAST	MAST has 25 questions	Items are scored either yes or no. In MAST a score of six or more indicates potential alcohol abuse.	Reliability estimates centre around 0.8 from 62 studies (Shields, Howell, Potter et al 2007)	MAST: 5 minutes
Brief Michigan Alcohol Screening test (Pokorny et al 1972)	B-MAST	B-MAST has 10 questions	In the B-MAST a score of more than 6 indicates 'probable' alcohol dependence.		B-MAST: 3 minutes
Short Michigan Alcohol Screening Test (Selzer, Vinokur, Van Rooijen 1975)	SMAST	SMAST has 13 items	In SMAST a score of 4 or more indicates potential alcohol abuse.		SMAST: 3 minutes
Cut down, annoyed, Guilty, Eye Opener (Mayfield et al 1974, Ewing 1984)	CAGE	Four item tool used to detect alcohol abuse and dependence	A point is scored for each positive response. A score of 2 or more is considered the cut off for probable alcohol dependence.	Test-retest reliability co efficient 0.80-0.95 (Dhalla and Kopec 2007)	30 seconds
Alcohol Use Disorders Identification Test (Babor, de la Fuente, Saunders et al 1989)	AUDIT	10 question survey. Can detect less severe forms of alcohol misuse	Individual answers are scored 0 to 4. Score range 0 to 40. A score of 8 or more (7 for women) indicates hazardous/ harmful alcohol consumption. A score of 14 or more in women and 15 or more in men is likely to indicate alcohol dependence.	Median reliability co efficient of 0.83 in most recent review (Reinert and Allen 2007)	2 minutes
Fast Alcohol Screening Tool (Hodgson, Alwyn, John et al 2002)	FAST	Developed from the AUDIT tool. Based upon four AUDIT questions.	Consists of questions 3, 5, 8 and 10 of AUDIT. Question 3 has been modified. Score of 3-8: Hazardous drinking. Score of 9-16: Probable dependent drinking.	Test-retest reliability of greater than 0.8	20-30 seconds

2.6 The Intensive Care Unit (ICU)

2.6.1 The ICU: a brief history

Despite much substantiation supporting the modern concept of critical care, there is an abundance of early evidence suggesting that intensive care medicine may have had its origin in the Bronze Age. A description of a healing throat incision (i.e. a surgical tracheostomy) appears in the *Rig Veda*, an ancient Hindu book of medicine (Szmuk, Ezri, Evron et al 2008). Additionally, Hippocrates (460BC-380BC) described intubation of the trachea in humans to support ventilation and life (Szmuk et al 2008). Florence Nightingale can be also seen to have an important role in the evolution of modern critical care during the Crimean War, where not only did she develop evidence based practice and measurable patient outcomes, she also explored the advantage of establishing a separate area of the hospital for the 'sickest' of the injured soldiers (Munro 2010).

Undoubtedly, one of the major events which heralded a new age for the critical care speciality was the Danish acute poliomyelitis epidemic (1952-1953) (Trubuhovich 2004). During this period, Dr Bjorn Ibsen established a new treatment for the respiratory complications of polio: manual Intermittent Positive Pressure Ventilation (IPPV) via a tracheostomy. This system was adopted throughout Copenhagen during this Polio epidemic and involved around the clock skilled nursing care and attention, supervised by anaesthetists (Andersen and Ibsen 1954). Using this combination of ventilation in a specified area of care, mortality rates were reduced by 50% (Lassen 1952). Dr Ibsen went on to open the first intensive care unit in 1953, which was then, in various forms, replicated throughout the world (Trubuhovich 2004). Over the following 60 years, intensive care medicine has evolved, despite opposition and resource management pressures, into a speciality providing clinical expertise to successfully care for the sickest patients, many of whom suffer from multi organ failure and who would undoubtedly die without this specialist care (Intensive Care Society (ICS) 2003).

2.6.2 Definition of critical care

The predominant role of critical care is to provide physiological support to patients with failing organs. In contrast to many other specialities which deal with specific organs or systems of the body, patients who present to critical care have a wide range of disease processes (ICS 2003). Consequently, the modern philosophy of critical care embraces a hospital wide perspective, with a focus on the level of care required by patients based on their severity of illness, regardless of their location (British Association of Critical Care Nurses (BACCN) 2009, ICS 2009). As a result, the Department of Health (DoH) (2000) recommended a classification that focuses on this level of care (Table 2.4).

Table 2.4: Classification of levels of care (DoH 2000)

Level of Care	Classification Definition
0	Patients whose needs can be met through normal ward care in the acute hospital setting
1	Patients at risk of their condition deteriorating, or those recently relocated from higher levels of care, whose needs can be met on an acute ward with additional advice and support from the critical care team
2	Patients requiring more detailed observation or interventions, including support from a single failing organ system, or post operative care, and those stepping down from higher levels of care
3	Patients requiring advanced respiratory support alone or the support of at least two organ systems. This level of care includes all complex patients requiring support for multi organ failure

2.6.3 Economic impact of critical care in the UK

Intensive care is commonly viewed as an expensive speciality due to its dependence on highly trained staff and the extensive use of technology (Ridley and Morris 2007). In 2011, the cost per day of an ICU bed in Scotland was £2044 and the cost of an HDU bed £702 (Information Service Division (ISD) 2011). However, the UK does spend less on healthcare and indeed ICU than most other Western Nations (ICS 2003) (Table 2.5). In the UK, relative to non intensive care treatment, the incremental cost per quality adjusted life year (QALY) gained from treatment is £7100, which is well below routine interventions and the

National Institute of Clinical Excellence (NICE) threshold for introducing new treatments into the NHS (Ridley and Morris 2007). However, a limitation of the Ridley and Morris (2007) economic evaluation of intensive care treatment is that it assumes that ICU survivors return to a normal quality of life at approximately one year post discharge. There is now an abundance of literature demonstrating that this is not the case (See Section 2.12). A contemporary economic analysis in this area is warranted.

Table 2.5: Availability of intensive care resources by country (Adapted from Adhikari, Fowler, Bhagwanjee et al 2010)

Country	Number of ICU beds per 100 hospital beds	Number of ICU beds per 100000 population
Germany	4.1	24.6
USA	9.0	20.0
Canada (excluding Quebec)	3.4	13.5
France	2.5	9.3
UK	1.2	3.5
Australia (public)	N/A	5.6
Australia (private)	N/A	2.4

2.7 Alcohol related admissions and the ICU

2.7.1 The assessment of alcohol related admissions to ICU

As previously stated, patients are admitted to critical care with a myriad of problems. Critically ill patients cannot always communicate due to the need for mechanical ventilation or sedative agents; therefore, a history of alcohol abuse is often not obtained (Boe et al 2009). As a result, assessment of AUDs and the potential for the development of alcohol withdrawal is easily overlooked (McKinley 2005). It is now recognised that the under evaluation of mental health, substance abuse and chronic pain conditions in the ICU carry significant implications for patient outcomes and resource utilisation (Broyles, Colbert, Tate et al 2008).

Few studies have analysed the impact of the assessment of substance misuse on admission to the ICU. Broyles et al (2008) in a longitudinal descriptive study, described clinician evaluation and management of co-existing mental health substance abuse (MHSA) and chronic pain (CP) conditions, in patients with

prolonged critical illness in a large academic medical centre in North America. Twelve patients with a MHSA or CP condition were extracted from a previous parent study data set (Happ, Swigart, Tate et al 2007) based on one of the following characteristics: current substance abuse or a psychiatric condition requiring regular narcotic or psychotropic medication before acute critical care hospitalisation. The study employed qualitative description to illuminate the specialised processes of patient management and clinical decision making from the perspective of ICU clinicians, through observation of their practice and interactions with families and the multi disciplinary team (MDT). The data set included in the analysis incorporated clinical records, interview transcripts and observational field notes (>400 documents) pertaining to the twelve patients. Uncoded text documents were imported into ATLAS, version 5.0, a qualitative database software programme for data coding, organisation and retrieval. Findings were organised into facilitators (causal conditions), barriers (intervening conditions), consequences and contextual factors consistent with the qualitative analytic paradigm model by Strauss and Corbin (Table 2.6). The findings from this particular study demonstrate that evaluation and management of MHSA and CP conditions were highly variable and inconsistent across cases. Further, the findings suggest that MHSA and CP conditions require monitoring and management similar to that required for other chronic conditions within the critical care environment. Lastly, the challenges involved in adequate assessment and the consequences of poor assessment were also highlighted (Table 2.6).

Limitations of this study included the sampling strategies employed by the research team. For the quantitative researcher, random sampling is an important technique and a necessary pre-requisite for statistical tests that can establish how likely it is that a pattern seen in a sample will be reproduced in a population (Harding 2013). However, qualitative researchers, who are less concerned with generalisation tend to use different techniques. Sampling strategies may include purposive and theoretical sampling of the population. As this study was a subset analysis of an ethnographic investigation, appropriate sampling strategies were not employed, which may have impacted on the appropriateness of the patients and clinicians involved. Consequently, specific dimensions of this qualitative analysis may have been missed.

Table 2.6: Facilitators, consequences, barriers and contextual factors in evaluation and management of mental health substance abuse and chronic pain conditions (Broyles et al 2008)

Facilitators	Family as history keepers; Use of sub speciality consultation; Anticipated alcohol withdrawal.
Consequences	Non integration of MHSA and CP medications and diagnoses; Episodic pharmacologic responses to psychobehavioural symptoms; Clinical-patient interpersonal tension.
Barriers	Limited history taking and assessment of MHSA and CP conditions; Use of cognitive shortcuts.
Contextual Factors	Ambiguous psychobehavioural symptomatology; Patients critical illness and inability to speak; Competing clinical goals.

In 2012, the PhD student distributed an electronic survey using the software package SurveyMonkey®. This study aimed to explore current practice in the use of assessment and management tools for alcohol related admissions to UK critical care units (McPeake, Bateson, O'Neill et al 2013) (Appendix II). There were nine questions in this survey, with two of the questions exploring alcohol related admissions to ICU (Table 2.7). The other seven questions in the survey explored the use of other validated tools used in the ICU setting, such as delirium and pain assessment tools.

Table 2.7: Questions relating to alcohol assessment and management (McPeake et al 2013)

1. Which tool(s) are used for the assessment of alcohol use?
   - Volume of alcohol consumption (i.e. 20 units per week)
   - Fast Alcohol Screening Test (FAST)
   - Cut down, Annoyed, Guilty and Eye Opener (CAGE)
   - Alcohol use disorders Identification test (AUDIT)
   - None

2. Which tool(s) are used for the management of alcohol withdrawal?
   - Clinical Institute Withdrawal Assessment (CIWA)
   - Glasgow Modified Alcohol withdrawal Score (GMAWS)
   - None
   - Other

Piloting a survey is one way of determining face and content validity (Parahoo 2006). Each question distributed in this survey was developed and tested in a pilot study. Two senior ICU consultants, one clinical academic and a lay

individual who had no knowledge on the subject were asked to complete the survey and comment on any section which was not clear or easy to answer. Several changes were made as a result of this pilot, including where in the email the link to the survey was presented and in which order the questions were offered.

A total of 248 lead consultants across England, Scotland, Northern Ireland and Wales were asked to complete the questionnaire; these consultants represented 260 ICUs (12 consultants represented two units). Lead consultants were approached as the researchers felt this would give a representative view of individual unit practice. Participants were asked to base their answers on level three patients only (Section 2.6.2). Three reminder emails were sent out at two week intervals.

In total, 103 (41.1%) participants completed the questionnaire. The number of respondents was greatest from mixed ICUs (n=82, 79.1%). There were 10 respondents from specialist units (9.1%); three from medical only units (2.1%) and eight participants gave no information about their ICU. There were 109 responses regarding the assessment of alcohol use (6 participants had two responses), 8% (n=9) of units used the CAGE tool, 1% (n=1) of units used the FAST tool, 67% (n=73) of units used volume of alcohol consumed, 23% (n=25) of units used no assessment tool and 1% (n=1) used a local trust protocol (Figure 2.2).

A full description of each of the screening tools mentioned in this survey is given in Appendix I and III.

There were 108 responses to the question analysing the management of alcohol withdrawal in the ICU. 11% (n=12) of units used the CIWA tool, 5% (n=5) of units used the GMAWS, 73% (n=79) of units used no tool, 5% (n=5) of units used a trust tool and 6% (n=7) of participants omitted this question (Figure 2.3).

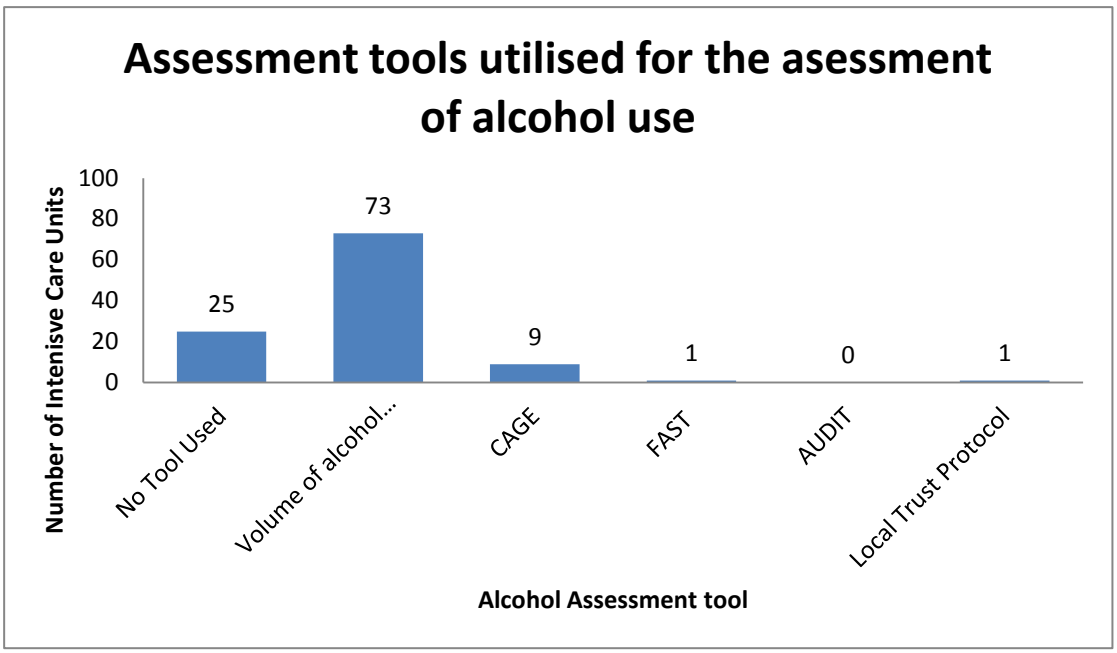

Figure 2.2: Assessment tools utilised for the assessment of alcohol use (McPeake et al 2013)

There are a number of limitations to this study. The response rate in this particular survey was 41.5%, however, it should be noted, this appears to be a reasonable response rate for this type of methodology (Scott, Jeon, Joyce et al 2011). It is well documented that despite the obvious advantages of using electronic surveys (McPeake, Bateson, O'Neill 2013; Appendix II), the response rate generated is generally lower compared to other survey types such as postal and telephone surveys (Bryman 2012a).

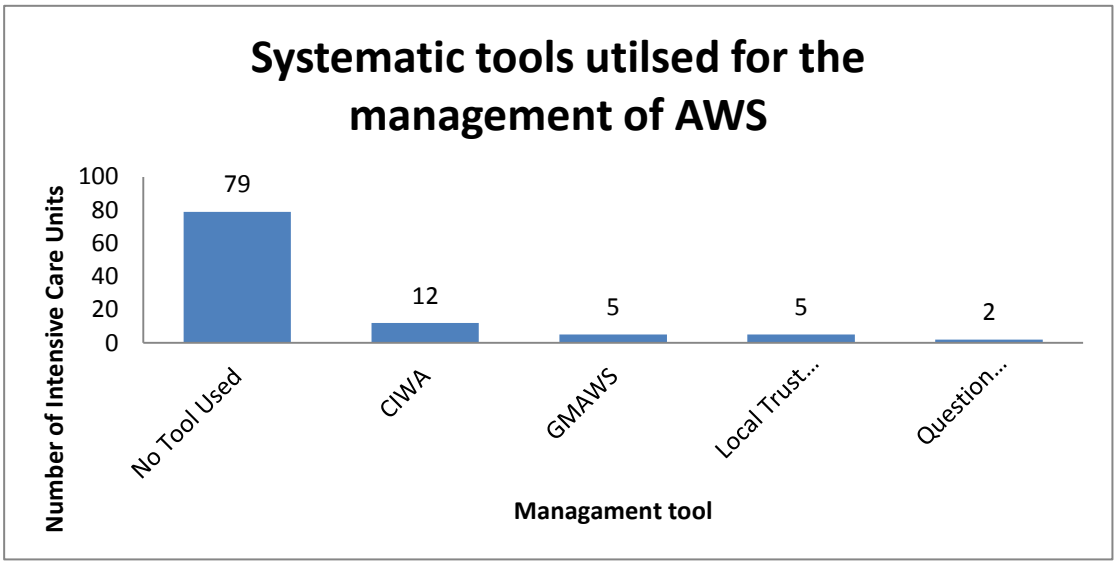

Figure 2.3: Systematic tools utilised for the management of AWS in the ICU (McPeake et al 2013)

This section of the literature review has demonstrated that AUDs are under reported within the critical care environment. Further, there is a haphazard approach to screening for AUDs across the UK.

2.7.2 Alcohol related admissions to ICU

There are a small number of studies which have specifically examined the frequency of alcohol related admissions to the ICU setting. In their widely quoted retrospective observational study, Baldwin, Rosenfeld, Breslow et al (1993) analysed the frequency of substance abuse related admissions to a tertiary referral ICU in Maryland, USA, over a 15 week period. Of the 435 ICU admissions in this 15 week period, 41 were alcohol related (9%), 59 were tobacco related (14%) and 22 were illicit drug related (5%). The researchers determined that patients admitted with a background of substance abuse had a longer ICU stay (by 0.8 days, $p<0.001$). Those with a substance abuse related admission also had higher average ICU costs (by US$1,860, $p<0.001$). Finally, substance abuse related admissions suffered a trend to less favourable outcomes, with 13% mortality in the substance related group vs. 7% mortality in the non-substance related group; however, this trend was not statistically significant ($p=0.10$).

Despite this study generating important results, there are factors which impact on its generalisability. For example, the study took place within one institution in the USA, which limits how applicable the results are to other settings due to extensive global differences in healthcare administrations (Polit and Beck 2009). Secondly, the researchers conducted retrospective case note analysis. Robson (2011) states that one of the main drawbacks of collecting retrospective data is that the researcher relies on existing data that were, most probably, not collected for research purposes and therefore lack the rigour with which research is carried out.

In 2002, Mostafa and Murthy were the first researchers to analyse alcohol related admissions to ICU in the UK. Mostafa and Murthy (2002) analysed alcohol associated admissions in a 12 month prospective audit in their University hospital. Using case note histories, patients were classified into three groups according to their history of alcohol intake and diagnosis (Table 2.8).

Total ICU admissions for the 12 months were 317. In 106 patients (33.3%) it was not possible to ascertain whether alcohol had a part to play in the patient's admission; therefore they were excluded from the audit. Thus, 211 patients were included for analysis. Although ICU length of stay was not significantly different between the three groups, mortality was significantly higher in Group 1 than that of overall mortality for all ICU admissions (41.6% vs. 23.7%, $p>0.001$).

This study was the first in the UK to describe frequency and related outcomes of alcohol related admissions in the ICU setting. However, these results may in fact be grossly under estimating the problem. Mostafa and Murthy (2002) used units of alcohol consumed per week as reported by the patient, to guide allocation of patients into different study groups. This approach to assessment is known to underestimate the scale of drinking habits and behaviours in different contexts (O'Brien et al 2008).

Table 2.8: Admissions groups and criteria (Mostafa and Murthy 2002)

Group	Number of Admissions	Group Criteria
One	89(28.1%)	Patients admitted with a condition that necessitated admission to ICU directly associated with alcohol consumption and patients who consumed > 21 units of alcohol per week for men and > 14 units per week for women.
Two	35(11%)	'Social drinkers': men who consumed less than 21 units of alcohol per week, and women who consumed less than 14 units of alcohol per week.
Three	87(27.5%)	Patients who deny any alcohol intake.

Uusaro, Parviainen, Tenhunen et al (2005) analysed the proportion of emergency ICU admissions related to acute and chronic alcohol use and the hospital resources utilised as a result of these admissions, in a single centre prospective cohort study in Finland. A total of 893 emergency admissions were analysed over a one year period. Similar to the Mostafa and Murthy (2002) study, three study groups were identified by the opinion of the admitting physician (Table 2.9). In contrast with the previous studies, ICU length of stay was shorter for patients with alcohol related admissions (1.2 days vs. 1.8 days, $p<0.001$) and there was

no statistically significant difference between ICU mortality (8.8% vs 10.5%, *p*=0.769).

Table 2.9: Admissions groups and criteria (Uusaro et al 2005)

Group	Number of Admissions	Group Criteria
A	156 (17.5%)	Patient has a definite relationship with alcohol.
B	678(75.9%)	No relationship with alcohol.
C	59(6.6%)	Alcohol is likely to contribute to the admission, but the relationship is not definite.

There are a number of possible explanations for reductions in the ICU length of stay seen in the Uusaro et al (2005) paper. For example, patients who are severely intoxicated are often admitted to the ICU because of altered mental status and respiratory depression and are promptly discharged after resolution of intoxication (Gentilello 2007). This indicates that rather than there being a beneficial effect of alcohol on outcome, it may be that alcohol related admissions may trigger an ICU admission for those with an otherwise low severity of illness (O'Brien et al 2007). A further limitation of this particular study is the use of a subjective opinion by the admitting physician to differentiate which study group the patient should be included. This clearly impacts on the internal validity of the study (Robson 2011). The use of a study protocol or an appropriate assessment tool for alcohol intake would have enhanced rigour within this particular element of the study (Bryman 2012a).

McKenny, O'Beirne, Fagan et al (2010) also prospectively recorded the number of patients admitted to an inner city tertiary referral hospital in Dublin as a result of alcohol. During the six month data collection period, 275 patients were admitted to their ICU, with 33 (12%) patients meeting the study's inclusion criteria for an alcohol related admission. The patient's admission was regarded as being related to alcohol misuse if excessive alcohol consumption had led to one or more of the following admission diagnoses: alcohol withdrawal syndrome, alcoholic liver cirrhosis with hepatic failure and/or upper gastrointestinal tract bleeding secondary to portal hypertension, alcoholic pancreatitis, alcoholic

hepatitis and trauma secondary to alcohol. The diagnosis of an alcohol related admission in this study was also made by the admitting ICU consultant. Patients within the alcohol related admission group had approximately double the length of ICU stay (12.3 days) compared with non-alcohol related admission group (the length of stay for the non alcohol related admission group is not presented in this paper). Alcohol related admissions also had a higher 30 day mortality rate compared to the non-alcohol related admission group (24.2% vs. 19%). No statistical analysis of the results is offered by the researchers in this particular study (McKenny et al 2010). This study may have also under represented the alcohol related ICU workload, as the researchers did not include those patients who had been admitted with a background of alcohol misuse not directly associated with their admission diagnosis. No information on alcohol intake pre admission was collected to establish this.

The most recent UK analysis of alcohol related admissions to ICU was a one month national audit in Scotland (Geary, O'Brien, Ramsay et al 2012). This study aimed to prospectively evaluate the incidence of alcohol related admissions to Scottish ICUs. Local co-ordinators were recruited at each ICU in Scotland (24 units in total) to collect data based on the criteria in Table 2.10. During October 2009, 771 patients were admitted to the 24 ICUs in Scotland. Of these admissions, 642 (83%) were unplanned ICU admissions and from these 196 (25.4%) had alcohol implicated either directly or indirectly in their admission. Although ICU stay was not statistically significant different between the two study groups (alcohol related 2.5 days vs. non-alcohol related 2.2 days, p=0.673), the alcohol related group did have significantly more ventilator days (2 days vs. 1 day, $p<0.001$). Further, there was no significant difference between either ICU mortality (18% vs. 16%, p=0.541) or hospital mortality (26% vs. 23.1%, p=0.541) between the study groups.

Despite the importance of this study in revealing the impact of alcohol related admissions to the ICU environment in Scotland, there are limitations in the study design. For example, Geary et al (2012) focussed on alcohol related admissions to ICU and their effect on the service rather than the impact on the individual. This was exemplified in their inclusion criteria, which included those patients with no AUD (i.e. assault by intoxicated assailant, Table 2.10). Further, this

audit was undertaken over one month only which may not reflect the entire yearly cycle and seasonal differences in admission.

Table 2.10: Group criteria for alcohol related admissions (Geary et al 2012)

Group	Group Criteria	Number
Not attributable to alcohol	• No evidence that the admission was related to alcohol. • No evidence of chronic alcohol use/dependency.	575 (74.6%)
Admission directly or indirectly (secondary alcohol related co-morbidity) attributable to alcohol	• Directly related to acute alcohol intoxication. • Secondary to chronic alcohol disease (i.e. hepatic encephalopathy, alcoholic liver disease, acute alcohol withdrawal). • The patient's admission was indirectly influenced by alcohol misuse with or without alcohol consumption (i.e. Assault by intoxicated assailant, road traffic incidents secondary to alcohol intake; disease process worsened by chronic alcohol consumption). • Did the patients have documented alcohol related disease which was not related to the reason for admission (alcoholic hepatitis, hepatic encephalopathy)? • Did the patients have documented alcohol excess/dependence?	196 (25.4%)

This section of the literature review has demonstrated that alcohol related admissions make up a significant proportion of admissions to critical care globally. However, there are significant limitations to the methodologies employed, especially regarding how alcohol related admissions have been classified.

2.8 Complications associated with alcohol related admissions to ICU

The consequences and complications of AUDs in the ICU environment have not been well described in the literature (de Wit et al 2007). Indeed, Gentilello (2007) calls attention to the fact that relatively little is known about the acute and chronic effects of alcohol on outcome, despite its frequent presence in the ICU population. However, there is emerging evidence, predominantly from North America, that AUDs are independently associated with a number of disease processes within the critical care environment (O'Brien et al 2007, Boe et al 2009). The following section will explore these complications and possible explanations for their increased presence in this population.

2.8.1 AUDs, sepsis and septic shock

Severe sepsis (acute organ dysfunction secondary to infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation) are major healthcare problems, affecting millions of individuals around the world each year (Dellinger, Levy, Carlet et al 2008). In the Scottish context, sepsis is associated with 1.7% of all admissions to Accident and Emergency departments, which equates to approximately 21,000 unscheduled visits per year (Scottish Trauma Audit Group (STAG) 2010). With an average hospital stay of around 7 days for each of these patients and 14% requiring admission to a critical care setting (Coronary Care Unit (CCU), High Dependency Unit (HDU) or ICU), sepsis has a huge impact on NHS service provision (STAG 2010).

AUDs have widespread effects on the immune system and leave abusers at an increased risk of a variety of infections (Gacouin, Legay, Camus et al 2008). Emerging literature also indicates an independent association between AUDs, sepsis and septic shock (O'Brien et al 2007, Gacouin et al 2008). O'Brien et al (2007) in their widely quoted five year retrospective cohort study analysed the association between alcohol dependence, sepsis, septic shock and hospital mortality among ICU patients. The initial cohort included 9,981 patients who had their first admission during the five year period in two inner city ICUs in North America. Of these patients, 1,222 (12.2%) were admitted with a background of alcohol dependence. Patients were allocated into the alcohol dependence group

if they had alcohol dependence recorded in their discharge summary from the hospital. Alcohol dependent patients had a higher rate of sepsis (12.9% vs. 7.6%, $p<0.001$), organ failure (67.3% vs. 45.8%, $p<0.001$), septic shock (3.6% vs. 2.1%, $p=0.001$) and hospital mortality (9.4% vs. 7.5%, $p=0.022$) on unadjusted analysis. Among those patients with liver disease and sepsis, alcohol dependence was associated with more than a twofold increase risk adjusted odds of hospital mortality (adjusted odds ratio, 2.31; 95% CI 1.26-4.24). Interestingly, among non-septic patients without liver disease, those with alcohol dependence had 71% (adjusted odds ratio, 0.3; 95% CI 0.20-0.46) lower odds of death than those without alcohol dependence, which may indicate that alcohol dependent patients without liver disease or sepsis are a relatively low risk population of ICU patients.

There are a number of methodological issues which may limit the results of this study. Firstly, the retrospective nature of this study is a major limitation (Robson 2011). The study relied solely on discharge documentation in the medical record to identify alcohol dependence. Gentilello (2007) argues that medical records are notoriously unreliable for documenting alcohol problems. Furthermore, the narrow criteria used for applying the diagnosis of alcohol dependence means alcohol use was probably severely underestimated (Gentilello 2007). Greater rigour would have been achieved by prospectively analysing the patient's records, enhancing validity and comprehensiveness of collected data (Bryman 2012a).

Gacouin et al (2008) also analysed whether excessive alcohol consumption increased the risk of ICU acquired infections, such as Ventilator Associated Pneumonias (VAPs) and acquired bacterial infections (i.e. Catheter Related Blood Stream Infections (CRBSIs), in a 21 bedded mixed ICU in a French university hospital. In this one year prospective observational study, a total of 358 patients were assessed using SMAST (see Section 2.5.1). Utilising the SMAST score, Gacouin et al (2008) then classified the patient as being *not at risk drinkers* or *at risk drinkers*. *At risk drinkers* were then further categorised into drinking more or less than 5 drinks per day (Figure 2.2). In total, 111 from the 358 (31%) patients assessed were found to be *at risk drinkers,* with 61 (55%) of these patients drinking more than five drinks per day. During the study period,

88 patients (26%) acquired bacterial infections and 69 (19%) acquired a VAP. The proportion of patients who acquired bacterial infections was significantly higher in the *at risk drinkers* group (19% vs. 36%, $p<0.001$). Similarly, the proportion of patients with one or more VAP was significantly higher in the *at risk drinkers* group (16% vs. 27%, $p=0.01$) and the number of patients who had septic shock associated with the acquired infection was also significantly higher in the *at risk drinkers* group (18% vs. 8%, $p=0.01$). Finally, amongst the *at risk drinkers,* the proportion of patients with acquired bacterial infection was higher in the patients who had a daily intake of five or more drinks, than the fewer than five drinks per day study group (44% vs. 13%, $p=0.046$).

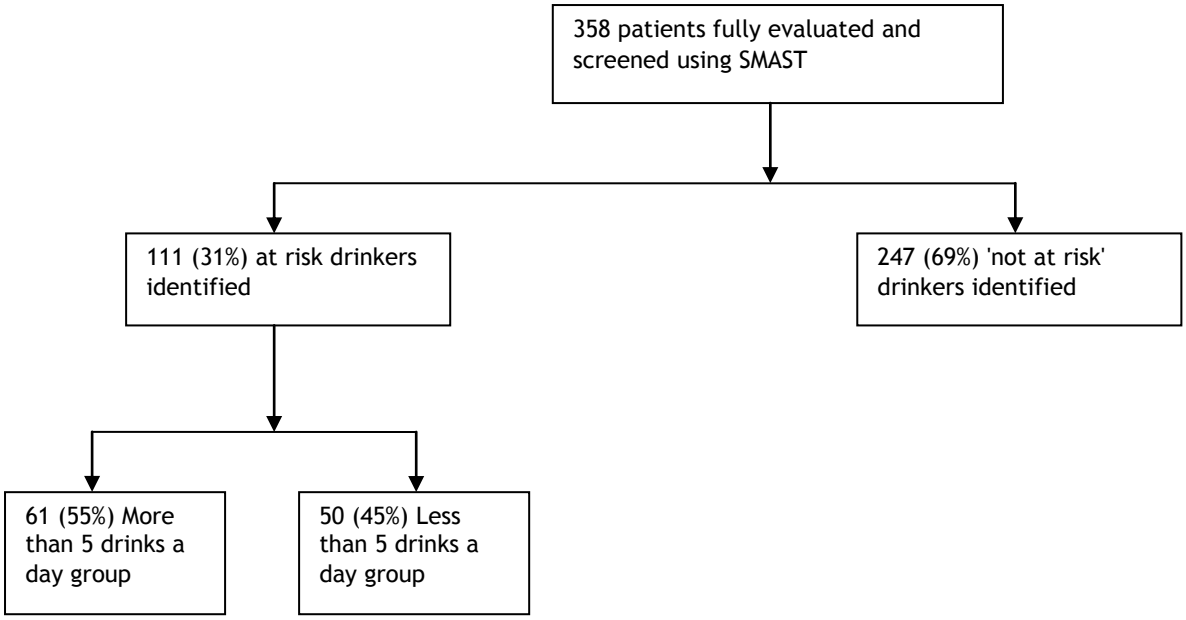

Figure 2.4: Details of study groups (Gacouin et al 2008)

There are several aspects of this study which require consideration. Gacouin et al (2008) offer no information regarding the treatment of alcohol withdrawal syndrome in the '*at risk drinkers'* group during the study period. Alcohol withdrawal syndrome is often treated with benzodiazepines and other sedative drugs which have been shown to impact on ventilation days, ICU stay and outcome (Pandharipande, Shintani, Peterson et al 2006). Therefore, higher rates of bacterial complications may have been expected in the *'at risk drinkers'* group if they received additional sedative agents for management of alcohol withdrawal syndrome (Yost and Gropper 2008).

2.8.2 Mechanisms for increased susceptibility to sepsis and septic shock

Immunological and non-immunological factors may contribute to increased susceptibility to infection in patients with chronic alcohol exposure (von Dossow, Schilling, Beller et al 2004, Gacouin et al 2008). For example, animal and human studies have demonstrated that chronic alcohol consumption may inhibit the production of important cytokines, modify neutrophil functions and suppress T- cell mediated immunity (Zisman, Strieter, Kunkel et al 1998, Moss and Burnham 2006, von Dossow et al 2008). Such differences could lead to an increased predilection to infection and once established, an increased risk of systemic complications (O'Brien et al 2007).

Another possible explanation for this increased susceptibility to infection is the relationship between AUDs and cortisol. Previous evidence has shown individuals with AUDs from the medical ICU setting have higher cortisol levels compared to individuals without AUDs (De Wit, Wiaterek, Gray et al 2010). It is well known that patients with sepsis who have increased cortisol concentrations or poorer responses to adrenocorticotropin hormone (ACTH) stimulation have a higher mortality than those with normal cortisol levels and a normal response to ACTH (Marik and Zaloga 2002).

2.8.3 Acute Respiratory Distress Syndrome (ARDS)

ARDS is a life threatening respiratory failure caused by a variety of disease processes and injuries, with mortality rates in the critical care environment ranging from 34%-64% (Del Sorbo and Slutsky 2011). Pathologically, ARDS is characterised by diffuse alveolar damage, alveolar capillary leakage and protein rich pulmonary oedema leading to clinical manifestations of poor lung compliance, severe hypoxemia and bilateral infiltrates on chest X-ray (Boe et al 2009, Hughes and Black 2011).

ARDS is a heterogeneous syndrome with multiple aetiologies including sepsis, pneumonia, surgery, trauma, burns, blood transfusion, pancreatitis, and aspiration (Berkowitz and Martin 2009, Boe et al 2009, Del Sorbo and Slutsky 2011). Recent evidence has also shown that a history of alcohol abuse is an

independent risk factor for the development of ARDS (Moss, Bucher, Moore et al 1996, Moss, Parsons, Steinberg et al 2003).

In their seminal paper in 1996, Moss et al prospectively examined the effect of alcohol abuse on the incidence of ARDS and the overall in-hospital mortality of a cohort of critically ill patients with one of seven identified at risk diagnoses (sepsis, severe pancreatitis, hyper-transfusion, aspiration of gastric contents, chest trauma and multiple fractures). A total of 351 medical and surgical patients were analysed over a four year period. A diagnosis of chronic alcohol abuse was made if the admission note included a diagnosis of chronic alcoholism, a previous admission to alcohol detoxification or a prior hospital admission for alcohol withdrawal. The incidence of ARDS in the entire population was 29% (102 of 351) and a history alcohol abuse was present in 34% (121 of 351). After adjusting for difference in sex, at risk diagnosis and Acute Physiology And Chronic Health Evaluation (APACHE) II scores, the effects of a positive history of chronic alcohol abuse on the incidence of ARDS was significant (p<0.001; OR, 2.79; 95% CI, 1.68 to 4.83). Further, in the subset of patients who developed ARDS, the in-hospital mortality rate was 65% for those with a prior history of alcohol abuse, which was significantly higher (p=0.003) than those patients without a history of alcohol abuse (36%).

In a more recent multicentre prospective epidemiologic study, Moss et al (2003) examined the role of chronic alcohol abuse on the development of ARDS and the possible effects on non-pulmonary organ dysfunction. In total 312 patients met the inclusion criteria for the study; however, 92 patients were excluded over the four sites (reasons for exclusion included: inability to obtain informed consent; pre existing 'do-not- resuscitate' status (n=6); patient did not live 72 hours in the unit (n=24) and the patient had an HIV positive status (n=11)). Thus, 220 patients were enrolled in into the study. Patients were enrolled only if they met a standard definition for septic shock and chronic alcohol abuse was determined using the SMAST tool (See Section 2.5.1) by either the patient or the patient's proxy. Thirty percent of all patients (66 of 220) were categorised as having a positive history of alcohol abuse based on a SMAST score of ≥ 3. After adjusting for difference in the source of infection, sex, age, chronic hepatic dysfunction, severity of illness, nutritional status and smoking status, the incidence of ARDS

in individuals with a positive history of chronic alcohol abuse was 70% (46 of 66) compared with 31% (47 of 154) in those patients without a history of chronic alcohol abuse (p<0.001; 95% CI, 1.51-3.42). Additionally, after adjusting for source of infection, sex, age, nutritional status, history of diabetes and smoking status, the effects of chronic alcohol abuse on the incidence of non pulmonary organ dysfunction was also significant (p=0.03; odds ratio, 2.07; 95 CI, 1.09-3.97).

This prospective multicentre epidemiologic study demonstrates that a history of chronic alcohol abuse substantially increased the risk of ARDS for critically ill patients with septic shock (Moss et al 2003). However, there are a number of factors which may impact on the reported results. Firstly, enrolment in this study was exclusively limited to patients with septic shock only, therefore it is not possible to generalise these results to all critically ill patients with other conditions (for example those patients with severe trauma who are at risk of developing ARDS). Another limitation is how the researchers utilised the SMAST tool. Whilst it has been studied and used extensively in critically ill patients, it has never been formally validated in the critically ill patient (either medical or surgical). Further, it has never been validated for use by a proxy within the ICU population. In this particular study, the SMAST was administered to 32% of patients (68 of 220) and to their closest available relative for the remaining 68% (152 of 220). The use of this tool with the patient's proxy may affect this study's internal validity (Polit and Beck 2009).

2.8.4 Mechanisms for the development ARDS

Extensive evidence suggests that there may be an association between AUDs and ARDS due to depleted Glutathione (GSH) stores in the lung (Moss, Guidot, Wong-Lambertina et al 2000, Moss and Burnham 2003). GSH is the most abundant non-protein thiol in living organisms and is essential for a number of vital biological functions including the synthesis of proteins and DNA, transport of amino acids, enzyme activity and protection of cells (Moss et al 2000, Moss and Burnham 2003). GSH has been considered a primary anti oxidant in the alveolar space, specifically in protecting the airspace epithelium from oxidative/free radical mediated injury and inflammation (Morris and Bernard 1994, Moss and Burnham

2003, Yeh, Burnham, Moss et al 2007). Impairment in GSH homeostasis results in increased permeability of the alveolar capillary barrier (Burnham, Moss, Harris et al 2004, Burnham, Halkar, Burks et al 2009), decreased fluid transport out of the alveolar space and alterations in surfactant production and secretions (Boe et al 2009, Berkowitz et al 2009) (Figure 2.5). Further, limited availability of GSH stores has been associated with a number of pulmonary diseases including ARDS (Yeh et al 2007).

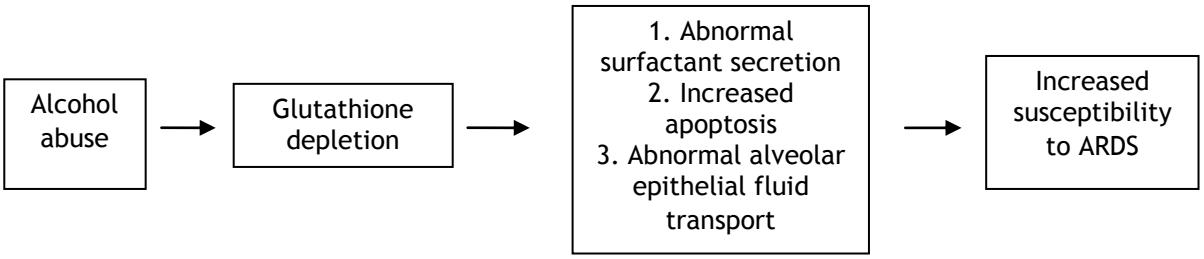

Figure 2.5: Proposed mechanisms for association between chronic alcohol abuse and ARDS (Moss and Burnham 2003)

Other possible mechanisms for the relationship between AUDs and ARDS include abnormalities in angiotensin II production and receptor expressions (Marshall, Webb, Bellingan et al 2002). Intoxicated individuals are also predisposed to a number of diagnoses associated with the development of ARDS, including trauma, sepsis and blood transfusion from gastrointestinal bleeding (Spies, Dubisz, Neumann et al 1996, Sarff and Gold 2010). Lastly, it is also possible that alcohol interacts with the development of ARDS through indirect effects such as impairment of hepatic function (Moss et al 1996). Alcohol abuse is associated with the development of hepatic dysfunction and the liver is a key organ in several host defence systems relevant to the pathogenesis of acute lung injury (Nesseler, Launey, Aninat et al 2012).

2.8.5 Other pulmonary complications associated with AUDs

AUDs have also been associated with other pulmonary complications within the ICU environment. Firstly, AUDs are associated with an increased risk of bacteraemia, with the most common cause of sepsis being pneumonia (Moss et al 2003, de Wit, Jones, Sessler et al 2010). AUDs may increase the risk of pneumonia through several mechanisms including increasing oropharyngeal colonisation and decreasing mucociliary clearance (Boe et al 2009). Secondly,

previous research suggests that patients with chronic alcohol abuse, including those with and or without ARDS, are at risk of greater quantities and slower resolution of pulmonary oedema, compared with patients with no history of alcohol abuse (Martin, Eaton, Mealer et al 2005, Berkowitz et al 2009).

Evidence also suggests that patients who are admitted to critical care with a background of alcohol misuse may spend longer on mechanical ventilation. De Wit et al (2007) carried out a retrospective cohort study using a national inpatient database which covers over 1000 hospitals in the USA, to examine the effects of a diagnosis of an AUD and alcohol withdrawal, on the initiation and duration of mechanical ventilation in patients with 6 medical conditions that are routinely associated with admission to the ICU (pneumonia, sepsis, gastrointestinal bleed; asthma, COPD, respiratory failure). There were a total of 785,602 patients who fulfilled one of the six diagnoses, 26,577 (3.4%) had an AUD, 3967 (0.5%) had alcohol withdrawal and 65,071 (8.3%) received mechanical ventilation (53% <96hours, 47% ≥ 96 hours). Independent of the medical diagnosis, an AUD was associated with an increased risk of requiring mechanical ventilation (13.7% vs. 8.1%, odds ratio, 1.49, 95% CI 1.41- 1.57, p<0.001), but was not associated with a prolonged duration of mechanical ventilation. The presence of alcohol withdrawal, however, was associated with a longer duration of mechanical ventilation (57% vs. 47% ≥ 96 hours, odds ratio, 1.48, 95% CI 1.26-1.72, p<0.001).

The generalisability of the study is affected as the researchers used only hospitals from an 'all payer' national, non-validated database. 'Non-paying patients' were not included in this study; therefore this study may not be fully representative of either the American or British population.

2.9 Alcohol Withdrawal Syndrome (AWS) and ICU related delirium

Complications related to alcohol withdrawal account for a significant demand in healthcare resources and are associated with an increase in morbidity and mortality (Eyer, Schuster, Felgenhauer et al 2011). AWS is the most common cause of alcohol related admission to the critical care setting, in some cases accounting for over 50% of alcohol related admissions (Marik and Mohedin 1996).

The following section aims to explore AWS, including treatment and management in the ICU. The challenges involved in differentiating and treating ICU related delirium and AWS will be critically examined. It should be noted that there is an abundance of recent literature on ICU related delirium; therefore this is a summary of the current understanding of the topic.

2.9.1 AWS- definition and pathophysiology

Despite its wide prevalence in the early 20th century, it was not until the late 1950s that AWS was definitively proven as a complication associated with abrupt cessation or reduction in alcohol consumption (Isbell, Fraser, Wikler et al 1955, Sarff and Gold 2010). AWS, which typically develops in the alcohol dependent patient within 6-48 hours of their last drink (Hall and Zador 1997, McKeon, Frye, Delanty 2008), is the hallmark of alcohol dependence. It is a 'constellation' of signs and symptoms that develop shortly after abstinence owing to complex neurobiological mechanisms (Hall and Zador 1997, Faingold, Knapp, Chester et al 2004, Campos, Roca, Gude et al 2011).

AWS is a result of the unmasking of the compensatory changes that occur during prolonged exposure to its depressant effects (Welch 2011). The complex mechanisms of alcohol intoxication, tolerance and dependence are not completely understood, but a clear relationship exists between alcohol and alterations in neurotransmission in the brain (Riddle, Bush, Tittle et al 2010). Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the CNS and its receptor is down regulated as a result of chronic alcohol abuse. There is also upregulation of N-methyl-D-aspartate (NMDA) receptors with chronic alcohol ingestion (Hall and Zador 1997) (Table 2.11). If a dependent individual abruptly stops drinking, the inhibitory effects of alcohol are lost whereas these adaptive changes persist (Welch 2011). This increased excitation and loss of suppression results in the clinical manifestations of autonomic excitability and psychomotor agitation (Sarff and Gold 2010). In addition, chronic alcohol use is thought to cause dysregulation of the dopaminergic system, a system whose transmission is enhanced in withdrawal (McKeon et al 2008, Lemon, Winstead, Weant 2010). These changes not only play a role in the rewarding and reinforcing effects of alcohol, they also contribute to the

characteristic hallucinations often associated with AWS (Heinz, Schmidt, Baum et al 1996, Saitz and O'Malley 1997).

Table 2.11: Acute and chronic effects of alcohol

	Effects on GABA	**Effects on NMDA**
Acute Alcohol Consumption	Antagonistic effect on receptors, reducing excitatory neurotransmission	Inhibitory effect on receptors
Chronic Alcohol Consumption	Down regulation of receptors	Upregulation of receptors

2.9.2 AWS- clinical manifestations

Presentation of AWS is part of a clinical continuum, which is inconsistent and dependent on the degree and type of alcohol abuse (Al-Sanouri et al 2005). There are four clinical stages of alcohol withdrawal (Al- Sanouri et al 2005) (Table 2.12). The withdrawal process is individual and each patient presentation will be influenced by the timing of abstinence (Corfee 2011). Furthermore, patients do not progress linearly from one stage to the next, often one or more stage may be missed out completely (Sarff and Gold 2010).

Table 2.12: The four clinical stages of AWS

Stage of Alcohol Withdrawal	Clinical Characteristics
Autonomic Hyperactivity Symptoms appear within hours of last drink, often peaking at 24 to 48 hours (Al Sanouri et al 2005)	• Tremors, sweating, anxiety, agitation, insomnia, nausea, vomiting (Hall and Zador 1997)
Hallucinations Manifests with 8-48 hours post abstinence, may last for several days (Corfee 2011)	• Visual and tactile hallucinations (Auditory relatively uncommon). Alcoholic hallucinations are distinguished from DTs by the presence of a clear sensorium (Sarff and Gold 2010)
Neuronal excitement Typically occur 6-48 hours after last alcohol use (Hughes 2009)	• Generalised tonic-clonic seizures (although partial seizures do occur). Sustained status epilepticus is typically not associated with AWS
Delirium Tremens (DTs) Typically occur 48-72 hours after last drink (Sarff and Gold 2011). DTs usually last for two to three days, or in severe cases up to two weeks (McKinley 2005)	• Severe hyperadrenergic state (hyperthermia, diaphoresis, tachypnoea and tachycardia), disorientation, impaired attention and consciousness as well as visual and auditory hallucinations (Lemon et al 2010) • Increased oxygen consumption, increased hyperventilation, respiratory alkalosis and decreased cerebral blood flow (Lemon et al 2010) • Dehydration and electrolyte abnormalities, specifically hypomagnesemia, hypophosphatemia and hypokalemia (Sarff and Gold 2010)

2.9.3 Incidence, assessment and management of AWS in the ICU

Patients experiencing AWS, especially DTs, often require ICU care (Moss and Burnham 2006). Dependent of their last drink, DTs might either be the main reason for admission to ICU or may complicate the clinical course of patients with non-alcohol related diagnoses (Moss and Burnham 2006).

The most widely utilised and validated tool for the measurement of symptom severity in AWS is the Clinical Institute Withdrawal Scale for Alcohol revised (CIWA-Ar) (Sullivan, Sykora, Schneiderman et al 1989) (Appendix III). This tool, which was initially developed by Shaw, Kolesar, Sellers et al (1981), uses a combination of objective data (vomiting, tremor and vital signs such as blood pressure and heart rate) and subjective data (anxiety, agitation and hallucinations) to score severity of withdrawal and trigger appropriate treatment (Corfee 2011). The scale can be used as frequently as every 30 minutes, but it is usually used hourly (Sullivan et al 1989).

The CIWA-Ar scale was not designed for non verbal patients in the hospital ICU, as a result the scale is difficult to implement within ICU, as seven out of ten of the questions requires a response from the patient (Sullivan et al 1989, de Wit et al 2010, Corfee 2011, Benson et al 2012). Although there are a number of studies which have utilised the CIWA-Ar scale within the critical care setting (Spies et al 1996, Spies, Otter, Huske et al 2003), as far as can be established, the scale has never formally been validated in this setting. A further drawback of the CIWA-Ar in critical care is that the CIWA-Ar may be too time consuming and complex, which may be incompatible with nursing duties which are fundamentally time driven (Benson et al 2012, McPherson, Benson and Forrest 2012).

More recently, the Glasgow Modified Alcohol Withdrawal Scale (GMAWS) has been proposed within the acute hospital setting as a tool for the management of AWS (Appendix III). This five variable tool, which is the modification of two AWS tools, identifies both alcohol dependency and harmful alcohol misuse and provides a simplified score to assess the level of AWS (Benson et al 2012). Although the CIWA-Ar scale has undergone extensive validation, there are clear indicators in the initial work surrounding the GMAWS that it may be more appropriate for the busy acute ward due to its simplicity (Benson et al 2012).

However, similar to the CIWA-Ar, there is yet to be formal validation work in the non verbal ICU population.

2.9.4 Pharmacological management of AWS in the ICU

The main goals of pharmacological therapy for the treatment of withdrawal from alcohol are:

- The reversal of the pharmacological effects of alcohol;
- Treatment and prevention of withdrawal symptoms and complications;
- Maintenance of abstinence from alcohol;
- Treatment of co-existing psychiatric conditions as appropriate (Saitz and O'Malley 1997).

Table 2.13 reviews the most commonly used drugs in the treatment of AWS, alongside their pharmaceutical properties, their impact on AWS and the influence of ICU related delirium.

Table 2.13: Commonly used drugs in the treatment of AWS and their impact on AWS and ICU related delirium

Drug name	Pharmaceutical group	Impact on AWS	Impact on ICU related delirium
Diazepam Lorazepam	Benzodiazepines. Benzodiazepines activate γ-aminobutyric acid A (GABA) neuronal receptors in the brain. Metabolised in the liver (Young and Prielipp 2001)	• Mainstay of therapy for alcohol withdrawal (Vincent, Smith, Winstead et al 2007) • Only agents that have been shown to reduce the risk of seizures, decrease the symptoms of alcohol withdrawal and lower the risk of delirium • They have anxiolytic, amnesic, sedating, hypnotic and anticonvulsant effects, but no analgesic activity • Longer acting benzodiazepines (i.e. diazepam) may offer a smoother recovery from withdrawal with fewer symptoms	• Drug class is implicated in causing delirium (Pandharipande et al 2006) • Prolonged benzodiazepine use in the ICU may lead to withdrawal symptoms when the drug is abruptly discontinued, manifesting as anxiety, agitation, tremors, headache, hyperactive delirium and occasionally seizures (Barr, Fraser, Puntillo et al 2013)
Haloperidol	Butyrophenone derivative antipsychotic (Allman and Wilson 2011)	• Antipsychotic agent used to treat symptoms like hallucinations • When used alone may increase seizure risk and does not reduce delirium • Recommended only as a adjunctive therapeutic option to benzodiazepines • Should be reserved for the psychiatric manifestations of AWS refractory to benzodiazepine therapy (Lemon et al 2010)	• Prophylactic treatment with haloperidol in ICU patients with a high risk of delirium may result in lower delirium incidence and more delirium free days (van den Boogaard, Schoonhoven, van Achterberg et al 2013) • However, further research is needed to determine the safety and efficacy of using antipsychotics to treat delirium in ICU patients (Barr et al 2013)
Carbamazepine	Anticonvulsant	• Well documented anticonvulsant activity and has shown to decrease seizures; however has not been shown to have any impact on delirium • Does not cause the respiratory depression seen by benzodiazepines • No abuse potential	• Not well documented. May in fact cause ICU related delirium (Weinhouse, Schwab, Watson et al 2009)

Clonidine Dexmedeto-midine	Alpha adrenergic agonists with anxiolytic and analgesic properties that reduce sympathetic outflow	• Does not treat the underlying pathophysiological mechanism of alcohol withdrawal and therefore must be used in conjunction with benzodiazepines (Sarff and Gold 2010) • This class of drugs does not have the seizure prophylaxis that is afforded by benzodiazepines (Kosten and O'Connor 2003) • Lowers the heart rate and limits tremor activity in AWS (Lemon et al 2010) • To date no published studies have compared the efficacy and safety of treating severe to moderate AWS with dexmedetomidine vs. benzodiazepines (Barr et al 2013)	• In mechanically ventilated patients Dexemedetomidine infusions administered for sedation may be associated with a lower prevalence of delirium compared to benzodiazepines (Pandharipande, Pun, Herr, et al 2007) • Provides sedation without respiratory depression, which is attractive in critical care (Savel and Kupfer 2014).
Propofol	Sedative that binds to multiple receptor in the central nervous system to interrupt neural transmission, including GABA, glycine and nicotinic receptors (Barr et al 2013)	• Short half life and predictable metabolism makes it an attractive choice for ICU patients with benzodiazepine resistance (Sarff and Gold 2010) • No RCT to date which has evaluated the efficacy of Propofol in isolation in AWS (Corfee 2011) • Does have anti convulsant properties	• There are no RCT's or high quality evidence available demonstrating a negative impact on ICU related delirium due to Propofol (Barr et al 2013) • Non benzodiazepine based solutions such as Propofol may have benefits in managing ICU related delirium due to short half life
Ethanol		• Few studies to support this form of treatment in any acute care setting • Efficacy, complications and optimum delivery strategies have not been well documented	• Ethanol use is a known risk factor for the development of ICU related delirium (Barr et al 2013)

There have been a small number of RCTs which have looked specifically at the pharmacological management of AWS in the ICU. In 2003, Spies et al carried out a prospective, double blinded randomised control trial in a surgical ICU, to examine the effect of bolus vs. continuous infusion therapy on the severity and duration of AWS. Patients who fulfilled the Diagnostic Statistical Manual of Mental Disorders (DSMD-IV) (Fourth Edition) criteria for alcohol abuse (not dependence) and with an alcohol consumption of greater than 60g/day were included in the study. The CAGE tool was also utilised to determine alcohol abuse (with proxy and patient) and informed written consent was obtained from either the patient of the patient proxy. Of note, no intubated patients were included in this particular study. In response to the development of the signs and symptoms of AWS, patients were randomized to either a continuous infusion of IV Flunitrazepam, Clonidine and Haloperidol (if needed), or the same combination of medications given as bolus adjusted doses. The administration of medication was determined using the CIWA scale (See Section 2.9.3). In total, 44 patients who developed AWS after admission to ICU were randomised, 23 into the Bolus Titrated Group (BTG) and 21 into the Infusion Titrated Group (ITG). Patients in the BTG had fewer AWS days compared with the ITG (2 vs. 6, $p \leq 0.01$), and had less requirement for mechanical ventilation (65% of patients vs. 90% of patients, $p= 0.05$). Further, ICU treatment days were significantly lower in the BTG group compared to the ITG (8 days vs. 14 days, $p \leq 0.01$).

Although these results clearly indicate that bolus therapy is preferred to infusion therapy in the ICU population for AWS management, there are several limitations which may affect the interpretation of this study. Firstly, patients were only included if they were diagnosed with alcohol abuse as oppose to dependency; however, dependent patients are the predominant population who will be treated for AWS within critical care. Of note, although the drug requirements in the BTG were significantly less than in the ITG, approximately one third of patients in each group required Propofol as a rescue medication, indicating that a single ideal approach for AWS therapy remains elusive in the ICU population.

Weinberg, Magnotti, Fischer et al (2008) compared the use of intravenous (IV) ethanol with diazepam for the management of AWS prophylaxis in a trauma ICU

over a 15 month period in Tennessee, using a non blinded RCT. All trauma patients admitted to the ICU with a history of chronic alcohol consumption (greater than or equal to five drinks per day), who independently consented, were randomised into one of two, four day prophylactic regimes. Treatment arm one was a 5% ethanol IV infusion and treatment arm two was scheduled -dosed Diazepam (IV or enteral route). Patients in each group were evaluated using the seven point Riker Scale (1=unrousable, 7=dangerous agitation) (Riker, Picard, Fraser 1999). According to the study protocol, regimens were titrated to achieve a Riker score of four (calm and cooperative). Deviation from a score of 4 during the course of treatment was then compared between the two groups. During the study period, 58 patients met the inclusion criteria, six patients were then excluded due to elevated liver enzymes, one further patient withdrew from the study and one patient was removed from analysis by the investigators for protocol violation involving the administration of supplementary benzodiazepines outside the study protocol. This left 50 patients for analysis, with 26 patients randomised to the ethanol group and 24 to the Diazepam group by way of a virtual computer generated coin flip. Overall, the ethanol group had a significantly greater proportion of patients who deviated from a score of four (p=0.02). Further, one patient in the ethanol group failed treatment (failure to achieve a score of 4, not caused by over sedation) whereas no patient failed in the diazepam group.

Despite the rigorous RCT design which was executed to evaluate these two treatment regimes, there are several important factors which may impact of the results from this trial. Firstly, because the researchers wished to obtain consent directly from the patient, no intubated patients were included in this study. Therefore, the participants of this study can be seen to be select group: patients who are significantly injured who could give an alcohol consumption history and informed consent. Another drawback is the use of the Riker Scale for the evaluation of sedation. The Riker Scale was not designed to monitor for AWS and therefore, may not have fully captured all the signs and symptoms associated with AWS which occur in the absence of generalised agitation. Lastly, this study was a non-blinded trial, which introduces a major element of measurement bias to this study, as the individuals assessing the Riker Scale score might allow their knowledge of the treatment affect their judgement (Nelson 2011).

More recently, the use of Dexmedetomidine has been tested in relation to the management of AWS within the critical care environment (Mueller, Preslaski, Kiser et al 2014). In a single centre, medical ICU in North America, Mueller et al (2014) undertook a randomised, double blind, placebo controlled dose range study to evaluate Dexmedetomidine as an adjunctive therapy to Lorazepam for severe alcohol withdrawal. Twenty four patients with a CIWA score of greater than 15, despite greater than or equal to 16mgs of Lorazepam, were randomised into three arms of the study: high dose Dexmedetomidine (1.2μg/Kg/hr), low dose Dexmedetomidine (0.4μg/Kg/hr) or placebo, in addition to the standard therapy for AWS (a symptom driven protocol of Lorazepam). The infusion of Dexmedetomidine was continued for up to five days or until the treating clinician judged that the patient was no longer in withdrawal. There were two primary outcomes measures: total Lorazepam requirements over the first 24 hours of the study intervention and the cumulative total dose of Lorazepam given over the first seven days of alcohol withdrawal.

Dexmedetomidine was infused for a median of 61 hours, while the placebo was infused for 70 hours. There was a significantly higher requirement for Lorazepam given in the first 24 hours in the placebo group compared to the Dexmedetomidine groups (p=0.04) (no difference between the high and low intervention group). Over the seven days of AWS, there was no significant difference in the total amount of Lorazepam given in any of the three study groups. There were a number of significant adverse events in the Dexmedetomidine groups, as hypotension and/or bradycardia occurred in 25% of patients. There was no difference in the need for, or duration of mechanical ventilation, ICU or hospital stay between any of the study groups. Fundamentally, this study demonstrated that Dexmedetomidine may have a short term benefit for the treatment of severe alcohol withdrawal within the critical care environment, however, there were significant side effects associated with its use.

This study provides valuable insights into the use of Dexmedetomidine as an adjunctive therapy to benzodiazepines such as Lorazepam, but the results should be interpreted with caution. Although, this study was adequately powered, the small sample size and the single centred nature of the study limits its

generalisability. Furthermore, this study also used the CIWA scale for the assessment of AWS. The use of these scales is controversial in the ICU due to their dependence of patient participation, which is not always possible.

The next section of this literature review will focus on ICU related delirium and the complex and challenging interplay between AWS and delirium.

2.10 ICU related delirium

2.10.1 Definition and pathophysiology

Delirium is a common manifestation of acute brain dysfunction in critically ill patients (Girad, Pandharipande, Ely 2008); it is defined in the American Psychiatric Association's DSMD-IV (2000) as *'a disturbance of consciousness and cognition that develops over a short period of time (hours to days) and fluctuates over time*'. Varying terminology is used to describe this syndrome of cognitive impairment in the critically ill patient including ICU psychosis, ICU syndrome, acute confusional state, septic encephalopathy and acute brain failure (Ely, Inouye, Bernard et al 2001a, Ely, Margolin, Francis et al 2001b, Ely, Siegel, Inouye 2001, Girad et al 2008). The current consensus is to consistently use the term delirium and subcategorise according to the psychomotor symptoms associated with the delirium (Pun and Ely 2007) (Table 2.14).

Table 2.14: Sub categories of ICU related delirium (Pun and Ely 2007, Arend and Christensen 2009)

Type of Delirium	Clinical Manifestations
Hyperactive (Previously ICU psychosis)	Restlessness, agitation, hallucinations, delusions, paranoia, disorientation, aggressive, combative.
Hypoactive	Withdrawal, apathy, lethargy, decreased responsiveness.
Mixed	Mixture if both of the above clinical manifestations.

The pathophysiology of ICU delirium is poorly understood but multiple promising hypotheses are subject to ongoing research (Girad et al 2008, Pun and Boehm 2011). Much of the evidence generated regarding the pathogenesis of delirium

has been conducted out with the ICU, highlighting the need for further research in the area. The pathophysiology of delirium does seem to be based around different neurochemical processes. Imbalances in the neurotransmitters regulating cognitive function, behaviours and mood are thought to be implicated (Truman and Ely 2003, Pun and Ely 2007, Arend and Christensen 2009, Van Rompaey, Elseviers, Schuurmans et al 2009). The main neurotransmittors thought to be involved are not dissimilar to those involved in AWS, namely serotonin, dopamine, GABA and acetylcholine (Morandi, Jackson, Ely 2009, Pun and Boehm 2011). In addition to these neurotransmitter systems, endorphin hyperfunction and increased central noradrenergic activity may play a part in the development of delirium as well as many systemic conditions, medications, medication withdrawal, substance intoxication, metabolic disturbance and hypoxemia (Morandi et al 2009, Pun and Boehm 2011).

2.10.2 Assessment of ICU related delirium

ICU related delirium has a reported prevalence of up to 80% depending on the severity of illness, the choice of sedation and the need for mechanical ventilation (Banerjee, Girad, Pandharipande 2011, Pandharipande, Cotton, Shintani et al 2008, Ely, Shintani, Truman et al 2004). There is an abundance of recent literature, predominantly from the USA, which focuses on accurate assessment of ICU related delirium, with most of the work centring on the development and validation of screening tools such as the Intensive Care Delirium Screening Checklist (ICDSC) (Bergeron, Dubois, Dumont et al 2001) and the Confusion Assessment Method for the ICU (CAM-ICU) (Ely et al 2001b) (Appendix IV). The purpose of delirium assessment tools such as CAM-ICU is to allow non-psychiatric physicians and other ICU personnel to diagnose delirium in ICU patients rapidly and reliably, even when the patient cannot speak because of endotracheal intubation (Girad et al 2008).

The ISCDS, originally validated with medical and surgical ICU patients against a consulting psychiatrist who served as a standard reference, is an eight item checklist with a sensitivity of 99% and specificity of 64%, with an inter-rater reliability of 0.94 (Bergeron et al 2001, Morandi et al 2009). The CAM-ICU, adapted from the Confusion Assessment Method (Inouye, van Dyck, Alessi, et al 1990), was originally validated by Ely et al (2001a and 2001b) in two cohorts of

38 and 111 medical ICU patients. CAM-ICU allows for delirium assessment in critically ill patients, including nonverbal mechanically ventilated patients. Delirium is present when three of the four features within the test are present (Pun and Boehm 2011). Both the ISCDS and the CAM-ICU are presented in Appendix IV.

Without the use of validated tools, it is estimated that delirium goes undetected by both medical and nursing staff in more than 65% of patients (Truman and Ely 2003). As a result, systematic use of validated assessment tools is necessary to detect delirium that would otherwise go undetected and consequently untreated.

2.10.3 Treatment and management of delirium

Unlike AWS, the main treatment option for ICU related delirium is not a pharmacological approach. Pandharipande et al (2006 and 2008) found that exposure to either Lorazepam or Midazolam was an independent risk factor for the development of delirium in various ICU populations. Furthermore, there is limited work on preventative or prophylactic drug regimes such as Dexmedetomidine or Haloperidol for ICU related delirium, although Haloperidol may be beneficial in some populations (Barr et al 2013, van den Boogard et al 2013).

As a result, much of the work surrounding the management and treatment of ICU related delirium has focussed on non pharmacological approaches such as the **A**wakening, **B**reathing trial, **C**hoice of appropriate sedation, **D**elirium monitoring and **E**arly mobility and exercise (ABCDE) bundle (Morandi, Brummel, Ely 2011). Despite this, the benefits of a daily sedation interruption in those patients with alcohol dependency remains unclear and requires further investigation (Barr et al 2013).

Other strategies which have been recommended for the prevention and treatment of ICU related delirium, include the promotion of sleep through non pharmacological approaches. Several small studies have demonstrated that sleep deprivation may contribute to the development of delirium and increased levels of physiologic stress (Figueroa-Ramos, Arroyo-Novoa, Lee et al 2009, Weinhouse

et al 2009). Other simple strategies to prevent delirium include: treating pain as needed; re-orientating patients; using aids as required (i.e. glasses and hearing aids) and the recommencement of psychiatric medication if necessary (Barr et al 2013).

From the sections above it is clear that AWS and ICU related delirium have similar clinical presentations. However, they have distinctly different treatment pathways, especially with regards to pharmacological approaches. What complicates this issue further is that patients with a history of previous alcohol misuse are likely to develop both AWS and ICU delirium, as previous alcohol misuse is a risk factor for its development (Barr et al 2013). More research is required into the assessment and management of both groups, especially the alcohol related group, with specific emphasis on delineating the two processes (Barr et al 2013).

2.11 Liver cirrhosis and the ICU

As well as acute problems such as AWS, patients with alcohol dependency are also at risk of developing serious long term complications such as liver cirrhosis. The next section of this literature review will explore the management of patients with liver cirrhosis in the ICU.

The ICU plays an integral role in the management of patients with complications of liver disease (Singh, Gayowski, Wagener et al 1998, Olson, Wendon, Kramer et al 2011). Indeed, patients with liver disease are amongst the most physiologically challenged of all in-patients with a high risk of ICU and hospital mortality (Foreman, Mannino, Moss 2003, Barclay, Forrest, Morris et al 2009, Thomson, Moran, Cowan et al 2010).

There is extensive evidence examining the impact of liver cirrhosis in the ICU population. The vast majority of this literature indicates a poor prognosis for this patient group (Cholongitas, Senzolo, Patch et al 2009). Thomson et al (2010) reported the weighted mean ICU and hospital mortality rates from seventeen studies as 45% and 58% respectively; however in some cases, mortality rates exceeded 70%. Interestingly, it appears that there has been little or no improvement in ICU survival rates for this group of patients over the last decade (Table 2.15).

The impact that alcohol induced liver cirrhosis has on outcome from critical care varies within the reported literature (Austin and Shawcross 2008). For example, Singh et al (1998) and Gildea, Cook, Nelson et al (2004), found that patients admitted with alcohol as a primary cause for their liver disease had a significantly lower mortality than those patients with liver disease not caused by alcohol (p=0.001). On the other hand, Thomson et al (2010) showed no statistical difference in hospital outcome for patients with and without alcohol related liver disease. Only one study appears to focus exclusively on patients admitted with liver cirrhosis as a result of Alcoholic Liver Disease (ALD) with each of the other studies focusing on cirrhosis of the liver from varying aetiologies (i.e. Hepatitis B, Hepatitis C, autoimmune disease and drug related).

Table 2.15: Outcome of patients admitted to ICU with liver cirrhosis

Study	Country	Total number of patients in study	Patients with alcohol induced injury (%)	Type of Unit	ICU mortality
Shellman, Fulkerson, DeLong et al (1988)	USA	100	Not Given	Two Centres, Medical Intensive Care Unit (MICU)	64
Singh et al (1998)	USA	54	54	Liver Transplant Unit	43
Aggarwal, Ong, Younossi, et al (2001)	USA	480	52.6	MICU	36.6
Arabi, Ahmed, Haddad et al (2004)	Saudi Arabia	129	2	Regional Referral Centre for Liver Disease	56.5
Gildea et al (2004)	USA	420	51.8	MICU	44
Rabe, Schmitz, Paashaus et al (2004)	Germany	76	72	MICU	59
Du Cheyron, Bouchet, Parienti et al (2005)	France	186	72	MICU	41
Chen, Tian, Liu et al (2006)	China	102	25	Gastroenterology ICU	68.6 (Hospital Mortality)
Mackle, Swann, Cook (2006)	Scotland	107	100	Tertiary Referral Liver Unit	58
Cholongitas, Calvaruso, Senzolo et al (2009)	England	412	69.4	Liver ICU	61.2 (in ICU or 6 weeks after discharge from ICU)
Juneja, Gopal, Kapoor et al (2009)	India	104	57.7	Liver ICU	42.3
Thomson et al (2010)	England	118	86	Two general ICU's	38
Tu, Jenq, Tsai et al (2011)	China	202	32	Hepato-gastroenterology ICU	59.9 (hospital mortality)
Levesque, Hoti, Azoulay et al (2012)	France	377	68	Liver Intensive Care Unit	43

Mackle et al (2006) examined the outcome of patients admitted with decompensated alcoholic liver disease to one general ICU in Scotland over a three year period using a retrospective observational design. It is worth noting that this particular unit contains a supraregional tertiary referral centre for hepatobiliary disease and also contains the National Liver Transplant Unit. A total of 110 admissions, involving 107 patients were analysed. The overall hospital mortality for this group was 58%. In patients who were ventilated, there was a 60% mortality rate. Interestingly, the mortality rate was only 4% in those patients who were ventilated and required no other system support (i.e. vasopressor support, Renal Replacement Therapy (RRT)). In patients with three failing organs, Mackle et al (2006) observed a 91% hospital mortality rate.

The retrospective nature and the relatively small sample size of the population studied may limit the generalisability of the reported results (Robson 2011). Further, the decision making process of treating physicians could not be analysed, especially those decisions related to RRT, vasopressor support or mechanical ventilation. No standard approach was used to make these decisions which impacts on the external validity of the results (Parahoo 2006). However, it could be argued this is, in fact, generally accepted practice in British ICUs. Despite the clear limitations of this study it does provide valuable information regarding this sub group of patients and the poor outcome which could be expected from multi organ support in the patient presenting with alcoholic liver disease to the ICU environment.

2.11.1 Liver cirrhosis: predicting outcome

It is becoming increasingly important to identify patients who may benefit from admission to the ICU, to ensure that aggressive treatment is targeted appropriately (Levesque et al 2012). A number of different scoring tools have been used for this purpose in the liver cirrhosis population. However, much of the data regarding the utility of these scores has come from either Asia, or from a limited number of transplant centres offering specialist hepato-gastroenterology ICUs. These centres have a different case mix of cirrhotic patients compared to the general ICU and it has been suggested that the application of scoring systems might differ between specialist and general ICUs.

A number of scoring tools are available to healthcare professionals admitting patients with liver cirrhosis to the ICU. Broadly speaking these can be split into two categories: liver specific scoring tools and ICU specific tools. Liver specific tools include: the Child-Turcotte Pugh (CTP) score (Pugh, Murray-Lyon, Dawson et al 1973); the Model for End Stage Liver Disease (MELD) (Kamath, Wiesner, Malinchoc et al 2001); the UK End Stage Liver Disease (UKELD) score (Neuberger, Gimson, Davies et al 2008); the Royal Free Hospital (RFH) score (Cholongitas, Senzolo, Patch et al 2006) and the Glasgow Alcoholic Hepatitis Score (GAHS) (Forrest, Morris, Stewart et al 2007). However, only one of these scores was created with the intention of optimising referral patterns for the ICU population: the RFH score. All of the other scores presented were designed for a specific clinical problem. For example, the CTP score was designed to predict mortality following surgical treatment of oesophageal varices and the UKELD was designed to assess patients for transplant in the UK.

General ICU and critical care tools include the Acute Physiolgy and Chronic Health Evalutaion (APACHE) tool (Knaus, Draper, Wagner et al 1985) and the Sequential Organ Failure Assessment (SOFA) score (Vincent, de Mendonca, Cantraine et al 1998). A recent study collaborative across European Gastronenterology units also created the Chronic Liver Failure- Sequential Organ Failure (CLIF-SOFA) score (Moreau, Jalan, Gines et al 2013) with the aim of bringing together the most predictive aspects of both sets of scoring tools.

Renal specific scoring tools have also been explored for their prognostic ability in this cohort of patients (Cholongitas et al 2009). Development of renal dysfunction is associated with poor prognois in patients with cirrhosis (Mackle et al 2006). Renal failure is also associated with severe complications of cirrhosis such as hepatorenal syndrome (HRS) (Cholongitas et al 2009). Renal specific scoring tools which are available are the Risk, Injury, Failure, Loss and End Stage Renal Disease (RIFLE) tool (Bellomo, Ronco, Kellum et al 2004) and the Acute Kindey Injury Network (AKIN) tool (Mehta, Kellum, Shah et al 2007).

Further details of the scoring tools discussed above are given in Appendix V.

2.11.2 Accuracy of current scoring tools

Over the last ten years there have been several papers documenting the accuracy of the above scoring tools in the critically ill cirrhotic population. As stated previously, many of these papers explored specific critical care areas, such as liver transplantation units (Thomson et al 2010, Levesque et al 2012).

In a recent systematic review, Flood, Bodenham, Jackson (2012) examined the prognostic value of liver-disease specific versus physiology based scoring systems in patients admitted to ICU with a background of alcoholic liver disease (ALD). In the nine studies analysed, the range of the study cohorts ranged from 76 to 486, with a total of 1742 patients across all nine studies. The mean age ranged from 50-55 years and the setting of these studies was a mix of general and liver specific ICUs. The ability of prognostic models to differentiate between survivors and non survivors was tested in all nine studies by examining the Area Under the Curve (AUC) of Receiver Operator Characteristic (ROC) curves.

Seven of the nine papers directly compared liver specific scoring tools against acute physiological scores. From these seven papers, six found physiology based systems more discriminating, with the SOFA performing most accurately (the majority of studies calculated the SOFA AUC >0.9). The exception was Rabe et al (2004) who rated the CTP higher than the APACHE II in a general ICU population. In general, the CTP (eight studies from nine) was rated the least predictive with an AUC ranging from 0.61-0.75.

Flood et al (2012) state that the increased prognostic ability of acute physiology scores is likely to reflect that patients admitted to the ICU with a background of ALD die of multi organ failure, rather than isolated decompensated ALD. This is reflected in Das, Boelle, Galbois et al (2010) who demonstrated that the severity of liver dysfunction was not a predictor of hospital outcome in patients with ALD admitted to the ICU. Liver specific scoring tools which focus on hepatic specific biomarkers (i.e. INR) may be insensitive to other organ failure (Flood et al 2012).

There are several limitations to this systematic review. Firstly, it included alcohol related aetiologies only, which limited the number of studies included in this analysis. Further, many of the studies included were in the form of abstracts

only. As a result, the authors of the systematic review accept that some key information may have been missed.

2.12 ICU survivorship

2.12.1 Quality of life after ICU

Intensive care medicine by definition treats the most critically ill patients who have an inherent risk of mortality; therefore it seems logical that for the last two decades the primary outcome parameter has been survival (Oeyen, Vandijck, Benoit et al 2010). It is now recognised, that while measuring mortality as an end point is crucial, the impact of intensive care treatment on Quality of Life (QOL) should also be considered in clinical decision making and as a research end point (Field, Prinjha, Rowan 2008).

The physical, psychological and social problems which patients face after discharge from the critical care environment have been described as post intensive care syndrome (PICS) (Needham, Davidson, Cohen et al 2012, Mehlhorn, Freytag, Schmidt et al 2014). The impact of PICS include: reduced QOL for both patients and their loved ones and reduced functional status (Oeyen et al 2010, Iwashyna, Ely, Smith et al 2010). The concept of PICS was created to raise awareness of the special needs of ICU survivors. Furthermore, by having an established group of signs and symptoms, it may make it easier to pave the way for more specialist and targeted interventions for ICU survivors (Mehlhorn et al 2014).

The following section of this literature review will firstly describe the most commonly utilised outcome measures for determining the different aspects of PICS. It will then describe more fully the physical, psychological and social problems faced by survivors of ICU. This review will then critically explore the current modes of rehabilitation used for patients after discharge from critical care which have attempted to overcome some of the issues related to PICS.

2.12.2 Current outcome measures

There are number of outcome measures which have been used within the literature to try and understand the physical, psychological and global problems

which survivors of ICU face (Table 2.16). These outcomes measures, which are predominantly patient reported, are used within many of the different studies which will be described in the following section of this PhD. It is outwith the remit of this thesis to provide detailed information on the original validation work surrounding this multitude of outcome measures. As a result, Table 2.16 gives an over view of these tools and information on the content of the measure.

2.12.3 Physical problems related to survivorship

An abundance of literature has been generated in the last decade describing critical illness associated disability (Corner and Brett 2014). Significant muscle loss, at a rate of up to 15% within 1 week of the onset of multi organ failure within the ICU environment, coupled with the negative effects of bed rest, can lead to life changing disability in the months following ICU discharge (Corner and Brett 2014). Table 2.17 demonstrates the wide range of physical problems and their incidence, which ICU survivors can encounter after discharge from the critical care environment. Table 2.17 does not represent an exhaustive or systematic review of the literature. It is intended to highlight the physical problems which ICU survivors encounter.

Table 2.16: Common outcomes measures utilised in ICU follow up studies

Outcome Measure	Type of Measure	Content of Tool	Scoring
EuroQol-5D (EQ-5D)	Global QOL	Short questionnaire containing five questions	Generation of a health utility score (0-1) which can be used for health economics studies
Medical Outcomes Study: 36 Item Short Form Health Study (SF-36) (Brazier, Harper, Jones et al (1992)	Global QOL	Contains 36 Items measuring 8 multi domains	Each domain is scored from 0 (worst score) to 100 (best score).
Six minute walk test (6MWT) (American Thoracic Society 2002)	Physical/ functional outcome measure	Measures the total distance an individual can walk in 6 minutes	Measure in metres
Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983)	Psychological outcome measure	Contains 14 statements related to mood: seven for anxiety and seven for depression	4 possible responses for each question (score 0-4). Scores 8-10= possibility of anxiety/depression, 11 and above= likely to be present
Impact of Events Scale (IES) (Horowitz, Wilner, Alvarez 1979)	Psychological measure	Scores for two of the core features of PTSD (intrusive thoughts and avoidant behaviour)	Score 0-8= low levels of symptoms Score 9-19= Medium levels of symptoms, Score 20= High levels of symptoms
Brief Pain Inventory (BPI) (Tan, Jensen, Thornby et al 2004)	Measure of Chronic Pain	Patients rate their worst, least, average and current pain intensity and the degree to which pain interferes with the 7 domains of functioning	Each Domain is measured on a scale of one to ten
Repeatable Battery for the Assessment of Neuropsychological Status (RBAWS) (Randolph, Tierney, Mohr et al 1998)	Neuropsychological measure/ cognition measure	Individual domains which focus on memory, attention, construction and language	Ten subsets give five scores

Table 2.17: Common physical problems associated with ICU Survivorship

Physical Problem	Studies	Key Results
Poor mobility	Herridge, Cheung, Tansey et al (2003)	At 3, 6, 12 months post ICU discharge, survivors of ARDS had significantly worse than population norm performance utilisng the 6MWT
	Herridge, Tansey, Matte et al (2011)	At 5 years post ICU discharge, survivors of ARDS had significantly lower performance on the 6MWT than the population norm (76% of predicted norm)
Chronic pain	Battle, Lovett, Hutchings (2013)	Using the Brief Chronic Pain Inventory, 44% of ICU survivors experienced chronic pain between 6 months and 1 year post ICU discharge
	Timmers, Vernofstad, Moons et al (2011)	57% of patients still experience a pain/discomfort long term (>6 years) after ICU discharge utilising EQ-6D
Sexual dysfunction	Ulvik, Kvale, Wentzel-Larsen, et al (2008)	Utilising the international index of erectile dysfunction- 41% of men stated they had impaired erectile dysfunction after a critical illness
	Griffiths, Gager, Alder et al (2006a)	Self Reported measure: 43.6% of patients reported symptoms of sexual dysfunction, 45% of patients and 40% of partners not happy with sex life.
Critical illness polyneromyopathy and muscle wasting	Fletcher, Kennedy, Ghosh et al (2003)	Motor or sensory deficits were present on clinical examination in 59% of the patients studied at a median of 43 months post ICU discharge
Dysphagia	Macht, Wimbish, Clark et al (2011)	Retrospective observational cohort study demonstrated dysphagia was present in 84% of patients post extubation
	Skoretz, Flowers, Marion (2010)	Systematic review demonstrated an incidence of dysphagia ranging from 3-62% post extubation
Nutritional problems and weight Loss	Kvale, Ulvik, Flaatten (2003)	During and after ICU stay, 40% of patients lost more than 10Kg

2.12.4 Psychological problems related to survivorship

Intensive care patients frequently experience memory loss, nightmares and delusional memories and some may develop symptoms of anxiety, depression and post traumatic stress (Aitken, Rattray, Hull et al 2013). There have been several studies which have explored the development of psychological morbidity after discharge from the critical care setting. Table 2.18 reviews some of the common psychological effects of ICU.

Self-efficacy has been proposed as an important psychological factor that may be related to a patient's physical and psychological recovery from critical illness (Connolly, Aitken, Tower 2013). The concept of self-efficacy, which is a core concept of social cognitive theory, assumes that health is a product of an individual's physical, psychological, cultural, spiritual and social environment (Bandura 1977). It is a person's confidence/belief in their ability to undertake a certain set of actions (Bandura 1977).

There are very few interventional studies examining self-efficacy in acute injury patients and none in the general critical care population. In other clinical areas, however, it has been identified that high self-efficacy is strongly associated with a better QOL and lower healthcare utilisation in patients (Tsay and Healstead 2002). Furthermore, self-efficacy has been found to influence various health outcomes including pain related disability and compliance with discharge instructions (Connolly, Aitken, Tower et al 2014).

Connelly et al (2014) aimed to identify factors associated with self-efficacy for managing recovery in the trauma ICU population. In this single centre study in Australia, 88 patients completed the 6 item Self Efficacy Scale (SES) at one and six months post hospital discharge with the aim of understanding the interplay between self-efficacy and recovery. Factors which were significantly associated with low self-efficacy and an individual's perceived ability to recover at six months post ICU discharge, were illness perception (consisting of cognitive and emotional aspects of health measured by the Brief Illness Perception Questionnaire) and continued psychological distress. The research team recommended that the screening of patients after hospital discharge for

Table 2.18: Common psychological problems associated with ICU Survivorship

Psychological Problem	Studies	Key Results
Post traumatic Stress Disorder (PTSD)/ PTSD symptoms	Wade, Howell, Weinman et al (2012)	27.1% survivors had probable PTSD using the Post Traumatic Stress Diagnostic Scale (PDS)
	Davydow, Gifford, Desai et al (2008)	Systematic review demonstrated a PTSD prevalence of 22% in ICU survivors
Poor sleep	Tembo, Parker, Higgins (2013)	Longing for normal sleep after ICU- Theme generated in a qualitative study
Personality changes and Mood	Karlsson and Forsberg (2008)	Swedish qualitative studies, (both using a phenomenological approach). Both studies generated a theme of 'changes in self' from the patients' perspective
	Corrigan, Samuelson, Fridlund et al (2007)	
Depression	Wade et al (2012)	46.3% of patients had probable depression on the Centre for Epidemiological Studies Depression Scale (CES-D)
Cognitive problems (Including memory and attention)	Pandharipande, Girad, Jackson, et al (2013)	3 months post ICU 40% of patients had global cognition scores below the population norm utilising the RBAWS
	Jackson, Hart, Gordon et al (2003)	6 months post ICU discharge, 32% neuropsychologically impaired using the Modified Blessed Dementia Rating Scale
Anxiety	Herridge et al (2011)	51% of ARDS population reported at least one episode of physician diagnosed depression, anxiety or both, between 2 and 5 years post ICU discharge

psychological distress and illness perceptions could help tailor appropriate interventions for vulnerable patients to help promote recovery. However, more research is required in this area to help understand the impact of self-efficacy in the critically ill patient, outwith the trauma population.

2.12.5 Social problems related to survivorship

A variety of social problems for ICU survivors have been described in the literature, with two studies specifically exploring this area. In 2013, Griffiths, Hatch, Bishop et al, undertook a multicentre questionnaire based study with survivors of critical illness at six months and 12 months post ICU discharge. Questionnaires sent included the EQ-5D and the SF-36. In addition, a novel questionnaire was designed specifically for the study to determine changes in family circumstance, socio economic stability and care requirements. Written informed consent was obtained from participants in the interval between ICU discharge and discharge from hospital. A small number of participants were also recruited at a routine outpatient visit to the ICU follow up clinic.

A total of 293 patients who had greater than 48 hours of level three care, in one of 22 UK ICUs, had a complete data set available at 12 months from this study. In terms of employment, a negative impact was reported by 33% of all patients at six months and 28% of patients at 12 months. Fifty percent of patients also reported a reduction in employment as their sole source of income at 12 months post discharge (19% vs. 11%) compared with pre ICU admission. Furthermore, 32% of patients reported an overall reduction in family income at 12 months post ICU. Requirements for additional care assistance were also explored by the researchers. In this cohort, they found that 22% of patients needed additional and continued care assistance as 12 months post critical care discharge, with 78% of this care provided by family members. As a result of this, in 8% of all cases examined in this study, a family member also experienced a significant reduction in employment activity in the year following ICU discharge. These findings were also consistent with the EQ-5D results, which demonstrated that 26% of patients still required support with self care at 12 months post ICU discharge.

This study by Griffiths et al (2013) is one of the first studies to specifically examine the social and economic problems which patients face after ICU discharge. Its strengths lie in the large sample size obtained and the large number of centres which were involved. However, there are limitations including a large dropout rate seen in recruitment. Eight hundred and thirty one patients were originally consented for this study with 90% of these patients still alive at 6 months and 89% alive at 12 months. Consequently, this equates to a response rate at 12 months of only 35%. This may have impacted the results of this study, as it may have been a specific population who replied (for example, those patients feeling well enough to respond or those who were feeling particularly negative about the ICU experience). Further, a newly developed questionnaire was developed for the purpose of this study. No information is given on how the authors attempted to achieve face or content validity which is crucial in instrument design (Robson 2011).

In a similar study, Quasim, Brown, Kinsella (2015) aimed to determine vocational outcomes of working age patients in terms of their ability to return to work and in the retired population and their ability to return to their home and live independently, two years after ICU discharge. The study was undertaken in one tertiary referral general ICU in Glasgow. The authors also explored how quality of life differed amongst patients when categorised by their work status post ICU. The study, which was posted to participants approximately two years following ICU discharge, utilised the EQ-5D questionnaire and a locally designed questionnaire which explored aspects of employment before and after ICU discharge.

One hundred and ninety nine patients were sent the surveys, the response rate in this study was similar to that in the Griffiths et al (2013) study, with 38% (n=75) of participants responding. At two years post ICU discharge, 28.8% of patients were categorised as being permanently long term sick, compared with only 15.4% of patients pre ICU. Those in employment post ICU discharge, reported significantly better Health Utility scores within the EQ-5D (p<0.001). However, of those patients who did return to work post ICU discharge, 17% had to take on a different role due to continuing health issues. Finally, within the

retired population, 50% of those who responded had a family member now acting as a carer.

This study gives a further insight into the social challenges faced by ICU survivors. Its generalisability is limited due its single centre nature and also because of the similar issues related to response rate and questionnaire design seen in the Griffiths et al (2013) study.

2.12.6 Risk factors for poor QOL: illness specific

A small number of studies have demonstrated that there may be specific risk factors for reduced QOL following ICU discharge.

There are a number of studies which have demonstrated the link between ARDS and poor QOL, in the months and years following critical care discharge. Herridge et al (2003) and Herridge et al (2011) followed 109 patients who had been diagnosed with ARDS over a five year period to explore the physical, psychological and social problems which these patients encountered after discharge from critical care. Both studies demonstrated that patients diagnosed with ARDS during their critical illness, suffered significantly worse physical, social and psychological problems, than an age and sex matched population more than five years after ICU discharge. These studies also demonstrated that this population incurred increased healthcare costs over the five year follow up period compared with the 'healthy population' comparison group.

Cox, Docherty, Brandon et al (2009) in a qualitative study, also described the negative impact on long term QOL after a diagnosis of ARDS, utilising in depth semi structured interviews, three to nine months post ICU discharge, with patients and relatives from medical and surgical ICUs in two medical centres in North America. Data Saturation was met after 23 patients and 24 caregivers had been interviewed. An overview of the participants and details of the interviews are given in Table 2.19. The authors undertook analysis of the interview transcripts using Colaizzis approach to analysis; the themes generated from this analysis are presented in Table 2.20.

Table 2.19: Overview of participants and interviews (Cox et al 2009).

Characteristic	Patients (n=23)	Caregivers (n=24)
Age (mean, range)	53 (30-70)	53 (38-64)
Female	7 (30%)	20 (83%)
APACHE II (Median, Inter Quartile Range (IQR))	23 (20-27)	n/a
Charlson Index (Median, IQR)	0 (0-2)	n/a
ICU length of stay (Median, IQR)	21 (14-28)	n/a
Location of Interview		
Home	22 (95%)	n/a
Nursing Facility	1 (5%)	n/a
Days from discharge to interview (Median, IQR)	92 (38-176)	95 (38-142)

This study has several strengths. The authors utilised several steps to ensure a rigorous approach to analysis was undertaken such as peer review of the manuscript and the presentation of a detailed audit trail. Further, it provided a unique insight into the challenges faced by survivors of ARDS and has helped support the quantitative results which have shown that a diagnosis of ARDS is a significant risk factor for poor QOL after ICU discharge. However, there are several issues which may limit the applicability of the findings. For example, the patients who took part in this study were predominantly young, white and male with a low rate of co-morbidities (Table 2.19). Therefore, it may not represent those with significant co morbidities and other sections of the general ICU population such as females and the elderly.

Table 2.20: Themes generated from Cox et al (2009) qualitative study

Coded Themes	Details
Pervasive memories of ICU	Participants described the co-existence of general amnesia of their ICU experience as well as vivid memories and terrifying dreams
Day to day impact of new disability	Patients reported physical problems, insomnia, fatigue, tremors, pain, emotional issues, depression, anxiety and fear and foreboding of becoming critically unwell again
Critical illness defining sense of self	Patients described altered body image, financial strain and work place and family upheaval. Some participants also described the lack of insight which others had about their mental and physical transformation post ICU
Relationship strain and change	This was apparent in both patients and carers. Discussions centred around changing social dynamics, intimacy and relationships
Coping	This theme focussed on coping and a lack of adjustments to a profoundly different situation. Coping strategies included the support of family, friends, spirituality, self sufficiency and the setting of specific goals such as returning to work
Care giver perspective	Care givers endorsed the main themes generated. They also described unique insights from the carers perspective including: the impact of change in cognition; a lack of support after hospital discharge; increasing distance in relationships; financial strain and some also described a sense of hopelessness

The development of sepsis and septic shock during the ICU stay has also been shown to be a significant risk factor for poorer quality of life in the months and years following ICU discharge. Winters, Eberlein, Leung et al (2010) performed a systematic review of long term mortality and QOL in patients with sepsis. Twenty six studies provided data for this review, with the follow up of patients ranging from three months to ten years. Furthermore, 13 of these studies compared patients with sepsis to a control population. Patients with sepsis showed ongoing, increased mortality up to two years beyond the standard 28 day in hospital mortality endpoint of most research studies. Furthermore, patients

with sepsis also had decrements in a variety of QOL measures after hospital discharge, with results consistent across varying severity of illness and different patient populations in different countries.

Finally, the development of delirium during the ICU is a well known risk factor for ongoing problems, especially cognitive problems, following ICU discharge. The ICU Delirium and Cognitive Impairment study group based in Vanderbilt University Nashville, have undertaken significant amounts of work exploring the poor long term outcomes of those patients who are delirious during the ICU stay. Most recently, in a 12 month prospective follow up study the study group demonstrated that approximately one quarter of patients, who developed delirium during the ICU admission, irrespective of age and co morbidities, had cognitive function scores similar to that of Alzheimer patients. Delirium duration was the only risk factor for worse global functioning found at three and 12 months (Pandharipande et al 2013). Furthermore, increased delirium duration has been shown to be associated with worse activity of daily living scores at 12 months post ICU discharge (Brummel, Jackson, Pandharipande et al 2014).

2.12.7 Risk factors for poor QOL: person specific

There is now emerging evidence that there may be certain subsets of the population who are more likely to develop complications and morbidity following discharge from critical care. Wade et al (2013) undertook a prospective study to investigate other risk factors (clinical, acute physiological, socio demographic and chronic health), for the development of complications following ICU discharge in a single, mixed general ICU setting in London. Level three patients were recruited in the ICU when the treating physician determined that the patient was showing signs of recovery, when the patient had the capacity to consent and were alert, awake and able to communicate. No information was given about delirium screening in this population. At this time point, patients completed a Profile of Mood States questionnaire and a newly developed Intensive Care Stress Reaction Scales (ICSRS). The validated Brief Illness Perception Questionnaire (BIPQ) was also used to determine the patients subjective illness perceptions during their ICU stay. Three months later via post, patients were asked to complete the Post Traumatic Stress Diagnostic Scale

(PDS), the Centre for Epidemiologic Studies Depression Scale (CES-D), the State-Trait Anxiety Inventory (STAI) and the SF-12.

A full data set (baseline and three month outcomes) was available on 100 patients (response rate 64%). At three month follow up, 55% of patients had psychological morbidity following ICU discharge; 27.1% had probable PTSD, 44.4% had anxiety and 46.3% had probable depression. The presence of a previous psychological illness was a significant risk factor in the development of PTSD, depression and anxiety. Similarly, lower socio economic position was associated with poorer quality of life, anxiety and depression at three months. Receiving inotropes or vasopressors was the strongest risk factor associated with anxiety at three months post ICU and was strong risk factor in the development of a poorer quality of life. Interestingly, a history of alcohol use was a significant risk factor in the development of PTSD at three months post ICU discharge. Unsurprisingly, increased duration of sedation in the ICU environment, especially with the addition of benzodiazpeines, was associated with anxiety, PTSD and depression three months post ICU discharge. ICU mood and the presence of intrusive memories during the ICU stay were independent risk factors for the development of PTSD and depression.

This is one of the first studies to look beyond clinical risk factors for the development of psychological morbidity following ICU discharge. Although it gives valuable insight about potentially modifiable factors, there are several limitations to this work. The exclusion of patients who remained incapacitated during their ICU stay is a significant limitation as an important cohort of patients may have been excluded. Further, no delirium screening tool was utilised when screening participants for enrolment in the study during the ICU stay. The presence of undetected delirium may have impacted on the information given during the ICU stay and be a clinical factor in poorer QOL following discharge from critical care.

2.12.8 Current approaches to rehabilitation

In 2009, NICE produced guidance on rehabilitation of the critically ill patient. These guidelines gave very little specific guidance, due to the limited evidence available at the time, on interventions which should be employed to improve

patient outcomes in this particular cohort (NICE 2009). The ICU rehabilitation manual was endorsed by the guideline as well as two other broad recommendations: provide a cycle of clinical assessments for patients leaving critical care and implement problem orientated treatments and patient agreed goals. The following section will provide a brief overview of the rehabilitation manual endorsed by NICE as well as a review of the other approaches to rehabilitation which have been evaluated since 2009.

The landmark study which analysed the use of the ICU rehabilitation manual was undertaken in two centres in England in 2003 (Jones, Skirrow, Griffiths et al 2003). The rehabilitation manual gives patients and family members information on what to expect after discharge from critical care. It included a self directed exercise programme as well as advice on psychological and psychosocial problems. In the RCT conducted into this approach (Jones et al 2003), patients also received ICU follow clinic appointments and telephone calls to discuss any issues in the six months following ICU discharge alongside the manual. This RCT demonstrated a significant improvement in QOL utilising the SF-36 tool (p=0.006) between the intervention and control group. However, there was no difference in levels of depression, PTSD or any significant changes in physical outcome measures at six months post ICU discharge.

Despite the positive psychological global benefits which seemed to emerge from this method of critical care rehabilitation, there are a great number of criticisms which can be made about this approach, especially in light of recent evidence. Firstly, since 2003 there is an abundance literature which details the cognitive problems which patients face after discharge home from critical care (See Table 2.18). As a result, a self directed manual which is over 100 pages in length, may not be appropriate for those patients with on-going concentration problems. In this RCT, standard care included telephone calls and the use of an ICU follow up clinic. This is not standard care elsewhere in the UK (Griffths, Barber, Cuthbertson et al 2006b) thus the generalisability of the results are debateable. Lastly, there are geographical areas across the UK which encounter major literacy problems. In post industrial cities such as Glasgow and Liverpool, up to 25% of the adult population have issues with reading and writing (GCPH 2012). As such, these manuals may not be appropriate for every group. Finally, it is now

widely accepted that information and education in isolation is unlikely to be successful as a rehabilitation approach and multifaceted approaches to support are required for patients (Health Foundation 2011).

Nurse Led follow up clinics for ICU patients have also been utilised widely as a method of rehabilitation. Nurse Led clinics seem to intuitively be the correct approach to improving outcomes for this patient cohort (Rattray and Crocker 2007). As a specified point in time, patients are invited back to the hospital setting where they can gain an understanding of their intensive care experience and appreciate the challenging recovery which they may be facing. However, there is very little empirical evidence to suggest that they offer any benefit to long term patient outcome. Cuthbertson, Rattray, Campbell et al (2009) undertook a non blinded RCT of Nurse Led follow up clinics in three hospitals in the UK. The main outcome measure was QOL as measured by the SF-36 at 12 months post ICU discharge. At 12 months post ICU discharge, there was no statistical difference in any component of the SF-36 between the control group and the intervention group and there was no significant difference in any sub group analysis or in any of the secondary outcome measures utilised in the study.

The ICU diary is a written record of the course of a patient's illness and treatment while in the ICU (Mehlhorn et al 2014). The patient is given the diary as a tool after or at ICU discharge so that they can understand factual events which occurred during their ICU stay. Perier, Revah-Levy, Bruel et al (2013) state that the diary has three main purposes: reconstruction of illness narrative; a debriefing tool to help deal with PTSD and to help transition patients from critical illness to normalcy. There is wide diversity of practice in the structure, content and process elements (e.g. the use of pictures and the timing of distribution of diaries) regarding the use of diaries in ICU (Aitken et al 2013).

The majority of the literature exploring the use of diaries in the ICU population is from Europe, specifically Scandinavia and the UK (Gjengedal, Storli, Jolme et al 2010, Jones, Backman, Capuzzo et al 2010). Many of these studies have shown a significant, positive psychological impact with the use of patient diaries in the critical care environment. In an RCT by Jones et al (2010), which included over 350 patients from six European countries and 12 ICUs, found that diaries reduced

the probable cases of PTSD significantly, at three months post ICU discharge (p=0.02). Similarly, Knowles and Tarrier (2009) in a RCT, with 36 patients in a single centre in the UK, found a significant decrease in feelings of anxiety (p<0.05) at three months post ICU discharge in those patients who received a diary.

Although the patient diary has been shown to have a positive effect on psychological well being after ICU discharge in a small number of studies, there are a number of methodological issues and limitations to its use within the critical care population. Firstly, the diary helps with aspects of psychological recovery following ICU discharge only. ICU survivors have complex problems which go beyond psychological issues. Secondly, there is currently an extremely diverse range of approaches to the patient diary utilised in each of the trials (for example, some have pictures some do not) (Aitken et al 2013). This is especially true for the timeframes for follow up. For example, Jones et al (2010) and Knowles and Tarrier (2009) both used the timeframe of three months for follow up. It is well documented that there are ongoing psychological problems after three months post ICU discharge, therefore, this may not been an adequate or appropriate timeframe to measure psychological outcomes. Finally, Engstrom, Grip, Hameren (2008) and Robson (2008) both found negative themes surrounding the use of patient diaries following critical care discharge. More work is undoubtedly required in this area.

A UK group aimed to evaluate the effectiveness of a supervised eight week, in hospital aerobic training intervention in an exploratory, single centred parallel-group RCT (Batterham, Bonner, Wright et al 2014, Walker, Wright, Danjoux et al 2015). The intervention consisted of two supervised, hospital based, physiotherapy led supervised sessions per week, 8-16 weeks post ICU discharge. During the supervised session, participants exercised either individually or in pairs for 40 minutes. The main outcome measure for this study was the relative oxygen consumption at the anaerobic threshold and health related quality of life utilising the SF-36. A qualitative evaluation of the programme was also undertaken utilising psychologist led focus groups. Data was collected after group allocation, at nine weeks (one week post intervention) and at 26 weeks post randomisation. A total of 30 patients were allocated to the control and 29

to the intervention. Although there appeared to be a trend to better outcomes at nine weeks in the intervention group, this intervention showed no significant improvement in physical or psychological health at any time point in the study.

In the qualitative arm of the evaluation, four focus groups, each with four participants, focussed on recovery from critical illness, quality of life following hospital discharge and perceptions of the exercise programme and its acceptability. Patients were purposively sampled, with the aim of recruiting equal numbers of patients from both the control and intervention groups, as well as equal representation of men and women of different ages. Thematic analysis was used to analyse the findings of each of the focus groups. The themes and sub themes generated are presented in Table 2.21.

The focus groups clearly demonstrated the positive impact that the exercise class had on recovery. However, participants (both those who did and did not receive the intervention) felt that more could be done by healthcare professionals to improve the recovery trajectory from critical illness.

There are a number of significant limitations with this mixed method evaluation. In terms of the RCT, there was a significant amount of missing data. For example, of the 29 allocated to receive the intervention, information on physical functioning was only available for 13 patients at week nine and 18 patients at week 26. In terms of the focus group, the authors state that they had intended to recruit 24 patients, but could not due to logistical reasons. They do not state if they felt data saturation was met within the sample size utilised. Therefore, caution should be taken with any generalisation of these results.

Table 2.21: Themes and subthemes generated from Walker et al (2015) focus groups

Themes	Subthemes
Significant biopsychosocial adjustment process post ICU	Negative and enduring physical and psychological effects; social withdrawal; boredom/inactivity; emotional impact on family and friends; difficult transition from 24 hours care to discharge home; positive psychological effects
Negative experience of community aftercare	Feeling abandoned/uncared for; lack of advice/info for self and families; delays for outpatients physiotherapy; battling the system
Positive biopsychosocial effects of the exercise programme	External source of motivation; reduced boredom, isolation and inactivity; intrinsically enjoyable; positive recovery focus enhanced well being; feeling cared about/emotional support from staff; improved fitness; accessible form of exercise
Suggestions for better aftercare	Group exercise/physiotherapy to enhance motivation; financial advice for families; better integration between inpatient and community services; meeting with others in a similar situation
Minor suggestions to enhance exercise programme	Greater duration; inclusion of upper body exercise; incorporated in rehab wards/general care; individualised targets

Another approach to rehabilitation for ICU survivors which has been evaluated is the use of a generic rehabilitation assistant (GRA). The GRA is a physiotherapy assistant with 4-6 weeks of training in occupational health and nutrition In 2015, Walsh, Sailsbury, Merriweather et al undertook a parallel group, RCT with blinded outcome assessment, in two units in Edinburgh to evaluate the effect of increasing physical and nutritional rehabilitation plus increased information, during the post ICU acute hospital stay for patients. This care was delivered to 240 (120 in each arm) patients who required greater than 48 hours of mechanical ventilation in the ICU by the GRA.

During the post ICU hospital stay, both groups received physiotherapy, dietetic, occupational and speech/language therapy input. Patients in the intervention group also received an increased frequency of exercise therapies, dietetic assessment and treatment, individualised goal setting and more illness specific information. The intervention group therapy was coordinated and delivered by the dedicated GRA. The main outcomes measures were the Rivermead Mobility Index at 3 months, health related QoL using the SF-36, psychological outcomes (HADS and the Davidson scale) and self reported symptoms (VASs for fatigue, breathlessness, appetite, pain and joint stiffness). At three months, 6 months and 12 months, there was no significant difference between the two study groups in any outcomes measures collected, including the self reported symptoms.

There are a significant number of limitations to these reported results. For example, the usual care group did have a rigorous approach to rehabilitation which is not usual care for the UK (Griffiths et al 2006b). Further, the length of stay in hospital post ICU can be influenced by a number of factors, for example, individual social circumstances of patients. This may have impacted on the delivery of care for patients in the acute hospital setting by the GRA.

In summary, ICU diaries and ICU rehabilitation manuals may have a positive impact of psychological health for some survivors of ICU however, there is no intervention which has showed improvement in global quality of health for the ICU population. The Walker et al (2015) study did give valuable insights into how care could be improved for patients during recovery from critical illness. Potential improvements included: meeting with others in a similar situation (peer support); more community and acute integration and financial advice for family members and patients. None of these potential interventions have yet been tested.

2.12.9 Long term outcomes: alcohol related admissions

The next section of the literature review will focus on the small number of studies which have explored long term outcomes for those patients admitted to critical care with an AUD.

Despite an emerging evidence base examining QOL in ICU survivors, there is a dearth of literature concerning the long term outcomes of patients admitted to the ICU with an AUD and how rehabilitation pathways can be targeted for this group. At present there are two studies published on longer term survival in this cohort, beyond the hospital setting. Christensen, Johansen, Pedersen et al (2012) conducted a prospective cohort study among 16,848 first time ICU patients between 2001 and 2007. Patients were admitted to three ICUs in Sweden, with 30 day and three year mortality examined in alcoholic patients. Alcoholic patients were defined as those patients who had redeemed at least one prescription for an alcohol deterrent within one year preceding ICU admission and/or had at least one hospital or outpatient clinical/emergency department visit with a diagnosis of an alcoholism related disease registered within one year of the ICU admission. Alcoholic patients were further categorised into two sub cohorts: patients with complications of alcoholism (i.e. psychosis; alcoholic pancreatitis, ALD etc) and patients without complications of alcoholism. One thousand two hundred and twenty nine (7.3%) of the patients admitted were classified by the researchers as current alcoholics. Among these patients, 785 (4.7%) had no complications of alcoholism and 444 (2.6%) were known to have complications related to alcohol. In alcoholic patients with no complications, 30 day mortality was 15.9%, compared with 19.7% among non-alcoholic patients. In the same group 3 year mortality was 36.2% compared to 40.9% among non-alcoholic patients, corresponding to an adjusted three year Mortality Rate Ratio (MRR) of 1.16 (95% CI:1.03-1.31). For alcoholic patients with complications, 30 day mortality was 33.6% and three year mortality was 64.5%, corresponding to adjusted MRRs with non-alcoholics as the comparator of 1.64 (95% CI:1.38-1.95) and 1.67 (95% CI:1.48-1.9) respectively (Table 2.22). Additionally, in the alcoholics with complications group, three year mortality for alcoholics with liver cirrhosis was 73.4% and 46.9% for alcoholics with non-cirrhotic complications. When compared with non-alcoholics, adjusted MRRs was 1.89 (95% CI: 1.64-2.18) for alcoholic patients with cirrhosis and 1.25 (95% CI: 0.98- 1.58) for alcoholics with non-cirrhotic complications.

Strengths of this study include its prospective nature and multi centre approach. Further, Swedish ICU's have many similarities to UK units including the same nurse ratio (1:1 nurse to patient ratio) and a similar free, tax supported, public

healthcare system. However, there are several factors which threaten the study's generalisability. Firstly, the use of previous hospitalisations and prescription drug redemption to identify alcoholic patients may have led to the inclusion of alcoholic patients with severe alcohol dependency only, and artificially inflated mortality rates in this particular group as a result. This may be responsible for the low levels of alcohol related admissions which were seen in this study compared to previously mentioned research (See Section 2.7.2).

Table 2.22: 30 data and three year mortality and corresponding crude and adjusted MRRs (Christensen et al 2012).

	30 Day Mortality			3 year mortality		
	Mortality % (95% CI)	**Crude MRR (95% CI)**	**Adjusted MRR (95% CI)***	**Mortality % (95% CI)**	**Crude MRR (95% CI)**	**Adjusted MRR (95% CI)***
Non-alcoholic patient	19.7 (19.1-20.3)	1	1	40.9 (40.1-41.6)	1	1
Alcoholic patient with complications	33.6 (29.4-38.2)	1.83 (1.55-2.16)	1.64 (1.38-1.95)	64.5 (60.0-69.9)	1.89 (1.68-2.13)	1.67 (1.48-1.90)
Alcoholic patient, no complications	15.9 (13.5-18.7)	0.79 (0.66-0.94)	1.04 (0.87-1.25)	36.2 (32.9-39.7)	0.84 (0.75-0.95)	1.16 (1. 03-1.31)

*Adjusted by Cox proportional hazards analysis for age group, gender, department providing care, primary diagnosis, surgery, Charlson Index Score, emergency/planned admission and marital status.

Another limitation is that despite the use of the Charlson Index Score for classifying and managing co morbidities, the study lacked clinical data on severity of illness at the time of ICU admission (e.g. APACHE, SOFA scores), which could have major implications for the adjusted MRRs presented.

Most recently, Gacouin, Tadie, Uhel et al (2014) aimed to determine whether at risk drinking was independently associated with survival in non trauma patients admitted to critical care in the year following ICU discharge. An observational cohort study was undertaken in a 21 bedded mixed ICU, in a large French teaching hospital. Baseline characteristics of patients were collected prospectively by the researchers and one year follow up data was collected

retrospectively. Patients who were older than 18, had an ICU stay of greater than 72 hours and were non trauma patients were recruited for the study. The study, which included 662 patients, was the combination of two previously published cohorts of patients (Gacouin et al 2008 and Gacouin, Roussel, Gros et al 2012). Data was collected from the first cohort between 2005-2006 and the second cohort between 2010-2011. The total number of admissions during these study periods is not given in this paper. However, when reviewing the original two papers, 33.4% of patients were excluded during these study periods as they were not screened for AUDs.

Patients were deemed to be 'at risk drinkers' using the definition from the National Institute on Alcohol Abuse and Alcoholism (USA). This was defined as drinking more than 14 units per week or more than 4 drinks on one occasion for healthy men between 18-64 years. For women and healthy men above 65, 'at risk drinking' was defined as consuming more than 7 drinks per week or more than three drinks per occasion. Those patients who met the criteria for 'at risk drinkers' were then broke into two further groups: those who drank more than 5 drinks per day and those who did not. Patients were only classified as 'at risk drinkers' when the excessive alcohol 'persisted for at least the entire year before ICU admission'. Of the 662 patients admitted during the two study periods, 208 (33%) patients were classified as 'at risk drinkers'. The proportion of patients who died in the ICU was significantly higher in the 'at risk' group than in the 'not at risk' group (50 (24%) patients vs. 61 (13%) patients, p=0.001). 'At risk' drinking was also independently associated with ICU mortality (adjusted OR 1.83; 95% CI of 1.16-2.89; p=0.01). At one year post ICU discharge, 41(24%) 'at risk' drinkers died vs. 56 (15%) 'not at risk' drinkers (p=0.008), (adjusted analysis HR 1.70; 95% CI of 1.15-2.52; p=0.01). Other factors independently associated with one year mortality were: Charlson Index Score, alcoholic cirrhosis and low BMI.

2.12.10 Interventions after ICU for alcohol related admissions

At present, there appears to be no studies which evaluate interventions for individuals admitted to critical care with an AUD, either in the ICU setting or in hospital. However, a well-known North American research group have recently

published a qualitative study which explored the potential for interventions for this patient group.

Clark, Jones, Cook et al (2013) conducted a qualitative study with the aim of identifying themes surrounding the decision to change drinking behaviours, that could be used to specifically tailor brief interventions for AUDs in medical ICU survivors in two medical centres in Denver, USA. Using purposeful sampling strategies, 19 semi structured interviews with 19 different patients were undertaken by the research team. Researchers recruited patients who had an AUDIT score of greater than eight (See Section 2.5.1), in the ICU before discharge from the unit. All patients provided consent for the interview at the time of interview and interviews took place in a private space in the ICU. Patients were excluded if they did not speak English, could not provide informed consent, or had a condition that prevented the completion of the interview. No information is given on the length of stay of participants, however, the median APACHE II score was nine, the median AUDIT score was 17 and 74% of participants were male. The final interview schedule after all revisions is shown in Table 2.23.

Table 2.23: Final interview schedule (Clark et al 2013)

1. Can you describe your alcohol use?
2. What do you like about it?
3. What do you not like about it?
4. What problems do you associate with it?
5. Can you describe any help you have sought for drinking in the past?
6. Why do you think it did or did not work?
7. How have people influenced your drinking?
8. Had you ever thought about changing you drinking before this admission?
9. Were you changing?
10. What made you more likely to change?
11. What made you less likely to want to change?
12. How has this changed based on your current illness?
13. Has anxiety or depression made it difficult for you to change?

This research identified five broad themes that facilitated the decision to stop drinking or cut down on drinking in survivors of ICU. Three themes related to barriers to cutting down drinking were also identified. One theme 'social network' was given as either a barrier or facilitator for reducing or stopping

alcohol intake. Table 2.24 highlights the themes identified and gives a short explanation to the background of each of these themes.

This is the first qualitative study of ICU survivors with AUDs and gives an understanding into how services could be designed to help this group of patients. It provides valuable insight into this difficult to capture group of patients. However, this study has a number of significant limitations. Firstly, patients were not screened for delirium using a validated tool (See Section 2.10) instead the researchers asked the nurse and the physician treating the patient if they felt the patient was delirious. It may be that these patients were suffering from hypoactive delirium (Table 2.14) which is very difficult to assess other than through the use of specific assessment tools. Further, no information is given on whether these patients were still actively being treated for AWS. Although the researchers stated that they obtained informed consent from the participants, it may have been appropriate to also ask patient proxy as this is a particularly vulnerable group of patients. Lastly, patients who did not want to change their drinking behaviours may have declined to participate in this study; therefore, key barriers to change may have been missed.

2.12.11 Readiness to change

It has been hypothesised that an ICU admission may represent a 'teachable moment' and may be an optimal time and opportunity to support change in patients with AUDs (Clark and Moss 2011, Clark, Smart, House et al 2012). Clark et al (2012) sought to determine the baseline readiness to change and its relationship with readiness to change, in survivors of ICU, in three medical centres in North America, utilising a cross sectional observational study. All patients admitted to the ICUs with an AUD, as defined by the AUDIT scale, were included in the study. Patients were asked to answer two questionnaires related to readiness to changes in terms of the behaviour towards alcohol: The Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) and the Readiness to Change Questionnaire (RCQ). Participants were also asked to complete a Visual Analogue Scale (VAS), which asked patients 'how ready are you to change your drinking habits?', with 0 being not ready to change and 10 being ready to change. All three tools have been through extensive validation work (Bertholet, Cheng, Palfai et al 2009, Lau, Freyer-Adam, Gaertner et al 2009).

Table 2.24: Facilitators and Barriers identified (Clark et al 2013)

	Theme	Description
Facilitators		
	Empathy of the inpatient healthcare environment	A feeling of understanding and lack of stigmatisation from the entire healthcare team as well as family members
	Recognition of the accumulating problems	Awareness of accumulating alcohol-related health, legal and financial consequences preceding and during ICU admission
	Religion	Strength from faith in god or from the community provided by the Church
	Pressure from others to stop drinking	An urging from family or friends to stop drinking
	Trigger events	Significant, life changing event related to alcohol use that results in changes in alcohol consumption
Barriers		
	Missed Opportunities	Failure to connect patients' excessive alcohol consumption with reason for hospitalisation/ severe acute illness
	Psychiatric co morbidity	Depression/anxiety frequently triggered patient to drink. However, some patients did not seek help due to stigmatisation.
	Cognitive Dysfunction	An impaired ability to think clearly
Barrier of Facilitator		
	Social network	A decision to change was guided by the probability that the patient's social network would be supportive if their decision

Of 731 medical ICU admissions, 161 patients met the inclusion criteria of the study, 49 patients were excluded, predominantly due to refusal. Of the remaining 112 patients, 101 (90%) completed their questionnaires and had sufficient data available for analysis. This study demonstrated high scores in all three measures used for Readiness to Change in patients with an AUD. Furthermore, patients with a higher APACHE II score had higher SOCRATES scores ($p<0.001$) and VAS scores ($p<0.01$). The authors concluded that medical ICU patients may represent a population who are open and ready to change their relationship with alcohol and may be a group who would benefit from brief interventions.

This work is unique and gives, for the first time, a valuable insight into readiness to change in the ICU survivor population. However, it does have several limitations, most notably the authors did not screen for delirium before asking patients to complete study questionnaires. If no delirium detection tool is used,

delirium may be missed in 65% of patients (Truman and Ely 2003). Therefore, completion of tools may not be a true reflection of intention from the patient's perspective.

2.13 Literature review summary

This literature review had four main aims. Firstly, it provided the context to alcohol misuse globally, nationally and for the purpose of this thesis, locally. It also provided an insight into the assessment of alcohol related admissions to critical care and the challenges involved with this. Prior alcohol dependence is often underestimated in ICU patients, making identification of patients at risk for AWS or DTs difficult (Barr et al 2013). Screening tools for AUDs and AWS have not been fully validated in the critical care setting and further research is required into optimal assessment and management of this patient group (Barr et al 2013).

This literature review also explored the complications related to AUDs in the ICU. It is clear that those patients admitted with an AUD, especially those with a background of alcohol dependency, are at particular risk of respiratory and circulatory problems such as sepsis. Further, those patients admitted with a background of alcohol dependency are more likely to die in the ICU and hospital. Although the critical care literature and practice guidelines do address the management of delirium, anxiety and pain and consider substance abuse as a possible etiological factor, evaluation and management recommendations are non specific (Broyles et al 2008). It is clear that more observational and interventional work is required in all of these areas to help develop effective and efficient solutions for this patient cohort.

Finally, this literature review has examined the long term outcomes and quality of life for ICU survivors with a focussed section on those patients admitted with a background of an AUD. Despite an abundance of observational data describing the challenges all survivors of intensive care face, there is limited work on interventions for this group, with the optimal, holistic model of rehabilitation remaining elusive for critical care practitioners. There is limited evidence in the area of long term outcomes for those patients admitted to critical care with an

AUD, with minimal work exploring the potential for behavioural changes in this group.

These substantial gaps in the literature form the justification for this PhD.

The overall research aim of this study is to explore the health and social consequences of alcohol related admissions to critical care.

This PhD aims to answer the following research objectives:

1. Analyse the nature and complications of alcohol related admissions to critical care

2. Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis

3. Explore patterns of recovery for patients with and without alcohol use disorders

4. Determine whether alcohol use disorders are associated with survival in critically ill patients at six months post ICU discharge

5. Examine the impact of critical care on future behaviour with regards to alcohol intake.

The following chapter will examine the literature pertaining to the methodologies employed within this thesis.

Chapter Three: Literature Pertaining to Methods

3.1 Introduction

In this PhD, a mixed methods approach was undertaken to answer the following research objectives:

1. Analyse the nature and complications of alcohol related admissions to critical care

2. Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis

3. Explore patterns of recovery for patients with and without alcohol use disorders

4. Determine whether alcohol use disorders are associated with survival in critically ill patients at six months post ICU discharge

5. Examine the impact of critical care on future behaviour with regards to alcohol intake.

In this chapter, theoretical issues pertaining to the selected methods will be discussed.

Research is conducted under two broad paradigms: the positivist paradigm and the naturalistic paradigm (Parahoo 2006). The positivist paradigm is associated with quantitative research, which is the investigation of phenomena that lends themselves to precise measurement and quantification (Polit and Beck 2009). Quantitative research is typically conducted with a traditional scientific approach, which is a systematic and controlled process (Polit and Beck 2009). Further, quantitative researchers base their findings on empirical evidence and strive for generalisibilty of their results beyond a single setting or situation (Parahoo 2006).

Researchers within the naturalistic paradigm emphasise understanding the human experience as it is lived through the collection and analysis of subjective,

narrative materials using flexible procedures which evolve in the field (Polit and Beck 2009). This paradigm is often associated with qualitative research. There are several approaches to qualitative research, most notably, Phenomenology, Grounded Theory and Ethnography.

Phenomenology can refer to a philosophy or a research method (Dowling 2007). Fundamentally, the phenomenological method's objective is to describe the full structure of an experienced lived, or what the experience meant to those who lived it (Sadala and de Camargo Ferreira Adorno 2002). The main purpose is to understand the experience as it is understood by the person who is 'living it'. Phenomenology is appropriate as a theoretical framework for nursing research, which frequently focuses on understanding the experience of patients (Campbell and Scott 2011, Dowling and Cooney 2012).

A variety of writers credit the history, and indeed start their description of the phenomenological philosophy, with reference to the Greek origin of the word and the translation of the word into English (Vivilaki and Johnson 2008). The term, which was first expressed by Immanuel Kant in 1764, is derived from the Greek 'phainein', meaning to appear (Priest 2003). However Edmund Husserl, a German mathematician and logician, is generally acknowledged as the father of Phenomenology, having introduced this movement at the beginning of the 20th century as a way of conducting philosophical reasoning (Tuohy, Cooney, Dowling et al 2013). He proposed Phenomenology as a theoretical perspective advocating the study of a direct experience taken at face value (Robson 2011).

There are two main phenomenological approaches: descriptive (eidetic) and interpretative (hermeneutic) (Flood 2010). Husserl's (1970) philosophical ideas gave rise to the descriptive phenomenological approach to enquiry. The aim of descriptive phenomenology is to describe a phenomenon's general characteristics rather than the individual's experiences and to determine the meaning or essence of a phenomenon (Flood 2010, Tuohy et al 2013). This requires that the researcher sheds all preconceptions and personal knowledge (termed bracketing) to minimise biases or judgements and enhance scientific rigour within a study (Beech 1999, LeVasseur 2003). Additionally, time and space, important concepts in interpretative phenomenology, are put aside in descriptive phenomenology to focus purely on the consciousness. The context of

the experience is disregarded and the focus is on the experience alone (Tuohy et al 2013). This phenomenological approach is arguably slightly confusing and indeed contradictory. It is contested whether it is actually possible to describe something without adding an interpretation at the same time (Pringle, Drummond, McLafferty et al 2011).

Heidegger, a student of Husserl, moved away from his professor's philosophy into interpretative phenomenology. Heidegger stressed the importance of interpreting and understanding; not just describing human experience (Polit and Beck 2009). Heidegger was critical of Husserl's emphasis on description rather than understanding, and on his use of bracketing. Interpretive phenomenology, also referred to as hermeneutics, goes beyond a description of core concepts and aims to look for meanings embedded in common practices: what people experience, rather than what they consciously know (Flood 2010). Within hermeneutics, existing personal experiences, pre judgements or prior knowledge should not be eliminated or suspended, but rather acknowledged as influencing the understanding of the phenomena (Priest 2003).

Grounded Theory was one of the first formally identified methods for qualitative research. It was developed by Glaser and Strauss (1967) and is a way of generating new theory grounded in the field, which is also set in the context of existing theory (McGhee, Marland, Atkinson 2007). The essence of Grounded Theory is the inductive-deductive interplay; beginning not with a hypothesis but with a research situation. Initially the approach taken is inductive and consequently hypotheses and tentative theories emerge from the data set. In this way inductive-deductive interplay is established (McGhee et al 2007). Sampling, which is central to this process, also proceeds on theoretical grounds: the sample is selected purposefully as the analysis progresses, and participants are chosen for their ability to confirm or challenge a theory. This process continues until the theory generated explains every variation in the data (Lingard, Albert, Levinson 2008). The resulting theory is a robust theoretical explanation of the social phenomenon under investigation (Strauss and Corbin 1998). This central principle of analysis is referred to as constant comparison (Lingard et al 2008).

Ethnography, which has its roots in anthropology, is a research approach where the researcher immerses themselves in a social setting for a period of time. During this period, they listen to what is said, observe behaviours and ask questions as appropriate (Bryman 2012a). Ethnography originally focussed on primitive and exotic cultures; however, it is now commonly used with a variety of research settings (Robson 2011). A key feature of an ethnographic approach to research is that people and cultures are studied over long periods of time. In contrast with the positivist researcher who undertakes experiments in a laboratory by controlling variable, the ethnographer aims to study the natural environment and observed behaviour (Parahoo 2006).

3.2 Selecting a research design

The last 20 years has seen a considerable increase in the interest around mixed methods research (Robson 2011, Ostlund, Kidd, Wengstrom et al 2011). The term is used as simple shorthand for research that integrates quantitative and qualitative approaches within a single project (Bryman 2012a). Although this approach can encompass the use of two types of qualitative or two types of quantitative data collection together, on the whole is refers to the combination of paradigms (Robson 2011). The primary philosophy of mixed methods research is that of pragmatism (Johnson, Onwuegbuie, Turner 2007). Pragmatic researchers consider the research question to be more important than either the method they use or the paradigm that underlies the methodology (Erzberger and Kelle 2003).

Mixed methods studies have the potential to provide a richness of detail and a more complete understanding of a phenomenon, especially when there are multiple perspectives to consider. This global view ensures convergent validation and confirmation of data (Halcomb and Andrew 2005). By providing a holistic view on phenomena, a mixed methods approach improves completeness and scientific rigour (Thurmond 2001, Jones and Bugge 2006, Johnson et al 2007). This is particularly important within the modern day NHS which is focused on person centred care and understanding the effect that social phenomena have on the delivery of care (Mandell 2009).

Much debate exists around utilising a mixed method approach. Using a combination of quantitative and qualitative methods can be a methodological minefield because of the complex ontological and epistemological issues that are involved (McEvoy and Richards 2006). Bryman (2012a) states that these arguments tend to be based on two main issues:

- The idea that research methods carry epistemological commitments
- The idea that quantitative and qualitative research methods are separate paradigms.

There is recognition that quantitative and qualitative research is connected with distinctive epistemological and ontological assumptions, but these views are not fixed and are wholly autonomous (Bryman 2012a). As a result, mixed methods research is both feasible and in many contexts both necessary and desirable (Bryman 2012a).

A limitation of a mixed method approach is that the use of two methods often reduces each to their most fundamental form. This often results in bias checking procedures being applied less than adequately (Ostlund et al 2011), compounding sources of error rather than heightening methodological strengths (Thurmond 2001). Researchers can reduce these sources of error by ensuring that a clear explanation of the decision trail for adopting a certain study design is included in the presentation of any research (Jones and Bugge 2006).

3.3 Study site and access

The study site is the overall location for the research (Parahoo 2006). The study site of any study should be selected to maximise the validity and reliability of any data collected (Polit and Beck 2009). Further, the study site must be consistent with the topic under study (Polit and Beck 2009).

It is increasingly common for researchers to carry out a study on the site in which they work (Robson 2011). There are clear practical advantages to this, including an intimate knowledge of the institution and how the relevant information required for the study can be accessed. Additionally, understanding

the hierarchy and culture of a workplace is also advantageous (Robson 2011). However, these advantages must be balanced with the disadvantages of carrying out research within the work setting. Obtaining objectivity of a problem, for example, may be challenging. Further, managing expectations and pressures from managers and colleagues on how they think the research study should be conducted can be time consuming and difficult (Robson 2011). These issues can potentially threaten the trustworthiness or validity of the study findings and results (Asselin 2003). However, these problems can be overcome by rigorous peer review and collaborating with managers and colleagues at the start of any research project to ensure that they understand the process (Robson 2011).

Therefore, on balance, although undertaking research in a work place setting can be challenging, these challenges can be overcome with careful planning and early communication.

3.4 Population and sample

A population is the entire aggregation of cases in which a researcher is interested. Sampling is the process of selecting a portion of the population to represent the entire population (Polit and Beck 2009).

3.4.1 Types of sample

There are two different types of sample in healthcare research: the probability and the non-probability sample. The main characteristic of a probability sample is that it is randomly selected from a target population (Parahoo 2006). Within probability sampling the researcher is aware of the known chance of selection for each unit involved in the research; that is the probability (Polit and Beck 2009).

Non-probability samples are made up of units whose chances of selection are not known (Parahoo 2006). Non-probability sampling is often utilised within qualitative research as the aim of qualitative methods is to understand complex phenomena and generate hypotheses, rather than to apply findings to a wider population (Bowling 2003). The primary methods of non-probability sampling are convenience, quota and purposive (Polit and Beck 2009).

Convenience sampling is the sampling of subjects for reasons of convenience (for example, easy to recruit, near to hand) (Bowling 2003). Although convenience sampling is the most commonly utilised sampling method in many disciplines, it is the weakest form of sampling and can introduce sampling bias (Polit and Beck 2009).

Quota sampling involves elements of purposive and stratified sampling without random selection (Parahoo 2006). With this approach to sampling, the researcher identifies population strata and determines how many participants are needed from each stratum. By using information about the characteristics of the population being studied, researchers can ensure that there is appropriate diversity in the population (Polit and Beck 2009). However, it is doubtful that utilising quota sampling will result in a representative sample being obtained as quota sampling shares the same inherent weakness of convenience sampling (Bowling 2003).

The goal of purposive sampling is to sample cases or participants in a strategic way so that those sampled are relevant to the research question being posed (Bryman 2012a). When purposively sampling, the researcher needs to be clear what the criteria are to ensure that this is relevant to the research objectives (Bryman 2012a).

One form of purposive sampling is theoretical sampling, which was advocated by Glaser and Strauss (1967) in the development of Grounded Theory. Theoretical sampling is the selection of sample members based on emerging findings from the study, to ensure adequate representation of the important themes (Polit and Beck 2009). In Grounded Theory, data collection continues until theoretical saturation has been achieved (Bryman 2012a). Hood (2007) argues that there may be an inclination among many researchers to label all qualitative research as Grounded Theory. This is particularly true when analysing sampling strategies within qualitative research. Theoretical sampling is not synonymous with purposive sampling rather it is a form of purposive sampling (Bryman 2012a). Theoretical sampling is generated in order to develop theoretical categories emerging from the data. General purposive sampling is not done on the basis of generating and developing emerging theory (Bryman 2012a).

3.4.2 Sample size: quantitative research

Quantitative researchers must explicitly justify the number of subjects required within any study to test hypotheses correctly (Polit and Beck 2009). The ability of a test to find an effect is known as its statistical power. The power of a test is the probability that a given test will find an effect assuming that one exists in the population (Field 2013). In general, most research aims to achieve a power of 0.8, or an 80% chance of detecting an effect if one genuinely exists. To calculate the sample size necessary to achieve a given level of power, researchers firstly decide upon the power which they require (i.e. 0.8). The likely effect size of any intervention in a population should then be estimated from previous research in the area (Field 2013). Given this information the number of participants required can then be estimated. This is commonly referred to as the power calculation.

3.4.3 Sample size: qualitative research

There is no definitive number of participants required in successful qualitative research. However, Bryman (2012b) states that several factors should be taken into account when deciding upon how many interviews should be undertaken (Figure 3.1).

Data saturation is the collection of data in a qualitative study to the point where a sense of closure is attained because different ideas or themes are no longer being acquired (Polit and Beck 2009). Researchers must carefully consider this issue when estimating the number of participants required in a qualitative study. The theoretical underpinnings of any study should also be carefully planned when estimating an appropriate sample size in qualitative work (Bryman 2012b). For example, Grounded Theory work requires a bigger sample size than many other theoretical approaches. Additionally, the heterogeneity of a population must be considered. In many specialities the population may be quite heterogeneous with a good deal of sub-group variability; the researcher may wish to capture this variability as it could affect the experiences and accounts of the participants involved (Bryman 2012b). The breadth and scope of the research questions posed must also be taken into account when deciding upon a sample size in qualitative research (Bryman 2012b). Morse (2004) stipulates that the

broader the scope of the qualitative study and the more comparisons between groups required, the more interviews will need to be carried out.

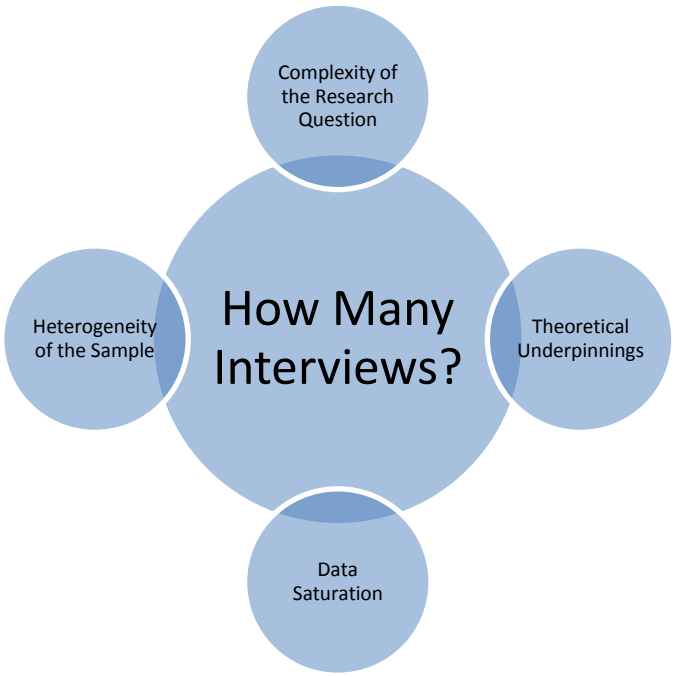

Figure 3.1: An approach to deciding upon a qualitative sample size (Adapted from Bryman 2012b)

3.5 An ethical framework for healthcare research

Ethical consideration should be included in any study design and the human rights of participants should always be guaranteed and protected (Polit and Beck 2009). The World Medical Association developed the Declaration of Helsinki, which was originally agreed in 1964, but is regularly revised (World Medical Association 2013). This declaration includes a number of important principles:

- The need for consent for all competent participants in research
- The rights of subjects to withdraw from research
- Human experimentation is to be used as a last resort, used only if other forms of research not involving human subjects is not possible
- There must be proportionality between the benefits of the research and the risks run by the subjects involved

According to the most widely quoted medical ethics text, Beauchamp and Childress (2001), there are four areas of moral principles that provide a

framework by which the ethical implications of a study design should be designed and reviewed. These are: respect for autonomy; beneficence; non maleficence and justice (Beauchamp and Childress 2001).

In many respects autonomy is the most fundamental principle in medical ethics (Herring 2006). Downie and Calman (1994) in their seminal work, state that to be an autonomous person is to have the ability to choose for oneself, or more extensively, to be able to formulate and carry out one's own plans and actions. To respect an autonomous individual is to take into account and understand that the individual is self-determining and self-governing and that he/she has feelings, desires and reason (Downie and Calman 1994). With respect to healthcare research, there are two primary ways in which autonomy can be respected. These are seeking informed consent and ensuring that participants of any research study are given the right and opportunity to withdraw at any point during the course of the research (Herring 2006).

Beneficence is the principle that healthcare professionals must do good for their patients (Herring 2006). Beneficence obliges researchers to weigh or balance potential benefits against potential risks before any research is undertaken (Herring 2006). Non-maleficence is the duty to avoid harming others or participants of research (Gaw and Burns 2011). The importance of this principle is that it urges against harming one patient to help another (Herring 2006).

The principle of justice insists on the fair distribution of both the benefits and the burdens of research (Christians 2013). Study participants have the right to fair and equitable treatment before, during and after their participation in any study (Polit and Beck 2009). This includes the fair, non-discriminatory selection of participants such that any risks and benefits will be equally shared. In addition, there should be non-prejudicial treatment of those who decline to participate in a study (Polit and Beck 2009). Justice also refers to the right to privacy and confidentiality. Participants have the right to any data they provide to be kept strictly confidential. This can occur through anonymity or through other confidentiality procedures (Polit and Beck 2009).

3.6 Data collection

3.6.1 Observational studies

Quantitative research studies use designs that can be divided crudely into experimental and observational (Healy and Devane 2011). In experimental studies the researcher plays an active role by introducing an intervention, whereas in observational research the researcher observes phenomena as it occurs naturally, without intervening (Polit and Beck 2009).

3.6.2 Cohort studies

Cohort studies are a particular kind of trend study in which specific subpopulations are examined over time (Polit and Beck 2009). Cohort studies are generally concerned with information regarding prevalence, distribution and the inter-relationship of variables in a population (Healy and Devane 2011). There are several different types of cohort studies and they are typically distinguished by the number of times data is collected. In cross sectional designs, data is collected at a single point in time, whereas in longitudinal designs, data is collected at more than one point in time (Robson 2011). The strengths and weakness of cohort studies are shown in Table 3.1.

Cohort studies can be either prospective or retrospective. Prospective studies follow a cohort forward in time and document specific variables in advance of the outcome of interest. Retrospective designs define the sample and outcome and look back in time to collect data about factors believed to be related to the already existing outcome (Healy and Devane 2011). Retrospective designs carry some advantages including ease of access and cost effectiveness (Robson 2011).

However, the main drawback of retrospective designs is that the researcher relies on existing data that were, most probably, not collected for research purposes and may lack the rigour with which research is carried out (Parahoo 2006). In contrast, researchers utilising a prospective design can have control over whom they want to include in their study and how data is collected (Parahoo 2006).

Table 3.1: Strengths and weaknesses of cohort studies (adapted from Healy and Devane 2011)

Strengths	Weaknesses
• The strength and consistency of associations found can be used to draw inferences about causation; • Can measure incidence rate; • Allows the study of multiple potential effects and permit flexibility in choosing the variables to be analysed.	• Do not establish causation; • Various types of bias including information bias, selection bias and confounding bias may be present with this methodology; • Loss of subjects can be high; • Practices or exposures can change over the study period making findings irrelevant; • Difficult to control extraneous variables.

3.6.3 Case note review

The manual abstraction of data from patient medical records is a method of data collection from clinical databases, audits and clinical research (Pan, Fergusson, Schweitzer et al 2005, Gregory and Radovinsky 2012). Obtaining data from charts for research purposes offers many advantages such as easy access, depth of information, a reduction in costs and flexibility in the time the study is conducted (Pan et al 2005, Gearing, Mian, Barber et al 2006). However, the limitations of incomplete documentation, difficulty interpreting information found in charts (i.e. jargon) and variance in the quality of information recorded have discouraged researchers from utilising this approach to data collection and indeed can call into question the reliability of data (Gearing et al 2006, Gregory and Radovinsky 2012).

Investigators must take a strategic approach to data collection efforts and implement a rigorous methodology when conducting clinical studies that utilise the medical record. Several strategies have been suggested to try and improve the rigour and in turn the reliability of the data collected from patient charts (Gregory and Radovinsky 2012). These include:

1. The development and testing of the data collection tool, including its organisation and structure. Organisation, simplicity and clarity are essential criteria from the development of a uniform data abstraction instrument. In addition, when designing, implementing and conducting case note review,

researchers must be specific about strategies to manage missing data (Gearing et al 2006).

2. The use of a coding manual which guides data collection. This includes the nature of the data to be collected and how it will be collected. This step ensures validity and accuracy (Gregory and Radovinsky 2012).

3. Ongoing communication and training with research staff to ensure a high degree of inter-rater reliability (Gregor and Radovinsky 2012).

Clinical information systems have evolved in the critical care setting over the last four decades. The healthcare industry began investing in information systems in the 1960's, with the primary focus being financial and business applications. Information systems have subsequently evolved and have been incorporated into almost every aspect of healthcare (Varon and Marik 2002). Utilising electronic records has many advantages for healthcare researchers including more complete, accurate, comprehensive, reliable documentation and information (Hayrinen, Saranto, Nykanen 2008), which overcomes, to a certain extent, many of the problems encountered when using case note review in research.

3.6.4 In depth semi structured interviews

The interview has become a favoured method in qualitative research, in research generally and in research into health care (Low 2013). In-depth interviews usually involve a face to face, or a one to one interaction between a researcher and respondent and are particularly useful with research topics where sensitive information may be disclosed (Liamputtong 2007). Fundamentally, an interview is a conversation that is directed towards the researcher's particular need for data. How far the researchers direct the interview in determining topics covered and from what angle they are explored, is one dimension by which interviews can be discussed (Green and Thorogood 2004).

The structured interview typically follows a specified set of questions in a specified order for each interview and generates comparable answers from each

respondent (Bryman 2012a). Unstructured interviews, on the other hand, use a brief set of prompts to help the researcher deal with a certain range of topics (Bryman 2012a). This type of interviewing tends to be very similar in character to a conversation. The most commonly utilised interview type in qualitative research sits between these two extremes, in what are called in depth or semi structured interviews. Semi structured interviews begin with a fairly clear focus, rather than a general notion of wanting to do research on a topic (Bryman 2012a). Unlike structured interviews where a very specific script is in place, semi structured interviews use a topic guide or an interview schedule.

There are many advantages to utilising semi structured interviews in healthcare research. Firstly, they are a relatively cost effective way of collecting a great deal of data in a short timeframe (Low 2013). They are also useful when exploring research areas that are complex as they allow researchers to pursue emergent themes thus gaining new insights (Low 2013). Interviews generate deeply contextual accounts of participant's experiences. The interaction which occurs between the researcher and participant can offer an opportunity to explore events which would otherwise be difficult to capture (Doody 2013). Lastly, semi structured interviews allow the researcher to develop new paths that emerge during an interview which may not have been considered initially (Doody 2013).

Semi structured interviews have several drawbacks which research teams must consider when utilising this approach. Interviews which are exploring sensitive areas may evoke strong feelings. These particular interviews require to be handled with a great deal of care and attention, which can be challenging for novice researchers. Additionally, novice researchers are often unable to identify where to ask prompt questions or probe responses; as a result, relevant and often important data can be missed. This problem can be overcome by ensuring that any interview schedule is piloted and there is extensive peer review throughout the period of data collection by a more experienced researcher in the field. Novice researchers can also listen back on an interview and transcribe it before the next interview. This will give the opportunity to critically appraise the interview and identify any areas for improvement (Doody 2013). Finally, semi structured interviews can be incredibly time consuming (Robson 2011).

Making arrangements to visit, securing appointments, allowing for participants who may not attend, transcription and finally analysis, all require to be built into the research timeframe.

3.6.5 Developing an interview schedule

An interview schedule can range from a brief list of memory prompts, to a somewhat more structured list of questions to be asked (Bryman 2012a). King and Horrocks (2010) suggest three sources to identify the topics which should be included in an interview guide: previous research literature in the area, personal experiences of the research and informal preliminary work. Good interviewing requires the researcher to accept that the course and content of an interview cannot be fully determined in advance (Smith, Flowers, Larkin 2009). The researcher must be able to respond by moving away from topics, rephrasing questions and in some cases pausing or ending the interview if required (Smith et al 2009).

In terms of the delivery of questions, Robson (2011) suggests that there is a common sequence to questions asked in a semi structured interview:

1. **Introduction**: Introductions, assurances of confidentiality, information on the conduct of the interview and gaining informed consent

2. **Warm up questions**: Easy, non-threatening questions

3. **Main body of the interview**: Covering main purpose of the interview. Any sensitive questions should be addressed within this section after trust has been built between the participant and researcher

4. **Cool off**: Usually a few straight forward questions to diffuse any tension

5. **Closure:** Ensure that the participant is aware the interview is ending and give them the opportunity to add any remarks or ask any questions.

When developing schedules, researchers must avoid long or double barrelled questions as the interviewee may only remember part of the question (Robson 2011). Further, jargon as well as loaded questions, should be avoided to ensure

that the participant can fully understand the question and feels free to answer. Researchers must also give participants adequate time to respond fully and express feelings to the questions posed, often by allowing long silences during the interview (Elmir, Schmied, Jackson et al 2011).

3.6.6 Conducting effective interviews

There are several issues which research teams must take in account when planning interviews. Firstly, the researcher must plan carefully where the interview will take place. Interviews should be conducted at a time and place of the participant's convenience, in a comfortable setting that is safe, private, non-threatening and free of interruptions (Doody 2013). This must be carefully balanced with the safety of the researcher and ensuring that all research governance safety procedures are adhered to. The timing of interviews also requires thought, especially when a personal traumatic experience is being explored (Liamputtong 2007, Elmir et al 2011). It may be important to capture experiences as close to the traumatic event as possible, as experiences may become less detailed, less vivid and more distant over time, however, this must be carefully balanced with potential psychological trauma for participants involved (Liamputtong 2007).

Research teams must also consider how the interview will be recorded. This can be from notes made at the time and/or a recording of the interview (Robson 2011). Novice researchers may struggle to take notes and maintain a rapport with the participant. However, in some circumstances written notes are preferable to audio recordings (i.e. certain cultural circumstances where audio recording is not an option) (Burnard 2005).

Lastly, the importance of the relationship between the researcher and the participant cannot be underestimated. During interviews, the researcher must establish a rapport with the participants, actively listen and ask questions that fulfil the research objectives. These approaches will enhance the researcher's access to the interviewee's life and experiences (Elmir et al 2011). Nurses and other healthcare professionals may often feel that they already possess these attributes. Although many of the skills which healthcare professionals have are indeed transferrable to this research environment, researchers must be aware of

their interviewing technique and ensure frequent critical appraisal of their research conduct to ensure that bias is reduced and participants are being approached in a respectful and sensitive manner (Doody 2013).

3.6.7 Field note observations

Field notes are the notes taken by researchers describing the unstructured observations that they have made in the field and their interpretations of observations (Polit and Beck 2009). Most field notes are not written while researchers are under-taking data collection but are written after a session of data collection has been completed (Polit and Beck 2009). These reflective notes which document the researcher's personal experiences and reflections serve a number of purposes including helping to understand what does and does not work within the interview process as well as helping to guide subsequent data collection. It is essential that qualitative researchers reflect on these feelings to ensure that these viewpoints do not influence what is being observed. These personal notes can also contain reflections about ethical dilemmas faced (Polit and Beck 2009). Stauss and Corbin (1990) argue that notes such as these help researchers to achieve analytical distance from the actual data and therefore play a critical role in the project's success.

3.7 Pilot study

A pilot study is a small scale version, or trial run of a data collection tool or approach done in preparation for a major study. A pilot study helps identify some of the inevitable problems of converting any research design into reality and gives the researcher experience with the data collecting instrument and analysis of the data collected (Parahoo 2006, Robson 2011). The study design will dictate what, how and when the pilot study should be conducted. Items and processes which can be piloted include: protocols; data collection instruments and sample and recruitment strategies (Polit and Beck 2009).

3.8 Quantitative data analysis

An important feature of quantitative research is the measurement of phenomena. Quantitative researchers carry out, wherever possible, appropriate, statistical tests to establish the probability of certain phenomena occurring

(Parahoo 2006). Statistics are either descriptive or inferential. Descriptive statistics are used to describe and synthesise data, for example, the use of the mean and standard deviation (Polit and Beck 2009). Inferential statistics are statistical tests that allow conclusions from the sample data to be generalised to a population on a probabilistic basis (Robson 2011).

Before quantitative data analysis can begin, Robson (2011) states that there are a number of steps a researcher must follow to ensure that reliable, rigorous analysis is carried out. These are:

1. The creation of a data set, including how and when the data set will be created, should be thought out at the research design stage. This step should ensure that the data is analysable and is as simple as possible. This is likely to be through the use of coding (Bowling 2003).

2. Deciding on the software package that the data will be entered and indeed analysed (e.g. RStudio).

3. Having processes in place to deal with missing data, and coding this appropriately within the software package being used.

4. Once all the data has been entered, it then requires to be 'cleaned' prior to analysis. There are a number of strategies for this including double data entry (Stratton and Neil 2005). Other methods for cleaning include range checks and consistency checks (Bowling 2003).

The next stage in the process of quantitative data analysis is determining the level of measurement. This is the relationship between what is being measured and the numbers which are being measured. Broadly speaking, variables are either categorical or continuous (Field 2013). Details of each are given in Table 3.2.

At this stage, researcher teams must also explore the distribution of the data they intend to analyse. This can be done through utilising Quintile Quintile (QQ) plots or Histograms. QQ plots are graphs which plot the quantities of a variable against the quantities of a particular distribution. If values fall on the diagonal

of the plot, the variable shares the same distribution as the one of interest (i.e. normal distribution) (Field 2013). A histogram is a graphic presentation of frequency distribution data (Polit and Beck 2009). In normally distributed data, if a vertical line was drawn through the centre of the histogram, the distribution would look the same on both sides (Field 2013).This step ensures that the theoretical assumptions of the statistical test utilised is being met (Lang 2004).

Once the distribution and type of data is known, appropriate and relevant statistical tests can then be selected. Many authors (Bowling 2003, Stratton and Neil 2005, Polit and Beck 2009) advocate that novice researchers must be seek statistical support. By undertaking this step, the accuracy and validity of results is also enhanced.

A full account of the statistical approaches utilised to examine the data in this thesis are given in Chapter 4, Section 4.10.1.

Table 3.2: Levels of measurement in quantitative data analysis

Level of measurement	Categorical or continuous	Definition
Binary Variable	Categorical	Data are split into two categories (Field 2013)
Nominal	Categorical	A variable that comprises categories that cannot be rank ordered (Bryman 2012a)
Ordinal	Categorical	A variable whose categories can be ranked ordered, but the distance between the categories is not equal (Bryman 2012a)
Interval Variable	Continuous	Data measured on a scale along which intervals are equal (Field 2013)
Ratio Variable	Continuous	The same as an interval variable but with the additional property that the ratio of the variable is meaningful (Field 2013)

3.9 Qualitative data analysis

3.9.1 Qualitative analysis

One of the most challenging aspects of conducting qualitative research lies in the analysis of the data (Priest, Roberts, Woods 2002). The purpose of data analysis is to organise, provide structure to, and elicit meaning from the raw

research data (Polit and Beck 2009). Theoretical frameworks or concepts are almost always present in studies that are embedded in a qualitative research tradition (Polit and Beck 2009). Theories provide complex and comprehensive conceptual understandings of things that cannot be pinned down, for example, how people interact in certain ways. Theories also provide a 'lens' through which to look at complicated problems and social issues; focusing attention on different aspects of the data and providing a framework within which to conduct their analysis (Reeves, Albert, Kuper et al 2008). This is in direct contrast to quantitative research theory, where the classic approach is to test a hypothesis deduced from a previous theory (Polit and Beck 2009).

3.9.2 Interpretative Phenomenological Analysis (IPA)

IPA is an approach to qualitative, experiential research that has gained momentum and popularity over recent years (Smith et al 2009). IPA has its roots in psychology and recognises 'the central role of the analyst' in making sense of the personal experiences of research participants (Smith 2004, Pringle et al 2011, Jirwe 2011). Therefore, IPA research involves a double hermeneutic approach. The participant is trying to make sense of their personal and social world and the researcher is trying to make sense of the participant trying to makes sense of their personal and social world (Smith 2004).

The aim of IPA is to illustrate, inform and master themes by firmly anchoring findings in direct quotes from participant accounts (Smith et al 2009). It stresses the importance of the interpretive and hermeneutic elements of phenomenology, seeking to capture examples of convergence and divergence, rather than focusing solely in commonalities, which for example Giorgi's (1997) approach to phenomenology suggests (Smith et al 2009, Pringle et al 2011).

Smith (2004), in his seminal paper, states that there are three main aspects to IPA. Firstly, IPA is idiographic. Idiography is concerned with the particular (Smith et al 2009). IPA's commitment to the particular is evident in two distinct ways. There is both commitment to the particular in the sense of depth of analysis, and also to understanding how a particular phenomenon has been understood from the perspective of particular people in a particular context (Smith et al 2009). IPA is also an inductive process that allows researchers to

employ techniques which are flexible enough to allow unanticipated topics or themes to emerge during analysis. Thus, IPA does not attempt to verify or negate specific hypotheses. Finally, IPA is an interrogative process which moves beyond the text to a more interpretative level (Smith 2004).

The analytical process of IPA involves six key steps (Figure 3.1). It is by no means a linear process, but a complex procedure which involves an iterative and inductive cycle (Smith et al 2009). The analyst must constantly reflect on their own perceptions, conceptions and processes to ensure that this conceptual framework is used effectively (Smith et al 2009). This process is not exhaustive; however, it does help provide a systematic and structured approach to analysis for IPA novices working their way through an often complex and daunting analytical process.

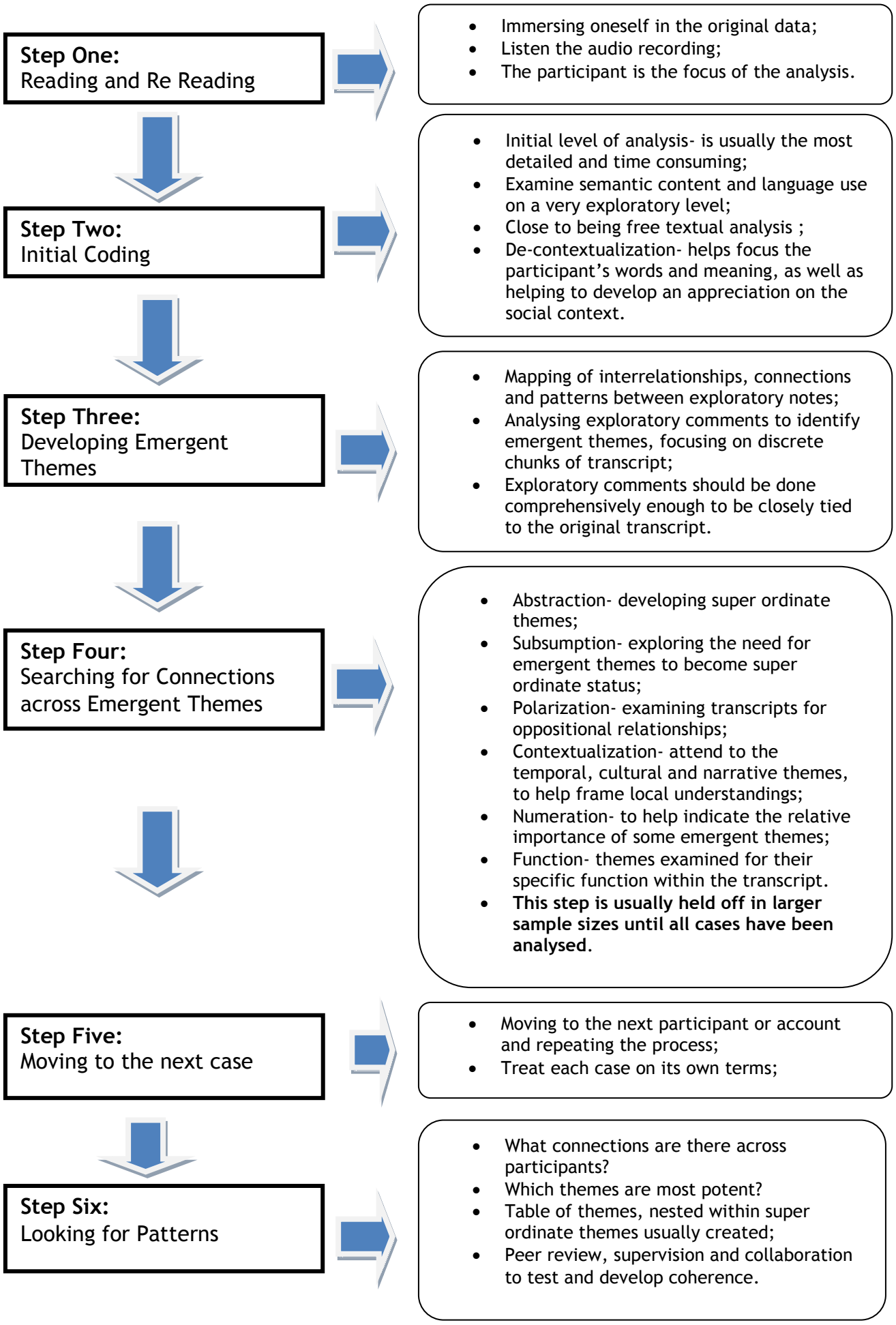

Figure 3.2: IPA Data Analysis Process (Smith et al 2009)

3.10 Issues of rigour

3.10.1 Rigour in quantitative research

Reliability and validity are traditionally used to evaluate rigour in quantitative research. Reliability is the degree of consistency or dependability with which an instrument measures the attribute it is designed to measure (Polit and Beck 2009). The concept of reliability is important when interpreting the results of statistical analyses. Statistical reliability refers to the probability that the same results would be obtained with a completely new sample of subjects. In essence the results are an accurate representation of the wider population (Polit and Beck 2009).

Validity is the degree to which an instrument measures what it is supposed to measure (Polit and Beck 2009). There are a number of different types of validity including:

Internal validity: The extent to which a study establishes that a factor or variable has actually caused the effect that is found (and that it has not been caused by other factors) (Robson 2011).

External validity: Refers to the generalisability of research findings to other settings. Adequate sampling is particularly crucial in establishing the external validity of any study (Polit and Beck 2009).

Construct validity: This refers to the extent to which a questionnaire or measurement scale reflects the entity which is being assessed or measured (Parahoo 2006).

Convergent validity: Is an approach to construct validation that involves assessing the degree to which two methods of measuring a construct are similar (i.e. converge). This is particularly important in mixed methods research (Polit and Beck 2009).

Face validity: Face validity is often confused with content validity. It simply refers to an investigators subjective assessment of the presentation and relevance of a questionnaire (Bowling 2003).

Content validity: Content validity is more systematic than face validity. It refers to judgements about the extent to which the content of an instrument appears logical and will comprehensively examine, in a balanced way, the full scope of the characteristics which it is intended to measure (Bowling 2003).

Statistical conclusion validity: Is the degree to which conclusions about relationships and differences from a statistical analysis of the data are legitimate. Threats to statistical conclusion validity include low statistical power and low precision (Polit and Beck 2009).

3.10.2 Rigour in qualitative research

There has been much debate in the last decade over the idea of quality and rigour in qualitative research and more specifically what, if any, criteria should be used to judge a qualitative piece by (Rolfe 2006 and 2007, Porter 2007). In his seminal and indeed controversial paper, Gary Rolfe (2006) argues that because of the absence of a unified qualitative paradigm, attempts to construct a predetermined framework to judge the quality of qualitative research are futile. In his somewhat elitist stance (Porter 2007), Rolfe (2006) goes on to argue that the appraisal of qualitative research is 'subject to individual judgement based on insight and experience' (pg 308), which appears to mean that qualitative research may be esoteric and can be judged only by those who have sufficient experience of performing research (Porter 2007). However, Porter (2007) in his critique of this viewpoint brings into question how non research active clinicians are to interpret evidence to ensure evidence based practice. Logically, research is a form of communication and communication by definition 'requires the active participation of at least two parties' (Porter 2007, pg 82). Further, science is concerned with rigour and if we reject scientific enquiry, we are undermining the belief that qualitative research is a scientific process and has a valued contribution to make to the advancement of knowledge (Tobin and Begley 2004).

In their seminal work, Lincoln and Guba (1985) argue that procedures to establish trustworthiness for 'naturalistic inquiry' need to be put in place. Guba and Lincoln were uneasy about the simple application of reliability and validity

standards to qualitative research, as these standards presuppose that a single, absolute account of reality is feasible. They were critical of the view that there are absolute truths about the social world, instead they argue that there can be more than one account (Bryman 2012a).

Trustworthiness can be divided into four components (Table 3.3) and there are now several methods available to researchers to demonstrate each aspect of trustworthiness in the qualitative research process. One major criticism about this approach to rigour is that this is a set of procedures to evaluate the process (post hoc) rather than a process which is done throughout the research course. Researchers must ensure that methods for ensuring rigour are underway during the data collection and analysis period (Tobin and Begley 2004).

Table 3.3: Criteria used to promote trustworthiness in qualitative research (adapted from Lincoln and Guba 1985)

Criteria	Quantitative comparable	Methods to validate criteria include
Credibility- Addresses the issue of 'fit' between the respondent's views and the researcher's interpretations of them.	Internal validity	Audit Trail Member Checking Utilising mixed methods studies Peer review
Transferability - Refers to the generalisability of the inquiry- this usually only concerns case to case transfer.	External validity	Peer Review Audit Trail
Dependability - Is the process logical, traceable and clearly documented?	Reliability	Audit Trail Reflexivity
Confirmability- ensures that the findings are clearly derived from the data	Objectivity	Audit Trail Member Checking Peer Review

3.10.3 Reflexivity

To do high quality work, qualitative researchers must be reflexive and conceptual throughout the project period (Polit and Beck 2009). Reflexivity involves ways of questioning our attitudes, thoughts, reactions and habitual actions to strive to understand our roles in relation to others (Clancy 2013).

Koch and Harrington (1998) advise that this is a process of ongoing self-critique and self-appraisal, including the moral, social and political stance of the researcher, and the affect that this can have on any presented analysis.

Between the two extremes of routine triviality and research as a self-exploration, are some 'good practice' approaches that demonstrate reflexive insight and in turn can increase the rigour of analysis (Green and Thorogood 2004). These are highlighted in Table 3.4.

Table 3.4: Good Practice approaches to demonstrate reflexive awareness (adapted from Green and Thorogood 2004)

Good Practice Approaches	Execution in Practice
Methodological openness	Be explicit about data production, analysis, decisions made and alternatives not pursued.
Theoretical openness	Theoretical starting points and assumptions should be addressed as well as how they shaped the study.
Awareness of the social setting of the research itself	Demonstrate an awareness of how your interaction as researcher influenced the data.
Awareness of the wider social context	How have politics and social values made the research possible and how have they constrained it?

3.10.4 Audit trail

One of the steps used to establish the credibility and confirmability of a qualitative study is the construction of an audit trail (Burns and Grove 2012). The audit trail, the origins of which arise in the work of Lincoln and Guba (1985), is used to establish the rigour of a study by providing the details of data analysis and information on some of the decisions that led to the findings (Wolf 2003). It is used by a peer reviewer, or auditor, to trace the textual sources of data back to the interpretations and vice versa (Wolf 2003). This step also allows the external reviewer to draw conclusions about the trustworthiness of the data and the dependability of the research (Cutcliffe and McKenna 1999).

3.10.5 Member checking

Member checking is a method of validating the credibility of qualitative data through debriefings and discussions with informants (Polit and Beck 2009). Usually, researchers return material such as transcripts, accounts and interpretations which have been made. These can be seen as a valuable means of guarding against researcher bias (Robson 2011).

Guba and Lincoln (1981) view member checks as a critical technique for establishing the credibility of any study. However, while member checking may be a commendable democratisation of the research process, there are several practical and methodological flaws with its use (Porter 2007). For example, perhaps an interpretation may be challenged or the participant may get cold feet and will seek to suppress certain material. Additionally, member checking involves enlisting a subset of participants for member checking. A challenge for any research team is deciding which participants should be approached (McConnell-Henry, Chapman, Francis 2011). Ethically, member checking may be challenging within research, especially when the research subject is sensitive and participants may not possess the emotional energy to recount the experience again (McConnell-Henry et al 2011). Furthermore, Heidegger's notion that time, space and context are pivotal, render the idea that follow up with participants is invalid. Heidegger's belief is that experience is relative to context, and re-visiting accounts with participants is outside this philosophical thinking (McConnell-Henry et al 2011).

3.10.6 Peer review

When researchers are generating patterns or themes from qualitative data, they can enhance the validity of the categorisation methods and guard against researcher bias by enlisting the assistance of a colleague, usually an experienced or expert colleague in the field (Cutcliffe and McKenna 1999). Both individuals then produce categories independently of one another and then come together to discuss these independent findings (Polit and Beck 2009). Qualitative researchers sharing their interpretations with colleagues are offered the opportunity to be challenged on the robustness of the emerging categories and themes that have been produced (Cutcliffe and McKenna 1999).

3.11 Chapter conclusion

This chapter has addressed the main theoretical issues around the methodologies employed in this PhD. The next chapter details how the research methodologies discussed in this chapter were used to answer the research aims of the study.

Chapter Four: Materials and Methods

4.1 Introduction

This chapter outlines the procedures and methods which were used to conduct this mixed method PhD. An observational cohort study, together with in depth semi structured interviews with patients after discharge from ICU, was used to answer the following research objectives:

1. Analyse the nature and complications of alcohol related admissions to critical care

2. Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis

3. Explore patterns of recovery for patients with and without alcohol use disorders

4. Determine whether alcohol use disorders are associated with survival in critically ill patients at six months post ICU discharge

5. Examine the impact of critical care on future behaviour with regards to alcohol intake.

Of note, the explanation and rationale for methods and materials utilised for the observational cohort study apply to both Chapter Five and Six of this programme of work.

4.2 Study design and research plan

4.2.1 Rationale: mixed methods approach

This work took a pragmatic approach with the research design being driven by the research aim and objectives. To fully answer the aim and objectives it was clear that neither quantitative nor qualitative methods in isolation were sufficient to develop a complete picture. A quantitative approach in isolation would have quantified the problem; a qualitative approach in isolation would

have explored the issues without developing context of the problem. By combining methods an overall account of the problem was formed and a more complete picture of the entire patient journey was created.

There are many different approaches to executing mixed methods studies. Within this PhD, there was a concurrent parallel data collection process. The separate data sets were then integrated after the analysis stage and discussed as one body of data.

4.2.2 Rationale: observational cohort study

An 18 month observational cohort study was utilised to determine: the nature and complications of alcohol related admissions to critical care; whether alcohol use disorders are associated with survival in the critically ill patients at six months post ICU discharge and to explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis.

All data was collected from Clinical Information Systems (Philips IntelliVue Clinical Information Portfolio (ICIP) (Revision D.03), WardWatcher (Critical Care Audit Limited, Yorkshire) and Orion Health Clinical Portal system within the ICU and from Information Services Division (ISD) Scotland (See Section 4.7.2). By utilising an observational cohort study the incidence rate could be measured and inferences drawn about causation, which was necessary to the address the research objectives (See Section 3.6). This approach also allowed the collection of relevant information required to complete the appropriate scoring tools utilised in Chapter Six.

4.2.3 Rationale: in depth semi structured interviews

In depth semi structured interviews were utilised to address the research objectives. They were chosen as a method of data collection as this area of research is complex and in some cases deeply sensitive. They also allow the researcher to gain insights into this area (Low 2013). Further, it was important to understand contextual accounts from participants about their recovery from ICU and behaviours regarding alcohol use. These contextual accounts would have been difficult to capture by any other research method.

4.2.4 Rationale: analytical framework

Interpretative Phenomenological Analysis (IPA) was chosen as an analytical framework for the qualitative aspect of this PhD (See Section 3.9.2). There are several reasons for this choice. Firstly, IPA is concerned with understanding, exploring and interpreting the personal, lived experience of a participant, which was a key aim of this particular study. Secondly, IPA gives clear guidance on how to contextualise and de-contextualise as well as how to understand and interpret different ideas and accounts from participants during the analysis process. Lastly, IPA offers a clear, systematic process for which to conduct analysis.

4.3 Study site

The study took place in the adult critical care unit of Glasgow Royal Infirmary (GRI), a University Teaching Hospital within NHS Greater Glasgow and Clyde. GRI is situated in an area of high socio economic deprivation, with 42% of the most deprived data zones in Scotland residing in this catchment area (Scottish Government 2012) (See Section 2.3.1). The GRI ICU cares for both level two and three patients, and the usual bed capacity is 12 level three beds (ICU) and eight level two beds (HDU) (See Section 2.6.2). In addition, GRI is a tertiary referral centre for pancreatic care, burn care, oesophageal surgery and some orthopaedic interventions.

The study site is the PhD student's place of work. Although undertaking research in a workplace setting has some disadvantages, these were offset by the advantages (See Section 3.3). For example, being part of the direct care team enhances the understanding of the complexities of the patient group which is a major advantage when requesting ethics approval. Additionally, training and expertise in the Clinical Information Systems required to access the appropriate data was essential for this particular piece of work.

4.4 Access

Access for this study was first granted by the Academic Lead for the critical care unit (also a Research Supervisor within this study) and also by the Lead Clinician for the unit. Access was then granted from NHS Greater Glasgow and Clyde's Research and Development Department and the Research Management

Department (See Appendix IV). All Nurse Managers were informed about the project and a Senior Charge Nurse was a member of the Stakeholder group for the study (See Section 4.5.1).

4.5 Research ethics committee approval

4.5.1 Potential ethical issues

A number of potential ethical issues were identified before the study commenced. Firstly, patients who were interviewed were within a vulnerable population. They had recently overcome a period of critical illness which, as discussed in Section 2.12, may cause ongoing physical and psychological problems. In addition, a proportion of the patients were struggling with addiction. To help overcome these sensitive issues a Stakeholder Group was formed to guide the conduct and execution of the study. Members of the Stakeholder Group included: a previous family member; a previous patient (who was admitted with alcohol related pancreatitis); a Senior ICU Charge Nurse; a member of the Critical Care Outreach team in the hospital; a lay member of a national healthcare group and Lead Nurse for Community Addictions in Glasgow. All members of the group were asked to comment on all patient documentation (i.e. Participant Information Sheets and Letters of Invitation) as well as the interview schedule. The PhD student had several meetings and phone calls with all members of the group. No formal meetings of the entire group took place to preserve confidentiality of the patient and family member.

4.5.2 Ethics approval

Ethics approval for this mixed methods PhD was granted on the 20th of March 2012 (Reference Number 12/WS/0039: West of Scotland Research Ethics Committee 5, Chairman Dr Gregory Ofili; See Appendix VI). During the course of the study two substantial amendments to the research protocol were requested and granted from the above Ethics Committee.

Amendment One (3rd January 2013): This was an amendment which allowed the PhD student to contact patients directly to participate in the in depth semi structured interviews. The initial research protocol stated that consent would be obtained through an existing system in the ICU, by which patients agree to

contact after discharge. However, due to a variety of factors, namely high workload in the unit and staff absence, this system did not seek permission from a large enough sample. In fact, only one patient had been recruited and interviewed through this system in several months. Therefore, the Ethics Committee allowed the research team to contact the patient directly without the need for approval during the ICU stay (See Appendix IV).

Amendment Two (17th of April 2013): The initial ethics application allowed for recruitment of patients who were 65 years and younger for interview participation. However, it was noted that a large section of the patient population (approximately 30%) would be excluded from the study. Therefore, permission was sought and granted by the ethics committee to increase the upper age limit for the semi structured interviews to 75 years (See Appendix IV).

Informed consent was obtained from every individual who participated in the interviews. It was not required for patients involved in the observational cohort study. Data collected for this part of the study was part of routine data collection for clinical purposes in the ICU.

4.6 Inclusion and exclusion criteria

4.6.1 Observational cohort: inclusion and exclusion criteria

The primary inclusion criterion for the cohort study was all patients admitted to ICU during the 18 month study period as level three patients. The only exclusion for the cohort study was patients younger than 18. Of note, readmissions to intensive care were not included in the analysis in Chapter Five; however, readmissions were included in the analysis in Chapter Six. Readmissions to the ICU were included in Chapter Six as this study addressed baseline liver function on admission to the ICU, which may have varied on different admissions for the same patient.

4.6.2 In depth semi structured interview: inclusion and exclusion criteria

The inclusion criteria for the interviews were:

1. Any patient admitted to the ICU as a level three patient (See Section 2.6.2)

2. Patients who had been admitted to the ICU and ventilated for greater than 72 hours

3. Patients who were older than 18 years of age at the time of ICU admission

4. Patients who were younger than 75 years of age at the time of ICU admission

5. All male and female participants

6. Patients who were able to give full consent at the time of interview

7. Patients who could speak English fluently (no requirement for translator).

The exclusion criteria for the interviews were:

1. Patients admitted to the ICU who did not meet the level three patient criteria

2. Patients who were admitted to the ICU and ventilated for less than 72 hours

3. Patients older than 75 years of age at the time of ICU admission

4. Patients younger than 18 years of age at the time of ICU admission

5. Patients who were unable to give their full consent at the time of interview

6. Patients who had ongoing mental health issues (such as alcohol related brain damage)

7. Patients who did not speak English and would require the support of a translator.

4.7 Data collection

4.7.1 Data definitions

Patients were assigned to one of three alcohol groups during the ICU stay. These groups, which were based on the WHO guidelines (See Section 2.4.1) for Alcohol Use Disorders (AUDs), were:

- Low Risk
- Harmful/Hazardous
- Alcohol Dependency.

These groups made up the three study groups presented in this research programme. Full information on each of these groups is shown in Appendix VII.

Patients were assigned to a study group based on information from family members, information from the patient, any assessment tool completed by the patient in the ward setting or any evidence from previous medical notes, including those available electronically. Ideally, the research team should have utilised a validated scoring tool for the assessment of AUDs (i.e. FAST or AUDIT, See Section 2.5.1). However, as highlighted previously, none of these tools have been through validation work in the ICU and as a result, they are rarely used in the critical care setting in the UK (McPeake et al 2013). Further, there is limited work on the use of patient proxies completing these tools in the acute healthcare setting. Therefore, the decision was made to use the above approach to assessment instead. Of note, if the patient had completed a scoring tool in the ward setting pre ICU admission, or at a pre-operative assessment appointment, this information could be directly transferred to the assessment in the ICU as the same classifications were utilised.

The sepsis variable was broken into three groups in the present study: No Sepsis, Sepsis/Severe Sepsis and Septic Shock. Patients were allocated to each of these groups based on the NHS Greater Glasgow and Clyde Sepsis Screening Tool (Appendix VIII). As the sepsis status of a patient could have changed over the duration of their ICU stay, the patient's worst clinical status was used to classify them into sepsis groups. For example, if a patient fell into the septic shock category at any point during their stay, there were allocated to the septic shock group. Patients were classified into a sepsis category during active treatment in the ICU only.

Cirrhosis was diagnosed either histologically or via clinical suspicion. Clinically, a patient was deemed cirrhotic if they had features of chronic liver disease with evidence of portal hypertension, ascites, encephalopathy or a liver-spleen scan consistent with cirrhosis. On completion of patient enrolment into the study, an independent clinician verified the diagnosis of cirrhosis by analysing each patient's medical notes.

This PhD also aimed to explore the use of vasopressors and Renal Replacement Therapy (RRT) in patients admitted to the ICU with an AUD. This information was particularly important in understanding the cirrhosis population. As documented in Section 2.13, the need for RRT and vasopressor therapy is a poor prognostic indicator for this patient cohort. Therefore, it was important understand these requirements in this population. The GRI ICU utilises both Continuous Veno-Venous Haemofilitration (CVVH) and Haemodialysis (HD). Patients were deemed to have a vasopressor day if they received any vasopressors in that 24 hour period. Similarly, patients were deemed to have a ventilation day or a RRT day if they received any invasive or non-invasive ventilation or any renal support during that 24 hour period. All blood results collected were those obtained on ICU admission.

Postcodes were collected from all patients in the study; the SIMD category was then calculated for each patient using the Scottish Governments 2013 revision of the score (See Section 2.3.1). In this study, deprivation was defined as the lowest two deciles of the SIMD.

No alcohol withdrawal tools are utilised with level three patients in the ICU. All patients are subject to the same sedation pathway in the unit, with no alterations made for alcohol related admissions.

4.7.2 Observational cohort study: data collection

Patients were followed at different points in time. The data collected and the time point at which it was collected is given in Table 4.1. To ensure reliable data was collected from the patients' notes, the data collection tool was piloted, a coding guide developed and all missing data was kept blank (See Section 3.6.3).

Quantitative data was collected both prospectively and retrospectively within the cohort study. Data collected during the ICU stay was collected prospectively from various Clinical Information Systems. The ICU utilises the Philips IntelliVue Clinical Information Portfolio (ICIP), locally known as CareVue (Revision D.03). CareVue incorporates patient observations, healthcare notes, drug prescriptions

and electronic recording of medication administration in the ICU (Warrick, Naik, Avis et al 2011).

The Orion Health Clinical Portal system, locally known as PORTAL was also used in this study. It is a repository of patients notes, including those from the acute care setting as well as those from community and out of hours systems. The system is used across NHS Greater Glasgow and Clyde and has been live since 2012. At present, not all clinical notes are uploaded onto this system however; it will become the sole case record for all patients in NHS Greater Glasgow and Clyde.

WardWatcher (Critical Care Audit Limited, Yorkshire) is a national audit system used to document a variety of patient observations and outcomes in all ICUs across Scotland. The system, which is managed by the Scottish Intensive Care Society Audit Group (SICSAG), is part of Information Services Division (ISD) Scotland. Analysts from ISD linked the ICU patient population being studied with the death registry for Scotland and extracted outcomes for patients at six months post ICU discharge. Due to the timeframes utilised by ISD (systems are updated every quarter), the outcomes of approximately one third of the study population could not be obtained by ISD. Therefore, the research team manually searched electronic records to obtain six month outcomes.

4.7.3 In depth semi structured interviews: data collection

Twenty of 22 in depth semi structured interviews took place in a room adjacent to the ICU. Three rooms were utilised: the ICU relatives' room, the ICU seminar room and the ICU quiet room. One interview took place in a sheltered housing facility as the participant was unable to attend the hospital independently. Another interview was undertaken in the University as requested by the participant. One supervisor attended the interview with the PhD student at the Sheltered Housing complex. This gave the opportunity for peer review and feedback. This was also in line with the research governance arrangements within the Health Board for ensuring the researcher safety. All interviews were undertaken by the PhD student.

Table 4.1: Data Collected from every patient in the observational cohort study

Data Collected	Time Frame	System Collected from
Alcohol group Admitting Speciality Admitting Area Days in Hospital pre ICU Is this a readmission? SIMD (postcode) APACHE II Smoking status and drug use Initial blood results	On admission to ICU	Ward Watcher PORTAL CareVue
ICU Length of Stay Ventilation Days Vasopressor Use RRT use Sepsis Status ICU outcome	On discharge from ICU	Ward Watcher CareVue
Hospital Outcome Days in Hospital post ICU discharge Total Hospital Stay	Hospital discharge	Ward Watcher PORTAL CareVue
Six Month Outcome	Six months to one year post discharge	Data provided from ISD Scotland PORTAL

An interview schedule was developed utilising the steps detailed in Section 3.6.5. The interview schedule was also disseminated to the Stakeholder group and feedback was received on wording and ordering of questions. All interviews were recorded using a digital audio recorder and then transcribed verbatim. The interview schedule, along with the Participant Information Sheet and Consent Form utilised in this study are presented in Appendix VI.

4.8 Population and sample

4.8.1 Observational cohort: population and sample

The primary outcome measure for this section of the study was to determine if there was an independent association between AUDs and ICU Length of Stay (LOS). Secondary outcome measures included differences in outcomes from ICU, hospital and at six months post ICU discharge, for patients with and without AUDs.

The sample obtained for this observational cohort was a convenience sample. The steps presented in Section 3.4.3 were used to estimate an appropriate sample size for the quantitative section of this study. It was estimated (based on previous admissions) that there would be approximately 600 first time level three admissions admitted in the 18 month study period. It was difficult to determine how many patients would fall into each study group as alcohol related admissions had not been explored previously. Based on expert opinion and a small one month audit in the ICU at GRI (O'Geary et al 2012), it was estimated that approximately 300 patients from the low risk group, 150 from the harmful/hazardous group and 150 from the alcohol dependency group would be admitted during the 18 month study period. Based on this estimated sample, the study would have 80% power to detect a difference of 12% between the large and small groups and an 80% power to detect a difference of 14% between the small groups. No power analysis was required for Chapter Six.

4.8.2 Semi structured interviews: population, sample and recruitment

The sample obtained for the in depth semi structured interviews was also a convenience sample. All patients admitted to the GRI ICU who were ventilated for greater than 72 hours were invited. This patient group was targeted as they were accessible to the research student. Patients from each of the three study groups were purposively sampled to understand recovery from ICU from all perspectives.

As highlighted in Section 3.4.3, it is challenging to estimate how many interviews are required to meet data saturation in a particular study. This was made even more challenging when looking at the literature in this field, where qualitative studies with patients after ICU have a wide range of participants (Range 6-250 participants, See Section 2.12). However, an estimated sample size is required when applying for ethics committee approval. It was decided after following the steps proposed by Bryman (2012b) (See Section 3.4.3), consulting the literature on the topic of ICU follow up (See Section 2.12) and discussing the issue with other researchers in both the field of ICU follow up and addictions, that a sample size of 20-25 patients would be adequate to reach data saturation. This would allow recruitment of between seven and eight participants from each study group and allow group analysis, as well as in depth analysis of each

individual interview. This sample would also allow for sub group variability and heterogeneity (Bryman 2012b).

The recruitment process utilised for the semi structured interviews is shown in Figure 4.1. Participants were recruited three to seven months after ICU discharge. This time frame was chosen as it was felt that this would allow the participants enough time to readjust to being home, but also allow the research team to look at recovery and decision making regarding alcohol use as it was actively happening. This timeframe was also chosen to help reduce memory bias or recall bias with regards to the ICU experience (Parahoo 2006).

4.9 Pilot study

The data collection tool for the quantitative section of the study was reviewed to ensure that the appropriate data was collected for each patient. It was then piloted with 10 discharged patients picked at random including two patients with a background of cirrhosis, to ensure that the appropriate data for this section of the study was collected. After this process, the order of the data collection tool was changed slightly to reflect how the Clinical Information Systems appeared on screen. This allowed data to be accessed more efficiently. The PhD student collected all data for the observational cohort study outwith the six month outcomes.

A pilot interview was also undertaken. After the pilot interview, the schedule was adapted to ensure that it reflected the patient journey more clearly. After transcription, the interview was discussed with the research supervisory team, to again refine and target the interview schedule more clearly. To ensure further peer review, one of the interviews was also directly observed by the research supervisor due to the location of the interview. This interview allowed further refinement of the approach to the interview. This process also gave the opportunity for feedback on asking questions that were more targeted and prompted more in depth responses from the participant.

4.10 Data analysis

4.10.1 Observational cohort: data analysis

The analysis of the observational cohort study was undertaken by the PhD student with the support of a clinical physicist in the departmental research group. All coded data was first entered into a Microsoft Excel (2010) spreadsheet.

The data was then transferred to the statistical package RStudio version 0.98.493 (R Foundation for statistical computing, Vienna, Austria) for statistical analysis. A screen shot of Rstudio can be seen in Appendix IX, along with the formula transcript used for analysis. All missing data fields were kept blank. There were a number of strategies used to clean the data, including range checks and consistency checks (See Section 3.8). In Chapter Six, the statistical analysis was undertaken using SPSS (SPSS Inc, IBM, Chicago, Illinois, USA, v.18). This analysis was undertaken in collaboration with undergraduate BSc students, who were required to use SPSS as part of their research programme.

The next step in the quantitative data analysis process was determining the levels of measurement. This was done through the use of both QQ plots and Histograms (See Section 3.8). A table was then constructed with the variables and information detailing the level of measurement (See Section 3.8). This step ensured that all assumptions for each of the statistical tests were met (Lang 2004).

4.10.2 Univariate analysis

The research team utilised a variety of statistical tests for the univariate analysis of the data. The two sample t-test is a parametric test utilised for continuous data. It assumes independent observations within and between groups and tests for a difference between the mean. The Mann Whitney *U* is a non-parametric test which looks for differences between two independent samples. Unlike the two sample t-test, it uses ranking instead of actual values as it tests for differences between median values (Field 2013). The ANOVA, an acronym for ANalysis Of VAriance (Field 2013), tests the mean differences across

three or more groups by comparing variability between groups to variability within groups (Polit and Beck 2009).

The Kruskall-Wallis test is the non-parametric version of the one way independent ANOVA (Field 2013). The Chi Square test (Pearson's Chi- Square test) was used to test for independence of two categorical variables (Field 2013).

In healthcare research it is rare that researchers achieve an answer to the research question or aim with the use of one statistical test (Field 2013). As a result, several tests are often conducted. The more statistical tests that are undertaken, the greater the probability of type one errors occurring. This type of error across statistical tests is known as experimentwise error rate. To reduce this build-up of errors, the level of significance for individual tests must be adjusted to ensure that the overall type one error rate remains at 0.05. One method for this adjustment is the Bonferroni correction. Within the Bonferroni correction, each test conducted should use a criterion of significance of the type one error, divided by the tests conducted (Field 2013).

In this research study, the Kruskall-Wallis test and the ANOVA were initially utilised to compare the three study groups. If there was a significant difference between the three study groups, a set of post hoc tests were carried out with the Mann Whitney test and the two sample t-test, to determine where the significant difference lay. At this point a Bonferroni correction was used to adjust the error rate.

4.10.3 Logistic regression

Logistic regression estimates the probability of an event occurring and transforms this probability into an odds. The Odds Ratio (OR) is the ratio of two probabilities: the probability of an event occurring to the probability that it will not occur. Logistic regression, which is a multivariate regression procedure, analyses the relationship between multiple independent variables and a categorical variable (Polit and Beck 2009). Logistic regression enables researchers to generate odds ratios that are meaningful results. In essence, the OR is an index of relative risk (Polit and Beck 2009).

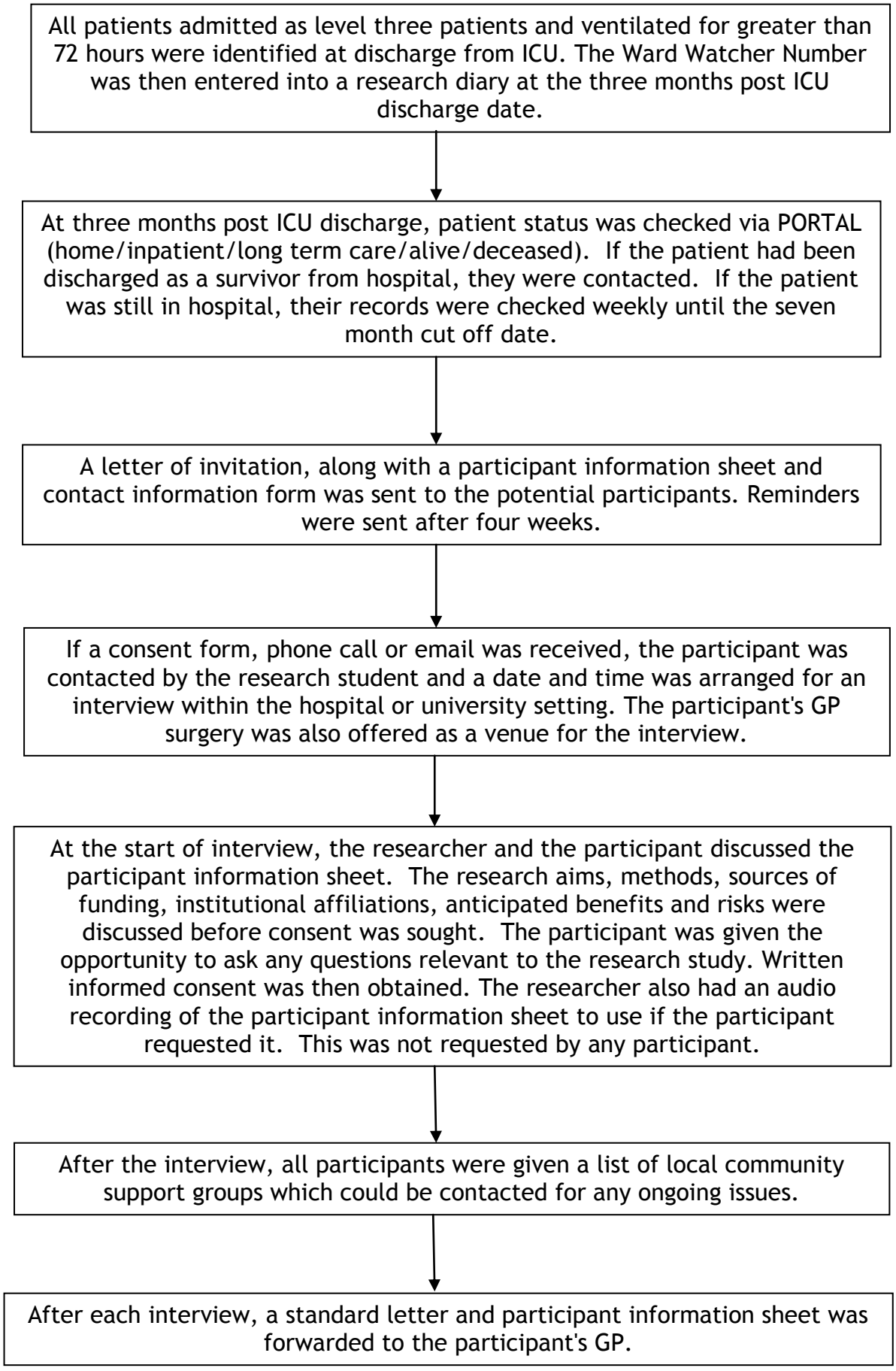

Figure 4.1: Recruitment process for the in depth semi structured Interviews.

4.10.4 Survival analysis

Survival analysis is widely utilised by medical researchers when conducting longitudinal studies (Polit and Beck 2009). The survival curve usually describes the probability of being event free (often alive or dead) at a given time point (Sur and Dahm 2010). Survival curves that are calculated using the Kaplan-Meier method allow study subjects with different lengths of follow up to contribute information (Sur and Dahm 2010). In preparing Kaplan-Meier survival analysis curves, each subject is characterised by three variables: the time they are involved in the study, their status at each time point (alive or dead) and the group they are classified into (Rich, Neely, Paniello et al 2010). Survival analysis also allows researchers to examine the determinants of survival transitions in a multivariate framework. In this type of analysis, independent variables are used to model the risk (or hazard) of experiencing an event (i.e. death) at a given point in time. The most common model utilised for this purpose is the Cox proportional hazards model (Polit and Beck 2009).

4.10.5 Statistical modelling strategy

There are many approaches to building and creating statistical models in medical research (Field 2013). Within this study, models were ranked using the Akaike's Information Criterion (AIC). The AIC is a goodness of fit measure that is corrected for model complexity. This measure in isolation is not intrinsically interpretable. However, it is useful to see how changing models and variables within the model affect the fit (Field 2013). A small value represents a better fit of the data. Although this approach was taken to determine the best available model for the data, clinical relevance and applicability was also used to ensure that the statistical models being created would be clinically meaningful. This approach was similar to that adopted by O'Brien et al (2007) in their widely cited paper on the same subject. In Chapter Six of this thesis, a multivariate, backward stepwise logistic regression analysis was undertaken. This is an automated version of the above approach, which has much less control over the process. Additionally, there is no clinical expertise involved in this process. However, as these were projects in collaboration with students, this approach was deemed to be most appropriate.

4.10.6 Receiver Operating Characteristic curve

Receiver Operating Characteristic (ROC) curves are frequently used in medical research to evaluate models for support, diagnosis and prognosis (Lasko, Bhagwat, Zou et al 2005). The ROC curve, which is essentially a mapping of sensitivity with specificity, is a useful tool in evaluating the accuracy of a statistical model that classifies subjects into one of two categories (i.e. survivor and non-survivor) (Perkins and Schisterman 2006, Zou, O'Malley, Mauri 2007). This comparison takes place through summary measures such as the Area Under the Curve (AUC), with higher levels indicating higher levels of diagnostic ability (Perkins and Schisterman 2006). An AUC equals 0.5 when a ROC curve corresponds to a random chance whilst 1.0 represents perfect accuracy in determining the precision of the tool under investigation (Zou et al 2007). In this study, as in many clinical studies, a model discrimination (an AUC) of greater than 0.8 was deemed a clinically useful level of ability (Johnson 2014).

4.10.6 Summary of statistical methods employed

Continuous variables were expressed as medians or means and inter quartile ranges and ranges respectively, using the Mann-Whitney *U* test and the two sample t-test. Categorical variables were compared using chi squared tests. All tests were two sided and a *p* value of less than 0.05 was considered significant. Kaplan-Meier curves with a log rank test were used to compare six month outcome between the three study groups. Logistic regression models were used to determine independent associations between variables and a Cox proportion model was used to determine the difference between the three study groups with the survival analysis. These results were expressed in terms of the Odd Ratio (OR) and the Hazard Ratio (HR) with a corresponding 95% Confidence Interval (CI). ROC curves and AUC values were used in Chapter Six of the thesis to analyse the utility of prognostic scoring tools in patients admitted to the ICU with liver cirrhosis.

4.10.7 Semi structured interviews: data analysis

All interviews were audio recorded and then transcribed verbatim. The research student transcribed the initial six interviews which allowed in depth reflection on the approach to the interview. The remaining interviews were then

transcribed by an experienced audio typist. IPA was utilised for analysis of the in depth semi structured interviews (Smith et al 2009, See Section 3.9.2).

Computer software, namely NVivo (Version 10 for Windows) and NUD*IST (Version 6) were considered for use during the qualitative analysis. Qualitative data management packages such as NVivo and NUD*IST allow researchers to analyse and visualise information on screen. Researchers can then organise material by topic and explore trends and emerging themes. There are a variety of advantages to utilising these software packages, including ease of data management and preparation and simple retrieval and movement of data (McLafferty and Farley 2006). However, conceptualising data on a computer screen can be difficult and the research student felt that this inhibited conceptualisation. Therefore, all coding and analysis was done manually using the steps detailed by Smith et al (2009).

4.11 Issues of rigour

While it is useful to collect multiple forms of data, it is also important that employing different methodologies adds value to the research. This can only be achieved if researchers demonstrate scientific rigour within each element of the study (Gelling 2014).

4.11.1 Observational cohort

Steps to ensure rigour in the 18 month observational cohort study included: the support of an expert in statistics and RStudio version 0.98.493 (R Foundation for statistical computing, Vienna, Austria) for data analysis. This step improved Statistical Conclusion Validity (See Section 3.10.1). The research student collected and entered all coded data into a Microsoft Excel (2010) spreadsheet using a coding guide derived from clearly stated data definitions (see Section 3.6.3). This improved the validity and accuracy of data collected. Additionally, the use of a validated and complete clinical information systems (CareVue) improved the reliability of data utilised (See Section 4.7.2).

4.11.2 Semi structured interviews

To ensure the credibility and confirmability of the findings of the qualitative section of this study, an audit trail was constructed (see Section 3.10.4). The audit trail included field notes, as well as all notes on the process of analysis. These notes, which were given to the peer reviewers of the data, also acted as a reflective diary for the research student. This allowed self critique of each interview and how her position as both a researcher and a critical care nurse influenced the approach to the interview and analysis of the data.

Peer review of all qualitative analysis took place by a research supervisor and two other critical care nurses with experience in qualitative research and nursing this specific population (see Section 3.10.6). This deepened both the credibility and the confirmability of the findings reported.

Member checking was not undertaken in this research project (see Section 3.10.5). Returning transcribed interviews to participants could be potentially upsetting for those involved, and some participants may not have had appropriate support in place if this was the case. Further, as stated in Section 3.10.5, revisiting the account is outside the philosophical thinking of IPA (McConnell-Henry et al 2011). However, one participant did request a transcript of his interview *'to aid in his journey to sobriety'*. Therefore, the research team sent him a fully transcribed account of his interview. No feedback was sought from this participant about the interview or interpretations made. However, the research team were confident that there was appropriate support in place for this participant to deal with any issues of revisiting the account.

4.11.3 Reflexivity

The steps recommend in Section 3.10.3 were utilised to demonstrate a reflexive insight with the aim of increasing the rigour of the qualitative analysis. The research student was aware of the influence of intersubjectivity when generating and analysing the data, and reflected on preconceptions of the topic and patient group. This allowed a more critical and open minded approach to the analysis of the data.

4.11.4 Ontological and Epistemological considerations

It is important to consider the Epistemological and Ontological foundations of any research process from the outset. Epistemological considerations centre on the theory of how things can be known; that is how we gain knowledge about a particular situation and how the research should be undertaken (Bryman 2012a). Ontological issues challenge social researchers on whether social entities can, and should, be considered objective entities that have a reality external to social actors (objectivism), or whether they can, and should, be considered as social constructions built up from the perceptions of actions and social actors (constructionism) (Bryman 2012a).

A traditional scientific, or positivist approach would not fully answer the research objectives set out. Moreover, a purely interpretive approach would not have been appropriate. Therefore, a mixed methods approach was chosen to fully understand the journey of critically ill patients with and without AUDs. The purpose of this study was to understand the social challenges which patients face following discharge from critical care and how patients cope and manage these challenges. Therefore, from an ontological perspective this research took a constructivist approach.

4.12 Chapter conclusion

This chapter has outlined the specific approach used in this mixed methods study. An 18 month observational cohort study, together with 21 in depth interviews with patients were used to answer the research objectives. The following three chapters will present the results and findings of this mixed methods study.

Chapter Five: Results

'Data do not give up their secrets easily. They must be tortured to confess.'

Jeff Hooper

5.1 Introduction

This chapter presents the results from the 18 month observational cohort study. Two research objectives were addressed in this chapter:

- Analyse the nature and complications of alcohol related admissions to critical care

- Determine whether alcohol use disorders are associated with survival in the critically ill patients at six months post ICU discharge.

5.2 Characteristics of patients

During the 18 month study period (1st June 2012-31st December 2013), 611 patients were admitted to the ICU.

A total of 31 patients were not allocated to a study group in their CareVue notes, ward notes or previous PORTAL notes. Therefore, 31 patients were excluded from the study. Table 5.1 details the baseline characteristics of all patients included for analysis. Of the 580 patients evaluated in this study, 380 (65.6%) patients were admitted with in the low risk alcohol group, 99 (17.0%) patient were admitted in the harmful/hazardous group and the remaining 101 (17.4%) patients were in the alcohol dependency group (Figure 5.1). A breakdown of the different clinical variables analysed and the differences in these variables across the three study groups are given in Table 5.2.

Table 5.1: Baseline Characteristics of patients

Baseline Demographic	**Patients (n=580)**
Age, Mean (Range)	57 (19-90)
Gender (Male)	339 (58.4%)
APACHE II, Mean (Range)	20.8 (2-50)
Known socio economic deprivation (2 lowest deciles of SIMD)	307 (53%)
Days in Hospital Pre ICU admission, Median (IQR)	1 (0-3)
Known current smoker	230 (39.7%)
Known current drug user	58 (10%)
Liver Cirrhosis (Alcohol or non-alcohol related)	75 (13%)
ICU Admission	
ICU Length of Stay, Median (IQR)	3 (2-8)
Ventilator Days, Median (IQR)	2 (2-6)
Vasopressor Therapy Used	327 (56.4%)
Vasopressor Days, Median (IQR)	2 (2-4.5)
RRT Therapy used	93 (16%)
RRT Days, Median (IQR)	3 (1-7)
Diagnosis of Septic Shock	140 (24%)
Non Survivor (ICU)	146 (25%)
Readmission to the ICU	56 (9.7%)
Post ICU	
Days in Hospital Post ICU, Median (IQR)	13 (6-29)
Total Hospital stay, Median (IQR)	17 (7-38)
Non Survivor (Hospital)	188 (32.4%)
Long Term Outcomes	
Discharged to long term rehabilitation	28 (4.8%)
Non Survivor (6 months)	215 (37%)

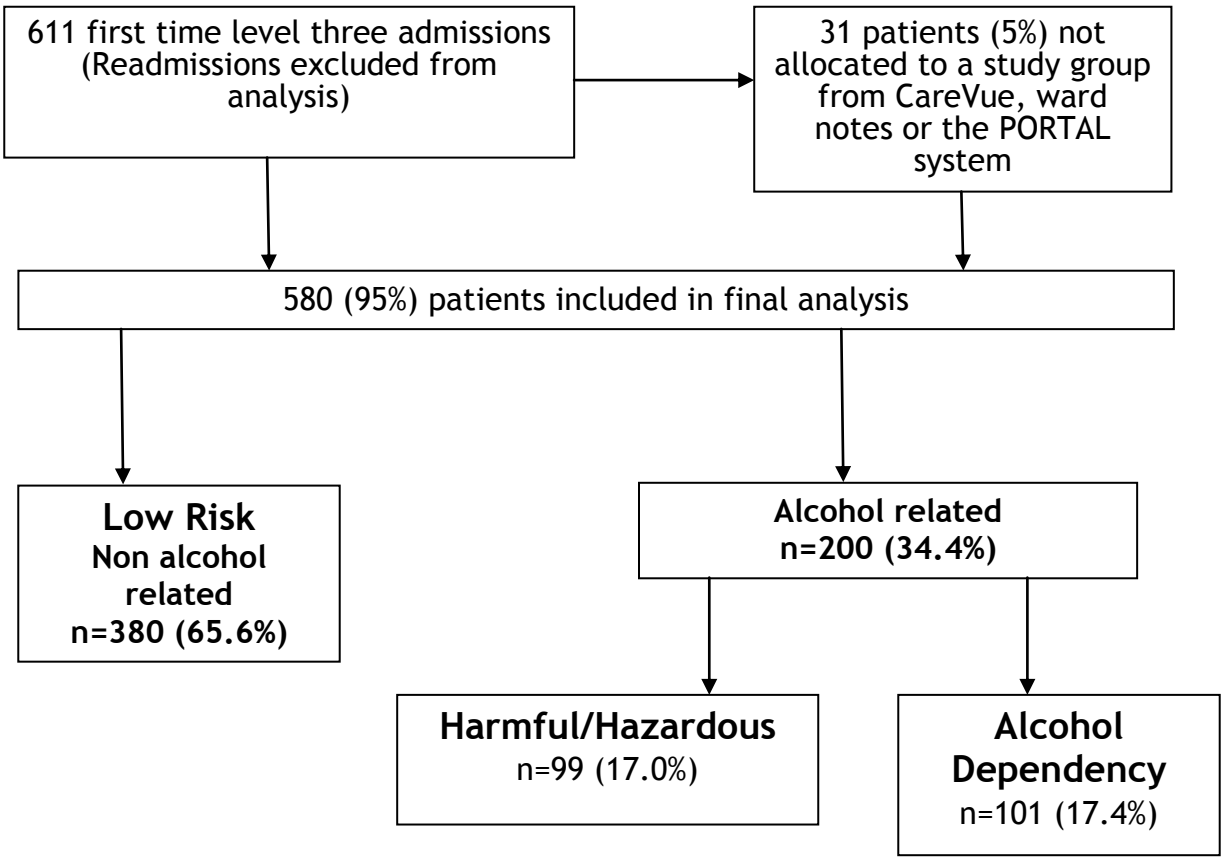

Figure 5.1: Included and excluded participants in the 18 month prospective cohort study

Table 5.2: Differences in clinical variables between the three study groups

Characteristics	Low Risk n=380 (65.6%)	Harmful/Hazardous n=99(17.0%)	Alcohol Dependency n=101(17.4%)	*p* value
Baseline Demographics				
Age, Mean (Range)	61.0 (19-90)	50.3 (19-81)	48.9 (27-76)	**<0.001**
Gender (Male)	186 (48.9%)	77 (77.8%)	76 (75.2%)	**<0.001**
APACHE II, Mean (Range)	20.6 (2-50)	20.2 (3-41)	22 (8-47)	0.22
Known socio economic deprivation (2 lowest deciles of SIMD)	178 (46.8%)	64 (64.6%)	65 (64.4%)	**<0.001**
Days in Hospital Pre ICU admission, Median (IQR)	1 (0-4)	0 (0-1)	1 (0-3)	**<0.001**
Smoking	117 (30.1%)	52 (52.5%)	61 (60.4%)	**<0.001**
Drug Use	13 (3.4%)	23 (23.2%)	22 (21.8%)	**<0.001**
Liver Cirrhosis (Alcohol or non-alcohol related)	14 (3.7%)	6(6.1%)	55 (54.5%)	**<0.001**
ICU Admission				
ICU Length of Stay, Median (IQR)	3 (2-7)	3 (2-7)	5 (2-13)	**0.01**
Ventilator Days, Median (IQR)	2 (2-6)	2 (1.5-4)	3 (2-9)	0.13
Vasopressor Therapy Used	225 (59.2%)	43 (43.3%)	59 (58.4%)	**0.02**
Vasopressor Days, Median (IQR)	2 (2-4)	2(2-4)	3(0-4)	**0.05**
RRT Therapy used	64 (16.8%)	10 (10.1%)	19 (18.8%)	0.19
RRT Days, Median (IQR)	3 (1-27)	5(2.25-10.5)	4(1-6)	0.59
Diagnosis of Septic Shock	78 (20.5%)	32 (32.3%)	29 (28.7%)	**0.03**
ICU Non Survivor	98 (16.9%)	18 (18.2%)	30 (29.7%)	0.15
Readmission to the ICU	37 (9.7%)	8(8%)	11 (10.9%)	0.79
Post ICU				
Days in Hospital Post ICU, Median (IQR)	14 (7-33)	7 (2-20)	14 (6-26)	**<0.001**
Total Hospital stay, Median (IQR)	18 (8-38)	9 (4-24.5)	19 (7-39)	**<0.001**
Non Survivor (Hospital)	128 (33.6%)	22 (22.2%)	38 (37.5%)	**0.04**
Long Term Outcomes				
Discharged to long term rehabilitation	19(5%)	6(6.1%)	3(3%)	**0.18**
Non Survivor (6 months)	145 (38.2%)	26 (26.3%)	44(43.6%)	**0.51**

5.2.1 Admitting speciality and environment

There was a clinically important difference in both admission source and the admitting speciality across the three study groups (Table 5.3). Of low risk patients, 65.7% were admitted via a ward in the hospital or theatre/recovery. This is in contrast to the harmful/hazardous group, where almost half of the admissions were directly from the Accident and Emergency department. Almost 80% of patients from the alcohol dependency group were admitted from either a ward in the hospital or accident and emergency.

5.3 Pre ICU admission

5.3.1 Days in hospital pre ICU admission

On initial analysis, there was a significant difference in the median number of days spent in hospital pre ICU admission between the three study groups ($p<0.001$) (Table 5.2). To ensure that the overall type one error rate remains at 0.05, a Bonferroni correction was applied. After this correction, there was a significant difference between the low risk group and the harmful/hazardous group ($p<0.001$) and between the alcohol dependency and harmful/hazardous group (1day vs. 0 days, $p= 0.01$).

5.4 Patient Demographics

5.4.1 Age

The mean age of patients admitted to the unit during the study period was 57 years (range, 19-90) (Table 5.2), with a significant difference in ages between the three study groups ($p<0.001$) (Figure 5.2).

Table 5.3: Admission Type: Originating Speciality

Admitting Speciality/ Admitting Area	Low Risk n=380 (65.6%)	Harmful/ Hazardous n=99 (17.0%)	Alcohol Dependency n=101 (17.4%)	*p* value
Admitting Speciality				**<0.001**
Respiratory Medicine	71 (19%)	15(15.2%)	14(13.8%)	
Gastroenterology	7 (2%)	1(1%)	23(22.8%)	
General Surgery	143 (38%)	26(26.3%)	22(21.8%)	
Burns and Plastics	32 (8%)	7(7%)	5(4.9%)	
Orthopaedics	10 (3%)	4(4%)	4(4%)	
Cardiology	28(7%)	5(5%)	3(3%)	
General Medicine	32 (8%)	31(31.3%)	19(18.8%)	
Gynaecology/Obstetrics	21 (5.5%)	0	0	
ENT	2 (0.5%)	0	0	
Neurology/Neurosurgical	32 (8%)	10(10.1%)	11(10.9%)	
Vascular	1 (0.3%)	0	0	
Urology	1 (0.3%)	0	0	
Area Admitted from				**<0.001**
Ward in hospital (GRI)	127 (33.4%)	26(26.3%)	41(40.6%)	
Accident and Emergency	89(23.4%)	45(45.4%)	39(38.6%)	
Theatre/Recovery	123(32.3%)	16(16.2%)	11(10.9%)	
External Transfer from other hospital	41(10.8%)	12(12.1%)	10(9.9%)	

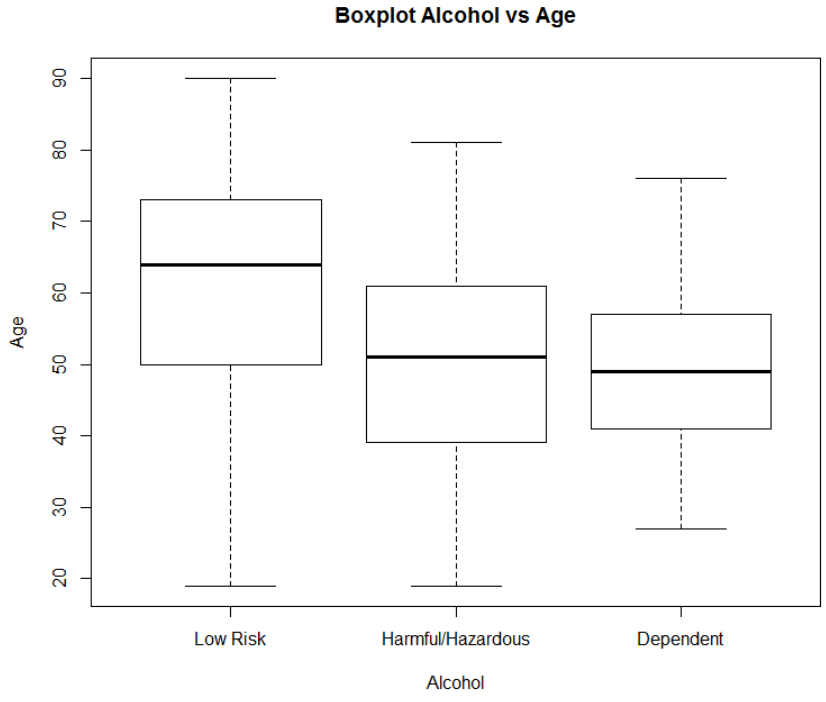

Figure 5.2: Boxplot of comparing mean age between the three alcohol groups

5.4.2 SIMD

Postcodes were collected from all patients on admission to the ICU. The SIMD decile for each patient was then calculated. Three hundred and seven (53%) patients were admitted from the two lowest deciles of society (Figure 5.3). However, those patients admitted with alcohol dependency had more than a twofold increased odds of being from the most deprived areas of society compared with those patients in the low risk group (OR 2.15; 95% CI 1.36-3.44, $p<0.001$).

5.4.3 Lifestyle variables

There was a significant difference in smoking and drug use between the three study groups. Only 30.1% of patients in the low risk group smoked compared with 52.5% in harmful/hazardous group and 60.4% in the dependent group ($p< 0.001$). Similarly, the number of patients admitted with a background of drug misuse (IV or other routes) was significantly higher in the alcohol related groups ($p< 0.001$). Furthermore, patients who were admitted with a background of drug misuse had more than fourfold increased odds of living in the two lowest deciles of the SIMD (OR 4.89; 95% CI 2.51-10.46; $p< 0.001$).

5.4.4 Liver cirrhosis

Seventy five patients were admitted to the ICU with a background of liver cirrhosis during the study period. Liver cirrhosis was more common in the alcohol dependent group (liver cirrhosis was present in 54.5% of admissions), compared with 6.1% of admissions in the harmful/hazardous group and 3.7% of admissions in the low risk group ($p<0.001$).

5.5 ICU admission

5.5.1 Severity of illness

APACHE II was utilised to determine severity of illness on admission to the ICU. There was no significant difference in mean APACHE II scores between the three groups ($p=0.22$) (Table 5.2). In addition, there was no significant difference in baseline Creatinine (Cr) and White Cell Count (WCC) levels on admission to the ICU between the three groups.

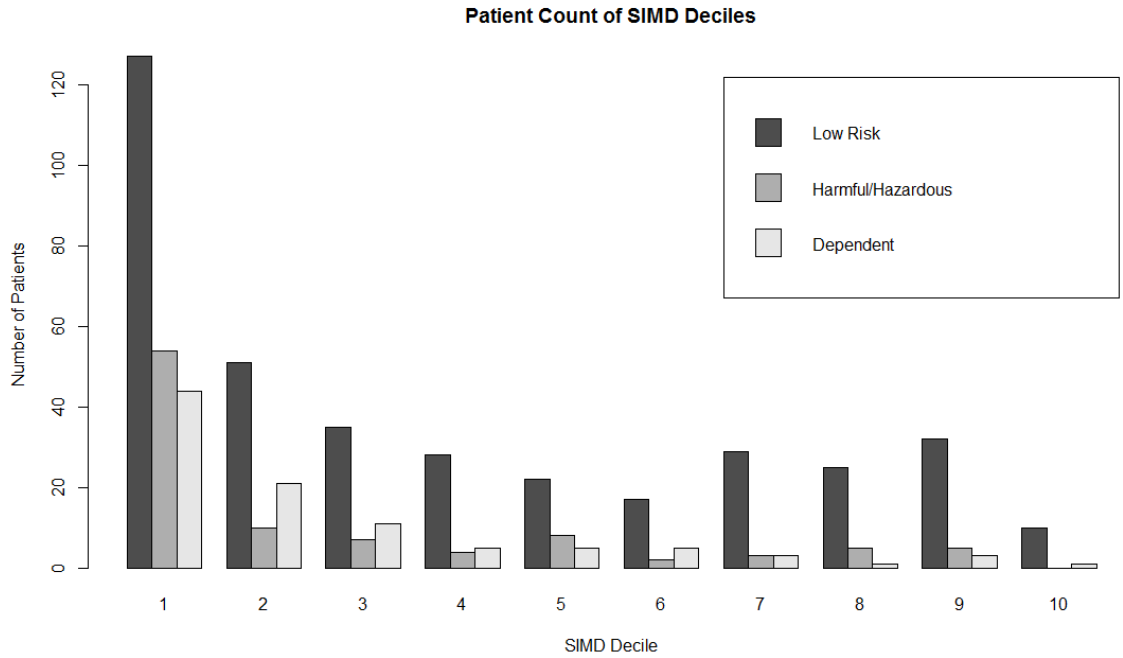

Figure 5.3: Bar Chart displaying distribution of SIMD deciles in the cohort

Table 5.4: Differences in baseline biochemical markers between the study groups

Variable	Low Risk n=380 (65.6%)	Harmful/Hazardous n=99(17.0%)	Alcohol Dependency n=101(17.4%)	*p* value
Urea, (µmmol), Median (IQR)	7.3 (4.7-12.8)	5.35 (3.65-8.85)	5.85(3.48-11.42)	**<0.001**
Cr, (µmol/l), Median (IQR)	75 (58-139.5)	68 (57-99.5)	73 (56.75-147.8)	0.26
WCC, ($X10^9$/l) Median (IQR)	12.7 (8.33-18.3)	11.95 (8.93-17.05)	12.75 (8.28-17.82)	0.89

However, there was a significant difference in Urea levels between the groups. Urea levels were significantly higher in the low risk group (Table 5.4).

5.5.2 Ventilation requirements

A total of 549 (94.7%) patients were ventilated during their ICU stay. Although there was a trend to a greater number of ventilation days in the alcohol dependency group, compared with the two other study groups, there was no significant difference (2 days vs. 2 days vs. 3 days, respectively; p=0.13) (Table 5.2).

5.5.3 Renal replacement therapy (RRT)

Ninety three (16%) patients required RRT during the study period and the median duration of RRT was 3 days (IQR, 1-7). There was no difference between the three study groups in the requirement for (p=0.19), or duration of RRT (p=0.59).

5.5.4 Vasopressor requirements

There was a significant difference in the requirement for, and the duration of vasopressor use between the three groups (Table 5.2). There was no significant difference in the need for vasopressor therapy between the low risk group and the alcohol dependency group. However, between the low risk and harmful/ hazardous group there was a significant difference in the need for vasopressor therapy (59.2% vs. 43.3%, p=0.02). There was also a significant difference between the harmful/hazardous and alcohol dependent groups in the need for vasopressors (43.3% vs. 58.4%, p=0.01).

The median number of days in which patients required vasopressor therapy was also significantly different between the three groups (Table 5.2). The difference within this test lies between the low risk and alcohol dependency group. Patients admitted with alcohol dependency required vasopressor support for significantly longer than those admitted in the low risk group (2 days vs. 3 days; p=0.04).

5.5.5 Septic Shock

During the study period, 139 (24%) patients had a diagnosis of septic shock at any point during their ICU stay, as defined by the NHS Greater Glasgow and Clyde Sepsis guidelines (Appendix VIII).

There was a significant difference between the three study groups with regards to the diagnosis of septic shock (Table 5.2). 20.5% of patients in the low risk group developed septic shock in comparison to 32.2% in the harmful/hazardous group and 28.7% in the alcohol dependent group. Those with an alcohol related admission (either the harmful/hazardous or alcohol dependent group) had an increased odds of developing septic shock during their ICU admission, compared with the low risk group (OR 1.67; 95% CI 1.13-2.47, p=0.01) in simple logistic regression. When adjusted for the presence of liver cirrhosis, the odds of developing septic shock increased in those with an alcohol related admission (OR 1.81; 95% CI 1.19-2.76, p=0.01).

5.5.6 Readmission to ICU

A total of 56 (9.7%) patients were readmitted to the ICU during the study period. There was no statistical difference in the number of readmissions in the alcohol dependent group compared to other two study groups (p=0.79) (Table 5.2).

5.5.7 ICU Length of Stay

The primary outcome measure of this study was to determine if there was a difference in ICU LOS between the three study groups. Median length of ICU stay was significantly different between the study groups (Figure 5.4). A log transformation was utilised to create this box plot to highlight the differences in ICU LOS which were being compared. However, after a Bonferroni correction had been applied, only the difference between the harmful/hazardous and alcohol dependency group remained significant (p=0.01).

Table 5.5: Difference in ICU LOS between the three study groups

	Low Risk	Harmful/Hazardous	Alcohol Dependent	*p* value
ICU Length of Stay, Days, Median (IQR)	3 (2-7)	3 (2-7)	5 (2-13)	**0.01**

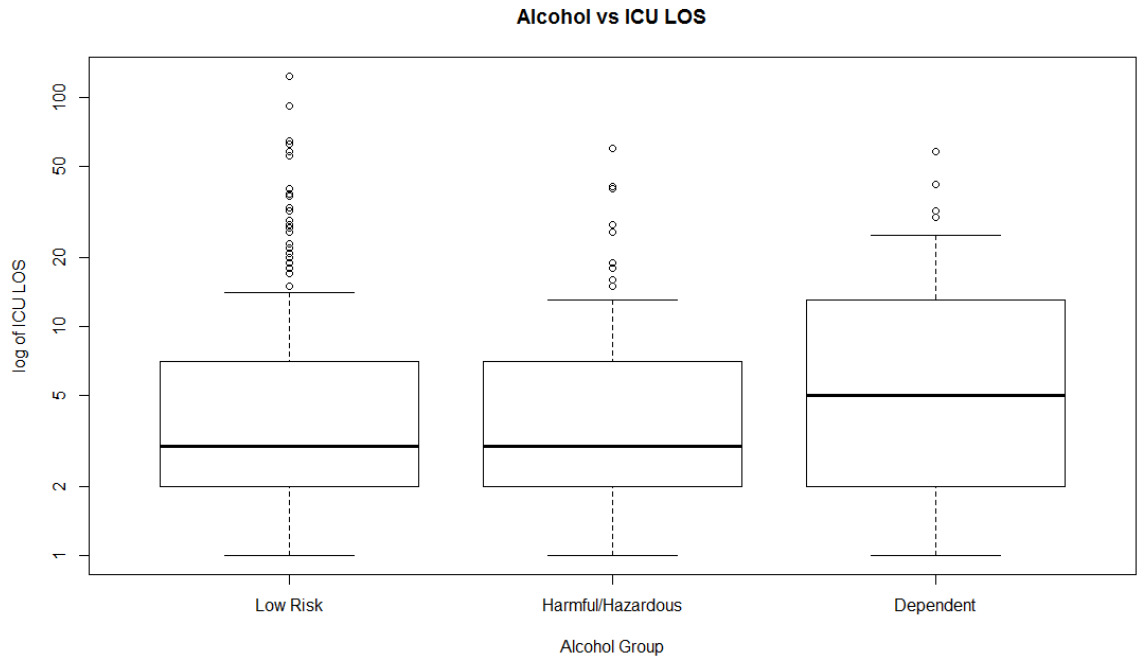

Figure 5.4: Boxplot comparing median ICU LOS between the three study groups

5.5.8 ICU Outcome

On unadjusted analysis there was no difference in ICU outcome between the three groups (p=0.15) (Table 5.2). As the primary aim of this study was to determine the impact of alcohol on the ICU stay, other lifestyle factors were adjusted for. After adjustment for all lifestyle factors that were significantly different between the groups (age, smoking and drug use, See Section 5.4.3), alcohol dependence was associated with more than a twofold increased odds of ICU mortality (OR 2.28; 95% CI 1.20-4.69, p=0.01) (Table 5.6).

Table 5.6: Risk adjusted association between alcohol dependence and ICU outcome

Variable	Adjusted Odds Ratio (95% CI)
Alcohol Dependence	2.28 (1.20-4.69)
Age	1.04 (1.03-1.06)
Smoking	1.24 (0.78-2.06)
Drug Use	0.44 (0.12-1.28)

There was no difference in ICU outcome for those patients with liver cirrhosis compared to those patients admitted without liver cirrhosis (p=0.19). A more detailed description of the outcomes of patients admitted with liver cirrhosis is presented in Chapter Six.

5.6 Post ICU: hospital stay

5.6.1 Days in hospital post ICU

The median number of days spent in hospital after ICU was 13 (IQR, 6-29), with a significant difference between the three study groups (p<0.001) (Table 5.2). The low risk group's median number of days in hospital post ICU discharge was double that of the harmful/hazardous group (14 days vs. 7days, p<0.001). Similarly, the alcohol dependent group had twice the length of stay in hospital post ICU compared with the harmful/hazardous group (14 days vs. 7 days, p=0.01).

5.6.2 Duration of total hospital stay

Total hospital stay was calculated from the date of admission to hospital to the date of discharge from hospital.

On unadjusted analysis there was a significant difference in total hospital stay between the three groups (p<0.001) (Table 5.2). Those in the dependent group stayed significantly longer than those in the harmful group (19 days vs. 9 days; p=0.01). Similarly, those in the low risk group stayed significantly longer than those in the harmful/hazardous group (18 days vs. 9 days, p=0.01). Although not significant, there was a longer total hospital stay for alcohol dependent patients (19 days vs. 18 days) compared to the low risk group.

5.6.3 Hospital outcome

On unadjusted analysis there was a significant difference in hospital outcome between the three study groups (p=0.04) (Table 5.2). However, after correction this difference did not remain significant. After adjustment for all lifestyle factors that were significantly different between the groups (age, smoking and drug use, See Section 5.4.3), alcohol dependence was associated with more than a twofold increased odds of hospital mortality (OR 2.43; 95% CI 1.28-4.62, p=0.004) (Table 5.7).

Table 5.7: Risk adjusted association between alcohol dependence and hospital outcome

Variable	Adjusted Odds Ratio (95% CI)
Alcohol Dependence	2.43 (1.28-4.62)
Age	1.04 (1.03-1.07)
Smoking	1.12 (0.71-1.77)
Drug Use	0.43 (0.13-1.66)

5.7 Discharge from hospital

5.7.1 Discharge destination

In this cohort of patients, 188 (32.4%) patients died during the hospital stay; 356 (61.4%) patients were discharged home; 28 (4.8%) patients were discharged to

long term care and 8 were lost to follow up (1.4%). There was no significant difference in discharge destination for patients (p=0.18).

5.7.2 Six month outcome

At six months post ICU discharge, mortality in this cohort of patients was 37%. With unadjusted analysis there was no difference in six month outcome between the three study groups (Table 5.2). However, after adjustment for deprivation category and age, alcohol dependence was associated with an almost two fold increased odds of mortality at six months post ICU discharge (HR 1.86; CI 1.30-2.70, p= 0.001) (Table 5.8, Figure 5.5). A log rank test on the Stratified Cox Proportional Hazards model demonstrated the influence the model had on survival (p<0.001).

Table 5.8: Risk adjusted association between alcohol dependence and six month outcome

Variable	Adjusted Hazard Ratio (95% CI)
Alcohol Dependence	1.86 (1.30-2.70)
Age	1.03 (1.02-1.05)
SIMD (deprived areas)	1.11 (0.84-1.45)

Additionally, the presence of liver cirrhosis was associated with an increased mortality six months after ICU discharge (HR 1.59; CI 1.12-2.26, p=0.01) (Figure 5.6). A log rank test was performed on the Stratified Cox Proportional Hazards model between the two groups which further demonstrated the impact that cirrhosis has on survival (p=0.01).

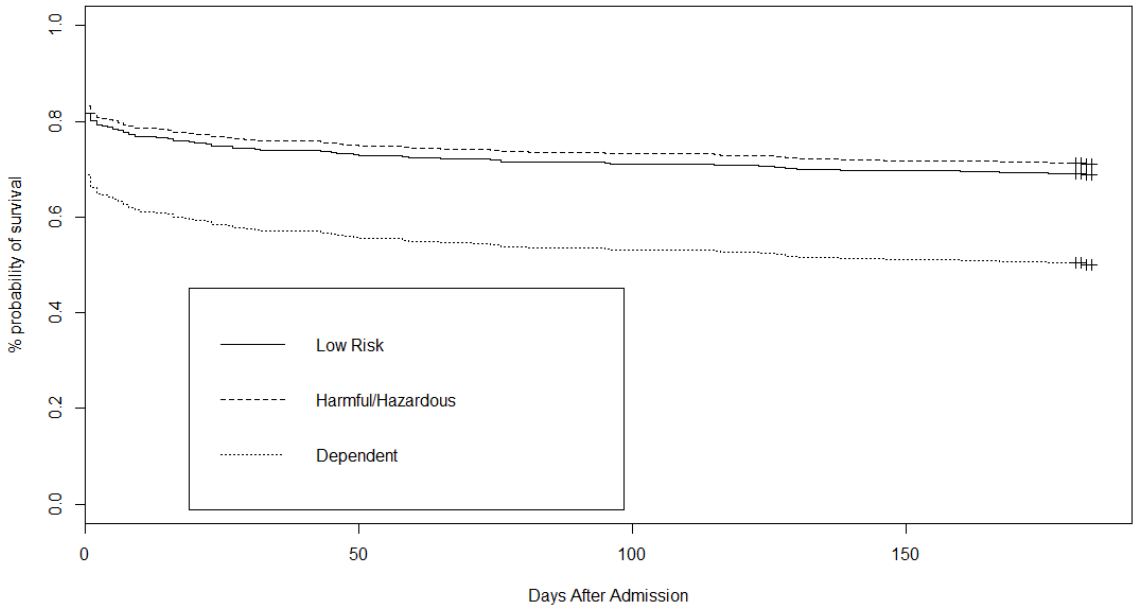

Figure 5.5: Kaplan Meier Curve for patients in the three different study groups at 6 months post ICU discharge (adjusted for the presence of deprivation and age).

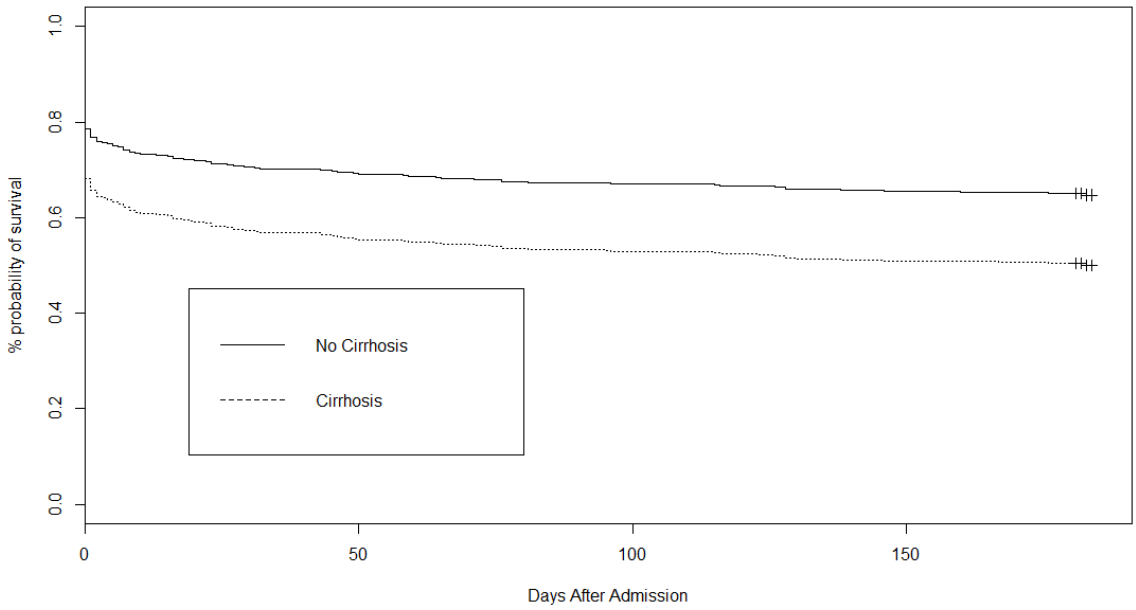

Figure 5.6: Kaplan Meier Curve for patients with and without liver cirrhosis at 6 months post ICU discharge.

5.8 Chapter Conclusion

This chapter presented the results from the 18 month observational cohort in this mixed methods study. These results demonstrate in our study cohort that:

- Patients with AUDs represent a high proportion of admissions to ICU (34.4%)

- Those patients admitted with a background of AUDs are more likely to smoke (p<0.001) and be current drug users (p<0.001). Patients admitted with AUDs are also more likely to live in the most deprived areas of society (p<0.001)

- ICU stay was significantly different between the three study groups, with those in the alcohol dependency group having a longer stay (p=0.01)

- Patients with alcohol dependency required vasopressors for a longer duration of time (p=0.05). Additionally, patients with an AUD had an almost two fold increased odd of developing septic shock during their ICU admission (OR 1.67, 95% CI 1.13-2.47, p=0.01)

- On adjusted analysis alcohol dependence was associated with more than a twofold increased odds of ICU mortality (OR 2.28; 95% CI 1.2-4.69, p=0.01)

- On adjusted analysis alcohol dependence was also associated with more than a two fold increase odds of hospital mortality (OR 2.43; 95% CI 1.28-4.62, p=0.004)

- Lastly, after adjustment for the presence deprivation and age, alcohol dependence was independently associated with mortality at six months post ICU discharge (HR 1.85; CI 1.27-2.70, p= 0.001).

The next chapter of this PhD thesis will explore the outcomes of patients admitted to the ICU with liver cirrhosis during the study period.

Chapter Six: Liver Cirrhosis in the ICU

6.1 Introduction

This chapter will briefly summarise the work carried out with two BSc Intercalated Medical Students (Critical Care and Peri-Operative Medicine), who were supervised by the PhD student in their research project. Phase One describes the work undertaken with the first BSc student, Phase Two describes work undertaken by a further BSc student. The work took place over two academic years and is complementary to the main body of work undertaken by the PhD student.

The primary research objective addressed in this chapter was:

- Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis.

Full information on each of these projects can be found in the relevant publications detailed in Appendix II.

6.2 Phase One

6.2.1 Background

A background to the public health issues related to liver disease and the challenges with cirrhosis related admissions to critical care is given in Section 2.3 and Section 2.11 of the literature review.

Scoring tools are now widely used throughout acute and critical care areas for a variety of purposes. For example, scoring tools are useful in stratifying severity of disease and helping to determine how, and in some cases, where a patient should be cared. Currently, there are no prognostic scoring tools validated to predict outcomes in patients with liver cirrhosis admitted to a general ICU setting. Although many hepatic scoring tools exist, they were designed for different purposes. For example, the Child-Turcotte Pugh (CTP) score was

designed to predict mortality following surgical treatment for oesophageal varices (Pugh et al 1973) and the UKELD was designed to assess patients for liver transplantation in the UK (Neuberger et al 2007).

The first phase of this study was undertaken over 12 months. This 12 month period represented the first 12 months of the 18 month observational study described in Chapter Five. This phase aimed to analyse the utility of prognostic scoring tools in patients admitted to the ICU with liver cirrhosis and to identify whether liver specific or general ICU scoring tools performed more accurately. It aimed to identify any independent predictors of mortality. In addition, the effect of incorporating lactate into a scoring tool was analysed and compared against the established scoring tools and for the first time, levels of deprivation and its impact on ICU outcome in this patient cohort was assessed.

6.2.2 Methods and materials: a short summary

Phase One was completed between June 2012 and June 2013. Eight scoring tools were analysed for the purpose of this initial study. Liver specific scoring tools analysed were: the Child Turcotte Pugh (CTP), the Model for End Stage Liver Disease (MELD), the UK End Stage Liver Disease model (UKELD), the Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) and the Glasgow Alcoholic Hepatitis Score (GAHS). APACHE II, the Acute Kidney Injury Network (AKIN) and the Sequential Organ Failure Assessment (SOFA) were also analysed. All scoring tools were collected on day one of ICU admission. In addition, the SOFA and the AKIN were calculated at 72 hours to investigate whether their prognostic accuracy differed after patients had received three days of intensive care treatment. Details of all scoring tools utilised for this study are shown in Appendix V.

The statistical analysis of this part of the study was performed using SPSS (SPSS Inc, IBM, Chicago, Illinois, USA, v.18). Univariate analysis was completed as described in Section 4.10.2. Multivariate, backward, stepwise logistic regression analysis was performed on selected significant variables to identify independent variables associated with ICU mortality. Scoring tools studied were compared using RO curves. The AUC provided the discriminative ability of the score (See Section 4.10.6).

6.2.3 Results

Sixty two patients were admitted with liver cirrhosis over the 12 month study period. Upon independent verification of cirrhosis, three patients were excluded as definitive evidence of cirrhosis could not be confirmed. Therefore, 59 patients were included in the analysis (for the criteria for liver cirrhosis See Section 4.7.1). Table 6.1 details the baseline characteristics of these patients and the factors which were associated with ICU outcome. Unlike the cohort utilised in Chapter Five, readmissions to the unit were included in this part of the study. This study aimed to explore baseline liver function on admission to the ICU, which may have differed on different admissions for the same patient.

A multivariate, backward stepwise logistic regression analysis was undertaken to identify any independent factors in determining ICU outcome. Prognostic scores were not included in this analysis as this study aimed to establish individual risk factors. Lactate (OR 1.69; 95% CI 1.15-2.49; p=0.01) and the presence of any grade of ascites (OR 5.91; 95% CI 1.35-25.88; p=0.02) on admission to the ICU were found to be independent predictors of ICU mortality.

ROC curves for all scores analysed are presented in Table 6.2. Of the established scoring tools, SOFA performed most accurately, with an AUC of 0.76 (95% CI 0.64-0.89), with CLIF-SOFA producing a similar AUC of 0.75 (95% CI 0.62 – 0.88). All the scores performed to a similar standard of between 0.70 and 0.76 (other than AKIN), although none reached the clinically useful AUC level of 0.8. Thirty seven patients remained in the ICU at 72 hours post admission. Of the 22 who were not in the unit at 72 hours, nine had died and 13 had been discharged to other areas. Both the SOFA and AKIN scores at 72 hours performed very similarly to the score at 0 hours.

Table 6.1: Predictive factors of ICU mortality by univariate analysis (Phase One)

Variable	All patients (n=59)	ICU Survivors (n=41)	ICU Non Survivors (n=18)	*p* value
Baseline Demographics				
Age (mean, range)	**51 ± 12**	50 ± 12	52 ± 12	0.45
Gender(male)	**40 (68%)**	27 (66%)	13 (72%)	0.43
Cause of Cirrhosis				
Alcohol	**47(80%)**	32(78%)	15(83%)	
Non Alcohol	**12(20%)**	9(22%)	3(17%)	0.47
SIMD				
Quintiles 1-2 (Most Deprived)	**48(81%)**	32(78%)	18(89%)	
Quintiles 3-5 (Non Deprived)	**11(19%)**	9(22%)	2(11%)	0.27
Reason for ICU admission				
Respiratory Failure		16(39%)	7(39%)	
Gastrointestinal Bleed		6(15%)	4(22%)	
Encephalopathy		4(10%)	1(5%)	
Sepsis		2(5%)	3(17%)	
Other		13(31%)	3(17%)	0.44
ICU admission				
ICU LOS	**5(42)**	5(32)	4(42)	0.17
Number of organs requiring support				
0	**1(2%)**	0(0%)	1(5%)	
1	**17(28%)**	16(39%)	1(5%)	
2	**30(51%)**	20(48%)	10(56%)	
3	**11(19%)**	5(12%)	6(34%)	**0.02**
Prognostic scores on ICU admission				
APACHE II (Mean, range)	**22(16-27)**	19(15-24)	23(21-33)	**0.01**
CTP (Median, IQR))	**9(7-12)**	9(7-11)	11.5(9-13)	**0.01**
MELD (Median, IQR)	**18 (8-23)**	13(7-21)	21(19-32)	**0.01**
AKIN (Median, IQR))	**0 (0-2)**	0 (0-2)	0 (0-2)	0.79
UKELD (Median, IQR)	**51(48-57)**	51(47-53)	58(50-62)	**0.01**
GAHS (Median, IQR)	**7(6-9)**	7(6-9)	8.5(7-10)	0.01
SOFA (Median, IQR)	**10(8-12)**	9(6-11)	11(10-14)	**0.01**
CLIF- SOFA (Median, IQR)	**10 (10-12)**	9(9-11)	11.5(10-14)	**0.01**
Biological parameters on admission				
Sodium (mmol/l, mean, range)	**137 (120-150)**	137 (120-150)	136 (128-147)	0.53
Creatinine (µmol/l, mean, range)	**124 (35-465)**	112 (35-389)	152 (49-465)	0.12
Bilirubin (µmol/l, mean, range)	**91(3-455)**	67 (3-390)	148 (5-455)	0.01
PT Ratio (mean, range)	**1.7(0.6-4.7)**	1.6 (1-3.6)	2.0 (0.6-4.7)	0.02
Lactate (mmol/l, mean, range)	**2.9 (0.6-20)**	1.8 (0.6-8.1)	5.5 (1-20)	**<0.001**
Urea (µmmol, mean, range)	**10.1 (1.3-46.3)**	10.1(1.3-46.3)	10.5(2.5-25.5)	0.85
WCC (x10/l, mean, range)	**14(0.8-41.7)**	13.7(0.8-36.4)	14.8(1.5-41.7)	0.64
Platelets (x10/l, mean, range)	**130(6-487)**	143(35-487)	102 (6-294)	0.09
Albumin (g/l, mean, range)	**20(8-37)**	20(8-37)	20(10-33)	0.93
Potassium (mmol/l, mean, range)	**4.2(2.8-6.6)**	4.1(2.8-6.6)	4.3(2.9-5.9)	0.48
Pa02:Fi02 ratio	**25.9(5.1-108)**	27.4(6.4-108)	23.1(5.1-77)	0.44
Clinical Parameters				
Encephalopathy	**19(32%)**	11(27%)	8(44%)	0.15
Ascites (Any Grade)	**26(44%)**	14(34%)	12(67%)	**0.02**
ICU Mortality	**28(48%)**			
Hospital Mortality	**18(31%)**			

List of Abbreviations

CTP: Child-Turcotte-Pugh Score; MELD: Model for End Stage Liver Disease; UKELD: Model for End Stage Liver Disease ; GAHS: Glasgow Alcoholic Hepatitis Score; APACHE II: Acute Physiology and Chronic Health Evaluation; AKIN: Acute Kidney Injury Network Score; SOFA: Sequential Organ Failure Assessment; CLIF-SOFA: Chronic Liver Failure Sequential Organ Failure Assessment; SIMD: Scottish Index of Multiple Deprivation; WCC: White Cell Count; Pa02: Arterial partial pressure of oxygen; Fi02: Fraction of inspired oxygen

6.2.4 The incorporation of lactate into a scoring tool

This study adds to the accumulating body of evidence that serum arterial lactate is an independent predictor of mortality (Burroughs, Garcovich, Vemala et al 2010). Therefore, the incorporation of lactate into existing scoring models was analysed. The CTP score was chosen as the model in which lactate would be incorporated because of its relative simplicity and ease of calculation. It can be calculated at the bedside without the need for a calculator or a computer programme, unlike MELD, UKELD, APACHE II and SOFA / CLIF – SOFA.

The two alterations to the CTP score created, termed CTP – L and CTP + L are presented in Table 6.3. The CTP – L involves the insertion of a new category: Lactate. As with the previous five categories a score ranging from 1 to 3 was assigned depending on the level of derangement. An admission lactate of < 2 mmol/l gave a score of one, of 2.0 – 4.0 mmol/l gave a score of 2, and > 4.1 mmol/l gave a score of three. The minimum available CTP-L score is 6, with the maximum being 24. These three ranges were chosen based on commonly reported values in the intensive care settings (Marino 2013).

The second alteration was termed the CTP + Lactate score (CTP + L). In this, the numerical CTP score for a patient was generated (with no defined units) and simply added to the ICU admission serum lactate (mmol/l). All measurement units were removed and the new score was produced. The CTP + L is therefore continuous, with the minimum score possible being 5, and the maximum being limited by the physiological range of serum lactate.

The AUC for the two CTP alterations to incorporate lactate (CTP-L and CTP + L) are also shown in Table 6.2. The incorporation of lactate improved the prognostic accuracies of the scores, with the CTP-L producing an AUC of 0.78 (95% CI 0.64 – 0.91). The CTP + L improved further and produced the highest AUC of any score, with an AUC of 0.86 (95% CI 0.75 – 0.97). The ROC curves of the CTP, CTP-L and the CTP+L are presented in Figure 6.1.

Table 6.2: Receiver Operating Characteristic curve analysis (Phase One)

Cut point and associated sensitivity and specificity determined by the Youden's index obtained from Receiver Operating Characteristic curves.					
Scoring Tool	**AUC**	**95% CI**	**Cut-Point**	**Sensitivity**	**Specificity**
CTP	0.7	0.55-0.85	9.5	0.61	0.62
GAHS	0.73	0.59-0.87	7.5	0.67	0.66
MELD	0.74	0.67-0.61	18	0.83	0.67
UKELD	0.7	0.55-0.85	54	0.61	0.97
APACHE II	0.72	0.58-0.85	22	0.61	0.68
SOFA	0.76	0.64-0.89	10.5	0.72	0.69
AKIN	0.52	0.35-0.69	2.5	0.22	0.93
CLIF-SOFA	0.75	0.62-0.88	10.5	0.83	0.59
72 Hour SOFA	0.74	0.57-0.90	10.5	0.78	0.68
72 Hour AKIN	0.52	0.30-0.75	2.5	0.22	0.85
CTP-L	0.78	0.64-0.91	11.5	0.72	0.68
CTP+L	0.86	0.75-0.97	14	0.78	0.90

Table 6.3: Methodology for calculating the CTP-L and CTP + L scores (Emerson, McPeake, O'Neill et al 2014)

The Child-Turcotte-Pugh - Lactate score (CTP - L)			
Variable	1 point	2 points	3 points
Bilirubin (µmol/l)	< 34	34-50	> 50
Albumin (g/l)	> 35	28 -35	< 28
INR (or PT ratio)	< 1.7	1.71 -2.30	>2.3
Lactate (mmol/l)	**< 2.0**	**2.1 -4.0**	**> 4.1**
Ascites	None	Mild	Severe
Hepatic Encephalopathy	None	Grade I / II	Grade III / IV
The Child-Turcotte-Pugh + Lactate score (CTP+L)			
Variable	1 point	2 points	3 points
Bilirubin (µmol/l)	< 34	34-50	> 50
Albumin (g/l)	> 35	28 -35	< 28
INR (or PT ratio)	< 1.7	1.71 -2.30	>2.3
Ascites	None	Mild	Severe
Hepatic Encephalopathy	None	Grade I / II	Grade III / IV
Serum arterial lactate	**Addition to overall score gained from above categories**		
The overall CTP score is calculated according to the five criteria above. THE CTP + L score is calculated via the addition to this score of the serum arterial lactate level **in mmol/l.** Once done, any units associated are removed, to give an overall, continuous score.			

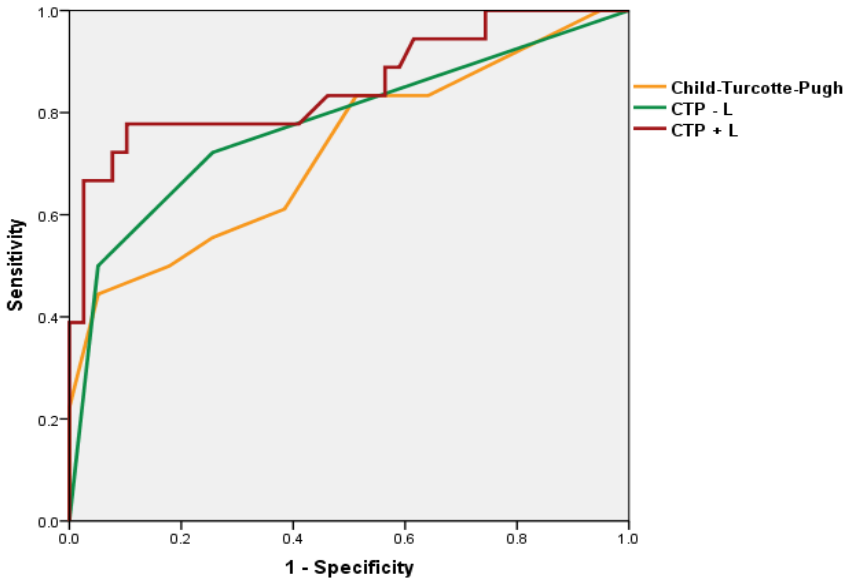

Figure 6.1: The Receiver Operator Characteristics curves of the CTP, CTP-L and CTP + L scores (Phase One)

6.3 Phase One: summary

This section has detailed the first phase of the study which aimed to investigate the utility of prognostic scoring tools in critically ill patients admitted to ICU with a background of liver cirrhosis.

From the existing scoring tools, the SOFA score performed most accurately, with an AUC of 0.76. From the liver specific scoring tools the MELD performed most accurately in this cohort (AUC 0.74). This phase demonstrated that lactate was an independent predictor of ICU outcome. In response to this, a novel scoring tool which included lactate was created. The aim of the next phase of this study was to externally validate this new scoring tool.

6.4 Phase Two

6.4.1 Background

The purpose of the second phase of this part of the study was to validate the new scoring tools created (CTP+L and CTP-L). To achieve this, the data collection period for GRI was increased from 12 months to 18 months (the same 18 months detailed in Chapter Five), and access to a second cohort of patients from an external centre was obtained.

The second cohort of 115 ICU patients was obtained from St Thomas' Hospital and St Georges Hospital in London. These patients were recruited from a demographic study of cirrhotic patients within a general ICU population (Thomson et al 2010).

6.4.2 Methods and materials

The same scoring tools which were completed in Phase One were also completed in this Phase Two study. Liver specific scoring tools were: CTP; MELD; UKELD; CLIF-SOFA and GAHS. In addition, during the second phase of this study a large scale study documenting the use and utility of The Royal Free Hospital (RFH) score was published (Theocharldou, Pieri, Mohammad et al 2014). As a result, we sought to undertake an external validation of this tool in a general ICU population and compare its prognostic accuracy with the other available tools. APACHE II and SOFA were also analysed. AKIN was not analysed by Thomson et al (2010) in their analysis. Further, the AKIN was the worst performing tool in Phase One. Therefore AKIN was not analysed during the second phase of the study. All scoring tools were collected at day one of ICU admission.

Of the two new scoring tools created in Phase One, CTP+L consistently performed more accurately. Therefore, CTP+L was the only tool analysed in this phase of the study (See Table 6.3).

Statistical Analysis was carried out using the SPSS (SPSS Inc, IBM, Chicago, Illinois, USA, version 21) and RStudio version 0.98.493 (R Foundation for statistical computing, Vienna, Austria).

6.4.3 Results

Eighty four patients from Glasgow and 115 patients from London were admitted with cirrhosis during the two study periods (Glasgow: June 2012-December 2013, London: October 2007-July 2009). However, during analysis 5 patients from Glasgow and 1 patient from London were excluded as they had missing values which were required for scoring tool completion. Therefore, 79 patients from Glasgow and 114 patients from London were included in the final analysis. Table 6.4 and 6.5 detail the characteristics of the patients admitted from each of the different cohorts.

Univariate analysis of the Glasgow data set demonstrated that significant predictors of mortality were lactate (p<0.001), bilirubin (p=0.01) and PT Ratio (p=0.01). Similarly, the London data set established that PT Ratio (p<0.001), lactate (p<0.001), Pa02/Fi02 Ratio (p=0.01) bilirubin (p=0.03) and the presence of ascites (p=0.03) were significant predictors of mortality.

6.4.4 Validation of CTP+L

All scoring tools were recalculated from the raw data on both cohorts. CTP+L continued to perform most accurately in the Glasgow data set (AUC 0.83). A comparison of the scoring tools for the Glasgow data set can be seen in Table 6.6.

In the London data set, the RFH score performed most accurately (AUC 0.76) with the CTP+L score performing to a similar level (AUC 0.75). No scoring tool reached the clinically useful level of AUC of greater than 0.8 in this data set (Table 6.7).

When creating one large data set with the two cohorts (to give a final cohort of 199 patients), the RFH and the CTP+L performed most accurately. The CTP+L obtained an AUC of 0.79 and the RFH an AUC of 0.78. There was no statistical difference found between the ROC curves (p=0.7) (Figure 6.2).

Table 6.4: Glasgow Cohort: Patient Characteristics and Univariate analysis (Phase Two)

GLASGOW COHORT

Variable	All patients (n=84)	ICU Survivors (n=59)	ICU Non Survivors (n=25)	*p* value
Baseline Demographics				
Age (mean, range)	**50.2(29-80)**	49.7(29-80)	51.4 (32-72)	0.55
Gender (male, number)	**59 (70.2%)**	41(69.4%)	18(72.0%)	1.0
Cause of Cirrhosis				
Alcohol	**70(83%)**	48(81%)	22(88%)	
Non Alcohol	**14(17%)**	11(19%)	3(12%)	0.54
SIMD				
Quintiles 1-2 (Most Deprived)	**68(81%)**	46(78%)	18(88%)	
Quintiles 3-5 (Non Deprived)	**16(19%)**	13(22%)	2(12%)	0.44
ICU admission				
Prognostic scores on ICU admission				
APACHE II (mean, range)	**23.5(2-47)**	21.5 (2-39)	28.3(14-47)	**<0.001**
CTP (median, IQR)	**9(7-11)**	9(7-10.5)	11(9-13)	**0.02**
MELD (mean, range)	**18.9 (6-43)**	16.7(6-43)	24.1(9-34)	**<0.001**
UKELD(mean, range)	**52.6(39-73)**	51(39-73)	56.3(46-65)	**<0.001**
GAHS (mean, range)	**7.7(5-12)**	7.4(5-12)	8.4(6-12)	**0.01**
SOFA (mean, range)	**9.7(3-20)**	8.7(3-15)	12(4-20)	**<0.001**
CLIF- SOFA (mean, range)	**9 (0-16)**	8.2(0-16)	11.1(7-16)	**<0.001**
RFH (median, IQR)	**-1.46(-2.41- -0.34)**	-1.88(-2.61- -0.92)	-0.31(-1.21- -2.82)	**<0.001**
CTP+Lactate (median, IQR)	**11(9-14.25)**	10(7-12.5)	15(13-19)	**<0.001**
Biological parameters on admission				
Sodium (mmol/l, mean, range)	**136.4(113-151**	136.7(113-151)	135.7(128-147)	0.52
Creatinine (µmol/l, median, IQR)	**81.5(57.8-158.8)**	75(57.5-138.5)	144(69-199)	0.06
Bilirubin (µmol/l, median, IQR)	**45.5(22.3-106.8)**	33(18-76.5)	71(40-182)	**0.01**
PT Ratio (median, IQR)	**1.5(1.2-2)**	1.5(1.2-1.8)	1.8(1.5-2.5)	**0.01**
Lactate (mmol/l, median, IQR)	**1.9(1.3-2.7)**	1.7(1.2-2.2)	4.1(2-8)	**<0.001**
Urea (µmmol, median, IQR)	**8.1(4.1-12.7)**	7.7(4.4-12.1)	9.2(4-14.5)	0.44
WCC (X10^9/L, mean, range)	**13.6(0.8-41.7)**	13.6 (0.8-36.4)	13.6(1.5-41.7)	0.99
Platelets (x10^9/l, mean, range)	**138.5(6-487)**	145.4(25-487)	122.2(6-371)	0.31
Albumin (g/l, mean, range)	**21.8(8-79)**	22.6(8-79)	19.8(10-33)	0.14
Potassium (mmol/l, mean, range)	**4.1(2.6-7)**	4(2.6-7)	4.3(2.9-5.9)	0.27
Pa02:Fi02 ratio(median, range)	**22.9(11.8-37.1)**	27.3(12.2-38.4)	16(11.7-25.3)	0.16
Clinical Parameters				
Ascites (Any Grade)	**35(42%)**	22(37%)	13(52%)	0.31
Encephalopathy (Any Grade)	**29(35%)**	19(32%)	10(40%)	0.66

Table 6.5: London cohort: Patient Characteristics and Univariate analysis (Phase Two)

	LONDON COHORT			
Variable	**All Patients (n=115)**	**ICU Survivor (n=72)**	**ICU Non-Survivor (n=43)**	***p* value**
Baseline Demographics				
Age (mean, range)	**50.9 (22-82)**	50 (28-71)	52.44 (22-82)	0.3
Gender (male, number)	**78 (67.8%**	51 (70.8%)	27 (62.8%)	0.49
SIMD*				
Quintiles 1-2 (Most Deprived)	**N/A**	N/A	N/A	
Quintiles 3-5 (Non Deprived)	**N/A**	N/A	N/A	
ICU Admission				
Prognostic Scores on ICU Admission				
APACHE II(mean, range)	**16.9 (5-29)**	15.4 (5-27)	19.4 (9-29)	**<0.001**
CTP (median, IQR)	**10 (8-11)**	9 (8-11)	11 (9.5-11)	**<0.001**
MELD (mean, range)	**19.2 (6-47)**	17.3 (6-47)	22.5 (6-47)	**0.003**
UKELD (mean, range)	**52 (39-75)**	50.1 (39-75)	55.1 (42-75)	**<0.001**
GAHS (mean, range)	**7 (7-8.5)**	7 (6-8)	8 (7-9)	**<0.001**
SOFA (mean, range)	**6.4 (0-14)**	5.4 (0-13)	8 (2-14)	**<0.001**
CLIF-SOFA (mean, range)	**10 (3-18)**	8.9(3-18)	11.9 (6-17)	**<0.001**
RFH (median, IQR)	**-0.61 (-3.27-1.39)**	-1.57 (-3.78-0.007)	1.29 (-0.57-2.58)	**<0.001**
CTP +Lactate (median, IQR)	**13 (10-16)**	11.5 (9-14)	15 (13-18)	**<0.001**
Biological Parameters on admission				
Sodium (mmol/l, mean, range)	**137 (133-142)**	138 (133.8-142)	137 (114-148)	0.34
Creatinine (µmol/l, median, IQR)	**86 (56-164.5)**	67.5 (52-135.2)	112 (75.5-180)	**0.05**
Bilirubin (µmol/l, median, IQR)	**40 (16-102)**	28 (15-82.3)	60.0 (23-197.5)	**0.03**
PT Ratio (median, IQR)	**1.5 (0.9-2)**	1.4 (1.2-1.7)	1.9 (15.-2.2)	**<0.001**
Lactate (mmol/l, median, IQR)	**2.4(1.5-4.8)**	1.9 (1.3-3.1)	3.9 (2.2-6.8)	**<0.001**
Urea (µmmol, median, IQR)	**7.5 (4.3-14.5)**	6.7 (4.2-11.6)	10.3 (4.7-15.2)	0.09
WCC (x10/l, mean, range)	**12.5 (0.7-35.5)**	12.7 (18.-35.5)	12.1 (0.7-31.4)	0.68
Platelets (x10/l, mean, range)	**120 (67-215)**	122 (80-235)	116 (46.5-174)	0.11
Albumin (g/l, mean, range)	**21.0 (17-27)**	22 (18-27.5)	19 (16.5-26.5)	0.16
Potassium (mmol/l, mean, range)	**4.2 (1.9-6.8)**	4.1 (1.9-6.8)	4.3 (1.9-6.4)	0.17
Pa02: Fi02 ratio (median, range)	**30.2 (6-77)**	34 (7-77)	23.9 (6-59)	**0.01**
Clinical Parameters				
Ascites (any grade, number)	**48(41.7%)**	24 (33.3%)	24 (55.8%)	**0.03**
Encephalopathy**	**N/A**	N/A	N/A	N/A

SIMD only available within a Scottish context
****Pre intubation encephalopathy scores not collected in London cohort. All patients were given an encephalopathy score of 2 for the purposes of the scoring tools (See Section 6.3.7)**

Table 6.6: Glasgow Cohort: Receiver Operating Characteristic curve analysis (PhaseTwo)

Cut point and associated sensitivity and specificity determined by the Youden's index obtained from Receiver Operating Characteristic curves.					
Scoring Tool	**AUC**	**95% CI**	**Cut-Point**	**Sensitivity**	**Specificity**
CTP+L	0.83	0.73-0.93	13.5	0.72	0.83
RFH	0.81	0.72-0.91	-1.4	0.84	0.66
MELD	0.78	0.67-0.88	16.5	0.88	0.59
CLIF-SOFA	0.77	0.67-0.87	8.5	0.92	0.54
SOFA	0.75	0.64-0.87	10.5	0.68	0.72
APACHE II	0.73	0.61-0.85	25.5	0.60	0.76
UKELD	0.72	0.60-0.88	54.5	0.68	0.81
GAHS	0.68	0.56-0.81	8.5	0.44	0.83
CTP	0.68	0.56-0.81	10.5	0.52	0.75

Table 6.7: London Cohort: Receiver Operating Characteristic curve analysis (Phase Two)

Cut point and associated sensitivity and specificity determined by the Youden's index obtained from Receiver Operating Characteristic curves.					
Scoring Tool	**AUC**	**95% CI**	**Cut-Point**	**Sensitivity**	**Specificity**
RFH	0.77	0.68-0.86	0.14	0.72	0.75
CTP+L	0.75	0.66-0.84	12.5	0.79	0.62
CLIF-SOFA	0.75	0.66-0.84	10.5	0.77	0.67
SOFA	0.72	0.62-0.81	5.5	0.77	0.61
APACHE II	0.71	0.61-0.80	14.5	0.81	0.50
GAHS	0.70	0.61-0.80	7.5	0.67	0.68
UKELD	0.70	0.60-0.79	49.5	0.79	0.58
MELD	0.69	0.59-0.79	16.5	0.81	0.56
CTP	0.68	0.59-0.78	8.5	0.88	0.47

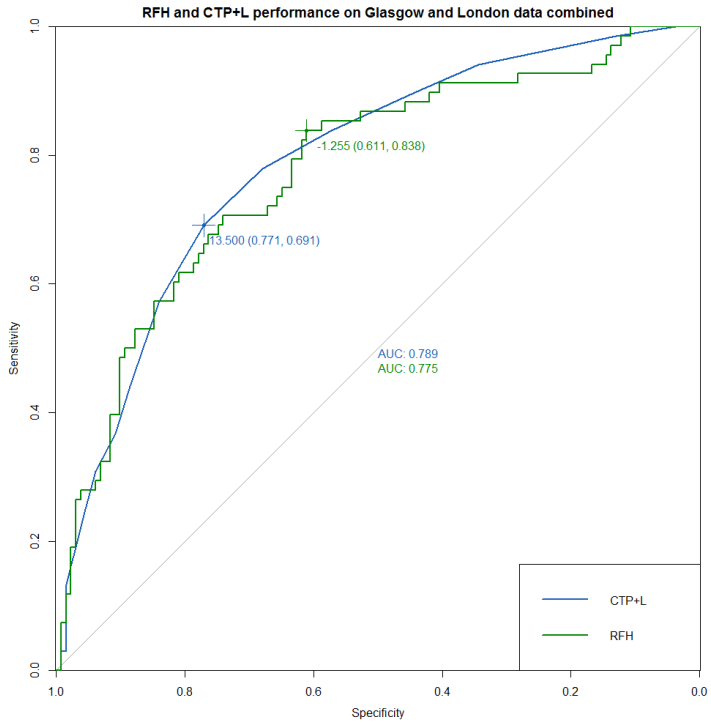

Figure 6.2: Receiver Operator Characteristics curves of the CTP + L and the RFH scores (Phase Two)

6.5 Chapter Conclusion

This chapter presented the outcomes of patients admitted to the ICU with liver cirrhosis during the study period. Further, it evaluated the impact of a wide ranging number and types of scoring tools in predicting outcome from ICU in two different cohorts of patients. These results suggest:

- Those patients with cirrhosis admitted to the general ICU setting have a lower severity of liver cirrhosis and have a better outcome than has been documented in speciality liver centre ICUs

- Of the newly created and established scoring tools, the RFH and CLIF-SOFA consistently perform well

- Despite recent evidence promoting the use of AKIN as a predictive scoring tool for this group of patients, it performed poorly as a predictive scoring tool in this cohort (AUC 0.52)

- Lactate was consistently an independent predictor of ICU outcome

- A novel scoring tool was created: CTP+L. This tool, which can be easily calculated at a patient bed space, may be a useful aid for critical care practitioners in decision making.

The next chapter of this thesis documents the findings from the qualitative arm of this mixed methods study.

Chapter Seven: Findings

'Whether the chicken crossed the road or the road moved beneath the chicken depends on your frame of reference'.

Albert Einstein

7.1 Introduction

This chapter presents the findings from the qualitative section of this mixed methods study. Two research objectives were addressed in this chapter:

- Examine the impact of critical care on future behaviour with regards to alcohol intake

- Explore patterns of recovery for patients with and without alcohol use disorders.

In keeping with the analytical framework utilised, the findings are accompanied with quotes from participants throughout. To ensure the principles of IPA are adhered to, this section will also aim to give detailed analytical interpretations of these extracts (Smith et al 2009). A full discussion of these interpretations is presented in Chapter Eight.

7.2 Characteristics of the participants

A total of 72 different participants were invited to take part in this section of the study. The responses to invitations sent are shown in Figure 7.1. Originally the research team had intended to recruit 24 participants (including one pilot interview). However, data saturation was met after 20 interviews. Two further interviews were completed to ensure no new themes were generated. In summary, one pilot interview and 21 interviews were undertaken.

An overview of the interviews and the baseline characteristics of interview participants are presented in Tables 7.1 and 7.2.

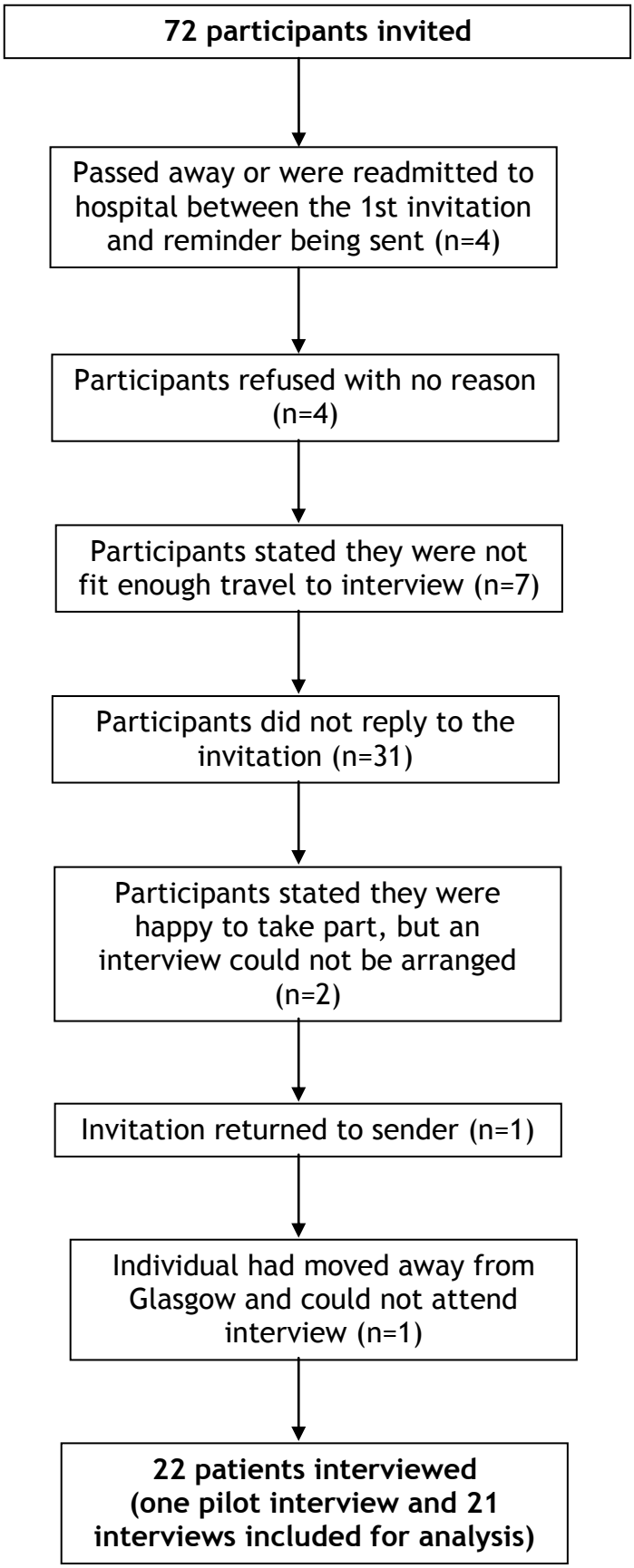

Figure 7.1: Responses to invitations sent for in depth semi structured interviews

Table 7.1: Clinical characteristics of interview participants

Participant Number	Age	Gender	Reason for ICU Admission	Alcohol Group	APACHE II	ICU LOS	SIMD (Decile)
PILOT	73	F	Pneumonia	Low Risk	14	4	2
P1	70	M	Alcohol related pancreatitis	Harmful/ Hazardous	17	3*	5
P2	34	F	Alcohol related pancreatitis	Alcohol Dependence	14	12	1
P3	52	M	Bowel obstruction	Low Risk	22	5	9
P4	23	F	Out of hospital Cardiac arrest	Low Risk	29	3	2
P5	57	M	Pneumonia	Alcohol Dependence	19	11	1
P6	57	M	GI tract sepsis (Salmonella)	Alcohol Dependence	31	58	4
P7	31	M	Serious Assault	Harmful/Hazardous	20	26 (Two readmissions)	1
P8	68	M	Necrotizing Fasciitis	Low Risk	30	6	9
P9	37	F	Urinary Tract Infection/Sepsis	Alcohol Dependence	29	5	1
P10	63	F	Pneumonia	Low Risk	16	8	2
P11	54	M	Pneumonia	Harmful/Hazardous Use	32	60	1
P12	52	F	Pneumonia	Low Risk	26	37	1
P13	63	F	Status Epilepticus	Low Risk	19	3	8
P14	60	M	Variceal Bleed	Alcohol Dependence	23	3	5
P15	22	M	Burn Injury	Harmful/Hazardous	14	6	4
P16	59	M	Accidental Overdose	Harmful/Hazardous	30	4	1
P17	38	M	Perforated DU	Alcohol Dependence	9	9	1
P18	50	M	Metabolic disturbance	Alcohol Dependence	32	4	2
P19	40	M	ARDS	Alcohol Dependence	33	9 (One readmission)	1
P20	60	M	Pneumonia	Alcohol Dependence	14	11	3
P21	39	M	Out of Hospital Cardiac Arrest	Harmful/Hazardous	23	4	5

***P1 was a tertiary referral for pancreatic care. He had been in another ICU for three weeks before admission to the ICU in Glasgow Royal Infirmary.**

Table 7.2: Overview of in depth semi structured interviews

Gender (% Male)	71.4%
Age (Mean, Range)	49 (23-73)
APACHE (Mean, Range)	22.5 (9-33)
Length of Interview in minutes (Mean, Range)	41(17-90)
ICU LOS (Median, IQR)	6(4-11.25)

7.3 Presentation of findings

Four themes were generated from the findings of the interview data. These are presented alongside the super-ordinate themes in Table 7.3.

When undertaking and analysing the findings from the interviews, it became apparent that participants from the three different study groups had similar problems and experiences during their recovery from ICU. However, for those admitted to ICU with an AUD, there was a significant interplay between alcohol and their recovery from critical illness.

To simplify the presentation of the findings and to demonstrate the research aims and objectives had been clearly met, the first three themes with their corresponding super-ordinate themes represent the entire cohort interviewed. Specific differences between the three study groups are highlighted. The final theme *'recovery and support for alcohol related admissions'* specifically explores the interplay with and the impact of, AUDs on recovery from critical illness. The findings presented in relation to alcohol relate to both the harmful/hazardous study group and the alcohol dependency study group, unless otherwise stated.

Although each super-ordinate theme will be presented discretely within the following chapter, how the themes and super-ordinate themes relate to one another will also be discussed.

Table 7.3: Themes and super-ordinate themes emerging from the interviews

Themes	Super-ordinate themes
Impact on Activities of Daily Living	• Psychological problems • Physical Problems • Discharge Planning
Impact of Psychological Resilience on Recovery	• Loss of control • Maintenance of self-efficacy • Ownership of the journey
Social Support and Cohesion	• The role of positive and negative social support • Social isolation (participants) • Social isolation and strain (families and carers)
Recovery and support for alcohol related admissions	• Interaction with healthcare professionals • Appropriate and timely rehabilitation • Impact of ICU on alcohol related behaviours

7.4 Impact on Activities of Daily Living

7.4.1 Psychological problems

It was clear from the interviews that participants suffered many complex psychological problems after discharge from critical care. These problems appeared to be similar across the three study groups. One problem which many participants described was low mood. P4 reflected on her mood after discharge:

> *P4: 'Some days it's a lot harder than others. Some days I'm just like, I can't be bothered, I just want to be better and just be getting on with things...And then other days I wake up and think, I'm never going to go anywhere because I will be too scared.'*

P12 also described her experience of low mood and the impact this had on her daily activities:

> *P12: 'I want to go out and I'll go to bed that night and I'll say I'm going out tha morra and I'm definitely going out the morra, and then the morra will come and it's just I'm in a mood. I just go in a mood and that's it. I just want to go upstairs and lock myself away...I've fallen out with everybody, it's just, I can't be annoyed with anybody.'*

Low mood and irritability not only had an effect of the participants; participants described how this change also had a significant effect on their relationships with loved ones. P11 explained the effect that his low mood had on his relationship with his partner:

> *P11: 'She says that, things will never go back, 'cause your mood swings are too terrible'. She says 'far, far, too terrible'.'*

Another key psychological problem which participants described was increased anxiety about adapting to changes in health and adjusting to life after critical care. Participants also discussed changes in anxiety at different points in their journey. For example, P3 discussed his time in an isolation room in the high dependency area:

> *P3: 'I just found it hard to sort of...I would pick up something to read and then your mind would just seem to go...AWOL and you would just start to be concerned and worried about...you know...why am I in here?'*

A number of the participants also discussed and described their experiences of starting to return to normal Activities of Daily Living (ADLs) and the anxiety that this often caused. P4 both discussed the impact of undertaking what previously had been normal activities to them:

> *P4: 'Well I have only stayed in my local area, like going to friends in the area, but one of my friends has asked me to go to dinner in the Southside and that's a big deal because I know that I am going to be further away... texting back I was like, can I have a think about it?'*

P17 highlighted how this anxiety had become much more serious for him and caused him to have panic attacks when attempting to do things that had previously been a part of his normal routine:

> *P17: 'I've went 20 yards to the bus stop from the hostel gates, or hostel doors and I've had panic attacks and I've had to run back in the house just to be safe and sound.'*

Some participants also discussed anxiety about their future health and the potential to become unwell again. Many patients related this feeling to a lack of insight and knowledge about what caused them to become so unwell. This was associated with a lack of tangible knowledge and indeed a poor memory about their admission to critical care. P10 explained how she felt about often simple and benign signs and symptoms:

> *P10: 'I don't know whether I have still got something in the back of my mind, if I start coughing or sneezing- is this going to come back again? You know? And I feel as if nobody has actually sat me down and said this is what happened.'*

Participants also explored how their anxiety caused strain on their relationships with their families and carers, consequently having a negative effect on their own moods and feelings:

> *P13: 'Robert used to meet my brother and go out for a pint, I was saying I'm fine, I'm fine. I said no, it's fine, you go. But when he was out I would panic and I was panicking in case something happened to him, cause I would think who's going to look after me? I'm totally selfish.'*

Another significant problem which many participants described was a change to sleeping patterns after discharge from intensive care and the effect that this had on other ADLs and energy levels. Poor sleeping patterns were reported at all stages of the journey to recovery for patients. For example, P8 discussed his sleeping pattern in hospital and how this routine continued for many months after discharge home:

> *P8: 'I just wasn't sleeping. I was sleeping to hospital sleeps...the 12 o'clock to four o'clock and all this at night. Then they were waking you up at six with your tablets and your breakfast and then you're awake all day, you know. That's the hardest, that's what I've found it, I just couldn't get to sleep with the same pattern.'*

Other patients described erratic sleeping patterns during their recovery period at home or in long term care. Some participants also discussed how their poor sleep had caused them to seek help from their GP:

> *P7: 'I have went to the doctors recently and got sleeping tablets, eh because of my patterns of sleeping. I'm not sleeping that great. It's broken sleep.*

P16 discussed their erratic sleeping patterns since discharge from critical care:

> *P16: 'That's all I was doing...sleeping. Then I would get up about 2 o'clock in the morning maybe for 2 hours, then I would go back to sleep again. My sleeping pattern was very erratic. Even now, if I don't get a sleep in the afternoon...well I get grumpy.'*

Fatigue, often as a consequence of poor sleeping patterns, was frequently cited as an issue which impacted on recovery. Participants described how they were frustrated by this, as for many this was a key issue which hindered their physical recovery:

> *P18: 'I don't feel great. To be honest with you, I don't feel 100%. I still feel knackered, absolutely knackered.'*

A further psychological problem, which had a significant interplay with sleeping patterns, was the difficulty which many participants had with their memory and concentration. Participants discussed poor memory not just in relation to memories concerning their ICU stay, but also their functional, mostly short term memory, after discharge home.

> *P16: I'm reading a book just now and I'm having to go back a couple of pages to try and see what happened, which I have never done before.'*

Participants also shared how their poor memory affected different aspects of their recovery. For example, P6 discussed how he found it difficult to remember advice and information given to him by healthcare professionals who he was consulting about his physical recovery:

P6: 'I can go to the doctor with one or two things wrong with me. I tell him about one because I forget to tell him about the second one. So I can come back out and she will say- did you tell him such and such? No ah forgot...So she gave me three exercises, just three exercises to do right- while I am sitting in the house on my back and I couldn't remember them!'

A significant ongoing issue participants reported was flashbacks of critical care. These flashbacks affected all facets of recovery for participants. P6 and P7 both described how they struggled with this topic:

P6: 'At the moment I struggle with sort of flashes and all that...the only common thing with the flashbacks I get is I'm still in the hospital bed and I still can't move.'

Similarly, P7 discussed the impact which nightmares had for him:

P7: 'And that night I had a dream...a nightmare...and I woke up sweating, sweating an awful lot. I actually had to check myself to see if I had urinated.'

7.4.2 Physical problems

Descriptions of poor mobility were typically the starting point for participants discussing their recovery. Participants discussed how poor mobility often had a negative impact on their mood and on other parts of their recovery. P7 highlighted the impact of poor mobility:

P7: 'I had stairs to climb, that was so hard so it was, a bit depressing, because before it I used to run up and down the stairs, do you know what I mean?'

P16 also discussed raised anxiety in relation to his initial physical rehabilitation:

P16: 'well...actually...I tried to get up and down stairs...with the two sticks, and I found it very, very hard. I was terrified actually. I was actually shaking.'

A small number of participants reported the benefits of personal, goal directed therapy during their physical recovery. P1 and P3 both discussed how these personalised goals helped highlight progress in their recovery which was meaningful. This process gave hope and indeed motivated them:

> *P1: 'I had to concentrate on what I was doing and work at it. And it was just a gradual process of moving...moving and eventually I got on to the wee trolley thing and eventually it was a wheelchair and walking and eventually I was getting up and holding on to handrails, no Zimmer.'*

P3 also discussed how he used to targets during his recovery:

> *P3: 'You have always got to set goals and targets and that's what my life has always been about. And I used that; I listened to that when that was getting said to me when I was in the hospital. Keep focused, set goals, you know and all these kind of things.'*

A further prominent physical problem which participants discussed was ongoing problems with pain. Some patients had very specific pain, which related to the cause of their admission. For example, P7, who was admitted after a serious assault and as a result had significant abdominal injuries, discussed how he had continuing problems with stomach pain:

> *P7: 'My stomach...my stomach is constantly sore; it's like a washing machine constantly bubbling.'*

However, six (almost one third) participants discussed a very specific site of pain; shoulder pain or a 'frozen shoulder':

> *P6: 'That's really bugging me at the moment, I've got a frozen shoulder...So that's sort of frustrating as well, it was really annoying.'*

> *P12: 'It's my shoulder. Down from the hip right down and now it's going to my knees.'*

P18:' I've had sore shoulders and things like that.'

P20: 'I've still got these exercises that I am doing for my neck and I get stiff over my shoulders...but the only ache is around my shoulder.'

7.4.3 Discharge planning

The was general agreement amongst all participants that discharge planning from intensive care and hospital did not adequately help individuals have an effective recovery from critical illness.

There were key areas identified by participants which required improvements, including: the journey through the hospital, medicine reconciliation, the GP interface, and access to appropriate housing or suitably adapted homes. These issues affected people's ability to carry out different ADLs in a way which was acceptable to them.

Discharge planning throughout the hospital and communication across different areas within acute care was seen as lacking and, in some cases, caused significant stress and upset for participants. P19 described his discharge from ICU to the ward environment:

P19: 'I came back from ICU, I was in the chair instead of the bed and she says right get into your bed. I said but I can't, I can't move, I can't walk, and she says aye you can. I says no I can't. She says right it should be in your notes. Checked the notes- wasn't in the notes.'

Participants also discussed a lack of preparation and information about what to expect when moving across the hospital. P6 discussed their anxiety about moving from an HDU ward environment to the general ward environment:

P6: 'Maybe if you had that in HDU, just before you were ready to go to the ward that would maybe prepare you a wee bit. You know. HDU where my bed was I could see the nurses' station. I couldn't see anybody. You know and that was a bit of a killer as well.'

Similarly, patient P17 discussed their apprehension about discharge from ICU:

> *P17: 'I was a bit scared cause I'd been in that long, like I felt safe there.'*

The impact of changes in medication regimes for individuals manifested as a significant area for discussion. There were many different aspects to this conversation. Lack of medication reconciliation by community services was one of these aspects.

P8 explained that he was still receiving antibiotics seven months after discharge from critical care. Further, during the discussion it was clear that P8 had no information about how long he should be taking antibiotics for. Ongoing antibiotic use has many significant physiological complications for example, P8 described how this affected his quality of life:

> *P8: 'But I am still on antibiotics...I asked him If I could come off of these tablets because I was scratching myself all over, especially in bed at night...scratch, scratch, scratch, he says well it's up to you and I says well you should be able to tell me!'*

Participants also discussed significant and potentially life threatening errors, which had occurred in their medicine reconciliation throughout their recovery. For example, P10 discussed how the medicine for her diabetes had not been issued in her dosset box for almost four months:

> *P10: 'Dr **** phoned me up and he said do you know you weren't getting Metformin and something else and something else when you were in the hospital? I went, 'to be honest with you doctor I haven't a clue what I was getting in hospital. I just took what I was given'. He said 'well, they took you off Metformin and they took you off, I think it was about five or six tablets.' I don't think he was too happy.'*

A further issue which related to medicine reconciliation was participants often had a lack of understanding regarding what certain drugs were used for and why

they had been prescribed them. Subsequently, some participants had a distinct lack of ownership related to this part of their recovery. For example:

> *P14: 'Have we just brought it down by the medication? Temporarily? Like if the medication was to stop would it all go back up again? Or not? I want to ask him that.'*

P21 discussed a lack of knowledge concerning their medication regime:

> *P21: 'I'm not sure what that's for either, but I'm just taking it cause I'm told to take it!'*

During the interviews, many participants discussed how their GP had been involved in their recovery. However, the experience which different participants had with their GP in the community varied extensively. For many participants, this relationship had a significant impact on ADLs and recovery from critical illness.

Some patients would have liked the opportunity to discuss their ICU experience with their GP, however only a few participants felt confident enough to ask, or were given the opportunity to do so. P13 would have liked the opportunity to discuss her recovery from critical illness, including the problems which she was experiencing with her memory:

> *P13:'It's never been mentioned...She's never ever mentioned anything to me about how am I feeling, how things are or anything like that.'*

Participants also described how they sometimes struggled with how different healthcare services interacted with one another and which services should be accessed for information and support. P14 was an individual who had been admitted to the ICU with a variceal bleed and did not know who he should speak to in response to changing bowel habits:

> *P14:'So the doctor is kind of seeing me, the GP. And these other things are cropping up. I'm thinking who's in the driving seat here?'*

Housing and living environments were also a significant issue for participants recovering. Several participants interviewed had to change or move house after being discharged home from intensive care because of changes in physical and social functioning.This had an effect on their relationship with community services as they could no longer attend their regular GP Practice.

> *P9: 'I miss my own doctor, because I am out of the catchment area.'*

Participants discussed how these housing and access issues impacted both themselves and their families from a psychological perspective and also from a privacy and dignity perspective. P6 described how he could not get out of the bath in his home because of weakness. He described his raised anxiety at the thought of having to ask his daughter to help him do this:

> *P6: 'As I says, I wanted a bath and I wanted to lie in the bath for a wee while... and no I just couldn't get out. Couldn't turn or nothing on my knee. Couldn't do that. We ended up having to run the water away. Sandra had to get in the bath behind me and lift me up...it was hysterical...She was like that: 'I'll need to go and get Emma', that's my oldest. I went: 'No way, you're not getting Emma'.'*

P2 also explained how challenging her living arrangements were and how ineffective re-adaptation to her existing home environment impacted on her physical recovery:

> *P2: 'A bit more support. I know I had my family, but from the medical side...it was just a case of: right, goodbye, away home and your family can deal with you. A wee bit more support from them. Nobody came out to my house. I couldn't get in and out of the bath unless there was somebody to help me.'*

Much more significant issues were also described by participants about housing and the affect this had on recovery. P7 discussed his experience:

> *P7: 'I went into the homeless unit. They put us up the top flat in a scheme. Then I got an occupational therapist. They got us a house in*

the area where I am just now- but that was a fight to get that. And it's temporary, I don't know whether they are going to let us keep it.'

In summary, across all three study groups there was a significant impact on ADLs during recovery from ICU. Participants discussed the key issues impacting their recovery and explored areas which may require significant improvements.

7.5 Impact of psychological resilience on recovery

Psychological resilience and its impact on recovery from critical illness was a major theme of this work. As discussed in Section 2.3.3, resilience is process which involves individuals being supported by the resources in their environment to provide positive outcomes in the face of adversity (GCPH 2014b). Psychological resilience was promoted and challenged in this cohort in several ways: loss of control during recovery; maintenance of self-efficacy; and individuals having ownership of their story or journey.

7.5.1 Loss of control

Many participants discussed how they felt they had lost all sense of control over their life after discharge from critical care. For many participants this lack of control hindered recovery from critical illness. For example, P20 described the impact of recovering from a critical illness and how he struggled with what he perceived as a lack of control:

P20: 'Strange...I always thought I was...I thought this wouldn't happen to me. You know, you hear all of these strange cases, but you think you have got your own mind...so you should be able to cope with anything...you always assume you are in control you know and then all of a sudden it had gone, you know?'

Many participants described how this lack of control during recovery from critical illness had caused them to have dependency on others. This was challenging for many reasons such as a feeling of loss of independence and in some cases a sense of embarrassment. P4, P7 and P15 were the three youngest people interviewed; they explained how frustrating and embarrassing they found this dependency:

P4: 'I didn't like being dependent on, almost having permission to do things sort of thing.'

P7: 'I moved in with her dad, eh the house wasn't adapted, I had to get lifted in and out of the bath, so I did, which was quite embarrassing.'

P15 was a young male who discussed the upset that his new dependency on others had caused him:

P15: 'Being in hospital and like the nurse wiping my bum and stuff like that- that never really bothered us in hospital. But when I went home and my mum had to do it the first couple of times that was sort of a step back. You never really want your mum to see you doing that.'

7.5.2 Maintenance of self-efficacy

Linking to the super-ordinate theme of loss of control is that of maintenance of self-efficacy.Self-efficacy as a concept is concerned with people's beliefs in their ability to influence events that affect their lives (Bandura 2010).

As previously stated, many participants described this loss of control and self-efficacy, however, many also explained how they had regained their self-efficacy. During the interviews, which attempted to understand how participants had regained their self-efficacy and a sense of control in their lives, many individuals described an *'inner drive'* or *'self-determination'*. P3 described how they had regained their control:

P3: 'What is the point in looking backwards?..you have just got to focus...What's the point of dwelling in the past? You have got to think positively all the time. You know if you are having a bad experience- correct it! You know, it easy to cope with life when you are winning things and doing things. But you have always got to be prepared for the worst; if you prepare yourself for the worst you will come through anything. You know, that was my attitude when I was in...As soon as I went home, I wasn't going back to my old self in the

hospital, going to bed and just lying down. I kicked myself into touch right away.'

P10 also discussed how they seen their own self determination:

P10: 'I don't know what it is. Honestly, I couldn't put my finger on it and say its determination or it's I don't like being ill- I couldn't give you an answer to that.'

Other individuals also described how they had gone about regaining self-efficacy. P15 described how he decided to go back to work, initially on a part time basis, to try and gain back some independence which he felt he had lost during his recovery:

P15: '6 Months down, I'm still not back to exactly what I was, I'm not as strong as I was or anything like that, but I can still do everything near enough that I am asked to do, so getting my independence back was more the point of going back to work.'

However, many participants had not regained control of their lives and some still felt that their lives were completely out of control. This issue was particularly stark in the group admitted with a background of AUDs. Many participants in this group felt that they still had no control over their lives. This had an influence on both their recovery from critical care and their relationship with alcohol.

Many participants discussed external factors, which they had no control over, being the reason for continued excessive alcohol intake. Consequently, patients could not regain this self-efficacy until these barriers or factors were removed. For example, P16 discussed how he was not able to give up drinking because he had significant pain issues after critical care and as yet, had not had an appointment at the regional pain clinic:

P16: 'But the reason I go on a binge is because of the pains...I was almost crying myself to sleep at night. I know that sounds like an excuse...'

Similarly, P9 discussed her change in living circumstances after critical care and how she perceived this as the primary obstacle for continued drinking:

> *P9: 'To have my own place, next to my family, and that will stop me drinking as well, because I won't drink in front of my dad.'*

P17 did not directly attribute his continuing alcohol problems to recovery from critical care or a tangible factor which could be altered. P17 felt that his problems with alcohol were the result of a predetermined issue:

> *P17: 'And I says, do you think I want to be here every three or four days with withdrawals?'*

However, part of the reason why many participants continued to drink excessively, and perhaps were unable to regain a sense of control, was because they felt that they had no meaningful future. For some participants this was because of the challenging health issues, both acute and chronic, which they were facing. P5 described how he felt about the future in relation to getting back to work:

> *P5: 'I don't think I will get a job. I'm 58 you know. No-one will take me now. With my legs- no one will take me.'*

In contrast, some participants with an alcohol related admission stated that recovering from critical illness had given them the chance *'to take stock'* of their life. Consequently, some participants had made significant changes to their life and drinking habits. P18 described how he felt after reflecting on his admission to critical care and the subsequent influence that this had on his relationship with alcohol. He spoke of his inner drive and determination to ensure that his admission to critical care had a positive influence on his health:

> *P18: 'I don't have any excuses for my alcohol abuse. That was a self-thing, know what I mean? That was down to me at the end of the day. Nobody asked me to lift a bottle and put it in my mouth that was my choice in life at the time...I was determined I wasn't going to sit in the house and let it get me down.'*

7.5.3 Ownership of the journey

Many participants discussed how they could not remember what had happened during their ICU stay and found it difficult to grasp how seriously unwell they had been. Some participants found this difficult to cope with as it was difficult for them to comprehend why they were now struggling physically and psychologically. Consequently, their ability to manage or even engage in their recovery was challenging.

Almost all patients interviewed discussed how they had received very little, or in some cases, no information about their time in the ICU and what had brought them there. Some participants would have liked to have known exactly what had happened during their critical illness. Many participants stated that this knowledge would have allowed them to move on with their lives more effectively. P6 and P10 were keen to learn what had happened to them and why they had become so unwell:

> *P6: 'It would have helped if somebody had actually explained, eh you're leaving ICU, this is what we have done for you...this is what's gone wrong and we've done this...you know, just to bridge the gap a wee bit.'*

P10 also discussed how she lacked an understanding of her critical illness:

> *P10: 'But I felt like I was getting nurses, but what was wrong with me? Why am I here and why was I intensive care? I feel as if someone could have sat in front of me and said listen- here is what happened. I think it would help the patient- it would help me, because I would have a better understanding.'*

On the other hand, some participants did not want to know about recovery and were not ready at this stage in the process to learn about their critical care stay. For example, P19 was very clear that he did not want know what had happened during his ICU stay:

> *P19: 'I don't want to know about it, because it'll probably be too scary for me to think about it.'*

During the interviews some participants discussed how they had attempted to piece together memories from intensive care, in the hope that this would give meaning to their physical and psychological recovery. However, there was a real challenge for participants in understanding what reality was and what were altered memories, this in turn was distressing for some individuals:

> *P6: 'I still get frightened when I think back. A few times when I have been feeling a bit depressed, a bit down and all that, I try and think and try and piece bits together and when I can't it gets really frustrating...It's hard to separate it from really happening to imagining it.'*

As a result of having no knowledge or ownership of the journey, participants explained how they struggled to comprehend why fundamental aspects of their life, such as physical functioning, were so difficult and different. As a result, they found it difficult to fully engage with their recovery. P6 spoke of his feelings:

> *P6: 'And then I just couldn't get it in there how ill I had been and it was going to take a long time because most of the organs in my body had shut down at some point. And my body had taken a lot of punishment...but I couldn't take this in. I still thought I should be able to do this.'*

Many participants described how upsetting this lack of memory was. P9 explained her feelings about this aspect of her recovery:

> *P9: 'It's scary. It's frightening. People think you are a nutter. Well that's what I think. It's...I don't know.'*

Participants also discussed how they felt slight resentment towards their families around this issue. Participants stated that although they had been the patient and the person at the centre of the event, their families and loved ones had greater knowledge and indeed ownership of this story and journey. P10 expressed how she felt about this:

P10: 'I just want someone to talk to me about me. Not taking it off my family. I know what they went through with me being in there. But it was me that was in there.'

An interesting finding from this work was that if participants with a background of an AUD understood how seriously unwell they had been, and had ownership of their story, they were more likely to make positive steps forward in their recovery and in changing their relationship with alcohol. P18 explained how understanding his experience motivated him to change his behaviour:

P18: 'I'm glad, I'm actually glad that I do remember things that happened to me. 'Cause when I got out of hospital I've got that in my mind now and see the thought of alcohol and all that, I just think of the way...lying in hospital and that's not going to happen to me anymore.'

Similarly, P17, a patient with a significant history of alcohol related admissions to the acute hospital environment, stated that he did wish he could remember more about the experience, to help give a clear idea of the impact of alcohol on his health:

P17: 'I can't remember it and as I says in a way I'm glad I can't remember. But in a way I wish I had because it would...A: for my sanity and B: my own peace of mind. But for the fact that they reminded me how bad things were and how close I was to death basically.'

Psychological resilience was a key factor in recovery from critical care. In this cohort, maintenance and promotion of self efficacy and resilience may have be promoted by patients having an understanding of the intensive care journey, as this helped them comprehend the changes to their life. However, many participants spoke of an inner drive and determination which was a key factor in promoting psychological resilience during recovery.

7.6 Social support and cohesion

7.6.1 The role of positive and negative social support

Many participants described what they perceived as positive and negative types of social support during recovery from ICU. Unfortunately, the sentiment that negative social circumstances were linked to recovery was shared with many of the participants. Those with an AUD spoke of negative social environments and negative social structures more frequently than those without an AUD. P17, who was discharged to a hostel after critical care, spoke about the challenging environment which he was attempting to recover in:

> *P17: 'Last night in the hostel, one of the boys started slapping me on the arms and all that, trying to punch me right...the guy is nice when he's sober but he's like Jekyll and Hyde with a drink in him...And another boy in the hostel...he can be alright with a drink in him, but when he runs out of money and he doesn't get any more drink...he starts getting, starts kicking the doors in and all that. I was sober last night obviously, as I says I'm trying to make an effort.'*

Other patients admitted with a background of alcohol misuse also spoke about challenging environments. For example, P17 spoke about having to avoid certain areas and circumstances:

> *P17: 'I'm trying to stay away from Parkhead Cross because that's where all the offies are. I go into the bookies and play a game of bingo and if I win at the bingo I'm just going to go straight over and buy a bottle of wine with the money.'*

Additionally, P18 was anxious about leaving the hospital because of the environment which he was returning to and how this may influence all aspects of his life:

> *P18: 'I was really afraid to go home because of the situation I'd been in. I didn't want to fall back into that. I was wanting to stay in hospital.'*

P11 also discussed the impact of the chaotic family environment which many individuals returned home to after discharge from critical care. For example, P11 described an incident with his daughter after they had both consumed a large amount of alcohol and the anxiety that this had caused him:

> *P11: 'My daughter, she's out on the street shouting at me.'*

However, many participants spoke about positive social support and how vital this was during their recovery. This included close family and carers as well as other forms of support, including employers and friends. P15 discussed how his employer had supported him throughout his recovery and the positive impact that this had:

> *P15: 'My work were a really good support as well.*

Similarly, P20 discussed how his family had been a constant form of support which was essential in his recovery:

> *P20: 'It's the family, you know. We were always a close family...I've had a lot of support...I am quite fortunate, I've got people around me all the time. I've got support. It would be very difficult presumably if they didn't have support at all.'*

7.6.2 Social isolation (participants)

Undoubtedly, the presence of an effective social support network helped individuals recover from critical illness. These formal and informal support networks were key at all stages of the journey to recovery including, for many participants, inside the hospital setting. When this infrastructure was not present, it could lead to a feeling of isolation for individuals. P3 reflected on his transfer from a single side room to a six bedded bay in the general ward:

> *P3: 'I found that a bit of a hold up to me, being in a room on my own, because, I had no-one to speak to and that, you know that sort of thing. I found that very lonely...I said I can't cope, I'm a mixer, because when you went into the ward, if you didn't have any visitors, you could always depended on the people next to you getting*

involved with you...When you went into a ward, I didn't have a care in the world. I got my old self back. I was laughing and joking, having laughs with people and mixing.'

P6, who was admitted to hospital due to Salmonella, spent his entire hospital stay (almost three months), in different side rooms throughout the hospital. P6 described how isolated he felt in the hospital environment:

P6: 'And it's even worse on a Monday because there was no afternoon visiting on a Monday. So you're waiting from six o'clock in the morning, not seeing any of your friends or family until six o'clock at night. It makes it one hell of a long day.'

Many participants spoke of a feeling of social isolation similar to P6, which lasted beyond their time in the hospital. P4 described how anxieties around her health had resulted in feelings of isolation:

P4: 'I was too nervous to go out by myself...like even now, I've not been out properly by myself. I always get dropped off if I'm like going to friends for a couple of hours. I'll get dropped off and picked up and I've not took a train or a bus or anything like that. I'm still a bit funny about things like that.'

Similarly, P11 discussed how they found it difficult to leave their home because of physical changes in their health which had led to significant social isolation for them:

P11: 'But I'm actually becoming a prisoner in my own home.'

P15 also explored their feelings of isolation due to physical changes following critical illness:

P15: 'So I just stayed the house a lot. A few days on end and that was the most frustrating bit. Because once I was down the stairs, I couldn't be bothered going back up the stairs and once I was up I

couldn't be bothered coming back down for maybe two or three weeks.'

Participants also described how they found it difficult to speak to either family members or professionals about their illness and time in ICU, which for many led to a feeling of isolation. Additionally, some participants felt isolated because they did not feel part of the recovery story or journey. P6, who spent 58 days in ICU, explained how he sometimes felt low because his family would speak about things which had happened in ICU, however, he remembered very little about ICU and could not relate to or participate in what was being said:

P6: 'I don't like talking about it in the house all the time, because it...she said it's getting boring and that...I mean they have been through it all. What they forget is I wasn't...That's the stuff that kills me, that ah, ah can't remember it. Sandra, ah mean she keeps talkin...the staff were brilliant and that one, and really, it's annoying when ah can't remember, you know?'

P16 also discussed this feeling of isolation. P16, a 59 year old man from the East End of Glasgow, found it difficult to discuss his feelings and emotions and as a result had felt isolated. He described how he knew that healthcare professionals could deal with the physical aspects of his recovery, but found it difficult to verbalise his emotions:

P16: 'I have found it hard to be honest with you. Emotionally as well- I feel as though I'm going to burst into tears at any time- it's depressing, It's actually quite hard...It's the emotional side of it that's not been dealt with yet and I feel it should be.'

7.6.3 Social isolation and strain (families and carers)

Participants were acutely aware of the impact of recovery on their families and carers. P5 and P6 discussed how their relatives had taken on the role of carer:

P5: 'I found it hard getting up and down the stairs. My brother wouldn't let me get messages. He was scared in case I fell.'

P6: 'Aye, I had a stalker, every time I opened the toilet door she was standing there!'

This new role and the stress of having to manage their loved ones' low mood and frustrations also took its toll on relatives. P11 and P16 spoke about the conflict this had caused within their relationships at home:

P11: 'Sharon, she's away now, she's been gone three weeks.'

P16: 'I was trying too hard. I was getting frustrated and angry because...I was taking it out on my wife...which isn't fair.'

This conflict and stress inevitably led to social isolation for loved ones and carers. P13 described how her anxieties had caused her husband to change his usual activities and work and subsequently led to social isolation for him:

P13: So it's got to the stage that he wasn't going out, 'cause I was so frightened in case something happened to him and there'd be nobody there for me.'

This section has highlighted that stable social support is key for recovery after critical illness. Many participants described feelings of social isolation for both themselves and their loved ones during recovery.

7.7 Recovery and support for alcohol related admissions

As previously stated, the final theme, *'recovery and support for alcohol related admissions*', specifically explores the interplay with and the impact of AUD's on recovery from critical illness.

Nine participants with alcohol dependency were interviewed. Of these nine participants, five stated that they had stopped drinking completely and four participants stated that they were still drinking excessively. Six participants were interviewed from the harmful/hazardous group: three participants stated that they had stopped drinking completely, one stated that he had changed his relationship with alcohol and two individuals continued to drink at a harmful level.

When undertaking these interviews, it became clear that to fully understand the impact of critical care on alcohol related behaviours, and to ensure that the IPA approach was being fully adhered to (See Section 3.9.2), it was vital to understand why participants, in their view, had a problematic relationship with alcohol. Therefore, this initial short section explores why participants felt they had a problematic relationship with alcohol; in essence it provides context.

The post industrial context of Glasgow was the starting point for many participants speaking about their health and social circumstances. They discussed this social and economic context and how this had caused them to start drinking more heavily. For example, P5 had worked in the steel industry. He was made redundant more than 20 years ago and had started drinking heavily when he could not find any future employment:

> *P5: 'It makes me feel bad. You see people out working. You cannie get a job. I used to work in the steel industry- steel fabrication I was...I was a machine operator and eventually through time the place shut down and that was what...24 years ago. I've not worked since. I got made redundant. I tried for jobs but there was nothing doing- not in the steel industry.'*

Other changes in employment were given as a reason for increased alcohol intake by a number of participants. P1 explored how he began drinking more during retirement:

> *P1: 'I drank more when I retired because I didn't need to bother with the driving, where before I had a driving job and I used to do lots of miles, which...alcohol was a bit, woooo...better watch.'*

Some participants also described their social network and how this had contributed to them having a difficult and unhealthy relationship with alcohol. P18 explained how his family had influenced his drinking patterns:

> *P18: 'I've come from a quite heavy drinking family. My sister's a heavy drinker, but I just knock it in the head. I don't go round to my sisters. My sisters hardly seen me since I got out of the hospital.'*

Participants also described how other significant health problems had caused them to start drinking more. For example, P19 explored his background to heavy drinking:

> *P19: 'But what really got to me over the last few eh, three or four years was the death of my sister, which put me down a bit and trying to decorate a new house and then taking a stroke in June. Which put me right back because I used to be a, a loch leader. Eh, outdoors person, going hill walking and gardening and things and an allotment and things like that. Eh, and then that put me on, on the drink again harder.'*

P17 described his background with alcohol and how he viewed his relationship with alcohol over the course of his life:

> *P17: 'I personally believe I was an alcoholic when I was born because I had all the traits of an alcoholic...my personal opinion: alcohol, drinking is a symptom, is a side effect and that's why people say things like you'll be an alcoholic 'til the day you die.'*

On the whole, the social context had a significant role to play in the development of unhealthy behaviours relating to alcohol. However, P14 was the exception to this. P14 was a former university academic who spoke about his relationship with alcohol:

> *P14: 'I've drank because I like it, and because I've enough money to do it. Not because you know, if I can't get any I'm going to break into your shed to sell your lawnmower type thing.'*

7.7.1 Interaction with healthcare professionals

Many participants discussed the importance of appropriate interactions with healthcare professionals during their recovery. A small number of participants stated that they were upset when their alcohol intake was not assessed properly and *'judgements'* were made about their alcohol consumption. P1 described how he became anxious when healthcare professionals appeared not to have listened to what he had said:

P1: 'I had said that I had drank...I said that I drank...the maximum I could possibly drink was, that I could possibly consume three bottles of alcohol...I said it could be whisky, Bacardi or vodka, they assumed three bottles of Bacardi, three bottles of vodka and three bottles of whisky...so I explained you would be dead drinking that in a week.'

Participants also discussed the positive influence of clear and honest communication about the impact of alcohol on their health. P19 reported the positive effect of these understandable, non-judgemental conversations:

P19: 'The consultants have told me and things like that. It's actually been drilled into my head that this is what's going to happen if you do it again.'

P20 also described this approach as being positive part of their recovery:

*P20: 'Dr ****** was very good, he told me the truth, he told me what the score was.'*

Interestingly, one participant spoke about how he had been unsure if alcohol had contributed to his acute pancreatitis. The conversation was perhaps not as focused and clear as the conversations above had been, the result of this was that P1 felt that he may have been '*unfortunate*':

*P1: 'I mean three bottles of spirit to me or to you is quite a lot. But that isn't a lot to a lot of people...That's the only thing I can put it down to, because no gallstones. Mr ***** says there is a bit of gravel there but nothing to cause any problems. So it has got to be alcohol related or maybe just unfortunate?'*

Several participants discussed negative experiences with healthcare professionals and how frank conversations should be balanced with empathy. P17 discussed his experience of this:

P17: 'I've had doctors in accident and emergency when I've come in with the DTs and withdrawals and all that and they shake their head

saying why don't you just stop? They've not tried to understand, they've not even listened to you.'

7.7.2 Appropriate and timely rehabilitation

A major aspect of recovery which was explored with participants was the role of rehabilitation and support for AUDs during recovery from critical illness. There were two key parts to this discussion: the need for appropriate interventions and the timing of these interventions.

Many participants discussed their pre-existing relationships with specific alcohol workers in the community. They stated that the rehabilitation offered within the acute care setting did not take these relationships into account. As a result these participants had refused the support offered in the ward setting. P2 and P11 discussed how they felt about this lack of continuity:

P2: 'I just told them straight that I have already got an addiction worker I said. So I don't really want to start discussing with a stranger'

P11: 'And I was getting on good with him, but then they changed it and I got somebody else and I was going and then they changed it again, so I just went: 'you are changing these people. I've got a rapport with people'; I says 'you're just changing, chopping and changing'. Eh and I says 'I don't want anything'.'

In contrast to this, a small number of participants had requested support from addiction workers within the acute care setting after discharge from critical care. However, this support could not be accessed:

P19: 'They asked me if I wanted anybody and I had previously said no, but this time I said yes. But nobody ever came.'

A small number of individuals stated that they did not wish to see an alcohol or addiction worker, with a variety of reason being offered for this choice. For example, P17 discussed his feelings to alcohol rehabilitation:

P17: 'Wouldn't have made any difference to be honest, in my personal opinion. Cause I'm either going to drink or I'm not. And I've had all the advice that I'm that I'm ever going to get. That's going to make any sense to me; nobody can tell me anything about alcoholism I don't already know.'

Participants articulated the importance of appropriate timing for addiction worker input. Many participants could not remember any contact during their time in the acute care setting, which may suggest that the timing of these interviews was not optimal:

P17: 'About alcohol...not to my knowledge. But, eh, I can't...maybe somebody did and I just can't remember.'

P20: 'I'm assuming that they must have, but I don't remember it. I don't doubt it happened, but I don't remember it at all.'

7.7.3 Impact of ICU on alcohol related behaviours

All participants with a background of an AUD stated that admission to ICU had an impact on their relationship with alcohol. During the interviews, many participants spoke about their admission to ICU admission acting as a *'wake-up call'*. For example, P2 reflected on their admission to critical care:

P2: 'It was just a shock to the system. I could see how bad I got...myself.'

Similarly, P7 discussed his time in the ward environment, after discharge from critical care, and how this had impacted on his relationship with alcohol:

P7: 'I'm not interested in drink...being in the wards where that's what they are dealing with, do you know what I mean? Some guys in there only drink recreationally- they only go out for a few pints and they are in here with pancreatitis. Do you know what I mean? It all catches up with you and at 31, I've been doing it since I was 13, do you know what I mean, drinking, I think now is the time to stop.'

The direct positive effect that admission to ICU could have on alcohol consumption was also discussed:

> *P18: 'Since coming out of hospital I've not touched a drop of alcohol or nothing.'*

> *P20: 'Oh, I feel much better, much better. I've stopped drinking entirely now. I've got my appetite back, I'm a bit lighter now, its healthier my lightness.'*

For those patients who had claimed to have stopped drinking completely, many reported positive benefits not just with their health, but in other aspects of their life. For example, P19 explained the positive impact that sobriety had on his relationship with his family:

> *P19: 'My health is a lot better. Not drinking...I'm more active with my wife and kids, getting more involved with them, I'm just trying to build my life back up to a good standard now compared to what it was previously. I'm more positive, positive life for myself now compared to what I was before. Because, I wasn't thinking about anybody else and I wasn't helping the kids, do their homework or anything like that. But now I'm more involved with them.'*

A small number of participants also described the stark difference to other aspects of their lifestyle and health, which in many ways influenced some of the other negative health and social consequences which they were experiencing as a result of ICU (See Section 7.4). P18 reflected on how their lives had changed since admission to critical care:

> *P18: 'I'm watching my medication...practically tried to turn my life right around. Changed all my diet and everything, actually went to college on Monday. It's a thing I never thought...everything's been positive since the day I came out of hospital. Just been a lot more...I've been a lot happier...When I got home I felt different about things. Got all my house squared up, starting living a normal life again, away from it all.'*

P21 also discussed the changes to his health following intensive care discharge:

> *P21: 'So, I mean I had to sort my life out. I've stopped smoking; stopped back in January...Doing more exercise and eating healthily...I'm 100% better than I was before.'*

However, some patients continued to drink harmfully after discharge from ICU. Many reasons were given for this, with social reasons being the most prominent. P9 discussed her social and housing situation and how she found it difficult to stop drinking because of this. Despite being only 37, P9 was discharged to Sheltered Housing after ICU, because of her complex medical and social history. She discussed this in relation to her drinking:

> *P9: 'To have my own place, next to my family, and that will stop me drinking as well, because I won't drink in front of my dad.'*

A small number of participants also discussed the physical and social effects of ICU and how this contributed to their ongoing problematic alcohol use. P11 had significant psychological problems after discharge from critical care and was finding these, difficult to cope with. He described how this had affected him the previous weekend:

> *P11: 'I was drinking a, a, it's no use telling lies. Last weekend I'd a, last weekend I was drinking from the Friday to the Sunday night, like, kind of nonstop. Eh, it was like, I was getting drunk, falling asleep on the couch, wakening up, starting again.That, that's, that's been about, that's the first time I've done that and oh, months, months and months, and it was vodka, it was just plain. I don't take anything in my vodka, it's just straight vodka. Eh, I washed that down with a couple of bottles of sherry.'*

Habit was also given as a reason for continuing to drink to excess. P17 explained how habit made it challenging for him to change his relationship with alcohol:

> *P17: 'The first thing I do when I wake up in the morning, it's hard to explain, but once my eyes are awake I'm gone. The first thing I do*

when I wake up is I put my hand down the side of the bed to feel for my bottle and even when I'm no drinking or I'm sober shall we say I still...it's a, you know, a natural habit. But, I'm doing a lot better now and I'm starting back at Alcoholic Anonymous.'

The negative impact on health and wellbeing that continued harmful alcohol consumption had was also described by participants. For example, P17 described how he was unable to be put on a housing list because of his drinking problems:

P17: 'Eh, the, the housing officer says to me, are you alcohol dependent? and I says yes. She says have you had a drink the day? I wasn't going to lie, she could obviously smell it. I says aye, I'd a bottle of cider before I came up to you...Eh, and she says well if you're alcohol dependent we can't put you back.'

Those participants admitted with a background of an AUD discussed both positive and negative consequences of admission to ICU. Additionally, this section has highlighted that for many patients, admission to critical care does influence alcohol related behaviours.

7.8 Chapter Conclusion

This chapter presented the findings from the in depth semi structured interviews undertaken as part of this mixed methods study. These findings suggest:

- Individuals recovering from a critical illness suffer persistent physical and psychological problems for many months after discharge from ICU

- Very few participants had clear memories of their ICU admission. This had a significant impact on their ability to recover, as many individuals could not comprehend why they now had considerable psychological and physical problems

- Participants described the importance of a stable social structure in their recovery

- Families and carers also experience challenges both during the ICU admission and throughout the critical care recovery period

- Those participants admitted with a background of an AUD discussed both positive and negative consequences of admission to ICU

- For many patients, admission to critical care does influence behaviour with regards to future alcohol use.

The following chapter presents the discussion section for this PhD Thesis.

Chapter Eight: Discussion

'We are all in the gutter, but some of us are looking at the stars'

Oscar Wilde (1892)

8.1 Introduction

The following chapter will present the discussion relating to this PhD.

This mixed methods study had five objectives:

1. Analyse the nature and complications of alcohol related admissions to critical care

2. Explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis

3. Explore patterns of recovery for patients with and without alcohol use disorders

4. Determine whether alcohol use disorders are associated with survival in critically ill patients at six months post ICU discharge

5. Examine the impact of critical care on future behaviour with regards to alcohol intake.

In this chapter, the results and findings from thesis will be discussed and mapped against an existing theory. The results and findings of this thesis will be discussed in relation to the salutogenic perspective of health. Salutogenesis, which is a term coined from the Latin *salus*=health and the Greek *genesis*=origin, is the theory of health proposed by the medical sociologist Aaron Antonovsky (1979).

In this chapter an overview on the key concepts of Antonovsky's (1979) model of Salutogenesis will firstly be discussed. Each of the five research objectives will then be addressed in relation to both the quantitative and qualitative data collected.

8.2 Salutogenesis

During this PhD, different theoretical models were explored in relation to this work. Two models which were explored in particular were Antonovsky's model of Salutogenesis (Antonovsky 1979) and Attribution Theory (Weiner 1972).

The Salutogenic approach was developed by Antonovsky as an alternative to the pathogenic approaches to health which existed. This approach emerged as a result of Antonovsky's concerns that a different paradigm was required in order to understand health not just in terms of the underlying process of illness and disease (Harrop, Addis, Elliot et al 2006). By focusing on Salutogenesis, in contrast to pathogenesis, Antonovsky hoped that healthcare professionals would create pathways of care leading in the direction of health on what Antonovsky referred to as the 'health/disease continuum' (Antonovsky 1996, Harrop et al 2006) (Figure 8.1).

Three core concepts are essential to the Salutogenic theory: the Sense of Coherence, Life Experiences and Generalised Resistant Resources (Antonovsky 1979).

8.2.1 Generalised Resistant Resources

Generalised Resistant Resources are key in understanding fully the concept of Sense of Coherence. A Generalised Resistant Resource can be defined as a characteristic, phenomenon or relationship of an individual group or society, that facilitates the avoidance of stressors or the resolution of stress generated (Antonovsky 1987) (Figure 8.1). Generalised Resistant Resources steer an individual's Sense of Coherence through Life Experiences.

8.2.2 Life Experiences

As highlighted in Figure 8.1, Life Experiences are crucial in shaping a sense of coherence. Antonovsky (1979) stated that from the time of birth, or perhaps even earlier, we constantly go through situations or challenges, stress, tensions and resolution. Antonovsky found that the more these experiences were characterised by consistency and participation in shaping the outcome, with an underload-overload balance of stimuli, the more individuals begin to see the world as being coherent and predictable. It is important to stress that participation does not necessarily mean control, rather participation in decision making (Antonovsky 1979). Life Experiences link with Generalised Resistant Resources and Sense of Coherence, in that Life Experiences lead to a Sense of Coherence being developed. Life Experiences depend on the available resources (Generalised Resistant Resources) which have been developed on the basis of the corresponding sociocultural and historical context.

8.2.3 Sense of coherence

Antonovsky (1991) described a Sense of Coherence as:

> *'a property of a person, a collective or a situation which, as evidenced or logic has indicated, facilitated successful coping with the inherent stressors of human existence.'*

In essence, a Sense of Coherence relates to the way in which individuals make sense of their world, use the necessary resources to respond to it and feel that those responses are meaningful and make sense (Harrop et al 2006). There are three components to make Sense of Coherence: comprehensibility, manageability and meaningfulness (Antonovsky 1979) (Figure 8.1). Confronted with a stressor, a person with a strong Sense of Coherence will wish to be motivated to cope (meaningfulness), believe that the challenge is understood (comprehensibility) and believe that the resources to cope are available (manageable) (Antonovsky 1991). According to Antonovsky, having a Sense of Coherence is decisive in facilitating the movement towards health. However, what is key to the concept of Sense of Coherence is that it can be shaped and manipulated, so that in turn people can be *'pushed towards'* health (Antonovsky 1987).

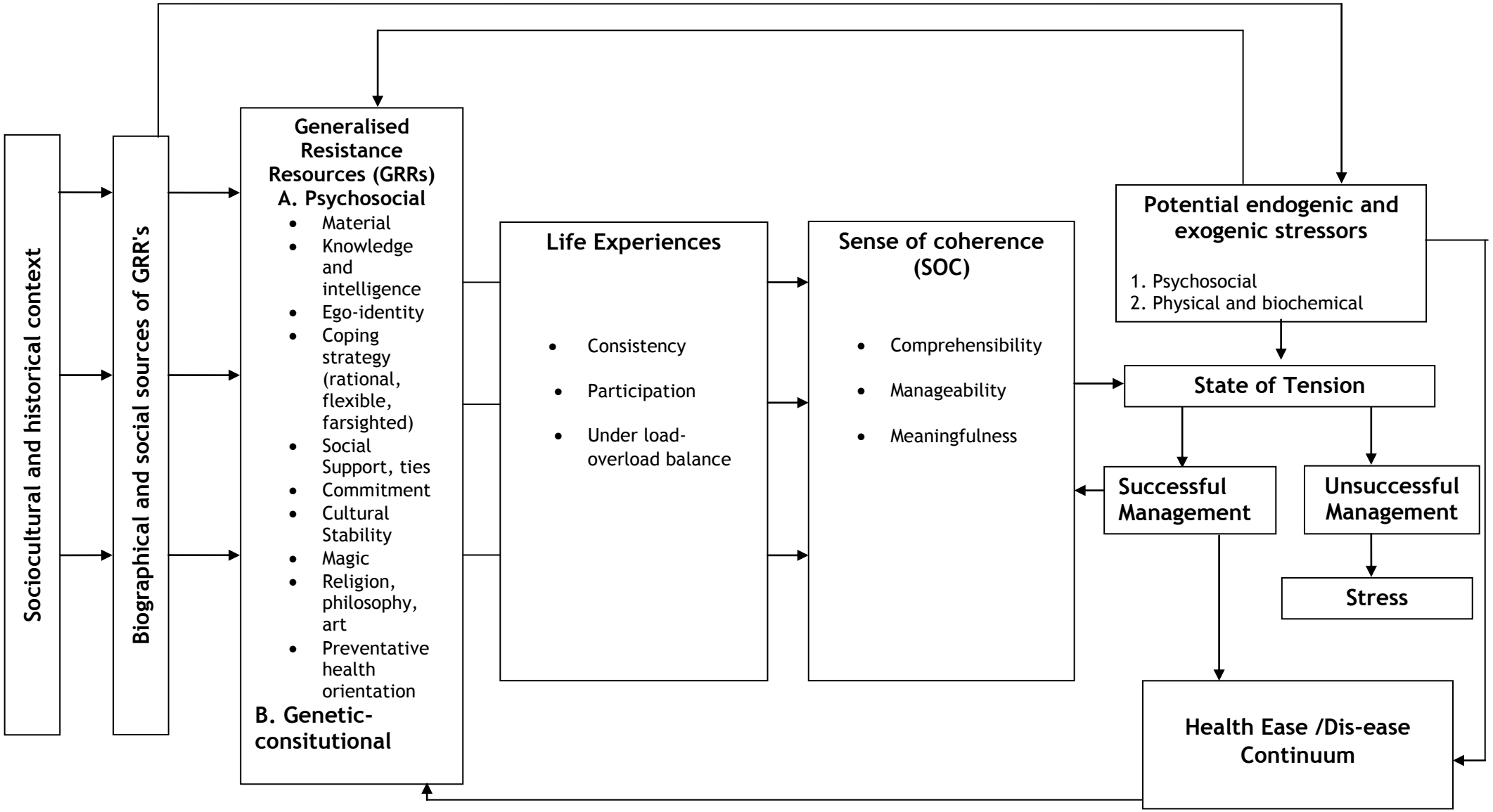

Table 8.1: Antonovsky's model of Salutogenesis (Antonovsky 1979)

The model of Salutogenesis clearly has many facets and influencing factors (Figure 8.1). To ensure clarity in the following section of this thesis, the discussion will relate to the three primary concepts of Salutogenesis: Sense of Coherence, Life Experiences and Generalised Resistant Resources.

8.3 Alcohol related admissions and the ICU

The first research objective of this study was to analyse the nature and complications of alcohol related admissions to critical care. A high proportion of patients admitted to the ICU had AUDs. Compared with other admissions to critical care, they were younger, more likely to take drugs and smoke and more likely to live in areas of higher socio economic deprivation. AUDs were also associated with an increased odds of developing septic shock in the ICU and poorer outcomes from both ICU and hospital.

The proportion of alcohol related admissions (34.4%) reported in this study is similar to the 33% of admissions reported in a recent French paper on the same topic (Gacouin et al 2014). However, this number is higher than previous research carried out in Scotland which explored alcohol related admissions to critical care. Geary et al (2012) estimated that 25.4% of ICU admissions in Scotland were related to alcohol. The difference in the present study may reflect the geographical area where the study centre sits, with a high proportion of patients residing in areas of deprivation. There is an abundance of evidence demonstrating that alcoholism and alcohol related deaths have a strong deprivation and gender gradient (Shipton et al 2013). This pattern was also observed within this study. Patients with alcohol dependency had more than a twofold increased odds of being from the most deprived areas of society compared with those patients in the low risk group.

The poor ICU and hospital outcomes in patients with alcohol dependency seen in this study are also consistent with the literature (O'Brien et al 2007,

Gacouin et al 2014). After adjustment for all lifestyle factors which were significantly different between the groups (age, smoking and drug use), alcohol dependence was associated with more than a twofold increased odds of both ICU mortality and hospital mortality.

Those with an alcohol related admission (either the harmful/hazardous or alcohol dependent group) also had an almost two fold increased odds of developing septic shock during their ICU admission, compared with the low risk group. This is consistent with previous papers which have demonstrated an increased incidence of sepsis and an increased risk of ICU acquired infections, such as Ventilator Associated Pneumonia and acquired bacterial infection (O'Brien et al 2007, Gacouin et al 2008). Immunological and non-immunological factors may contribute to increased susceptibility to infection in patients with chronic alcohol exposure (Gacouin et al 2008). Animal and human studies have demonstrated that chronic alcohol consumption may inhibit the production of important cytokines (Von Dossow et al 2004), modify neutrophil functions and suppress T-cell mediated immunity (Moss and Burnham 2006). These cellular changes could lead to an increased predilection to infection which may contribute to systemic problems and contribute to increased ICU mortality (O'Brien et al 2008).

Median length of ICU stay was significantly different between the study groups (p=0.001). However, after a Bonferroni correction had been applied, only the difference between the harmful/hazardous and alcohol dependency group remained significant (p=0.01). Clinically this result is logical: those in the harmful/hazardous group are quite often individuals who require a short term stay as a result of being involved in an incident as a consequence of being inebriated (i.e. those patients who may have taken an overdose). Therefore, these patients are more likely to have a short ICU stay for reversal of, for example, respiratory depression.

A limitation of this study was that there was minimal data collected on patient co-morbidities and long term conditions. Co-morbidities can have

an impact on ICU outcomes and may have had an impact on LOS in both the ICU and hospital (Docking, Mackay, Lewsey et al 2012). Future work should explore this in relation to AUDs.

8.3.1 Summary

The first research objective of this PhD thesis was answered fully. Alcohol related admissions represent a high proportion of admissions to ICU and patients with AUDs (both harmful/hazardous and dependency) have significantly more complications during the ICU stay. Further, patients with alcohol dependency have poorer ICU and hospital outcomes compared to those admitted without an AUD.

8.4 Liver cirrhosis and the ICU

A sub study within this PhD was undertaken to explore the utility of prognostic scoring tools in critically ill patients admitted to a general ICU with a background of liver cirrhosis. This section of the work was completed in two phases.

Both phases demonstrated that the outcomes of patients admitted with a background of liver cirrhosis to the general ICU setting are better than previously documented in the literature (Cholongitas et al 2009, Levesque et al 2012). These figures are also comparable to another recent UK study in a non transplant setting which demonstrated improved outcomes for patients with a background of cirrhosis admitted to the general ICU setting (Lewis, Reynolds, Lillis et al 2012).

The reduction in mortality seen in the present study may reflect referral patterns in this patient cohort locally. Furthermore, within the general ICU context, patients are often admitted to ICU with cirrhosis rather than because of decompenstated liver failure which is often the case within the transplant setting. This is reflected in the low degree of liver dysfunction

which was seen in the London and Glasgow cohorts. In the latter cohort for example, the mean CTP score is lowest of any published data in this field.

Phase One of this sub study demonstrated that of the existing scoring tools available, the SOFA score had the best discriminative ability, with an AUC of 0.76. From the liver specific scoring tools, the MELD performed most accurately in this cohort (AUC 0.74). These results are consistent with a recent systematic review which demonstrated the accuracy of the SOFA score in both the transplantation and general ICU settings (Flood et al 2010).

The AKIN tool was also utilised as a predictive scoring tool in Phase One. Previous research in the liver transplantation setting has demonstrated the importance of renal failure in critically unwell patients with cirrhosis (Cholongitas et al 2009). The AKIN performed poorly in this cohort of patients, with an AUC of 0.52. Furthermore, there was no significant relationship with AKI and outcomes from ICU. It may be that patients who had developed AKI were not referred to the ICU due to the notoriously poor outcomes demonstrated in the literature for patients with liver cirrhosis and renal failure (Mackle et al 2006). There is no data on referral patterns in the present study. Future research in this field should explore this to help understand the relationship between liver cirrhosis and renal impairment more fully.

The results of the first phase of this study add to the accumulating body of evidence that serum arterial lactate is an independent predictor of mortality (Burroughs et al 2010). As a result, lactate was added to an existing scoring tool (the CTP) to generate an appropriate scoring tool for the general ICU setting. This novel tool was the only tool which achieved an AUC of greater than 0.8 in the initial phase of the study. The lack of tools to achieve this clinically useful level is in line with other previously published work in the general ICU, with none of the established prognostic

scoring tools achieving the clinically useful threshold of an AUC of greater than 0.8 (Thomson et al 2010).

Utilising a previously published cohort (Thomson et al 2010) the second phase of the study aimed to establish the discriminative ability of the newly developed tool. A further aim was to externally validate another newly developed scoring tool, the RFH, in the general ICU setting (Theocharidou et al 2014).

The primary findings from the second phase of the liver cirrhosis study were that the CTP+L continued to perform well in a larger cohort from Glasgow (AUC 0.83). However, in the London cohort it did not reach the clinically useful level of 0.8. The tool which provided the best discriminative ability in the London cohort was the RFH score (AUC 0.77). However, when the two datasets were combined, the CTP+L did perform slightly better than the RFH (AUC 0.79 vs. AUC 0.78); however, there was no significant difference between these AUCs.

It could be argued that the two scoring tools specifically examined in this phase of the study have two different purposes. The RFH score is a calibrated score, but is complex to calculate:

$$-6.611 + \text{bilirubin}\ (0.004) + \text{urea}\ (0.057) + \text{lactate}\ (0.274) + FiO_2\ (3.126) + K$$

In this formula K represents the number of failing organs as defined by the SOFA score (Theocharidou et al 2014). Therefore, this is not a tool which can be quickly and easily calculated at the patient's bed space without a medical calculator and may be more appropriate for use within a research context. In contrast, the CTP+L is simple and can be calculated within the clinical context, as it uses categorical variables which are easily accessible. Additionally, the CTP is routinely used within a gastroenterology setting and is often already calculated for this cohort of patients.

There are specific limitations in this phase of the work. For example, the lack of pre intubation encephalopathy grades in the London cohort may impact on the reported results. Encephalopathy scores are a key component of the CTP score; consequently the presented results of the CTP+L in the London cohort may not have been accurate. Future validation work with this clinical scoring system should include a cohort where pre intubation encephalopathy scores are available.

8.4.1 Summary

The second research objective of this PhD thesis was answered fully. The utility of prognostic scoring tools for critically ill patients admitted to a general ICU with a background of liver cirrhosis were explored. Of the established scoring tools, the SOFA has the best discriminative ability. New scoring tools were also explored in two cohorts of patients. Both these scoring tools demonstrated superior discriminative ability compared with the pre existing scoring tools available.

8.5 Recovery from ICU

8.5.1 Physical and psychological problems

Similar to many previously published studies, participants described ongoing physical, psychological and emotional problems during recovery from critical illness. Physical problems discussed were consistent with previous literature on recovery from intensive care and included poor mobility and ongoing pain issues (Herridge et al 2011). These influenced many parts of the ICU recovery including psychological health and dignity. For many participants with a background with an AUD, it also impacted on their ability to move forward in reducing their alcohol intake.

Ongoing pain appeared to be an important issue for many participants interviewed. As described in Section 7.4.2, many participants also described shoulder pain as been a specific site for pain. There is evidence from many studies which highlights ongoing pain as an issue which impacts

on quality of life for ICU survivors (Herridge et al 2011, Broyle, Murgo, Adamson et al 2004). However, only one previous study has highlighted shoulder pain as being a specific issue. Battle et al (2013) in a retrospective analysis found that 22% of ICU survivors had ongoing shoulder pain at six months post discharge. Further studies are required to investigate interventions both during and after the ICU to address this long term issue.

Many participants discussed how they had attempted to overcome issues, such as pain and poor mobility, through the use of goal directed therapy and through setting individualised goals for both physical and psychological recovery. The recent study by Walker et al (2015) also discussed the benefits which patients gained from making such focused, individualised care plans with staff. Future rehabilitation for this cohort should explore this approach to supporting patients during recovery.

The emergence of serious psychological issues following intensive care discharge was discussed extensively in the in depth semi structured interviews. Low mood, anxiety, poor memory and concentration and persistent fatigue were some of the commonly encountered issues. The impact of poor sleeping patterns on all aspects of recovery was also apparent for both patients and carers. There is an abundance of literature which has extensively described ongoing psychological issues for ICU survivors (Davydow, Gifford, Desai et al 2008). There are some promising, positive changes in psychological outcomes emerging from the use of ICU diaries in this population (Jones et al 2010). However, more work focusing on appropriate and timely rehabilitation is required in this population, for both patients and carers, to help support psychological recovery.

8.5.2 Discharge planning

A strong theme which emerged from this study, relating to patterns of recovery, was the lack of discharge planning for patients and carers at all stages of the patient journey. This is a finding which has been described recurrently within the literature (Strahan and Brown 2005).

The lack of health and social integration and communication amongst health care professionals was described frequently by participants. This was especially true in the working age population. Unlike patients who are older than 65, and have access to care of the elderly rehabilitation services, the working age population did not seem to have any of these services and support. This was particularly apparent when discussing housing and adaptation to living, with one patient having to declare himself and his young family homeless in order to gain appropriate accommodation. This is consistent with recent work which has demonstrated that very few patients of working age recovering from critical illness are referred to community rehabilitation teams or services (Soulsby, McPeake, Ashcroft et al 2015). Future rehabilitation services for this group should focus not just on physical and psychological recovery from critical illness, but also on social support. Furthermore, within clinical practice, more support must be given to those patients of working age who do not automatically qualify for certain support and benefits. This will allow patients and their family members to better manage their recovery which according to Antonovsky (1979) is key to developing a Sense of Coherence and thus wellbeing.

A startling finding of this study was the impact of new pharmacy regimes, or indeed the lack of medicines reconciliation for participants when discharged home from hospital. There were a number of participants who had no understanding of their drugs and there were a small amount of errors discussed within the interviews. This was particularly true for a patient who had not been restarted on her diabetes drugs until three months after discharge home from hospital. There is some emerging evidence regarding the impact of medication issues post intensive care discharge. More work is required in this area to ensure potentially life threatening errors are reduced and appropriate interventions put in place (Eijsbroek, Howell, Smith et al 2013). This will ensure that patients have the knowledge and intelligence they require, which according to Antonovsky (1979), is a key Generalised Resistance Resource for the creation of health and wellbeing.

As previously described, intensive care treatment is expensive, especially when there is a reduced quality of life and high healthcare utilisation costs following discharge (Lone, Marta, Wild et al 2013). To ensure that this investment in healthcare costs is justified and to ensure that the ordeal of ICU is worthwhile, there must be a greater emphasis on all aspects of rehabilitation for patients and their family members.

8.5.3 Psychological resilience and self efficacy

Psychological resilience and its impact on recovery also emerged as a theme from the in depth semi structured interviews. Patients frequently discussed how they felt they had lost control over their health and in some cases they felt they had no command over their future. This problem was particularly prevalent in those patients with a background of an AUD. This is consistent with the small body of literature in the field. Connelly et al (2014) found that patients with ongoing psychological distress or problems found the maintenance of self efficacy particularly challenging.

This theme relates closely with the elements of consistency and manageability within the model of Salutogenesis. Significant events such as critical illness are hugely disruptive and are usually unforeseen. Consequently, they can have a major impact on all aspects of a person's life and greatly influence the ability to manage life and one's health.

One of the reasons many participants gave for this feeling of loss of control, was a lack of ownership over their experience, health and critical care journey. This lack of ownership was related to poor memory and the inability to differentiate between delusional memories and reality. There has been a focus on producing the 'patient story' in various forms as part of different approaches to rehabilitation. Within nurse led clinics, patients receive information on their ICU experience. Further, the entire purpose of the ICU diary is to reconstruct the illness narrative for the patient (Perier et al 2013). The findings from this work would suggest that these are helpful interventions. However, the evidence suggests that these approaches in isolation are not enough to support patients and family

members through the difficult recovery trajectory which is often encountered. It would appear that a more holistic model of care, which features a component on rebuilding the patient journey, is needed.

8.5.4 Social support

According to Antonovsky (1979) social support and social ties are key Generalised Resistance Resources for the creation of health and wellbeing. When exploring patterns of recovery from critical care, the importance of stable social support networks and the avoidance of social isolation were key for the creation of health and wellbeing.

Participants of the interviews discussed social isolation at all points of the recovery journey, including isolation within the hospital environment and social isolation in the community when discharged home.

ICU is unique to most other specialties within the acute care setting, in that the population is diverse and heterogeneous. This is in contrast to specialties such as stroke, where patients with a similar disease process are generally admitted to one ward and have, one the whole, similar treatment pathways. The organisation of care based on different organ systems (i.e. respiratory, cardiology) means that patients have an instant informal support network within the hospital setting and quite often within the community, with parallel support available for family members. This is not available for ICU survivors and as demonstrated in some of the interviews undertaken for this study, quite often members of the multi disciplinary team outwith the ICU have no insight into the challenges ICU patients encounter. Similar themes emerged from the Walker et al (2015) study, where patients stated that it was useful to interact with patients and family members who had been through similar experiences. In essence, patients appear to be looking for peer support.

Peer support has been shown to promote recovery amongst a variety of different populations such as patients with newly diagnosed cancer and those recovering from cancer and burn injuries (Davis, Gorgens, Shriberg et al 2014, Cameron, Both, Schlatter et al 2007). Furthermore, a recent

randomised controlled trial of peer support demonstrated an improvement in blood sugar control in patients with diabetes (Heisler, Vijan, Makki, et al 2010). Peer support could be embedded within current rehabilitation programmes such as the nurse led follow up clinic and with the use of rehabilitation manuals, in several ways. For example, previous patients could interact with current patients at nurse led clinics or visit patients during the recovery phase in the ward setting. This model could also extend to carers. More research is required to be undertaken to understand how the use of peer support could improve the recovery trajectory for this patient group.

The use of side rooms within the hospital environment also seems to be a challenge for some patients and led to a sense of isolation and in some cases depression. Although single rooms are required for infection control purposes and patient safety, more work is required into the psychological impact that long term isolation can have on patients within the acute healthcare setting.

Social isolation within the community setting was also common in this population, with a variety of reasons such as low mood, physical inability (such as poor mobility), anxiety and lack of purpose given as reason for this work. Appropriate recognition and the facilitation of psychological support following ICU discharge may help this. Furthermore, integration and awareness from the community healthcare setting of these potential problems is necessary. This support is also key for family members as the participants of the interviews described similar issues for their loved ones.

When analysing the literature around recovery for this patient cohort, a model for care which has not been attempted is a self management model of care. The self management model of care has an emphasis on education and active participation with the aim of empowering patients to improve their own health with appropriate scaffolding from relevant healthcare professionals (Health Foundation 2011). An area for future research, in collaboration with patients and relatives, may be to develop a model of self management for ICU survivors which encompasses social and peer

support, which are key to many other disease self management programmes (Heisler et al 2010). This model of care could also include personal and individualised targets for patients and relatives, which would align with the findings of this study and the NICE (2009) guidelines.

8.5.5 A sense of purpose

According to Antonovsky (1979) a sense of meaningfulness is key to ensuring a Sense Of Coherence and fundamentally to ensure the creation of positive health and wellbeing. Many participants described a lack purpose and meaning in their life following discharge from critical care and as a result, found it difficult to focus on recovery. This has been previously presented in the literature. Cox et al (2009) also described how both patients and family members felt hopeless about the future. More work is required to help support these patients and family members in the community from a social perspective. Furthermore, peer support with people further along the recovery trajectory may also be useful, as this may provide hope and insight about potential recovery for the physical and psychological problems which individuals may be encountering.

8.5.6 Summary

The third research objective of this PhD thesis was answered fully. Patterns of recovery for patients with and without AUDs were explored. There were many similarities in the recovery process for those with and without and AUDs. More work is required into optimal rehabilitation for all patients recovering from critical illness, with particular focus on developing patient self efficacy.

8.6 Long term outcomes from ICU

A key objective of this study was to determine whether AUDs were associated with survival in critically ill patients at six months post ICU discharge. At six months post ICU discharge, mortality in this cohort of patients was 37%. After adjustment for deprivation category and age,

alcohol dependence was associated with an almost two fold increased odds of mortality at six months post ICU discharge.

This is the first UK study which has documented long term outcomes in this cohort of patients. Further, this is one of only three prospective studies worldwide which have studied the long term outcome of patients with AUDs admitted to ICU. The data generated on long term outcomes for this patient cohort reflect the results of the two other European papers on this topic, which demonstrate the negative impact of AUDs on longer term outcomes from critical care (Christensen et al 2012, Gacouin et al 2014).

There are a variety of reasons for the poor long term outcomes seen in those with alcohol dependency and the liver cirrhosis population. For example, the poor long term outcomes seen in this cohort may be due to the social problems which many of these patents may face after discharge from critical care. These social challenges were explored in the qualitative interviews undertaken. Patients with an AUD described poor social networks and poor social cohesion more frequently than those from the low risk study group. The chaotic surroundings and relationships which many patients with an AUD described may therefore influence their ability to recover. These chaotic surroundings may lead to a lack of consistency, manageability and a lack of balance regarding stress in a participant's life; all key elements within the model of Salutogenesis.

Those participants who took part in the in depth semi structured interviews with a background of an AUD described a lack of control and self efficacy in their life after ICU more frequently than those from the low risk/no use group. Self-efficacy is known to influence outcomes, adherence to discharge instructions and physical recovery (Connolly et al 2013). This lack of self-efficacy may also have impacted on the poorer long term outcomes seen in this patient population.

Other factors which may account for poor long term outcomes include the association between alcohol related admission and the development of

septic shock during the ICU stay. Patients with an AUD were more likely to develop septic shock when in ICU; the development of septic shock is known to impact on long term mortality from ICU (Winters et al 2010). Furthermore, patients admitted to ICU with alcohol dependency are more likely to develop ARDS (Moss et al 2003). The development of ARDS during critical illness is also associated with poor long term outcomes (Herridge et al 2011). However, information on patient co-morbidities was not collected during this study. It may be that patients in the alcohol dependency group had multiple co-morbidities which impacted on both long and short term outcomes from intensive care. Future research should explore co-morbidities in this group of patients to determine what impact, if any, that these have on long term outcomes.

This study also explored the long term outcomes of patients admitted to the ICU with a background of cirrhosis. The presence of liver cirrhosis was associated with an increased mortality six months after ICU discharge. Poor long term outcomes in patients admitted to the ICU with liver cirrhosis is consistent with previous literature (Mackle et al 2006). Social reasons, such as those detailed above, may have accounted for the poor outcomes in this patient group. A limitation of this study is that it did not determine which patients continued to drink alcohol after discharge from ICU, outwith those participants who took part in the semi structured interview. Future research should explore this more fully in this patient population.

8.6.1 Summary

The fourth research objective of this PhD thesis was fully answered. Alcohol dependency is associated with mortality in critically ill patients at six months post ICU discharge

8.7 Future behaviour in relation to alcohol use

Finally, the study aimed to examine the impact of critical care on future behaviour with regards to alcohol intake. This is the first study which has

explored recovery in patients with AUDs and looked specifically at the challenges this group of patients encounter after ICU.

Approximately half of the participants who took part in the interviews with a background of an AUD continued to consume alcohol. The other half of participants reported that they had changed their relationship with alcohol or stopped drinking completely. For many participants admission to critical care was a turning point in their decision, with one individual describing it as a *'shock to the system'*. This is consistent with the literature: patients in two recent studies described both quantitatively and qualitatively of their 'readiness to change' after a stay in critical care.

Post ICU recovery may be an optimal time to deliver interventions aimed at reducing alcohol consumption (Clark and Moss 2011, Clark et al 2012). More work, across different countries and populations, is required in this area to understand the delivery of an optimal model for this.

After intensive care many patients have persistent physical, psychological and social problems and a reduced QOL. From these interviews it appeared that participants with an AUD, who positively changed their behaviour with alcohol after ICU, were the only group who could possibly have a constructive and indeed positive change in their wellbeing after ICU. Those patients who had stopped consuming alcohol described better relationships with family members and a healthier outlook on life. Of note, all of those who had stopped drinking after ICU stated that social support was fundamental to this progress.

However, social support and social structures were described as an external driver for both stopping and continuing to consume alcohol following intensive care discharge. Vicious social cycles were harrowingly described by some participants. Individuals discussed negative environments related to their recovery from both ICU and alcohol. For example, living in poor geographical areas or temporary accommodation such as hostels, or having family members or peers with problematic social

issues, or ongoing problems with harmful alcohol use all impacted negatively on the decision to stop drinking excessively. However, for many participants, until they had stopped drinking, they could not be moved out of these often harmful environments, which consequently led to an almost impossible situation for some of the participants interviewed. As previously stated, lack of social support when leaving intensive care and a lack of communication between the acute and community sectors has been highlighted previously in the literature (Cox et al 2009, Walker et al 2015). This was particularly true for this vulnerable population.

Another interesting finding from this work was that those patients who had clear memories of the ICU stay and how seriously unwell they had been, discussed changing their relationship with alcohol more frequently. It may be that interventions such as the ICU diary may be appropriate for this group to give meaning and comprehensibility to their critical illness. This could be an area of future research regarding ICU diaries and AUDs within the critical care environment.

Similar to the study undertaken in 2013 by Clark et al, participants described the importance of compassionate, clear and non judgemental interactions with healthcare professions during their recovery from critical illness. Furthermore, participants discussed the importance of timely and appropriate rehabilitation after critical care for optimal support for their addiction. This includes the delivery of support when a patient is aware of the intervention, at a time which is suitable for the individual and the delivery of support by and the appropriate health or social care practitioner. These findings link closely to the idea that an admission to critical care may be a *teachable moment* in terms of delivering interventions for health related behaviours.

These discussions about recovery map almost identically to the Life Experiences section of the model of Salutogenesis (Antonovsky 1979). These steps to rehabilitation will ensure *consistency* (working with an individual's own support worker), *participation* (the individual is able to

work as an active partner in their recovery) and will ensure that that the individual can control the *balance* of the interventions, thus ensuring they are in control and their future can be predictable and coherent. As far as we can establish, no work has focused on alcohol rehabilitation within the hospital setting after critical care discharge. Based on the findings from this thesis, future research should focus on the delivery of sensitive support in the acute healthcare setting.

8.7.1 Summary

The final research objective of this thesis has been fully explored. Future behaviours regarding alcohol intake were examined after hospital discharge. Furthermore, potential rehabilitation strategies for optimal recovery were also discussed.

8.8 What does this study add to the existing body of literature?

The results and findings of this study add new information and perspectives to the existing international knowledge base concerning alcohol related admissions to the ICU. This includes:

- This is the first British study which has demonstrated the link between septic shock and alcohol related admissions in the critical care environment

- This is the first study in the ICU environment, as far as we can establish, which has demonstrated the link between deprivation and social demographics such as alcohol use, smoking and drug use

- This is the first British study to monitor patients with alcohol related admissions beyond the hospital environment. Moreover, this is one of only three prospective studies worldwide which have studied the long term outcomes of patients with AUDs admitted to ICU

- This is one of the first studies to externally validate the CLIF-SOFA and RFH score

- This work adds to the existing body of literature, which demonstrates the link with admission lactate in critically ill cirrhotic patients and outcomes from ICU

- This works has developed a bedside tool which demonstrates good sensitivity and specificity in predicting the outcomes of patients from ICU in three different centres

- The qualitative aspect of this study is completely novel. This is the first study, as far as can be established, which has explored recovery in patients with AUDs and looked specifically at the challenges this group of patients encounter after ICU

- The findings of this study also explore unique social challenges which all ICU survivors encounter after discharge home.

8.9 Study Limitations

The prospective approach to assessing patients within the cohort study does have strengths. The research team could have utilised a validated scoring tool for the assessment of AUDs (i.e. Fast Alcohol Screening Tool (FAST) or Alcohol Use Disorders Test (AUDIT) (Babor et al 1989, Hogson et al 2002). However, none of these tools have been through extensive validation work in the non verbal ICU population and as a result are rarely used in the critical care setting in the UK (McPeake et al 2013). Despite being validated for use with proxies in specialities such as accident and emergency, there appears to be no study which has validated this approach within the European critical care setting (Donovan et al 2004). More work is required on the use of these tools with non verbal patients and their proxies within the ICU environment.

The prospective cohort study and the semi structured interviews were undertaken in a single centre, residing in an area of high deprivation where alcohol related illness is a significant public health issue. Glasgow has high rates of unemployment, with a high number of individuals out of work because of ill health. Glasgow also has low levels of general health compared to wider UK and Scottish populations (Brown, Hanlon, Turok et al 2008). Therefore, the high numbers of alcohol related admissions captured may not be representative of all ICUs. Furthermore, due to the single centre nature of this study, it can only provide information on the range of experiences described by the participants interviewed. As a result, conclusions about how prevalent such experiences are cannot be made. However, this work does offer a unique insight into the impact of alcohol and its link with deprivation in the critical care setting.

A further significant limitation of this work is that those patients who participated in the semi structured interviews may be a self selecting group, not completely representative of the population being explored. Of the 72 patients invited to participate, 35 (48.6%) either did not reply or did not wish to be interviewed. However, this study does give a valuable

insight during the challenging recovery period, which no other study has offered.

In relation to the cirrhosis sub study in this thesis, the lack of pre intubation encephalopathy scores in the London dataset may have impacted on the reported results. Additionally, clinical values for the scoring tools at admission were taken as soon as possible following arrival in the ICU, but in some cases this was delayed. This variability in time may have affected the predictive ability of the scoring tools. However, this work does represent one of the biggest data sets available for the general ICU setting and gives contemporary data on the outcomes for this patient group.

8.10 Reflection on the research process

8.10.1 Issues of rigour

The following section will detail the steps undertaken throughout this PhD thesis, to ensure a rigorous approach to the research process.

The PhD student undertook the steps detailed in Section 3.10.3 (see Table 8.1) to ensure a reflexive approach to the research process. Throughout this PhD, information on how data was produced, the process of analysis, including decisions on the type of analysis to be used, has been made explicitly clear. Field notes were kept throughout the duration of the study period; these detailed and specified key decisions made throughout all stages of the research process. These notes, as well as all transcripts from the interviews, were available to the peer reviewers of the qualitative aspect of this study.

Throughout the study period, the evolving results and findings have been presented in various peer reviewed journals and at international multi disciplinary conferences (See Pages 13-14). This step has also ensured continuous peer review of the process and outputs from this body of work.

Table 8.1: A framework for Reflexive Practice (Adapted from Green and Thorogood 2004)

Good Practice Approaches	Execution in Practice
Methodological openness	Be explicit about data production, analysis, decisions made and alternatives not pursued.
Theoretical openness	Theoretical starting points and assumptions should be addressed as well as how they shaped the study.
Awareness of the social setting of the research itself	Demonstrate an awareness of how your interaction as researcher influenced the data.
Awareness of the wider social context	How have politics and social values made the research possible and how have they constrained it?

Epistemological and ontological standpoints were considered frequently throughout the research process and decisions were made in and attempt to ensure objectivity. Reflective debriefs with supervisors and the use of reflective field notes with each interview undertaken, helped ensure that no assumptions were being made by the PhD student and that interpretations were based on the content of the interview, rather than clinical insights, knowledge or beliefs that the PhD student held. Furthermore, transcribing interviews as soon as possible and revisiting the IPA process frequently, allowed the research student to stay focused on and seek out as fully as possible the experience of the patient.

Finally, throughout this PhD the wider political and social context within and outwith the research process was considered. For example, the SIMD was used at every stage of this research to understand the socio economic context of the study and participant. Further, throughout the interviews, the PhD student sought to understand the context for alcohol misuse to help understand the drivers and influences for current decision making.

8.10.2 Relationship between the participant and the researcher

The in depth semi structured interviews were undertaken over a nine month period. Participants shared personal and sometimes very sad experiences, which were often created as a consequence of clinical environment where the study was undertaken. As a result, the role of PhD student and ICU nurse often became blurred in this observational capacity as researcher. This was especially true of one participant who was isolated and had no social support networks to help with recovery. Although the participant's GP was informed and support processes put in place as described within the Ethics application, this was an incredibly complex situation. Debriefing sessions with supervisors and academic peers helped ensure objectivity and indeed internal validity. Furthermore, the process of peer review ensured all interpretations were based on the evidence gathered rather than on the PhD student's personal standpoint and world view. However, this process has given insight into the challenges of undertaking qualitative research with vulnerable populations from the researcher's perspective and the need for support networks to be put in place for professionals undertaking this type of work.

Many of the family members who attended the interviews did remember the PhD student from their time in the ICU. This undoubtedly will have impacted on what the participants discussed and indeed who participated in the study. However, at the start of each interview, how the data would be handled and a thorough explanation of the purpose of the interview was given in the hope of reducing this bias. The PhD student also encouraged participants to describe everything in their own language and how they understood events. This was with the aim of reducing assumptions made by the PhD student during the interpretation of results.

The limitations of having the interviews take place within the hospital environment may have also influenced the data collected during the interviews, as this may not have been a comfortable place for those involved. Furthermore, it may have appeared that there was a gradient of

inequality in terms of knowledge and status within the interview setting. Ideally, the interviews should have taken place in a more naturalistic location. However, due to research governance structures and safety issues, this was not possible.

8.11 Chapter Conclusion

This chapter has presented the discussion related to the results and findings of this PhD thesis. It has provided future directions for research in this area and has presented the limitations to the PhD. The next chapter will provide a brief conclusion to this work.

Chapter Nine: Conclusions and Recommendations for Practice

9.1 Introduction

In this final chapter, the main results and findings of this mixed methods PhD are summarised. Recommendations for future research, clinical practice and education are also presented. A final section on the student's future work is also given briefly.

A high proportion of patients admitted to the ICU had AUDs. Compared with other admissions to critical care they were younger and more likely to take drugs and smoke. AUDs were also associated with an increased odds of developing septic shock in the ICU and with poorer outcomes from the ICU, hospital and at six months following ICU.

At present there is minimal information on optimal rehabilitation for patients with an AUD. Some recent studies have suggested that early intervention within the ICU environment in the form of brief interventions may be beneficial and an ICU admission may represent a 'teachable moment' for patients with an AUD (Clark and Moss, 2011). Much of this research has been undertaken with patients during the ICU stay (Clark et al 2013), which may not give a full picture of the multifaceted interventions which may be required for this cohort in the longer term. More research into optimal rehabilitation is required in this area.

This study has demonstrated that all patients leaving ICU need more support to ensure a timely and effective recovery. This work has contributed, especially from a social perspective, to the body of evidence regarding QOL from ICU. It would appear that some of the current approaches to rehabilitation may have some use for patients, however, a model which focuses on encouraging self efficacy and promoting patient ownership of their care may be of use when moving forward with rehabilitation for this patient group.

9.2 Summary of results and findings

The main results and findings from this PhD thesis are:

- Individuals recovering from a critical illness suffer persistent physical and psychological problems for many months after discharge from ICU

- Very few participants had clear memories of their ICU admission. This had a significant impact on their ability to recover, as many individuals could not comprehend why they now had considerable psychological and physical problems

- Participants described the importance of a stable social structure in their recovery

- Families and carers also experience challenges both during the ICU admission and throughout the critical care recovery period

- Those participants admitted with a background of an AUD discussed both positive and negative consequences of admission to ICU

- For many patients, admission to critical care does influence behaviour with regards to future alcohol use.

9.3 Recommendations

9.3.1 Recommendations for future research

This PhD thesis has identified that alcohol related admissions make up a high proportion of admissions to the ICU environment. However, significant amounts of work are required to understand assessment and management of these patients within the critical care setting.

Referral patterns in this patient cohort, especially those with liver cirrhosis, need analysed further. This is especially true for those patients with a combination of an AKI and liver cirrhosis.

This PhD has highlighted more work is required to support this vulnerable population from an emotional, social and psychological point of view after discharge home from hospital. The same level of support is also required for family members and carers. Future research must go beyond the traditional biomedical approach which has been utilised in the past and focus on health and social care integration. Rehabilitation must also move away from a focus on physical rehabilitation and/or isolated psychological interventions such as patient diaries. This PhD has demonstrated that there must be an emphasis on encouraging individuals to take control of their health. Furthermore, this work has highlighted that health care and social care practitioners must focus on goals which are person centred and not service defined.

9.3.2 Recommendations for clinical practice

The findings from this programme of research have several implications for future practice. Many patients feel 'abandoned' after a critical care stay. Critical Care Practitioners must communicate effectively with patients, families and downstream wards in the acute care setting, to help facilitate a smoother journey for this patient cohort. A further recommendation for practice is that more education and communication is needed between acute and primary care. Critical Care Practitioners must also raise awareness within General Practice to ensure that patients have the appropriate support they require when returning to their home.

Greater emphasis must be placed on discharge planning at all stages for this cohort of patients. Significant problems with housing and access to rehabilitation services were experienced by participants and family members. More focus on discharge is required to ensure a seamless transition to recovery.

Finally, Critical Care Practitioners must communicate more effectively with patient and family members about the long term consequences of critical illness and the challenges which they are likely to encounter. This will help individuals plan more carefully for their future from a health and social perspective.

9.4 Current work

The PhD student is already engaging with future work in this area as a direct result of the results and findings of this study.

It was clear from this data that both patients and family members experienced significant problems throughout their hospital stay and beyond. A result, the PhD student also aimed to understand the solutions from a patient's perspective. With the support of Dr Tara Quasim, a grant was obtained from the Foundation of Nursing Studies to create a Patient and Family Advisory Council in the ICU at Glasgow Royal Infirmary. This Council, which is chaired by participants, has helped develop novel solutions to the issues raised within this PhD.

A grant has also been obtained from the Health Foundation, again with Dr Tara Quasim, to pilot an innovative five week rehabilitation programme for ICU survivors. This programme (Intensive Care Syndrome: Promoting Independence and Return to Employment: InS:PIRE) is based on a cardiac rehabilitation model. The main outcome measures are return to employment; GP visitations and self efficacy. Patients also set individual goals or personal outcomes, which are co produced with staff at the clinic and various community organisations. This work has been created, in part, from the results of this study.

The research group are also working closely with a Health Economist to critically appraise the economic impact of a poor quality of life in the ICU survivor population. This work is focusing on increased healthcare

utilisation costs as well as low quality of life and changes to employment after critical care.

The PhD student is collaborating in a project which is evaluating the use a proxy assessment for patient alcohol use during the ICU admission. Furthermore, a BSc student is continuing to build on the cirrhosis work undertaken in this PhD. This work is now focusing on longer term outcomes for this patient group.

Finally, a CSO Nursing and Midwifery Clinical Academic Fellowship was obtained in January 2015. This Fellowship will allow the development of the above work, with the aim of improving outcomes in this vulnerable patient group.

9.5 Thesis conclusion

This work has demonstrated the difficult recovery trajectory which all patients face. Providing ICU care is expensive and more work is required to ensure that this investment is worthwhile and patients are given the support they require during recovery from critical illness.

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Appendices

Appendix I: Alcohol Screening Tools

Michigan Alcohol Screening Test (MAST) (Selzer 1971):

Questions are asked in relation to the last 12 months.
1. Do you feel you are a normal drinker? ('normal'- drink as much or less than most other people)
Circle Answer: YES NO

2. Have you ever awakened the morning after some drinking the night before and found that you could not remember part of the evening?
Circle Answer: YES NO

3. Does any near relative or close friend ever worry or complain about your drinking?
Circle Answer: YES NO

4. Can you stop drinking without difficulty after one or two drinks?
Circle Answer: YES NO

5. Do you ever feel guilty about your drinking?
Circle Answer: YES NO

6. Have you ever attended a meeting of Alcoholics Anonymous (AA)?
Circle Answer: YES NO

7. Have you ever gotten into physical fights when drinking?
Circle Answer: YES NO

8. Has drinking ever created problems between you and a near relative or close friend?
Circle Answer: YES NO

9. Has any family member or close friend gone to anyone for help about your drinking?
Circle Answer: YES NO

10. Have you ever lost friends because of your drinking?
Circle Answer: YES NO

11. Have you ever gotten into trouble at work because of drinking?
Circle Answer: YES NO

12. Have you ever lost a job because of drinking?
Circle Answer: YES NO

13. Have you ever neglected your obligation, your family, or your work for two days in a row because you were drinking?
Circle Answer: YES NO

14. Do you drink before noon fairly often?
Circle Answer: YES NO

15. Have you ever been told you have liver trouble such as cirrhosis?
Circle Answer: YES NO

16. After heavy drinking have you ever had delirium tremens (D.T's), severe shaking, visual or auditory (hearing) hallucinations?
Circle Answer: YES NO

17. Have you ever gone to anyone for help about your drinking?
Circle Answer: YES NO

18. Have you ever been hospitalized because of drinking?
Circle Answer: YES NO

19. Has your drinking ever resulted in your being hospitalised in a psychiatric ward?
Circle Answer: YES NO

20. Have you ever gone to any doctor, social worker, clergyman or mental health clinic for help with any emotional problem in which drinking was part of the problem?
Circle Answer: YES NO

21. Have you been arrested more than once for driving under the influence of alcohol?
Circle Answer: YES NO

22. Have you ever been arrested, even for a few hours because of behaviour while drinking?
Circle Answer: YES NO

Scoring
Please score one point if you answered the following:
1. NO
2. YES
3. YES
4. NO
5 through 22:YES

Add up the scores and compare to the following:
0-2: No apparent problem
3-5: Early or middle problem drinker
6 or more: Problem drinker

Cut-down, Annoyed, Guilty, Eye-Opener' (CAGE) (Mayfield et al 1974)

1. Have you ever felt you needed to **C**ut down on your drinking?
2. Have people **A**nnoyed you by criticizing your drinking?
3. Have you ever felt **G**uilty about drinking?
4. Have you ever felt you needed a drink first thing in the morning (**E**ye-opener) to steady your nerves or to get rid of a hangover?

Two 'yes' responses indicate the possibility of alcoholism.

Fast Alcohol Screening Tool (FAST) (Hodgson et al 2002)

FAST	**Scoring system**					**Your score**
	0	**1**	**2**	**3**	**4**	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Only answer the following questions if the answer above is Never (0), Less than monthly (1) or Monthly (2). Stop here if the answer is Weekly (3) or Daily (4).						
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

If score is 0, 1 or 2 on the first question continue with the next three questions

If score is 3 or 4 on the first question – stop here.
An overall total score of 3 or more is FAST positive.

What to do next?
If FAST positive, complete remaining AUDIT questions (this may include the three remaining questions above as well as the six on the next page) to obtain a full AUDIT score.

Alcohol use Identification Test (AUDIT) (Barbor, et al 1989)

Scoring: 0 – 7 Lower risk, 8 – 15 Increasing risk,
16 – 19 Higher risk, 20+ Possible dependence

AUDIT	**Scoring system**					**Your score**
	0	**1**	**2**	**3**	**4**	
How often do you have a drink containing alcohol?	Never	Monthly or less	2 - 4 times per month	2 - 3 times per week	4+ times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	1 -2	3 - 4	5 - 6	7 - 9	10+	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you needed an alcoholic drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Have you or somebody else been injured as a result of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Appendix II: Publications Related to this Programme of Study

Appendix III: Alcohol Withdrawal Assessment Tools

Clinical Institute Withdrawal Scale for Alcohol revised (CIWA-Ar) (Sullivan et al 1989):

Clinical Institute Withdrawal Assessment Scale for Alcohol, Revised (CIWA-Ar)

Nausea and Vomiting
0 – No nausea or vomiting
1
2
3
4 – Intermittent nausea with dry heaves
5
6
7 – Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats
0 – No sweat visible
1 – Barely perceptible sweating, palms moist
2
3
4 – Beads of sweat obvious on forehead
5
6
7 – Drenching sweats

Agitation
0 – Normal activity
1 – Somewhat more than normal activity
2
3
4 – Moderate fidgety and restless
5
6
7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances
0 – Not present
1 – Very mild photosensitivity
2 – Mild photosensitivity
3 – Moderate photosensitivity
4 – Moderately severe visual hallucinations
5 – Severe visual hallucinations
6 – Extreme severe visual hallucinations
7 – Continuous visual hallucinations

Tremor
0 – No tremor
1 – Not visible, but can be felt at finger tips
2
3
4 – Moderate when patient's hands extended
5
6
7 – Severe, even with arms not extended

Tactile Disturbances
0 - None
1 – Very mild paraesthesias
2 – Mild paraesthesias
3 – Moderate paraesthesias
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Headache
0 – Not present
1 – Very mild
2 - Mild
3 - Moderate
4 – Moderately severe
5 - Severe
6 – Very severe
7 – Extremely severe

Auditory Disturbances
0 – Not present
1 – Very mild harshness or ability to frighten
2 – Mild harshness or ability to frighten
3 – Moderate harshness or ability to frighten
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Orientation and Clouding of the Sensorium
0 – Oriented and can do serial additions
1 – Cannot do serial additions
2 – Disoriented for date but not more than 2 calendar days
3 - Disoriented for date by more than 2 calendar days
4 – Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0 – 8	No medication needed
9 – 14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

Glasgow Modified Alcohol Withdrawal Scale (GMAWS) (McPherson et al 2012):

Tremor 0) No tremor 1) On movement 2) At rest	
Sweating 0) No sweat visible 1) Moist 2) Drenching sweats	
Hallucination 0) Not present 1) Dissuadable 2) Not dissuadable	
Orientation 0) Orientated 1) Vague, detached 2) Disorientated, no contact	
Agitation 0) Calm 1) Anxious 2) Panicky	
Score	
Treatment	

Score: (Do not use scoring tool if patient intoxicated, must be at least 8 hours since last drink.)

0: Repeat Score in 2 hours (Discontinue after scoring on 4 consecutive occasions, except if less than 48hrs after last drink)

1 – 3: Give 10mg Diazepam: Repeat Score in 2 hours

4 – 8: Give 20mg Diazepam: Repeat Score in 1 hour

9 - 10: Give 20mg Diazepam : Repeat Score in 1 hour; discuss with medical staff

Appendix IV: ICU Delirium Screening Tools

Intensive Care Delirium Screening Checklist (ICDSC) (Bergeron et al 2001)

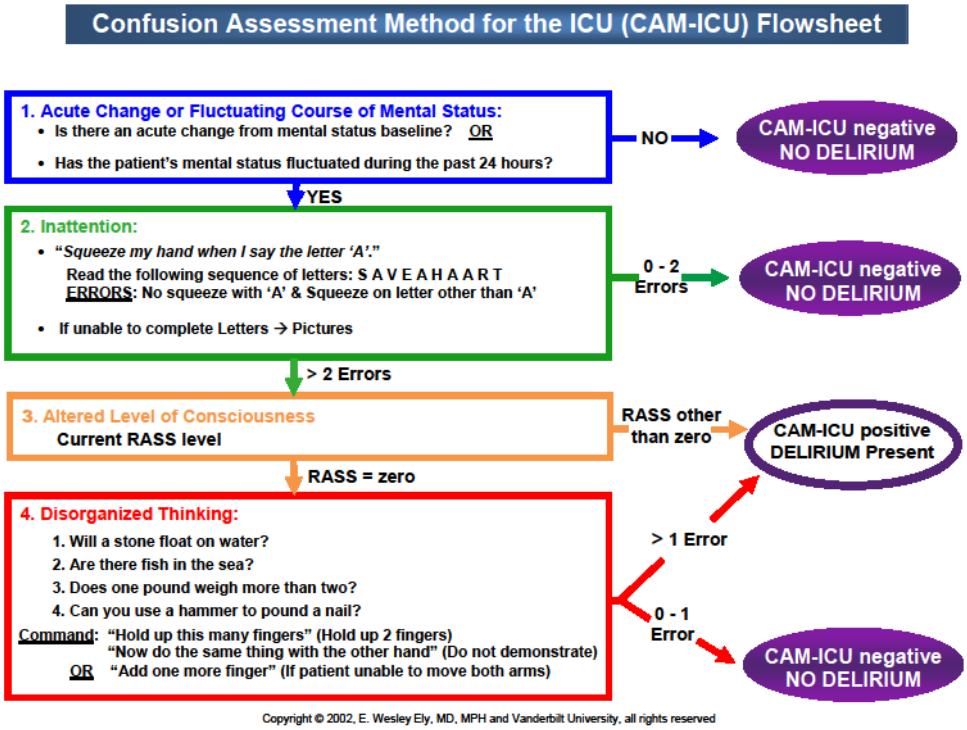
1. Altered level of consciousness. Choose one from A to E		
A. Exaggerated response to normal stimulation	SAS = 5, 6, 7 or RASS = +1 to +4	(1 point)
B. Normal wakefulness	SAS = 4 or RASS = 0	(0 points)
C. Response to mild or moderate stimulation (follows commands)	SAS = 3 or RASS = −1 to −3	(1 point)
D. Response only to intense and repeated stimulation (e.g., loud voice and pain)	SAS = 2 or RASS = −4	Stop assessment[a]
E. No response	SAS = 1 or RASS = −5	Stop assessment[a]
2. Inattention (1 point if any present)		
A. Difficulty in following commands or		
B. Easily distracted by external stimuli or		
C. Difficulty in shifting focus		
Does the patient follow you with their eyes?		
3. Disorientation (1 point for any abnormality)		
A. Mistake in either time, place, or person		
Does the patient recognize ICU caregivers who have cared for him/her and not recognize those who have not? What kind of place are you in? (list examples)		
4. Hallucinations or delusions (1 point for either)		
A. Equivocal evidence of hallucinations or a behavior due to hallucinations (hallucination = perception of something that is not there with no stimulus) or		
B. Delusions or gross impairment of reality testing (delusion = false belief that is fixed/unchanging)		
Any hallucinations now or over past 24 hr? Are you afraid of the people or things around you? (fear that is inappropriate to the clinical situation)		
5. Psychomotor agitation or retardation (1 point for either)		
A. Hyperactivity requiring the use of additional sedative drugs or restraints in order to control potential danger (e.g., pulling IV catheters out or hitting staff) or		
B. Hypoactive or clinically noticeable psychomotor slowing or retardation		
Based on documentation and observation over shift by primary caregiver		
6. Inappropriate speech or mood (1 point for either)		
A. Inappropriate, disorganized, or incoherent speech or		
B. Inappropriate mood related to events or situation		
Is the patient apathetic to current clinical situation (i.e., lack of emotion)?		
Any gross abnormalities in speech or mood? Is patient inappropriately demanding?		
7. Sleep/wake cycle disturbance (1 point for any abnormality)		
A. Sleeping < 4 hr at night or		
B. Waking frequently at night (do not include wakefulness initiated by medical staff or loud environment) or		
C. Sleep ≥ 4 hr during day		
Based on primary caregiver assessment		
8. Symptom fluctuation (1 point for any)		
Fluctuation of any of the above items (i.e., 1–7) over 24 hr (e.g., from one shift to another)		
Based on primary caregiver assessment		
Total Intensive Care Delirium Screening Checklist score (add 1–8) _____		

[a]Delirium assessment can not be completed in patients who are stuporous or comatose.

SAS = Riker Sedation-Agitation Scale, RASS = Richmond Agitation-Sedation Scale.

Modified from Devlin JW, Marquis F, Riker RR, et al: Combined didactic and scenario-based education improves the ability of intensive care unit staff to recognize delirium at the bedside. *Crit Care* 2008; 12:R19.

Confusion Assessment Method for the ICU (CAM-ICU) (Ely et al 2001)



Appendix V: Scoring Tools In Critical Care

Child-Turcotte Pugh (CTP) score (Pugh, et al 1973):

	1	2	3
Total Bilirubin	<34	34-50	>50
Serum Albumin	>35	28-35	<28
INR	<1.7	1.71-2.3	>2.3
Ascites	None	Mild	Moderate to Severe
Heaptic Encephalopathy	None	Grade I-II	Grade III-IV

Score	Class
5-6	A
7-9	B
10-15	C

Model for End Stage Liver Disease (MELD) (Kamath et al 2001):

MELD Score = (0.957 * ln(Serum Cr) + 0.378 * ln(Serum Bilirubin) + 1.120 * ln(INR) + 0.643) * 10 (if hemodialysis, value for Creatinine is automatically set to 4.0)

Note: If any score is <1, the MELD assumes the score is equal to 1.

UK End Stage Liver Disease (UKELD) score (Neuberger et al 2008):

(5.395 x lnINR) + (1.485 x lnCreat) + (3.13 x lnBilirubin) - (81.565 x lnNa) + 435

The Royal Free Hospital Score (RFH) score (Cholongitas et al 2006):

RFH score = -6.611 + bilirubin(0.004) + urea(0.057) + lactate(0.274)+FiO_2(3.126) + K

Where K is a constant that depends on the number of failing organ systems. The number of failing organ systems for the RFH score is defined by a sofa score of ≥3 for each organ system.

Glasgow Alcoholic Hepatitis Score (GAHS) (Forrest et al 2007):

	1	**2**	**3**
Age	<50	>50	
WCC	<15	>15	
Urea	<5	>5	
INR	<1.5	1.5-2	>2
Bilirubin	<125	125-250	>250

Sequential Organ Failure Assessment (SOFA) score (Vincent et al 1998):

Organ/System	**0**	**1**	**2**	**3**	**4**
Liver (Bilirubin (mg/dL)	<1.2	1.2-1.9	2-5.9	6-11.9	>12
Kidney (Creat, mg/dL or urine output ML/day)	<1.2	1.2-1.9	2-3.4	3.5-4.9 or<500ml	>5 or <200ml
Central Nervous System (GCS)	15	13-14	10-12	6-9	<6
Coagulation (Platelets, x 10^9/L)	>150	≤150	≤100	≤50	≤20
Circulation	MAP ≥70mmHg	MAP <70mmHg	Dopamine ≤5 or Dobutamine any dose	Dopamine >5, epinephrine ≤ 0.1 or norepinephrine ≤0.1	Dopamine >15, epinephrine >0.1 or norepinephrine >0.1
Respiratory (PaO_2/FiO_2)	>400	>300-≤400	>200-≤ 300	>100-≤200	≤100

Doses for catecholamines are in μg/Kg/min.

Chronic Liver Failure- Sequential Organ Failure (CLIF-SOFA) (Moreau et al 2013)

Organ/System	0	1	2	3	4
Liver (Bilirubin (mg/dL)	**<1.2**	**≥1.2-≤2.0**	**≥2.0-<6.0**	**≥6.0-<12.0**	**≥2.0**
Kidney (Creat, mg/dL	**<1.2**	**≥1.2-<2.0**	**≥2.0-<3.5**	**≥3.5-<5.0**	**≥5.0**
					Or use of RRT
Cerebral (Hepatic encephalopathy Grade)	**No HE**	**I**	**II**	**III**	**IV**
Coagulation (INR)	**<1.1**	**≥1.1-<1.25**	**≥1.25-<1.5**	**≥1.5-<2.5**	**≥2.5 or platelet count ≤20 (10^9/L)**
Circulation	**MAP ≥70mmHg**	**MAP <70mmHg**	**Dopamine ≤5 or Dobutamine any dose**	**Dopamine >5, epinephrine ≤ 0.1 or norepinephrine ≤0.1**	**Dopamine >15, epinephrine >0.1 or norepinephrine >0.1**
Lungs					
$Pa0_2/Fi0_2$ or	**>400**	**>300-≤400**	**>200-≤ 300**	**>100-≤200**	**≤100**
$Sp0_2/Fi0_2$	**>512**	**>357-≤512**	**>214-≤357**	**>89-≤214**	**≤89**

Acute Physiolgy and Chronic Health Evalutaion (APACHE) tool (Knaus, et al 1985):

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

APACHE II Score	
Sum of	
	A + B + C
APS-Score	A
Age points	B
Chronic points	C
Total APACHE II	

C - Chronic Health points

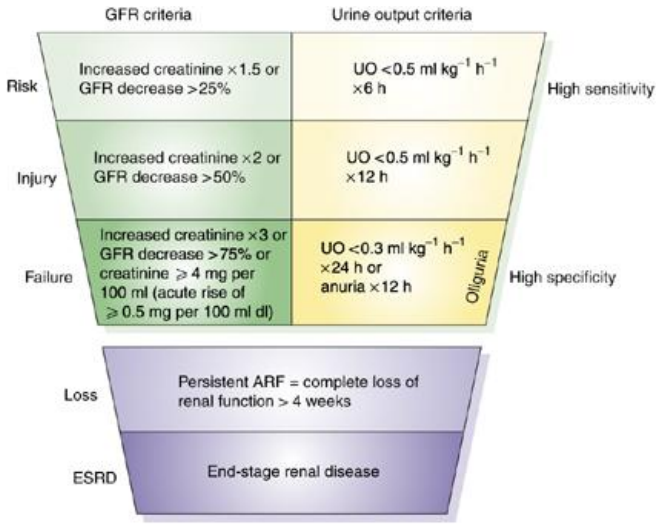
If the patient has a history of severe organ system insufficiency or is immuno-commpromised assign points as follows

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

Risk, Injury, Failure, Loss and End Stage Renal Disease (RIFLE) tool (Bellomo et al 2004)



Acute Kindey Injury Network (AKIN) tool (Mehta et al 2007):

Table 1 | Classification and staging systems for AKI

System	Serum creatinine criteria	Urine output criteria
RIFLE class		
Risk	Serum creatinine increase to 1.5-fold OR GFR decrease >25% from baseline	<0.5 ml/kg/h for 6 h
Injury	Serum creatinine increase to 2.0-fold OR GFR decrease >50% from baseline	<0.5 ml/kg/h for 12 h
Failure	Serum creatinine increase to 3.0-fold OR GFR decrease >75% from baseline OR serum creatinine ≥354 μmol/l (≥4 mg/dl) with an acute increase of at least 44 μmol/l (0.5 mg/dl)	Anuria for 12 h
AKIN Stage		
1	Serum creatinine increase ≥26.5 μmol/l (≥0.3 mg/dl) OR increase to 1.5–2.0-fold from baseline	<0.5 ml/kg/h for 6 h
2	Serum creatinine increase >2.0–3.0-fold from baseline	<0.5 ml/kg/h for 12 h
3	Serum creatinine increase >3.0-fold from baseline OR serum creatinine ≥354 μmol/l (≥4.0 mg/dl) with an acute increase of at least 44 μmol/l (0.5 mg/dl) OR need for RRT	<0.3 ml/kg/h for 24 h OR anuria for 12 h OR need for RRT

Small but important differences are observed between the two systems. A time constraint of 48 h for diagnosis (using either serum creatinine levels or urine output) is required in AKIN criteria. GFR decreases are used for diagnosis only in RIFLE criteria. In both systems, only one criterion (creatinine or urine output) has to be met to qualify for a given class or stage of AKI. Classes L and E of the RIFLE criteria are not reported. Owing to the wide variation in indications for and timing of initiation of RRT, individuals who receive RRT are considered to have AKIN Stage 3 AKI irrespective of their serum creatinine level and urine output.[6,15] Abbreviations: AKI, acute kidney injury; AKIN, AKI Network; GFR, glomerular filtration rate; RIFLE, Risk, Injury Failure, Loss, End-stage renal disease; RRT, renal replacement therapy.

Appendix VI: Approvals required for this study

Appendix VII: Study Group Definitions

Definitions of Alcohol Use (Version Three)

If a FAST score has been obtained prior to ICU admission please use this to determine group allocation. Use the following scoring system:

FAST 0-2: No Risk/Low Risk
FAST 3-8: Harmful Use
FAST 9-16: Alcohol Dependency

No Risk/Low risk:
Individuals who:

- Consume no alcohol;
- Have experienced no or minimal harm as a result of alcohol use.

Harmful Use:

- Alcohol is responsible for or has substantially contributed to physical or psychological harm, including impaired judgement or dysfunctional behaviour ;
- The nature of harm is clearly identifiable (i.e. falls/ absence from work);
- The pattern has persisted for at least one month previous to

Alcohol Dependence (should be made if <u>three or more</u> of the following are present):

- A strong desire or sense of compulsion to take alcohol;
- Difficulty in controlling drinking in terms of: onset, termination or level of use;
- A physiological *withdrawal* state is present when drinking has ceased or been reduced;
- Drinking to relieve or avoid withdrawal symptoms;
- Evidence of *tolerance*, such that increased doses of alcohol are required in order to achieve effects originally produced by lower amounts (examples are when individuals take daily doses sufficient to incapacitate or severely hurt non-tolerant users);
- Preoccupation with alcohol use to the detriment of other interests (e.g. social or occupational)
- Persistent alcohol use despite awareness of harmful consequences, such as physical harm (liver impairment), depressive mood states consequent to periods of heavy drinking, or alcohol related impairment of cognitive function.

Appendix VIII: NHS Greater Glasgow and Clyde Sepsis Screening tool

Appendix IX: RStudio version 0.98.493 (R Foundation for statistical computing, Vienna, Austria): Screen Shots