A clinical investigation to examine the proportion of posttraumatic stress disorder after discharge from critical care.

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Summary

The psychological impact of a critical care admission is sufficient to precipitate significant psychiatric morbidity for those who survive it. The true proportion of posttraumatic stress disorder (PTSD) is unclear.

A prospective longitudinal study of 90 survivors was conducted to examine the proportion of PTSD, using a structured clinical interview and compared to that identified through a self-report questionnaire. Assessments of anxiety, depression, cognitive function and quality of life, were also performed. The primary aim was to determine the true prevalence of PTSD after critical care discharge

The proportion of survivors of critical care treatment who developed PTSD, according to a structured clinical interview after discharge was modest and lower than that reported previously in most critical care studies or compared to that identified through self-report questionnaires. However, the identified proportion of 10% PTSD still represents a significant minority who could potentially benefit from detection and treatment. A model stepped care pathway is proposed, to support survivors in their psychological recovery after discharge from critical care.

Thesis Chapters and Contents

METHODOLOGY

5. Methods

6. Statistical Methods

RESULTS

7. Recruitment, baseline characteristics and attrition

8. PTSD Assessment Outcomes

9. Comparison of Assessment measures 107

Tables

Chapter 7

Chapter 8

Chapter 9

Linear regression - 1 month data

Chapter 11

Chapter 12

Figures

Figures

Figures

ABBREVIATIONS

AAA - ABDOMINAL AORTIC ANEURYSM

ACER- ADDENBROOKE'S COGNITIVE EXAMINATION

ALI - ACUTE LUNG INJURY

APA - AMERICAN PSYCHIATRIC ASSOCIATION

APACHE - ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVAUATION

ARDS - ACUTE RESPIRATORY DISTRESS SYNDROME

ASD - ACUTE STRESS DISORDER

BAI - BECK ANXIETY INVENTORY

BDI - BECK DEPRESSION INVENTORY

CAM-ICU - CONFUSION ASSESSMENT METHOD

CAPS - CLINICIAN ADMINISTERED POSTTRAUMATIC STRESS DISORDER SCALE

CES-D - CENTRE FOR EPIDEMIOLOGICAL STUDIES DEPRESSION

DSM - DIAGNOSTIC AND STATISTICAL MANUAL

DTS - DAVIDSON TRAUMA SCALE

E/A - EMERGENCY ADMISSION

HADS - HOSPITAL ANXIETY AND DEPRESSION SCALE

HSC - HAYLING SENTENCE COMPLETION TEST

ICD - INTERNATIONAL CLASSIFICATION OF DISEASE

ICNARC - INTENSIVE CARE NATIONAL AUDIT AND RESEARCH CENTRE

ICU - INTENSIVE CARE UNIT

IES - IMPACT OF EVENTS SCALE

IES-R - IMPACT OF EVENTS SCALE-REVISED

IQCODESF - INFORMANT QUESTIONNAIRE ON COGNITIVE DECLINE SHORT FORM

ISS - INJURY SEVERITY SCORE

mBDRS - MODIFIED BLESSED DEMENTIA RATING SCALE

MCS - MENTAL COMPOSITE SCORE

MMSE - MINI MENTAL STATE EXAMINATION

MTBI - MILD TRAUMATIC BRAIN INJURY

MTI - MULTIPLE TRAUMATIC INJURIES

MVA - MOTOR VEHICLE ACCIDENT

NRS-R - REVISED NEUROBEHAVIOURAL SCALE

PCS - PHYSICAL COMPOSITE SCORE

PMH- PAST MEDICAL HISTORY

PPH - PAST PSYCHIATRIC HISTORY

PTSD - POSTTRAUMATIC STRESS DISORDER

PTSS - POSTTRAUMATIC STRESS SYMPTOMS

PTSS-10 - POSTTRAUMATIC STRESS SYMPTOM SCALE - 10 ITEMS

PTSS-14 - POSTTRAUMATIC STRESS SYMPTOM SCALE - 14 ITEMS

QOL - QUALITY OF LIFE

RASS - RICHMOND AGITATION SEDATION SCALE

RCT - RANDOMISED CONTROLLED TRIAL

RSPM - RAVEN'S STANDARD PROGRESSIVE MATRICES

SAPS - SIMPLIFIED ACUTE PHYSIOLOGY SCORE

SBI - SEVERE BRAIN INJURY

SCID - STRUCTURED CLINICAL INTERVIEW FOR THE DIAGNOSTIC AND STATISTICAL MANUAL

SD - STANDARD DEVIATION

SET - SIX ELEMENT TEST

SF-12 - SHORT FORM HEALTH SURVEY

SOC - SENSE OF COHERENCE

STAI - STATE TRAIT ANXIETY INVENTORY

TISS - THERAPEUTIC INTERVENTION SCORING SYSTEM

TSQ - TRAUMA SCREENING QUESTIONNAIRE

WHO - WORLD HEALTH ORGANISATION

ZDRS - ZUNG DEPRESSION RATING SCALE

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Chapter 1 -Post traumatic stress disorder

1.1 - A Brief Historical Perspective

The psychological burden after exposure to traumatic experiences has long been recognised. Even as far back as the Industrial Revolution a syndrome was observed among travelling Post Office employees who had been involved in railway crashes, which was referred to as "Railway Spine", (Lasiuk & Hegadoren 2006). The symptoms of Railway Spine included sleep disturbances, nightmares about collisions, tinnitus, intolerance of railway travel, and chronic pain.

Soldiers of the American Civil War were reported to have suffered with Da Costa's Syndrome, a condition first thought to be cardiac in origin, but later found to more closely resemble that of emotional responses, specifically fear (Paul 1987). Fifty years later, thousands of soldiers were invalided out of the trenches in Northern France with precisely the same symptoms (Le Fanu 2003) and Shell Shock, the more generic term, was said to have affected some 40% of those injured during the Battle of the Somme (Macleod 2004). Numerous other contemporary nomenclatures have been used to fit both the patients and diagnosis of the time, but a reluctance to separate the post traumatic syndromes meant that formulation of Post traumatic stress disorder (PTSD) did not take place until the advent of the DSM III (APA 1980), when it first became recognised as a diagnosable psychiatric disorder. This marked the beginning of contemporary research on the psychiatric response of traumatic event victims (Breslau 2002).

1.2 - PTSD .

According to the DSM IV (APA 1994), PTSD is an anxiety disorder that may develop following the exposure of an individual to an event that generates intense fear, helplessness or horror and is followed by characteristic symptoms. Exposure can occur through direct experience, or through witnessing or learning about a traumatic event that caused "actual or threatened death,"serious injury," or "threat to the physical integrity" of oneself or others (APA 1994). The traumatic event may be naturally occurring such as an earthquake, tornado or medical

illness, or man made such as accidents, war, domestic or community violence, rape or acts of terrorism.

The distinguishing symptoms of PTSD are re-experiencing the trauma, avoidance of anything that may be associated with the event, generalised numbing of emotions and increased arousal. The symptoms need to be present for at least one month and cause clinically significant distress or impairment in social, occupational, or other important areas of functioning, in order to fulfil the diagnostic criteria.

In the first three months, it is classified as acute PTSD and beyond that chronic PTSD. Symptoms usually occur shortly after a trauma, but in some cases symptoms may not appear until six-months after the event, in which case it would be delayed onset PTSD. The ICD-10 Classification of Mental and Behavioural disorders (WHO 1992), is an international guideline for the diagnosis of PTSD and differs slightly to the American DSM-IV (APA 1994) in terms of diagnostic criteria. The differences between the ICD-10 and the DSM-IV criteria have been previously examined and discrepancies identified between prevalence rates (Peters et al 1999) and in the reporting of symptoms between genders (Peters et al 2006). Table 1.0 and Table 1.1 display the characteristic symptoms according to the DSM-IV and ICD-10, respectively.

- **Table 1.1 - PTSD according to the ICD-10**

CRITERION B RE-EXPERIENCING (1 SYMPTOM)	CRITERION C AVOIDANCE (1 SYMPTOM)	CRITERION D INCREASED AROUSAL (EITHER D1, OR 2 OF D2)
• INTRUSIVE FLASHBACKS • VIVID MEMORIES OR RECURRING DREAMS • EXPERIENCING DISTRESS WHEN REMINDED OF THE STRESSOR	• ACTUAL OR PREFERRED AVOIDANCE	• D1- INABILITY TO RECALL • D2- TWO OR MORE OF ○ SLEEP PROBLEMS ○ IRRITABILITY ○ CONCENTRATION PROBLEMS ○ HYPERVIGILANCE ○ EXAGGERATED STARTLE RESPONSE

CRITERION A - NO SUBJECTIVE STRESSOR CRITERION; CRITERION E - ONSET OF SYMPTOMS WITHIN SIX MONTHS OF STRESSOR

- Table 1.2 - PTSD according to the DSM-IV

RE-EXPERIENCING (AT LEAST 1 SYMPTOM)	AVOIDANCE AND NUMBING (AT LEAST 3 SYMPTOMS)	INCREASED AROUSAL (AT LEAST 2 SYMPTOMS)
• RECURRENT AND INTRUSIVE RECOLLECTIONS • RECURRENT, DISTRESSING DREAMS • ACTING OR FEELING AS IF EVENTS WERE RECURRING • INTENSE PSYCHOLOGICAL DISTRESS TO REMINDERS • PHYSIOLOGICAL REACTIVITY TO REMINDERS	• AVOIDANCE OF THOUGHTS, FEELINGS AND CONVERSATIONS. • AVOIDANCE OF REMINDERS. • PSYCHOGENIC AMNESIA. • GREATLY REDUCED INTEREST IN ACTIVITIES. • DETACHMENT OR ESTRANGEMENT FEELINGS. • RESTRICTED RANGE OF AFFECT. • SENSE OF FORESHORTENED FUTURE.	• DIFFICULTY SLEEPING • IRRITABILITY OR OUTBURSTS OF ANGER • DIFFICULTY CONCENTRATING • HYPERVIGILENCE • EXAGGERATED STARTLE RESPONSE

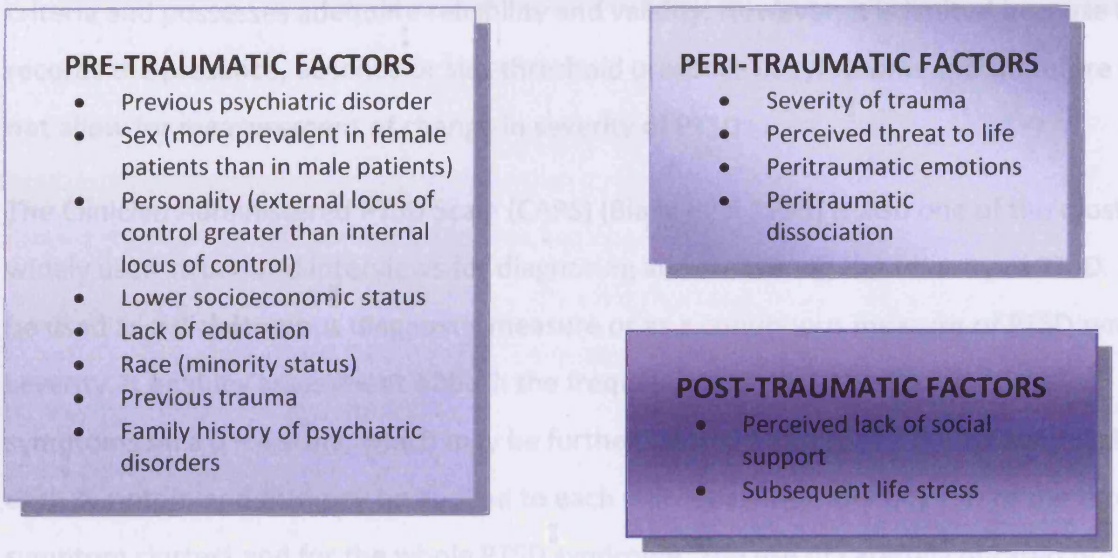
1.3 - Risk Factors for PTSD

In recent years, several epidemiological studies have examined PTSD prevalence and risk factors within the general population. The findings from the National Co-morbidity study (Bromet et al 1998) and those of a larger community study (Breslau et al 1991) suggested that a family history of psychopathology, prior affective and anxiety disorders were strongly associated with higher risk of PTSD.

Individual characteristics were also found to be associated with higher risk of PTSD in two meta-analyses (Brewin et al 2000; Ozer et al 2003) although the effect sizes of these were small and factors operating around the time of the trauma or after it were more strongly associated with a higher risk of PTSD. Both of these studies reached similar conclusions in

that the identified risk factors accounted for relatively little variance. The factors associated with PTSD from the meta-analyses are illustrated in Figure 1.0

Figure 1.0 - Factors associated with post-traumatic stress disorder (Ozer et al 2003; Brewin et al 2000)



1.4 - Assessment of PTSD

There are a number of structured clinical interviews for the assessment of PTSD. In the evaluation of an adequate measure for PTSD, Watson et al (1990) suggested four standards.

- It should correspond with the current diagnostic criteria
- Provide dichotomous and continuous data for each symptom and the diagnosis,
- Be useable by trained paraprofessionals
- Possess adequate reliability and validity.

Blake et al (1995) reviewed six clinical interviews and found they varied widely in their relative merits when the standards proposed by Wilson et al were applied and all had one or two limitations. The most widely used structured clinical interviews are the Structured

Clinical Interview for the DSM-IV Axis 1 disorders (SCID 1- PTSD Module) (First et al 1996) and the Clinician administered PTSD scale (CAPS) (Blake et al 1995).

The PTSD module of the SCID is the most widely used clinical interview across a range of trauma populations (Bryant & Harvey 2000 p.64). It comprises 17 questions corresponding to the DSM IV criteria. Standard questions are provided for each symptom and these are rated as *absent, sub-threshold* or *present.* The SCID-PTSD is said to correspond to diagnostic criteria and possesses adequate reliability and validity. However, it is limited because it records the presence, absence or sub-threshold presence of symptoms and therefore does not allow for measurement of change in severity of PTSD.

The Clinician Administered PTSD Scale (CAPS) (Blake et al 1995) is also one of the most widely used structured interviews for diagnosing and measuring the severity of PTSD. It may be used as a dichotomous diagnostic measure or as a continuous measure of PTSD symptom severity. It enables assessment of both the frequency and the intensity of individual symptoms on a 0 – 4 scale, which may be further summed to create a 0-8 severity scale for each symptom and this may be applied to each individual symptom of PTSD of the three symptom clusters and for the whole PTSD syndrome. The use of carefully phrased prompt questions for each symptom and the use of follow-up prompts along with explicit rating scale anchors, promotes uniform administration and scoring. Following its development in 1990, the CAPS has undergone considerable revision based upon user feedback and in line with changes in the PTSD criteria. Having been extensively tested, it has been found to be a psychometrically sound, practical and flexible structured interview that may be used within a wide range of clinical and research applications, with many different traumatised populations (Weathers et al 2001). It has strong test-retest reliability (.90-.98), high internal consistency (.94) and good convergent validity with the SCID (r=.89). Weathers et al (2001) are opposed to the reliance on a single instrument in the assessment and instead advocate multimodal assessment reliant on converging evidence from multiple sources, including measures of PTSD and comorbid disorders whenever possible.

Self-report questionnaires are the most commonly used instruments to detect PTSD symptoms. They are quick and easy to administer and may be used by non-trauma specialists to screen for adverse psychological responses. Unlike clinical interviews for PTSD, self report measures need not include items corresponding to specific diagnostic criteria but

may be based on any measure (e.g., demographic, biological, or self-report items) that successfully predicts the criterion diagnosis (Brewin et al 2005).

There are numerous self-report questionnaires to detect PTSD and Brewin et al (2005) systematically reviewed thirteen instruments that had been validated against a structured clinical interview. The instruments varied considerably in relation to the number of items on the questionnaires. The shortest being the SPAN (Meltzer-Brody et al 1999) which comprises four items and the longest being the PDS (Foa et al 1997) which comprises thirty items. Brewin and colleagues' concluded that the performance of some currently available instruments was near to their maximal potential effectiveness, and instruments with fewer items, simpler response scales, and simpler scoring methods performed as well as if not better than longer and more complex measures.

The validity of questionnaires for PTSD, are normally determined by comparison to a "gold standard" test, such as the SCID or the CAPS. The effectiveness or performance of the questionnaire, as compared to the gold standard is then clarified through a number of tests. The most frequently used tests are those of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The percentage of respondents correctly classified by the tests as having or not having PTSD, is referred to as the overall efficiency of the test. Sensitivity refers to the probability that someone who is found to have PTSD will have had a positive test result. Specificity refers to the probability that someone who is found not to have PTSD will have had a negative test result. The sensitivity and specificity of tests are not affected by population prevalence and can be compared across studies, whereas the predictive values are affected. The predictive values answer the particular questions "What is the probability that someone who has a positive test result will report a diagnosis of PTSD" (PPV) and "What is the probability that someone who has a negative test result will not receive a PTSD diagnosis" (NPV).

The Impact of Event Scale (IES) (Horowitz et al 1979) is a 15-item questionnaire that contains questions about intrusion and avoidance that are based upon a four-point scale that quantifies the frequency of the reaction. Scores are summed to obtain total IES scores or separately to obtain total intrusion or avoidance scores. Although the original cut off score of 19 proposed by the authors was found to have a perfect sensitivity (Wohlfarth et al

2003), a cut off score of 35 was found to yield the best screening performance (Neal et al 1994). It has since been revised to include a 22-item version that includes hyper-arousal symptoms.

The Davidson Trauma Scale (DTS) (Davidson et al 1997) was developed as a self-reporting scale, based upon the symptom definitions of the DSM IV (APA 1994). It was designed to evaluate symptoms of PTSD in individuals exposed to trauma and evaluate the effects of treatment. It contains 17 items that correspond to each DSM IV symptom. Subjects are asked to rate each symptom on a scale of zero to four for frequency and likewise for severity of symptoms during the previous week. Scores are summed to obtain total DTS scores or separately to obtain total frequency or severity scores

The Post Traumatic Stress Symptoms Scale (PSS) (Foa et al 1997) considers twelve preliminary questions related to the occurrence of specific traumatic experiences. After nominating the most traumatic event, patients answer four questions related to the nature of the stressor, 17 questions about the frequency, on a four-point scale, of the intrusive, avoidance and arousal criteria and finally nine questions related to impairment. A validation study compared to the SCID found the PDS to have a high sensitivity.

The SPAN (Meltzer-Brody et al 1999) is a four-item questionnaire derived from the DTS questionnaire that consists of questions relating to Startle, Physiological arousal, Anger, and Numbness. Each question has a severity score rating on a scale of zero to four. Using a severity cut off score of five, the sensitivity of the SPAN was found to be higher than that of the DTS although specificity was lower.

The Trauma Screening Questionnaire (TSQ) (Brewin et al 2002) consists of five re-experiencing and five hyper arousal questions taken from the PTSD Symptom Scale–Self Report version (PSS–SR) (Foa et al, 1993). This modified questionnaire requires either a *yes (score 1)* or *no (score 0)* response, indicating whether symptoms were experienced in the past two weeks. The best overall diagnostic efficiency of the questionnaire was found with a cut off score of six (Brewin et al 2002). Table 1.3 illustrates the performance of the questionnaires described, as identified by Brewin et al (2005).

- TABLE 1.3 - SELF REPORT QUESTIONNAIRE PERFORMANCE (ADAPTED FROM BREWIN ET AL 2005)

AUTHOR	MEASURE (CUT OFF)	ITEM NO.	SAMPLE (SIZE)	PTSD %	SENSITIVITY	SPECIFICITY	PPV	NPV	OVERALL EFFICIENCY
NEAL ET AL (1994)	IES (35)	15	MIXED (70)	51%	.89	.88	.89	.88	.89
WOHLFARTH ET AL (2003)	IES (35)	15	CRIME VICTIMS (79)	13%	.89	.84	.67	.99	.94
DAVIDSON ET AL (1997)	DTS (40)	17	MIXED (129)	52%	.65	.95	.92	.79	.83
FOA ET AL (1997)	PDS (CLUSTER)	30	MIXED (248	52%	.89	.75	.79	.86	.82
SHEERAN ET AL (2002)	PDS (27)	17	MH O/P (774)	11%	.67	.91	.49	.96	.88

- TABLE 1.3 continued

AUTHOR	MEASURE (CUT OFF)	ITEM NO.	SAMPLE (SIZE)	PTSD %	SENSITIVITY	SPECIFICITY	PPV	NPV	OVERALL EFFICIENCY
MELTZER-BRODY ET AL (1999)	SPAN (5)	4	MIXED (121)	46%	.84	.91	.89	.87	.88
MELTZER-BRODY ET AL (1999)	SPAN (5)	4	MIXED (122)	51%	.77	.82	.81	.78	.80
BREWIN ET AL (2002)	TSQ (6)	10	TRAIN CRASH SURVIVORS (41)	34%	.86	.93	.86	.93	.90
BREWIN ET AL (2002)	TSQ(6)	10	CRIME VICTIMS (157)	27%	.76	.97	.91	.92	.92

1.5 - Prevention and Treatment of PTSD

1.5.1 - Prevention of PTSD

Psychological debriefing (PD) was one of the first psychological interventions used in the hope it would prevent the development of permanent emotional injury, by enabling cognitive appraisal and emotional processing of the traumatic experience (Kaplan et al 2001).
The origins of PD have been traced back to efforts to maintain morale and reduce psychiatric distress amongst soldiers after combat (Rose et al 2002). It was initially, designed for ambulance personnel and was seen as an opportunity for individuals to share their common normal response to extreme circumstances with team members, at least one of whom was familiar with the culture of the work system (Litz et al 2002).

For many years, PD was the most common form of early intervention for some individuals. Some advocates of PD claimed convergent evidence to support its' efficacy (Mitchell and Bray 1990; Robinson & Mitchell 1993). More recently, evaluation into the efficacy of this practice from randomised controlled trials suggested that providing formal psychological interventions to all those involved in traumatic events was ineffective (Rose et al 2005). In some cases, the provision of one-off interventions based upon critical incident stress debriefing even resulted in more negative outcomes (Bisson et al 1997; Mayou 2000).

The key recommendations (NCCMH 2005) regarding the initial response provided to those who have experienced a traumatic event are for watchful waiting for mildly symptomatic individuals, with further contact arranged within one month. The provision of brief, single session interventions should not be routinely provided. For those with severe symptoms, provision of TFCBT is the only proven effective treatment in the first month, conducted on an outpatient basis. Some forms of medication in the short term, such as hypnotics, for the management of sleep disturbances may be considered, but in the longer term, the use of suitable anti-depressants are more suited as an adjunct to psychological therapy.

Recovery of individuals in the aftermath can be facilitated by assessment and provision of identified needs of practical and social support of individuals and significant others, in addition to education of individuals in respect of the range of emotional responses that may develop, along with methods of alleviating them or accessing the relevant support. The NICE clinical guidelines for the first three months are illustrated in Figure 2.

1.5.2 - Treatment of ASD and acute PTSD

The inclusion of acute stress disorder (ASD) in the DSM IV (APA 1994), although not without out criticism (Marshall et al 1999; Wakefield 1996; Bryant et al 2000), facilitated additional research into early traumatic stress symptoms and prompted more investigations into early interventions that may prevent PTSD. The emergence of the benefits of trauma focussed cognitive behavioural therapy (TFCBT) provided one - three months after trauma, to symptomatic individuals influenced the recommendations of the National Institute for Health and Clinical Excellence guidelines (NCCMH 2005).

The conclusions reached by the NICE Guideline Development group (GDG) following the examination of evidence from 24 intervention studies, were that although TFCBT was effective for those at risk of PTSD, there was considerable variation in how the therapy was delivered, how responses to treatment were measured, the number of therapy sessions, the expertise of the therapist and the length of therapy sessions. The pharmacological studies reviewed by the GDG did not provide convincing evidence of efficacy and the conclusion drawn from this was that no drug treatment helped as a routine early intervention. Some drugs however, were thought to have a place in the symptomatic treatment of those who were acutely distressed or experiencing sleep problems. For example, hypnotic medication was considered appropriate for short-term use but if longer-term drug treatment was required, consideration should also be given to the use of suitable antidepressants at an early stage in order to reduce the later risk of dependence (NCCMH, 2005).

There is increasing evidence that suggests that TFCBT is best for those with a diagnosable condition within three months of a traumatic event. Studies have shown that TFCBT offered within the first few months of a trauma to symptomatic individuals are effective, but there is a growing need for additional evidence to support this and for the detection of those most vulnerable. More recently a systematic review of 25 studies of early intervention

following trauma (Roberts et al 2009) found that TFCBT was the only early intervention with convincing evidence of efficacy in reducing and preventing traumatic stress symptoms, but this was only for symptomatic individuals and particularly for those who met the diagnostic criteria for acute stress disorder or acute PTSD.

- **FIGURE 2 - NICE GUIDELINES FOR THE FIRST THREE MONTHS AFTER TRAUMA (NICE 2005)**

➢ **EARLY INTERVENTIONS @ 1 - 4 WEEKS**

WATCHFUL WAITING

- SYMPTOMS MILD, PRESENT < FOUR WEEKS
- PRACTICAL SOCIAL AND EMOTIONAL SUPPORT ONLY
- FOLLOW UP CONTACT WITHIN ONE MONTH
- NO DE-BRIEFING OF TRAUMATIC INCIDENT

➢ **INTERVENTION WITHIN 3 MONTHS OF TRAUMA**

TFCBT (INDIVIDUAL)

- SYMPTOMS SEVERE
- SEVERE PTSD WITHIN ONE MONTH OF TRAUMA (5 SESSIONS)
- PTSD WITHIN 3 MONTHS (8-12 SESSIONS)
- 90 MINUTE SESSIONS FOR TRAUMA DISCUSSION
- REGULAR, DELIVERED AT LEAST 1X WEEK, SAME THERAPIST
- NO NON TF INTERVENTIONS THAT DO NOT ADDRESS TRAUMA MEMORY

CONSIDER

- HYPNOTICS - SHORT TERM USE
- SUITABLE ANTI DEPRESSANTS, EARLY INTRODUCTION, LONGER TERM USE

Trauma-focused CBT comprises a group of treatment programmes that involve, imaginal and in-vivo exposure to the memory and reminders of the trauma coupled with cognitive therapy (Brewin et al 2008).The Key elements of trauma-focused psychological treatment include:

- Confronting the traumatic memory in a controlled and safe environment (imaginal exposure).
- Identifying, challenging and modifying biased or distorted thoughts and interpretations about the event and its meaning (cognitive therapy).
- In-vivo exposure.

  (Forbes et al 2007)

1.5.3 - Treatment of chronic PTSD

A Cochrane Collaboration (Bisson & Andrews 2007) systematic review of 33 randomised controlled trials of psychological treatment in the treatment of PTSD, found that the use of non-trauma focused psychological treatments delivered to individuals did not reduce PTSD symptoms as significantly as those which were trauma focussed (Individual TF-CBT, EMDR). The review also suggested that although Individual TF-CBT and EMDR were superior to Stress Management at between two and five months following intervention, all three were superior to other therapies. The authors'concluded that in the treatment of individuals with PTSD, either TF-CBT or EMDR should be considered.

EMDR uses a structured eight-phase approach and addresses the past, present, and future ramifications of dysfunctionally stored memories (Shapiro, 2001). During the therapy, the client is instructed to focus both on a disturbing image or memory and on the emotions and cognitive elements connected with it, whilst following a bilateral stimulation with his/her eyes of the therapist's fingers moving back and forth, in front of the client's face (Seidler & Wagner 2006). It may also involve other bilateral stimulation such as alternate hand tapping or bilateral auditory tones. The process of alternating dual attention and personal reflection is repeated many times during the session, and if successful, associations to the targeted memory become positive, the patient's distress is relieved, and related cognitions become realistic and adaptive (Maxfield 2007).

These psychological treatments have been recommended in the current guidelines (NCCMH 2005) for all chronic PTSD sufferers, on an individual outpatient basis and regardless of the time since trauma (Bisson 2007). Pharmacological treatment was not recommended as a first line treatment because of the limited evidence base. However, individuals may be prescribed pharmacological treatment if they choose not to participate in the psychological therapy, or where they are unable to participate in psychological therapy due to an ongoing threat of further trauma, or for those for whom psychological therapy was not beneficial, or for symptom relief to aid successful progression through the therapy.

Chapter 2 - Posttraumatic Stress disorder after critical illness admission.

2.1 - Critical Care as a Traumatic Stressor

The psychological impact of a critical care admission has received much attention over the past two decades. It is now well recognised, that the emotional stress of an admission, often contributed to by multi-organ dysfunction, severe systemic infection and the intensive care treatment itself (Schelling 2002) is sufficient to precipitate significant psychiatric morbidity for those who survive it.

In one evaluation of Intensive care treatment (Dyer 1985), it was compared to an Amnesty International publication describing psychological torture

> *"Psychological techniques used such as "DDD"; debility, dependency and dread, were reported to have been used in over 60 countries. These included methods such as sensory manipulation, pharmacological manipulation with psychotropic drugs, prolonged immobility, mutilation, isolation, being forbidden to speak, uncertainty about one's fate, humiliation and re-regulation of the biological clock by the changing of sleep patterns and mealtimes".*

For most patients the experience of critical illness is considered stressful and post-discharge recollection by survivors, suggests that ICU patients commonly experience distressing symptoms at levels of severity that are substantial and underestimated by caregivers. (Puntillo 1990; Bergbom-Engberg & Haljamae 1989).

In a review of recovering critical care survivors, it was noted that in addition to a barrage of physical deficits, survivors reported significant psychological burden in the form of distressing memories of nightmares and delusions (Griffiths & Jones 1999). At the time, this was attributed to a combination of factors, which included the illness itself, the use of opiate and sedative drugs, and the unnatural environment of intensive care with its lack of proper day and night, and to constant noise. Others had observed that their patients were not doing so well overtime despite improvements in physical recovery and attributed this to

psychological factors, specifically posttraumatic stress disorder (PTSD) (Michaels et al 1999), confirming the findings from previous studies of psychosocial difficulties in survivors of traumatic injury (Michaels et al 1998; Holbrook et al 1998).

Framers of the original posttraumatic stress disorder (PTSD) diagnosis had only considered catastrophic events such as war, torture, rape, the Nazi Holocaust, the atomic bombings of Hiroshima and Nagasaki, natural disasters, and human-made disasters in the conceptualisation of a traumatic stressor (Friedman et al 2006). The addition of a life-threatening illness in the diagnostic criteria for PTSD in 1994 (DSM IV) (APA 1994), generated a further outcome measure for survivors of critical illness.

Whilst the experience of being a patient in an intensive care unit is recognised as having the potential to precipitate PTSD (Lloyd, 1993), arguably it is a cascade of events experienced by the survivor and the meaning they attribute to the whole experience that will determine, alongside vulnerability factors, if they develop PTSD.

The presence of pure PTSD prevalence studies is limited within the critical care literature, although some have been conducted. The estimated rate of PTSD ranges from 4.1%, two weeks after ICU discharge (Schnyder et al 2000), to 59%, ten years after admission for septic shock (Schelling et al 1999). The diversity in the reported prevalence rates is considerable and consequently there is uncertainty regarding the true prevalence of PTSD after discharge form critical care.

2.2 Literature Search Methodology

A systematic review of the literature was performed to determine the prevalence of PTSD following critical care admission. Six electronic databases were searched (Medline, EMBASE, Psych-Info, British Nursing Index, All EBM reviews and CINAHL), using the key words, post traumatic stress disorder, PTSD, intensive care, critical care, psychological outcome and critical illness. The results of the search resulted in the identification of 560 citations. Following the removal of duplicated studies, 445 citations remained.

Criteria for selection of relevant papers had been previously decided and comprised –

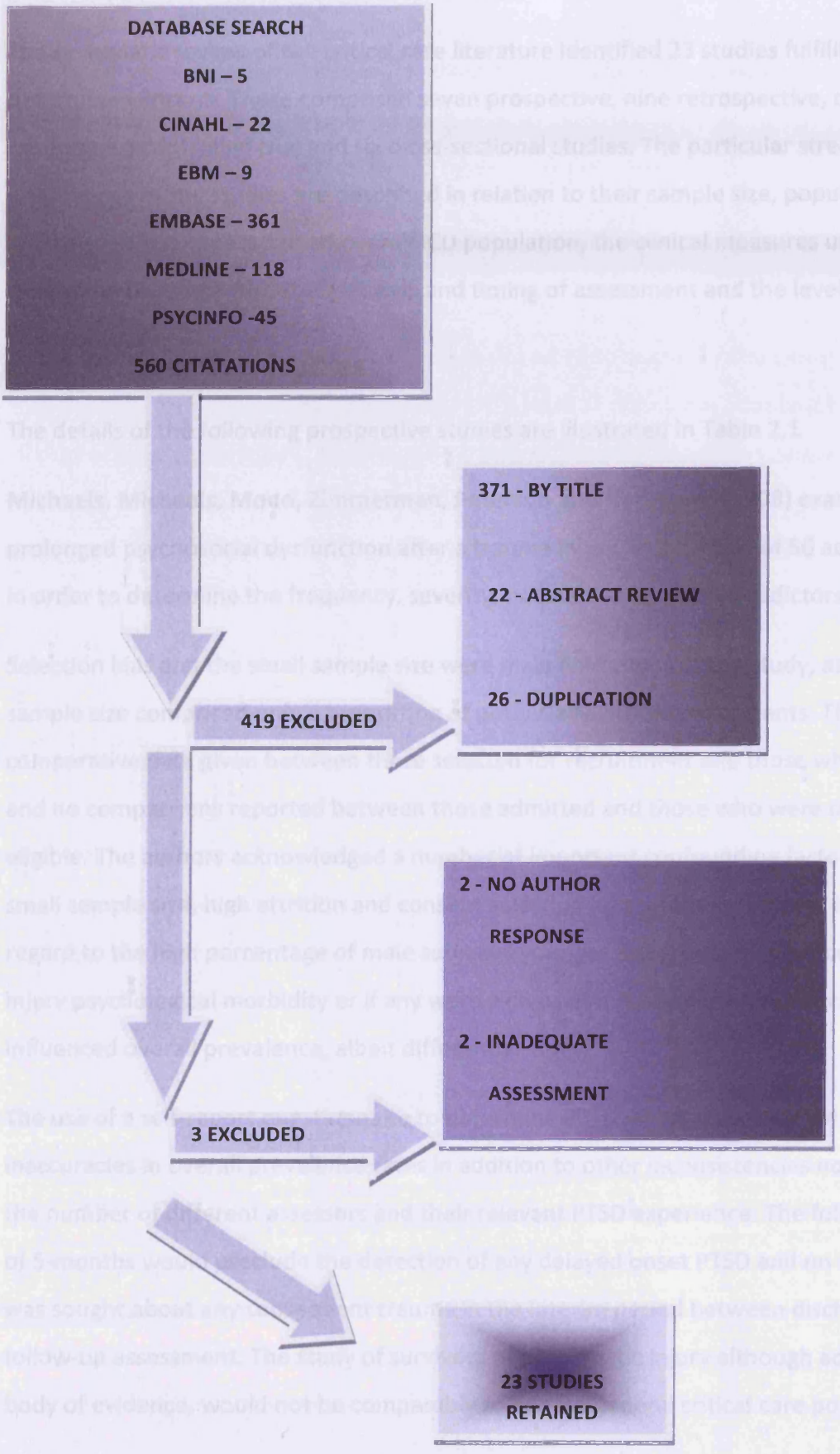
- Quantitative Research Studies
- Sample size > 25
- Adult ICU patients
- General ICU admission
- Validated PTSD measure
- PTSD prevalence estimate documented
- English Language
- Published Studies

Citations were individually reviewed; 371 were excluded by title, 22 by abstract review and 26 for duplication. The remaining 26 abstracts were scrutinised for potential inclusion. The reference lists of each relevant paper obtained were examined to identify any papers not previously found through other methods, in addition to a hand search of Critical Care Medicine, Intensive Care Medicine and the American Journal of Respiratory and Critical Care Medicine and the online intensive care journal, Critical Care. All appropriate studies were identified and critically read.

The full text articles of the studies fulfilling the specified criteria were appraised using tools developed by the Critical Appraisal Skills Programme (CASP) (Milton Keynes Primary Care Trust 2002). Where statistical detail was lacking, for example where prevalence data were omitted, authors were contacted for clarification of statistical results. If this was obtained, the reference was included in the review. The summary of the literature that follows discusses the 23 studies identified in the systematic review that fulfilled the inclusion criteria.

A literature review flow chart illustrates the review process Figure 2.1.

FIGURE 2.1 - LITERATURE REVIEW FLOW CHART



2.3 –PTSD after Critical Care Admission - A Review of the Literature

The systematic review of the critical care literature identified 23 studies fulfilling the pre-determined criteria. These comprised seven prospective, nine retrospective, one randomised controlled trial and six cross-sectional studies. The particular strengths and weaknesses of the studies are described in relation to their sample size, population studied and relevance compared to an overall ICU population, the clinical measures used to determine rates of PTSD, the methods and timing of assessment and the level of attrition.

2.3.1 Prospective Studies

The details of the following prospective studies are illustrated in Table 2.1

Michaels, Michaels, Moon, Zimmerman, Peterson and Rodriguez (1998) examined prolonged psychosocial dysfunction after a trauma injury, in a sample of 56 adult survivors, in order to determine the frequency, severity, nature and any early predictors of PTSD.

Selection bias and the small sample size were main limitations of the study, as the initial sample size comprised only a proportion of potentially eligible participants. There were no comparative data given between those selected for recruitment and those who were not and no comparisons reported between those admitted and those who were considered eligible. The authors acknowledged a number of important confounding factors, such as the small sample size, high attrition and consent selection bias, but no reference is made with regard to the high percentage of male subjects, younger age group, high percentage of pre-injury psychological morbidity or if any were victims of intentional injury which may have influenced overall prevalence, albeit differently.

The use of a self-report questionnaire to determine PTSD status may have led to inaccuracies in overall prevalence rates in addition to other inconsistencies noted, such as the number of different assessors and their relevant PTSD experience. The follow-up period of 5-months would preclude the detection of any delayed onset PTSD and no clarification was sought about any subsequent trauma in the interim period between discharge and follow-up assessment. The study of survivors of a traumatic injury although adding to that body of evidence, would not be comparable to a more general critical care population.

The retention of the selected participants from the consenting sample was below that normally required (62.5%). Demographic comparisons were made between those who completed and those who did not but overall this was a very small proportion (28%) of all survivors of trauma who fulfilled inclusion criteria and with no other demographic comparisons given.

Michaels, Michaels, Zimmerman, Smith, Moon, and Peterson (1999) examined the factors related to the development of PTSD in 250 injured adults.

The high recruitment rate (83%) and sample size were strengths of the study. However, the study was biased in favour of male gender (75%) and 14.5% of the population studied were victims of intentional injury. No comparisons were provided between those who took part in the study and those who did not, particularly given that the more severely injured patients were not available for interview, which may have influenced the overall prevalence identified.

Although PTSD measures were valid for assessment of traumatic stress symptoms, these were self-report questionnaires and there was inconsistency in the assessment method, where some questionnaires were completed by mail and others through telephone interviews. This suggested further potential for inaccuracies in overall PTSD prevalence estimation. It was noted that patients who developed PTSD were younger and more likely to have been assaulted. The authors acknowledged some of the confounding factors of the study but did not take into consideration that patients lost to follow-up were also younger and more likely to have been assaulted, which may have influenced the overall results.

The demographic comparisons between those who completed the study and those who did not showed a number of significantly different characteristics, in that those lost to follow up had fewer years of education, were mostly male and had lower injury severity scores. More importantly, those lost to follow up had similar baseline IES score, quality of life mental health scores, perceived threat to life and percentage of dissociation at the time of the trauma, compared to those retained in the study. These similarities were relevant given that dissociation and poor baseline mental health were identified as two of six predictors of PTSD in the subjects who completed the study.

Whilst the follow-up to 6 months post trauma is acceptable; there was no clarification of whether subjects were asked about subsequent trauma in the interim period between discharge and the follow-up. Although the study comprised a good sample size in addition to a moderate attrition (30%) at 6-months, a sample of survivors of a traumatic injury would not be wholly comparable to that of a typical ICU population.

Schnyder; Moergeli, Klaghofer and Buddeberg (2001), conducted a one-year follow-up study of severely injured accident victims, in order to assess the incidence of PTSD and predict the presence of PTSD symptoms at a 12-month follow-up.

The sample size, the high response rate and consecutively admitted patients were strengths of this study in addition to the provision of comparative data between those who took part and those who did not, which enhanced generalizability of the overall results. Further positive features of the study were the use of a gold standard measure (CAPS) for PTSD assessment, in addition to a self-report measure and the assessment of patients by experienced personnel who were trained in traumatic stress research.

The authors acknowledged the limitations in respect of the strict study criteria and that the exclusion of subjects with prior mental health problems may have explained the very low rate of PTSD identified. They also acknowledged the exclusion of patients unable to speak German, recognizing that proficiency in the official language is a strong determinant of social integration, which may have excluded patients with greater than average difficulties in dealing with the consequences of the accident. In addition to the strict selection process, the population was biased in favor of male gender (74.5%), participants with high levels of education and those in paid employment, which may also have contributed to the very low prevalence identified in the sample.

One important factor, which was relevant to clinical practice, was that none of those with PTSD at the two-week assessment had PTSD at the one-year follow-up, but two patients with a sub-clinical PTSD at two-weeks, had developed PTSD. There was a very low attrition (12.4%) at the time of the 1-year follow-up and the sample comprised 79% of all those considered eligible for inclusion. This was further supported by the inclusion of all relative comparative data for those who had dropped out of the study. Despite the admission to the

ICU for a life threatening illness, a population sample of survivors of serious accidental injury only would not be comparable to that of a typical ICU population.

Creamer, O'Donnell and Pattison (2004) examined the relationship between acute stress disorder (ASD) and subsequent PTSD development in 363 seriously injured trauma survivors. Of these only 31% were admitted to ICU.

This was a particularly large sample size however only 31% (99 patients) were admitted to ICU because of their injuries. By comparison to some ICU studies, the sample size was a strength and represented one of the larger samples of consecutive admission studied.

As the publication was based upon the full recruitment sample and not the sample of ICU survivors, it was not possible to comment further on the differences between participants, non-participants or any loss to follow-up. The use of a structured clinical interview for PTSD and assessment by trained mental health personnel were strengths of this study, particularly in view of the method of assessment at follow-up, by telephone.

The exclusion of subjects with mental health problems and a male gender bias (75%) may have contributed to the lower rate of PTSD identified in the study. Conversely the acquisition of a younger age group which comprised mainly survivors of motor vehicle accidents may have resulted in higher prevalence overall. The high retention rate reported by the authors is a further strength, but the lack of comparative data for the critical care participants precluded further comment. The sample of survivors of accidental injury would not be comparable to an ICU population overall.

Rattray, Johnston and Wildsmith (2005) assessed the levels of and changes in emotional outcome after Emergency admission to Intensive Care.

The initial sample size of 109 patients would have been a strength of the study, but incomplete data and a change in study protocol reduced this to a somewhat smaller sample size of 60 subjects. The broad inclusion criterion was a strength of the study and although the final sample size was small, some compensation was made for this by the comparison of data between those who consented and those who did not. .
There was consistency in the assessments conducted through in-person interviews, although no information was given in relation to the PTSD experience of the assessors. The

use of the IES was a limitation as this could not generate a diagnosis of PTSD, although it does possess good psychometric properties. The use of a self-report questionnaire in conjunction with particularly high rates of anxiety and depression in the sample may have resulted in some misinterpretation of PTSD symptoms and the high rate of PTSD observed.

Given the time to study completion, clarification of any subsequent trauma in the interim period from the initial assessment to that of the follow-up, would have been helpful, particularly in view of a slight increase in PTSD, but there was no mention of this having been done. The change in study protocol and attrition at follow-up resulted in IES data for 60 patients only, which represented just 24% of the eligible population. However, the broad inclusion criteria resulted in a broad case mix of participants, which although comprising emergency admissions only, were comparable to that of a typical ICU population.

Hamanaka, Asukai, Karnijo, Hatta, Kishimoto, and Miyaoka (2006) investigated the prevalence of acute stress disorder (ASD) and PTSD at six-months and early predictive factors for the development of PTSD in survivors of motor vehicle accidents.

The sample size, recruitment of consecutive admissions and low rate of exclusions (17%) were strengths of this study. However, the report lacked data comparisons between subjects who refused to take part and those excluded which limited any conclusions of sample representation. The exclusion of subjects with a history of a pre-existing mental health disorder and an overall bias in favour of male gender in the sample may explain the low prevalence observed and was a limitation of the study.

The use of structured clinical interviews, conducted by experienced assessors were strengths of this study, as well as the use of an additional measure the IES-R, which the authors reported showed a better correlation with ASD symptoms than any other measure used. The use of a telephone interview as opposed to a face-to-face interview however, may not have been as reliable in terms of diagnostic accuracy. The PTSD rate was particularly low, considering that 46% of survivors sustained severe physical injuries and that the mean age of the sample overall was 32.8 years. The authors suggested that the low rate of PTSD might have been due to a cultural-based reticence among Japanese that may have prevented survivors admitting to their symptoms.

The excellent retention rate (82%) at the 6-month follow-up was an added strength although data comparisons between completers and non-completers were not provided in the report, which was a limitation. In terms of comparing the sample to that of an overall ICU population, a sample of motor vehicle accident survivors only, would not be typical.

Jones, Backmann, Capuzzo, Flaaten, Rylander and Griffiths (2007) explored relationships between post-traumatic stress disorder, patients' memories of the intensive care unit (ICU) and sedation practices in 304 patients, recruited from two British and three European Hospitals.

The large sample of consecutively admitted patients, comprising a varied case mix of ICU survivors from five study centres, with a minimal exclusion rate were strong points of this study. However, the number of subjects who consented to take part represented only 38% of the total population and the exclusion of those admitted for deliberate self harm, or with a pre-existing or concomitant psychotic illness (14.6%) added some limitations in terms of overall sample representation. In addition to the exclusion of some mental health conditions, there was slight male gender bias (62%) and the study comprised a sample of older patients, which may have contributed to the lower PTSD prevalence observed. Whilst the multi-centre recruitment resulted in a larger sample population, the downside of this is that clinical practice between the five participating ICU's may have varied and the impact of this on PTSD prevalence is unknown.

There was a standardized assessment of PTSD at the three-month follow-up, conducted at outpatient clinics in the respective countries which is favorable, however this involved five different assessors, whose experience of PTSD is not known and may have induced further bias. The PDS is a well-validated instrument, although use of a self-report measure to diagnose PTSD may be unreliable and there is very little detail given regarding the translation of it into the different languages used and whether any cultural differences were acknowledged in doing so. In addition to this the authors used DSM-IV criteria only, with no cut off score, to determine categorical PTSD diagnosis, which may have resulted in further inaccuracies.

All participating study centres offered a dedicated follow-up service to survivors after hospital discharge and although the authors acknowledged this might have influenced the

prevalence of PTSD, no current evidence exists to either support or challenge this. Further potential confounding factors at a three-month follow-up may have included such things as physical impairment, particularly in light of the age of the population studied, and the common presence of anxiety and depression after the critical care experience, but these would be more likely to have increased overall prevalence.

Given the potential for confounding, the particularly low rate of PTSD observed in this study, compared to some other studies is somewhat surprising in a sample where 25% reported prior mental health problems. However, the prevalence rate reported was that at a follow-up three months after ICU discharge. The absence of prevalence data for the two earlier follow up sessions, precludes any determination of symptom resolution over time. Although demographic data was given for participants, there was no comparable demography for those who dropped out, refused to participate or who were missed which limited generalisability, particularly since the overall sample studied represented only 36% of the total population. Although the retention of participants (78%) was very good, there were no data comparisons between those who completed and those who did not, which limited the interpretation of the overall PTSD prevalence observed at study completion. The broad case-mix of the study sample suggested that this was comparable to a typical ICU population.

- Table 2.1 - Prospective Studies

AUTHOR	SAMPLE SIZE	SUBJECTS STUDIED	AGE M (SD)	PPH EXCLUDED	CLINICAL MEASURE	ASSESSMENT TIME	PTSD/PTSS PREVALENCE
MICHAELS ET AL (1998)	35	TRAUMA MECHANISM	38 (1.75)	NO	IES SASQ MISSISSIPPI PTSD-C	POST INJURY I MONTH 5 MONTHS	51% 34% ASD 38%
MICHAELS ET AL (1999)	176	TRAUMA MECHANISM	38 (0.88)	NO	MCEPS MISSISSIPPI PTSD-C	PRE DISCHARGE 6 MONTHS	NOT GIVEN 42%
SCHNYDER ET AL (2000)	106	ACCIDENTAL INJURIES	38 (13.1)	YES	CAPS/IES CAPS/IES	2 WEEKS 1 YEAR	4.1% 1.9%
CREAMER ET AL. (2004)	99	MOTOR VEHICLE ACCIDENT	36(13.4)	YES	CAPS IV	8 DAYS 3 MONTHS 12 MONTHS	2% ASD 7.4% 11.6%
RATTRAY ET AL 2005	60	E/A'S >24HR STAY	55(17.6)	NO	IES	PRE-DISCHARGE 6 MONTHS 12 MONTHS	32% 24.5% 27.5%
HAMANAKA ET AL (2006)	100	MVA	33(14.5)	YES	IES-R/ASDI SCID/IES-R	1MONTH 6 MONTHS	9% ASD 8.5% PTSD
JONES ET AL (2007)	238	BROAD CASE-MIX	61	PART	PTSS-14 PDS	1-2 WEEKS 2 MONTHS 3 MONTHS	NOT GIVEN NOT GIVEN 9.2%

2.3.2 - Retrospective Studies

Table 2.1 illustrates the details of the nine retrospective studies.

Schelling, Stoll, Haller, Briegel, Manert, Hummel, Lenhart, Heyduck, Polasek, Meier, Preub, Bullinger, Schuffel, and Peter (1998) carried out a retrospective, cohort, case controlled analysis, to investigate adverse experiences during ICU treatment and subsequent impact on PTSD and on health related quality of life in long-term survivors of Acute Respiratory Distress Syndrome (ARDS), to those of two other groups.

This was a moderate sample size by comparison to other critical care studies and with a high recruitment rate (92%) of eligible patients. Although the sample comprised ARDS patients, this consisted a broad case mix of patients and so it would be comparable to an ICU population overall. However, the treatment of the ARDS participants, who are known to represent some of the sickest patients treated within an ICU, often involves long periods of time weaning from mechanical ventilation, which results in stays that are more prolonged. It is possible, that the prolonged exposure to the ICU would have contributed to the overall high prevalence identified. It is possible, that the prolonged exposure to an experience, may serve to desensitize patients and thus reduce overall PTSD, although the high rate of PTSD in this study does not this happened. Other factors, which may have influenced overall prevalence rate in the study, were the exclusion of patients with mental health problems, the young age of the sample (35 years (M)), the high percentage (45%) of trauma survivors and a preadmission history of disability.

The use of a self-report measure only was a weakness of this study and at the time of the study, the questionnaire had not been validated in an ICU population. The use of a retrospective design in PTSD research was a further limitation because of the potential for recall bias and it was unclear if clarification, was obtained regarding the exposure to other stressful events in the interim period, particularly given the long period of time since the admission.

A 92% return for mailed questionnaires was a strength of this study in addition to a 70% representation of all known survivors of ARDS; however no comparisons between those

who refused participation, those who were excluded and those who agreed to take part were made, which limited further conclusions.

Schelling, Stoll, Kapfhammer, Rothenhausler, Krauseneck, Durst, Haller, and Briegel (1999) tested the hypothesis that stress doses of hydrocortisone during septic shock would reduce the incidence of PTSD and improve emotional well-being in survivors of Sepsis. Twenty-seven patients who received standard therapy for septic shock served as controls and were compared with an equal number of patients who received hydrocortisone in addition to standard treatment.

This was a very small sample size of surviving patients, which reduced validity and robustness of conclusions. The control comparison is an obvious strength of the study, validity could have been improved by the use of a further population based group and a larger sample size.

The patients were selected from a database detailing age, gender, and cause of septic shock, to be as similar as possible to control patients. This would normally be considered a strength but the groups differed in that there were a higher percentage of trauma admissions in the control group (26%) than in the intervention group (20%) and the control group also differed in that they were 10 years post ICU discharge compared to 4 years in the intervention group.

The retrospective design of the study in relation to PTSD research has potential for recall bias and there was no indication in the report, if patients were asked about any additional traumatic experiences in the interim period between ICU treatment and follow-up.

The use of the PTSS-10 through self-report was considered a weakness, although it was noted that a sample of study participants were interviewed by psychiatrists as part of a parallel validation study of the PTSS-10. In the validation exercise, the psychiatrists were blinded to the treatment option and PTSD status according to the PTSS-10, but only interviewed 38% of the total sample. This was, partly compensated for by the inclusion of comparative data between those who were interviewed by the psychiatrists and those who were not, which showed no significant differences between the two groups.

Prevalence rates for PTSD were higher in the control group, but equally concerning was the high level of PTSD in the intervention group and indeed overall. One important factor was the inclusion of a predominantly female population (67%) which may have contributed to the high prevalence observed. Other factors considered to have influenced the overall rate of PTSD identified were the broad exclusion criteria, particularly since patients with a psychiatric history were excluded, as were patients who were unable to speak German.

The study lacked comparative data for those who were excluded from the study and other septic patients not included in the study and who were not matches for the study groups. Given the period of time since treatment, which in the control group ranged from 1 - 12 years, it was likely that the sample of septic patients studied was a very small and probably non-representative sample.

Scragg, Jones and Fauvel (2001), investigated psychological distress and predictive variables amongst responders of a postal questionnaire survey, previously treated in a general ICU.

This study included a moderate sample size of subjects with broad inclusion criteria. The inclusion of subjects with past mental health problems and an equal distribution of male and female patients added to its' strengths. Although subjects who had experienced accidental and non-accidental injuries were excluded, this was purposeful as the authors wished to investigate distress associated with the ICU environment. However, this may have contributed to the lower prevalence of PTSD observed. Other factors that may have resulted in the lower prevalence of PTSD were the inclusion of a "less sick population", as only patients who had ICU stays of 2 days or less were included.

The use of a self-report questionnaire only was a weakness of the study; the authors acknowledged this. The IES although well validated, only records symptoms of intrusion and avoidance and therefore cannot be used to diagnose PTSD. Added to this is the potential for confounding factors such as anxiety and depression, as these may have influenced the reporting of PTSD symptoms, particularly since it was reported that all 12 PTSD positive patients who scored above 30 on the IES also scored above the anxiety and depression threshold scores on the HADS.

The use of a retrospective design in PTSD research may be unreliable because of a potential for recall bias, furthermore the postal questionnaire method allows no opportunity for checking interim traumatic events. The sample of patients studied was small (22%) by comparison to the overall population of surviving patients prior to the exclusion criteria. No comparisons of patients' characteristics were reported between those excluded and those who were not. The 80 patients who returned completed questionnaires represented 56% of the eligible population and although the authors reported that baseline characteristics of those returning and not returning the questionnaires were similar, the only characteristics that were presented in the report were age and gender.

Kress, Gehlbach, Lacy, Pliskin, Pohlman and Hall (2003) investigated long-term psychological impact of daily sedative interruption in survivors of critical illness. The primary aim of the study was to identify if daily interruption of sedation was associated with long-term psychological harm.

The final sample studied was very small and the number of patients assigned to the respective groups unequal, with 19 (59%) having received continuous sedation (control group) and 13 (41%), sedation interruption (intervention group). The use of a broad case-mix of ICU patients studied was a strength, and would be comparable to an overall ICU population. The use of a structured clinical interview in conjunction with a self report questionnaire conducted by experienced psychologists were strengths of the study as was the blinding of psychologists to the treatment group, but there was no mention of patient blinding or if the integrity of the blinding process was checked.

Whilst retrospective PTSD research has its limitations in terms of the potential for recall bias, the use of a structured clinical interview may have reduced this risk. The absence of PTSD in the intervention groups would be an important finding in terms of clinical practice but a sample size of 19 patients imposes considerable limitations in terms of overall validity. The authors provided data comparisons between the two groups who were studied, which included confidence intervals to compensate for the small sample sizes of the groups. This showed no significant differences between a number of particularly relevant characteristics, which added weight to the study findings. This was further supported with comparisons between participants and non participants, although this showed that those not enrolled in

the study were younger which may have impacted on overall prevalence of PTSD, had they taken part.

Kapfhammer HP, Rothenhäusler HB, Krauseneck T, Stoll C, and Schelling G (2004), investigated psychiatric morbidity and negative effects on health-related quality of life in long-term survivors of acute respiratory distress syndrome.

The sample investigated were 46 long-term survivors from a previous study and was very small. Although the authors provided a comprehensive comparison between participants and non-participants that showed no significant differences between the two groups, the use of non-parametric statistics to compare the two groups in addition to the small sample size suggested that a type II error could not be ruled out.

The considered strengths of the study were the use of a structured clinical interview (SCID) by two psychiatrists in addition to the administration of a self-report questionnaire (PTSS-10), prior to the interview and that the psychiatrists were blinded to participants' prior PTSD status reported in the previous study. A limitation was that the SCID was only administered in a sample of 15 patients and there was a discrepancy between the SCID and the PTSS10 of three patients.

The reported results of the study were somewhat confusing. There were frequent references to a previous study and an additional retrospective assessment of PTSD symptoms in the current study, to identify PTSD present at the time of discharge and eight years previously. The authors concluded that the PTSD reported at an earlier time, could have been inaccurate.

The rate of PTSD was based on the results of the PTSS10 and although high was most likely due to the small sample size, and a prolonged ICU stay. The retention rate of 58% was low and represented only 40% of the original sample of ARDS patients, which cannot be considered a representative sample. A sample of ARDS survivors would comprise a broad case mix of patients and would be comparable to an overall ICU population, although these patients typically have longer stays within critical care, than that of a normal critical care population.

Richter, Waydhas and Pajonk (2006) investigated the prevalence of PTSD in survivors of prolonged ICU treatment, with a view to identifying any differences between trauma patients and patients admitted with other diagnoses.

The sample size of participants studied was very small although it was highly representative of survivors (80%) of a prolonged ICU stay. In addition to this, the authors did not exclude patients with histories of mental health problems or those with evidence of traumatic brain injury, which may have influenced overall PTSD prevalence.

Compared to non-participants, which included those who did not survive to follow-up, the patients who took part in the follow-up were similar in terms of gender, the duration of ICU stay and injury severity score but were found to be significantly different in that they were younger and had lower APACHE II scores. However, statistical significance in such a small sample size may not be accurate and no confidence intervals were given to support the findings.

A further confounder in terms of PTSD within a general ICU population was the high percentage (78%) of trauma survivors who took part. The AMDP System was reported as a comprehensive psychopathological assessment by the authors, although it is not commonly referenced in PTSD research and no details were provided to support its validity. However, an assessment by a psychiatrist may have increased the reliability of PTSD diagnosis particularly in view of the retrospective design of the study.

Déjà, Denke, Weber-Carstens, Schröder, Pille, Hokema, Falke and Kaisers (2006) evaluated the relationship between PTSD symptoms and long term health related quality of life in survivors of ARDS.

The sample size in this study was small although the authors provided a concise and comprehensive comparison of data between survivors who participated and those who did not, which was a strength of the study. No significant differences were found between participants and non-participants except for the length of time between discharge and follow-up, but no confidence intervals were provided for this and the study lacked power to detect any differences.

The use of a self report measure was considered a weakness of this study, as was the retrospective study design. The authors reported that participants with PTSD according to the PTSS-10 also recorded high scores for other multiple aspects of psychopathology according to the Symptom Checklist 90-R which suggested further confounding for symptoms of PTSD, particularly in view of the use of a self-report questionnaire. Other potential confounders for PTSD were the presence of disability both pre-admission and post-discharge and the use of a postal questionnaire survey.

This was a particularly high rate of PTSD, although it was acknowledged that survivors of ARDS were among the most critically ill patients admitted to ICU. The broad case mix represented by ARDS survivors would be comparable to an overall ICU population, but with more prolonged stays both within ICU and on the general wards, compared to other less sick discharged ICU patients. Despite concerted efforts by the authors to achieve a good sample size, only 50% of survivors returned the completed questionnaires and the participant sample represented just 35% of the total population of ARDS survivors.

Boer, Mahler, Unlu, Lamme, Vroom, Sprangers, Gouma, Reitsma, De Borgie and Boermeester (2007), investigated long term prevalence of PTSD symptoms following secondary peritonitis, to determine whether prevalence of PTSD-related symptoms differed between patients admitted to critical care and patients admitted only to the surgical ward.

Although the overall sample size was reasonable compared to some ICU studies, only 61% of the sample was admitted to the ICU. These comprised a sub-population of ICU patients, who were survivors of peritonitis, which would not be comparable to that of an overall ICU population. In addition, although comparisons were given in respect of responders and non-responders, this suggested that the groups were different which reduced the generalisability of findings and may also have influenced the overall rate of PTSD identified.

There were a number of other confounding factors in relation to PTSD in the ICU sample in that patients had a prolonged period of mechanical ventilation, ICU and hospital stay, 22 (36%) patients had open abdomens after surgery, 44 (72%) patients had re-laparotomies, surgery related complications (72%), sepsis (57%) and hospital readmissions (12%). The eventful and complicated recovery period may have further exacerbated the stress of critical illness and influenced the overall prevalence of PTSD.

The use of the PTSS-10, may have contributed to the overall higher rate of PTSD identified in addition to the use of a postal survey and the retrospective design. Additionally, no clarification was sought in respect of any interim traumatic experiences between discharge and follow-up, which extended to a median duration of 5 years.

The overall sample size was small (61%) and although some comparisons were made between participants and non-participants, these showed that non-responders were younger, had fewer co-morbidities at initial surgery, were less sick and had a lower Mannheim Peritonitis Index than responders. Although this suggested that the participant sample was not representative of a larger population, the significant p values were not supported by confidence intervals, which served to prevent any further conclusions.

Jackson, Obremskey, Bauer, Greevy, Cotton, Anderson, Song and Ely (2007) conducted a pilot study to determine 12 to 24-month cognitive, emotional and functional outcomes in a cohort of Trauma ICU survivors with a high illness severity but no radiographic evidence of intracranial haemorrhage.

Sample size was small in this study and this, in conjunction with a failure to provide a comparison of patient specific characteristics between those who participated and those who did not were considered weaknesses of the study. The inclusion of patients with mental health problems was a strength, but the restriction to a population of patients who were survivors of trauma would not be comparable to the usual ICU population.

The patients who took part, comprised a young population who were mostly male (67%) and 81% were survivors of motor vehicle accidents, with a large proportion of mental health problems of different categories. All of these factors may have influenced the overall prevalence rate of PTSD identified in the sample. There was an inconsistency in the method of assessment, some survivors were interviewed at home and some in an outpatient clinic, and the use of the DTS questionnaire for detection of PTSD were additional weaknesses. The prevalence of PTSD was high and, in addition to those confounders already identified, the impairments in physical functioning identified at assessments may have added to this. The retention of 60% of the original sample was low and would not be representative of an overall trauma population due to the lack of comparative data.

- **Table 2.1 - Retrospective Studies**

AUTHOR	SAMPLE SIZE	SUBJECTS STUDIED	AGE	PPH EXCUDED	CLINICAL MEASURE	ASSESSMENT TIME	PTSD PREVALENCE
SCHELLING ET AL (1998)	80	ARDS	35	YES	PTSS-10	3-6 YRS	27.5%
SCHELLING ET AL (1999)	54	SEPSIS	53.5	YES	PTSS-10	IG 4 YEARS CG 10 YEARS	IG - 18.5% CG - 59% OVERALL - 39%
SCRAGG ET AL (2001)	80	BROAD CASE-MIX	57	NO	IES	3-5 YEARS POST DISCHARGE	15.6%
KRESS ET AL (2003)	32	BROAD CASE-MIX	48.5	NO	INTERVIEW	6-MONTHS +	IG – 0% CG – 32% OVERALL – 19%
KAPFHAMMER ET AL (2004)	46	ARDS	37	YES	SCID/ PTSS10	8 YEARS MEDIAN	23.9%**
RICHTER ET AL (2006)	37	TRAUMA/ NON-TRAUMA	48	NO	INTERVIEW	35 MONTHS	19%
DEJA ET AL (2006)	63	ARDS	39	YES	PTSS-10	57 MONTHS	29%
BOER ET AL (2007)	61	PERITONITIS	54	NO	PTSS10	88 MONTHS POST DISCHARGE	28%
JACKSON ET AL (2007)	58	TRAUMATIC INJURY	45	NO	DTS	1 – 2 YEARS POST INJURY	38%

**-prevalence based upon PTSS10

2.3.3 - Randomized Controlled Trial

Table 2.2 illustrates the details of the only Randomized Controlled Trial identified

Jones, Skirrow, Griffiths, Humphris, Ingleby, Eddleston, Waldmann and Gager (2003) examined the effectiveness of a rehabilitation programme following critical illness on patients' physical and psychological recovery.

This was a multi-centre study with recruitment of consecutive admissions. The recruitment of a sample size of 126 subjects was very good compared to other ICU studies; unfortunately, a limitation to this was that the required sample size was not achieved. A comparison between participant groups was conducted and this showed no significant differences, however no comparisons were given between participants and patients who either were excluded or did not want to take part, which restricted the generalization to an overall population.

A randomization procedure was carried out appropriately and participants allocated to a routine follow-up (control Group) or a routine follow-up plus a rehabilitation package. Unfortunately, the numbers of patients were different in the two groups, which was a minor limitation. Blinding was well described and the authors took all measures to ensure that this was effective, however it is unclear if the integrity of the blinding process was checked.

A considerable limitation in the study was the lack of baseline PTSD data prior to commencement of the follow-up programmes, particularly since the primary aim of the study was to test whether the provision of a six week rehabilitation programme post-ICU improved patients' physical and psychological recovery. This was not assessed until 8 weeks and then again at six-months in an outpatient clinic. The IES was used to identify symptoms of PTSD, which was a further limitation. The actual prevalence of symptoms at 8 weeks was not given in the report, although the authors reported that symptoms were significantly lower in the intervention group compared to the control group at that time. At the six-month follow-up prevalence of PTSS was given and the authors reported that IES scores for participants in the intervention group had increased.

A further confounding issue in this study was the prescription of benzodiazepines and anti-depressants. Twenty two percent of participants in the Intervention group and 18% of

participants in the control group were prescribed anti-depressants and benzodiazepines were prescribed in 21 %(IG) and 15.7 %(CG).

A further important limitation of the study was the use of delusional recall as a surrogate end-point. The authors reported a significant correlation for delusional recall with anxiety and IES scores, which was somewhat misleading and distracted meaning away from the primary aim and clinical outcome of this study. Retention rates were excellent with 81% of participants completing the study at six-months; this consisted of 84% in the intervention group and 77% in the control group.

- **Table 2.2 - Randomized Controlled Trial**

AUTHOR	SAMPLE SIZE	SUBJECTS	AGE	PPH EXCLUDED	CLINICAL MEASURE	ASSESSMENT TIME	PTSD/PTSS PREVALENCE
JONES ET AL (2003)	126	BROAD CASE MIX	58	PART	IES (CUT OFF >19)	8 WEEKS 6 MONTHS	51% IG- 48% CG- 53%

2.3.4 - Cross-sectional Studies

The six cross-sectional studies reviewed are shown in Table 2.3

Cuthbertson, Hull, Strachan and Scott (2004), investigated the incidence and severity of symptoms related to the diagnosis of PTSD in a cohort of 78 general ICU patients, three months after discharge.

The sample size in this study was moderate in comparison to other critical care studies reporting PTSD, but strengths of the study design were the use of consecutive admissions and broad inclusion criteria, which meant that patients with prior mental health problems were not excluded. The inclusion of comparative data between participants and non-participants that showed no characteristic differences between them were initially considered strengths, in terms of generalization of results, although skewed distributions

and heterogeneity of variance resulted in the use of nonparametric statistics, which may be a limitation in respect of any reported significance.

Participants were contacted by a research nurse 3-months after ICU discharge and a telephone interview was conducted. There was no information regarding the Research Nurse's experience of PTSD or the use of the Davidson Trauma Scale. The use of a self report measure was a limitation of the study and the particularly low rate of PTSD as compared to other studies using self report questionnaires was noted. It was possible that this low rate compared to other studies may have been partly due to an older participant population and a shorter stay within ICU. Further confounding factors for PTSD may have been co-morbid anxiety and depression, physical impairment known to be common in the early stage of recovery after critical illness, but no assessments for these problems were carried out.

The overall retention rate was adequate (70%) and 24% of the attrition was considered unavoidable, due to the premature death of some participants. The recruitment of a broad case-mix of patients suggested that this study would be comparable to a typical ICU population.

Nickel, Leiberich, Nickel, Tritt, Mitterlehner, Rother and Loew (2004) examined the relationship between PTSD and prior psychiatric illness and the reliability of the PTSS-10 in conjunction with a structured clinical interview (SCID I and II) for the DSM-IV in a random sample.

The main limitations of the study were the small sample size. A clear description of the aims of the study was given and the target population represented a good cross-section of medically ill patients, although slightly biased in favour of male gender.

The broad inclusion criteria that included patients with ICU stays of at least 24 hours was a strong point, however, no demographic comparisons were given between those who participated and those who did not which limited generalisability to a larger population.

The use of a validated structured interview in diagnosing PTSD , conducted by experienced personnel were strengths of the study, in addition to the use of a self report questionnaire. The number of participants found to have PTSD according to the PTSS-10 was nearly twice

that identified by the SCID. Although the study showed that the PTSS-10 over diagnosed PTSD, this appeared to have been based solely on descriptive analysis as no other statistical results were given. In conjunction with a small sample size, this posed restrictions in terms of the overall validity of the findings.

Recruitment of an historical sample of patients into the study with varying lengths of time since ICU discharge was a further confounding factor in terms of detection of PTSD symptoms, because of the potential for recall bias. The sample represented 6% of the overall population and 19% of those considered eligible. Although the response rate in the random sample was excellent (82%), no efforts were made to improve this when nine patients declined participation despite the fact that other participants were known to have survived to the time of the study.

Liberzon, Abelson, Amdur, King, Cardneau, Henke, and Graham (2006) examined the development of posttraumatic stress and depressive symptoms in survivors of aortic aneurysm or occlusive disease, six-months to 2 years after discharge

The sample size was among one of the larger ones in studies conducted after ICU admission, the authors did not exclude patients who had a prior history of mental health problems and these were considered strong points of the study. Some of the confounding issues in respect of PTSD prevalence were that patients who were unable to complete the assessment because of language difficulties or those who were physical frail were excluded. In addition, the sample comprised a large proportion of male patients (73%) and this may have affected the overall prevalence identified in the sample.

The use of a gold standard assessment (CAPS) and interviews conducted by a trained research associate were considered further strengths however; no scoring rules were given with regards to how a diagnosis of PTSD was determined, from the CAPS. Further confounding issues were the considerable variation between the timing of follow-up for participants (6-month – 2 years) since it is likely that some resolution of symptoms would have occurred over time, and the use of an historical sample, because of the potential for recall bias.

The recruitment of 85% of potential subjects was excellent. There were two limitations to this however, in that the sample was confined to a sub population of ICU admissions and no demographic comparisons were given between patients who consented and those who were either excluded or did not want to take part. As a result, this study would not be comparable to an overall ICU population and was limited with regards to comparison to a larger population of survivors of treatment of abdominal aortic aneurysm.

Griffiths, Gager, Alder, Fawcett, Waldmann, and Quinlan (2006) investigated the incidence of sexual dysfunction and the association of demographic and clinical variables in ICU survivors in the first year after treatment.

The initial sample size and broad case mix were strengths of the study, however PTSD data was provided for only 56 patients, which reduced over all vigor as compared to the larger sample. There were a number of weaknesses in terms of the study sample, all of which may have contributed to the identified rate of PTSD. These included failure to include subjects who spent less than 3 days on ICU, a male gender bias (66%), inability to read or understand English, and those who were unable to complete a self-report measure, due to cognitive disability.

The rate of PTSD in the sample studied was one of the highest identified following critical care admission, which may have been influenced by the use of a self report measure, the TSQ, which had not been previously used within the ICU population. Other potential confounders for PTSD included a prolonged stay on the ICU that suggested that patients were very sick, as indicated by the number of patients requiring more complex treatment such as, inotropic support (49%), haemo-filtration (17%) and tracheostomy (57%), all of which may have added further stress to the burden of critical illness.

Although the number of patients taking part in the study was high, the number of patients who had completed assessments for PTSD represented only 46% of those who agreed to take part and 24% of those originally deemed eligible. Added to this, there were no comparative data between those who took part in the study and those who did not.

Samuelson, Lundberg and Fridlund (2007), investigated patients' psychological distress in relation to memory and stressful experiences in the intensive care unit (ICU) and examined early predictors for the development of high levels of acute PTSD related symptoms.

The large sample size, the participation of patients from two ICUs and the inclusion of comparative data between those who agreed to participate and the sixty who were lost to follow-up at the two-month assessment, were particular strengths of the study.

The use of a self-report questionnaire, the IES-R, to determine PTSD, was a weakness and there was no reference to the experience or training in PTSD, of the interviewer. The particularly low rate of PTSD identified may be due to a number of confounding issues such as the exclusion of patients with a previous mental health history and a relatively short stay within ICU, which suggested less sick patients. The authors also suggested that the use of a telephone interview may have resulted in a failure by the patient to fully reveal their inner fears and subjective memories to the researcher, which may also have contributed to the lower rates of PTSD identified.

Despite an excellent sample size, the population studied only represented 12% of the overall surviving population and there were no comparisons of patient characteristics between those who took part and those who were either excluded from the study, or refused to take part.

Girard, Shintani, Jackson, Gordon, Pun, Henderson, Dittus, Bernard and Ely (2007) conducted a pilot investigation to identify factors associated with the development of PTSD symptoms in ventilated patients.

The small sample size and high rate of attrition were weaknesses of the study. The exclusion criteria were appropriate, although the exclusion of non-English speaking patients and those with sensory deficits may have introduced an element of bias with regards to the overall prevalence of PTSD identified. However, the sample of patients studied would be comparable to an overall ICU population because of the broad case mix of the sample.

A strength of the study was the inclusion of a comprehensive comparison of patient characteristics between those who took part and those who survived to hospital discharge but did not take part. A down side to this however was the use of non-parametric statistics

to determine the differences between the two groups of patients. Non parametric statistics tend to be less sensitive than parametric statistics and may fail to detect differences between groups that do actually exist (Pallant 2000). Despite some apparent differences between the groups, such as age, gender and critical care length of stay, these were not found to be significantly different between the groups, according to the non parametric tests.

Other limitations of the study included the use of a telephone interview as opposed to a face to face interview, the use of the PTSS-10, a self report measure to identify PTSD and the lack of information with regards to the assessors' experience of PTSD and subsequent assessment of the participants. The sample investigated represented only 47% of the total population of survivors and no comparison between the participants and those who were either excluded or did not want to take part was given, which limits overall generalisation of results.

- Table 2.3 - Cross-Sectional Studies

AUTHOR	SAMPLE SIZE	SUBJECTS	AGE	PPH EXCLUDED	CLINICAL MEASURE	ASSESSMENT TIME	PTSD PREVALENCE
CUTHBERTSON ET AL. (2004)	78	BROAD CASE-MIX	58	NO	DTS	3 MONTHS	10%
NICKEL ET AL. (2004)	47	BROAD CASE-MIX	48	NO	SCID PTSS-10	3 – 15 MONTHS	9.8% 17%
LIBERZON ET AL (2006)	109	ABDOMINAL AORTIC ANEURYSM	64	NO	CAPS	6 MONTHS – 2 YEARS	11%
GRIFFITHS ET AL (2006)	56	BROAD CASE MIX	57	NO	TSQ	3-MONTHS	52%
SAMUELSON ET AL (2007)	226	VENTILATED PATIENTS	63	YES	IES-R	2 MONTHS	8.4%
GIRARD ET AL (2007)	43	BROAD CASE MIX	52	NO	PTSS10	6 MONTHS	14%

2.4 - Discussion

Three systematic reviews have been carried out in the past five years examining PTSD reported after medical illness and treatment (Tedstone & Tarrier 2003), PTSD after medically related critical illness (Jackson et al 2007), and PTSD after at least 24 hours of ICU treatment (Griffiths et al 2007).

Whilst the first two were not representative of a "typical" ICU population, in that they only considered PTSD in studies of critically ill medical patients, all three reviews reached similar conclusions, in that overall prevalence of PTSD after critical care admission was largely inconclusive due to the numerous methodological shortcomings. The shortcomings were selection bias, loss to follow-up, the wide use of screening (as opposed to diagnostic) instruments (Jackson et al 2007), case mix, demographic variables, method and timing of PTSD assessment (Griffiths et al 2007), and use of measures that had the potential to confound symptoms of illness with those of PTSD (Tedstone & Tarrier 2003).

Griffiths et al (2007) recommended rigorous longitudinal studies because deficiencies in design, methodology and reporting made interpretation and comparison of quoted prevalence rates difficult. Jackson et al (2007), more conservatively, suggested that studies should be methodologically rigorous because the magnitude of the problem posed by PTSD in survivors of critical illness was unknown. Tedstone & Tarrier however suggested that because medical trauma may act as a trigger in individuals with a predisposition to PTSD, that the clinical measures of PTSD after physical illness required standardisation.

The purpose of this review was to examine the existing evidence for, a) the prevalence of PTSD/PTSS following ICU admission, b) whether the clinical measures used contribute to the confusion regarding prevalence, and c) if there is a need for specialist psychological intervention for survivors after discharge from critical care.

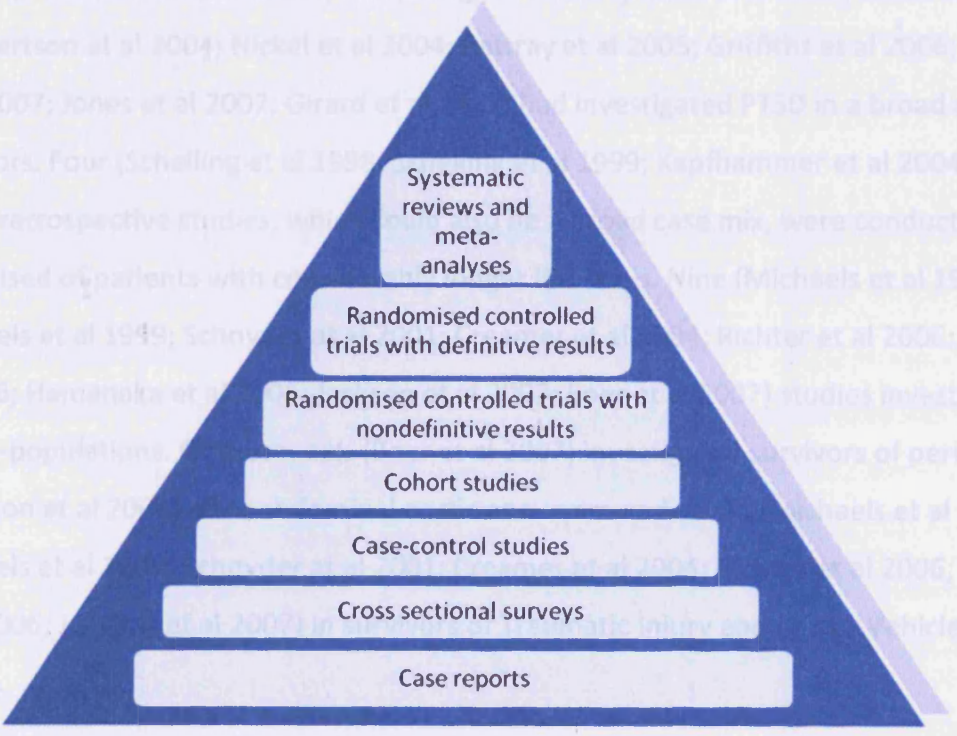
2.4.1 - Study Design

In terms of rigour and the search for best sources of evidence, a "Hierarchy of Evidence" that graded research studies according to their quality was developed in the early 60's by two social scientists. Whilst this has helped to raise awareness that some forms of evidence,

are more trustworthy than others (Glaziou et al 2004), it is not without criticism. In this particular example according to the Hierarchy of Evidence, the best source of evidence is that of a Meta Analysis or a Systematic Review. Unfortunately, those conducted have re-enforced what was already known, in that PTSD after ICU shows considerable variation. The next best evidence would the RCT but this is not the best way to consider prevalence and in this study (Jones et al 2003), PTSD prevalence was confounded by the provision of two interventions that may or may not have influenced the rate of PTSD at study completion.

Concato (2004) suggested that a more balanced and scientifically justified approach would be to evaluate the strengths and limitations of well conducted experimental and observational studies, recognizing the attributes of each type of design. More specifically, Petticrew and Roberts (2003) suggested that it is more useful to think of how you can best use the wide range of evidence available and particularly to consider what types of study are most suitable for answering particular types of questions.

Figure 2.2 - Hierarchy of Evidence



Although there were no "perfect" studies, the research conducted thus far has provided a wealth of information. Retrospective studies help to focus the study question, clarify the hypothesis, determine an appropriate sample size, and identify feasibility issues for a prospective study (Hess 2004). The prospective studies allow us to measure a variety of variables that might be relevant to the development of the condition and observe the people in the sample, to see whether they develop the outcome of interest (Mann 2008). The cross-sectional studies provide a snapshot of PTSD prevalence at different times after ICU discharge and fill some of the gaps not accounted for in some of the prospective studies. All the studies have provided insight into PTSD after critical care treatment, even if in some cases, it has only been to highlight the methodological challenges faced by investigators.

One challenge was the generalization of study results to that of a "typical" critical care population. In order to compare and discuss this the studies were divided into three categories , studies of trauma and serious accidental injuries, studies of prolonged ICU stay and studies with a broad case mix of participants.

Of the 23 studies reviewed, only ten (Scragg et al 2001; Kress et al 2003; Jones et al 2003; Cuthbertson et al 2004; Nickel et al 2004; Rattray et al 2005; Griffiths et al 2006; Samuelson et al 2007; Jones et al 2007; Girard et al 2007) had investigated PTSD in a broad case mix of survivors. Four (Schelling et al 1998; Schelling et al 1999; Kapfhammer et al 2004; Déjà et al 2006) retrospective studies, which could also be a broad case mix, were conducted but comprised of patients with considerably longer ICU stays. Nine (Michaels et al 1998; Michaels et al 1999; Schnyder at al 2001; Creamer et al 2004; Richter et al 2006; Liberzon et al 2006; Hamanaka et al 2006; Jackson et al 2007; Boer et al 2007) studies investigated PTSD in sub -populations. Of these, one (Boer et al 2007) investigated survivors of peritonitis, one (Liberzon et al 2006) after abdominal aortic aneurysm and seven (Michaels et al 1998; Michaels et al 1999; Schnyder at al 2001; Creamer et al 2004; Richter et al 2006; Hamanaka et al 2006; Jackson et al 2007) in survivors of Traumatic Injury and Motor Vehicle Accidents (MVA).

Whilst knowledge of the sub-population prevalence rates usefully inform practice when such patients are cared for within ICU, prevalence rates of PTSD after MVA have been found

to range from 8% (Malt & Blikra 1993) to 39% (Blanchard et al 1995) and those in response to physical assault from 23% - 39% (Kilpatrick & Acierno 2003). This may partly explain the high prevalence of PTSD observed in some of the sub-population ICU studies, but other factors may also have contributed to the variation and confusion of prevalence.

2.4.2 - Sub-population studies

Four (Schnyder et al 2001; Creamer et al 2004; Liberzon et al 2006; Hamanaka et al 2006) of the sub-population studies, had particularly low prevalence rates and these had used structured clinical interviews to identify PTSD symptoms. Four (Michaels et al 1998; Michaels et al 1999; Jackson et al 2007; Boer et al 2007) studies with a high prevalence rate used self-report questionnaires. One remaining study conducted by Richter et al (2006) used a structured clinical interview to identify PTSD, but this was not one of the more commonly known gold standard assessments for PTSD. This particular study comprised a very small sample size, of young subjects of whom 49% had a history of prior mental health problems, with a prolonged ICU stay and an assessment time of nearly 3 years post trauma.

The inclusion of patients with prior mental health problems in studies of PTSD is likely to result in an increased prevalence, as a past psychiatric history is known to be associated with PTSD (Brewin et al 2000). Studies with higher prevalence rates had included these patients and those with the lowest prevalence had excluded them.

Other confounding factors in relation to high prevalence of PTSD within the sub-population studies were sample size. All but one (Michaels et al 1999) of the studies with the highest prevalence had samples of 61 subjects or less. Although Michaels and colleagues' study was large (176 subjects), the study included subjects with a prior history of mental health problems including previous trauma/abuse, who were younger, with perceived poor social support and a high percentage of intentional injuries. Studies with lower prevalence of PTSD were those with sample sizes of 99 or more and although all of them had a higher proportion of males, the samples included subjects who were all relatively young and were assessed by personnel proficient in the field of PTSD.

2.4.3 - PTSD in survivors of prolonged ICU admission

Other studies reviewed with high prevalence rates were those in which participants were survivors of a prolonged ICU stay, such as survivors of ARDS and Sepsis. These undoubtedly represent some of the sickest patients treated within an ICU. Whilst for much of the ICU treatment patients may be sedated for comfort whilst mechanically ventilated, progression to spontaneous breathing necessitates a period of weaning from mechanical ventilation, during which time sedation would cease. During this often prolonged period of time, patients learn of their illness from others, are restricted by technological "attachments" and are exposed, to what many consider an extremely stressful environment. It has been suggested that the physiological or psychological consequences of being awake and intubated make this experience a particularly potent inducer of psychiatric sequelae (Liberzon et al 2006). As a result, this period of awareness and the individuals' perception of it may be crucial in relation to the development of later PTSD, in that factors operating during or after a trauma such as trauma severity, lack of social support, and additional life stress, have been found to be associated with PTSD (Brewin et al 2000).

Whilst this may be a contributing factor for higher prevalence in survivors of prolonged ICU treatment, other additional confounding factors were evident. Overall sample size was small to moderate, all studies used a retrospective design and the same self report questionnaire to determine PTSD status, subjects were mostly of a younger age group, with prolonged ICU stay, and follow-up assessments were conducted from 3 to 10 years after discharge. In addition, the study with the highest prevalence (Shelling et al 1999) had a female gender bias of 67%. This was particularly relevant given the evidence from epidemiological studies that have found women to be approximately twice as likely as men to succumb to PTSD following traumatic events (Breslau 2002).

2.4.4- PTSD in a broad case mix ICU population

The studies that recruited a broad case mix of patients considered most representative of the typical ICU population also had varying rates of PTSD. Two of these (Griffiths et al 2006; Jones et al 2003), found the highest prevalence of PTSD of all the studies reviewed with reported prevalence rates of 52% and 51% respectively.

When examined in more detail, these studies showed, rather surprisingly, an older population, evidence of male gender bias, and exclusion or part exclusion of patients with prior mental health problems, all factors which have been associated with lower prevalence of PTSD. However, participants in both studies had slightly longer ICU stays than other studies in this category.

Both studies had used self-report questionnaires to determine PTSD and one of them (Griffiths et al 2006) used a questionnaire which, although not previously used in an ICU population, had been previously found to perform consistently well as a screening instrument and was considered better than most longer instruments (Brewin 2005). It is possible that this particular questionnaire was not suited to this particular population.

In Jones and colleagues' study (2003), a randomised controlled trial examining two follow-up interventions, participants completed the IES at a dedicated ICU follow up clinic. Whilst the IES may detect very clinical symptoms of PTSD, it can not be used to make a clinical diagnosis because it only includes questions for intrusive symptoms and avoidance. But of particular relevance was the authors used the originally proposed lower total cut off score of 19 (Horowitz et al 1979) instead of the more frequently used higher cut off of 35 which may explain the high prevalence reported. The lower cut off score of 19 has been found to have perfect sensitivity when compared to the (PSS-R) according to the DSM-IV criteria for PTSD, although with low specificity (78%) (Wohlfarth et al 2003). Interestingly it appeared from presentation of graphical data that neither of the study groups in Jones' study met the cut-off score of 35 recommended by Neal et al (1994).

A further factor and one being currently investigated (Cuthbertson et al 2007) was that both authors' study centre routinely follow up patients after ICU discharge as do 30% of other centres according to a national survey (Griffiths et al 2006) despite no evidence to date to support service provision.

The studies with the lowest prevalence for PTSD (Jones et al 2007; Samuelson et al 2007) in this group of studies had the largest sample sizes of all the reviewed studies and used self report questionnaires to detect PTSD. In Samuelson and colleagues' study, potential recruits were excluded from taking part if they had a previous history of mental illness. Those who did take part were also older (63 years) than participants in the other studies. Prevalence of

PTSD in subjects ≥ 60 years of age in the National Comorbidity Survey (Kessler et al 2005) was found to be only 2.5%, which was much lower than the total population prevalence. One noteworthy point in relation to PTSD prevalence in Samuelson and colleagues' study was the slight excess of female (48%) participants, when compared to a normal critical care female population (44%) (ICNARC 2007), this would usually increase PTSD prevalence.

In Jones and colleagues' study, (2007) patients were also in the older age group and participants with some mental health problems were excluded from taking part. There was also an excess of male participants (62%), compared to a normal critical care male population of 56% (ICNARC 2007).Two (Kress et al 2003; Nickel et al 2004) studies used clinical interviews to determine PTSD, but both had small sample sizes. One (Nickel et al 2004) of these, compared the clinical interview to the PTSS10 and found that the PTSS10 identified almost twice as many cases of PTSD to that of the SCID.

All the remaining studies used self report questionnaires to determine PTSD status and five of these recruited samples of 60 patients or fewer. Two studies with moderate PTSD prevalence had a female gender bias and the same, slightly prolonged mean stay within ICU. The variability in PTSD prevalence observed with the numerous self report questionnaires suggested that further validation studies in this population of survivors, with gold standard structured clinical interviews as a comparison would be useful, help determine which instruments are best to use and would comply with previous recommendations for the standardisation of clinical measures for PTSD (Tedstone & Tarrier 2003).

2.4.5 - Attrition and Representation

Identifying dropouts and specifying the sources of information necessary to determine attrition are critical in research (Pekarik 1985). Although some studies provided comparative data between participants and those who were lost to follow-up, many did not. In some studies only the outcomes of participants were reported, which may have resulted in falsely inflated outcomes (Matthieu & Ivanoff 2007).

Studies of ICU patient populations are notoriously difficult due to increased mortality during the ICU stay, after discharge to the wards and following discharge from hospital. These frequently present problems in relation to recruitment and retention of subjects. The

overall sample size therefore is considered particularly important, as is the comparison of data between participants and non-participants. Very few of the studies reviewed provided this information, which limits generalisability within the larger population.

2.5 - Conclusions

The variation in prevalence of PTSD after discharge from ICU may be accounted for by various factors, methodological differences in studies, small sample sizes and the type of population studied, (e.g. sub-populations of ICU patients, survivors of a prolonged ICU admission or the typical ICU population involving a broad case-mix of admissions) are likely to be major factors. Overall, survivors of a prolonged ICU stay appear to present with a higher prevalence rate of PTSD than those whose stay is shorter, which may require further investigation. The variation in PTSD prevalence in studies recruiting samples comprising a broad case mix of patients, most comparable to the typical ICU population, may be due to simple methodological problems, such as the sample size recruited, a gender bias, selection of clinical measures to determine PTSD and the inclusion or exclusion of patients with a prior psychiatric history.

There was a distinct lack of prospective longitudinal data for a "typical" ICU population and a lack of data for early traumatic symptoms, which in terms of prevention is important. The natural course of PTSD symptoms following critical care admission is largely unknown and is vital to determine the appropriate evidenced based support that may, or may not, be required in order to improve overall outcome of survivors.

The disparity between prevalence of PTSD identified through the numerous self report questionnaires used and that of a gold standard structured clinical interview requires further investigation and possibly standardisation of measures may be achieved. However, in view of the difficulties in the recruitment of adequate sample sizes, given the recommendations that sample size for PTSD prevalence should be in the region of 1000 participants (O'Donnell et al 2006), this may only be realistically achieved through multi-centre studies. A further consideration may be that formal power calculations need to consider attrition rates most likely in the region of 20-30%, in order to obtain adequate representative samples.

2.6 - Factors associated with PTSD

The studies that presented predictive models for PTSD are shown in Table 2.4

TABLE 2.4 - PREDICTORS OF PTSD

AUTHOR	STUDY DESIGN	SAMPLE (SIZE)	PREDICTORS
MICHAELS ET AL (1999)	PROSPECTIVE	TRAUMA (176)	INTENTIONAL INJURY; DISSOCIATION; MALE GENDER; YOUNGER AGE; BASELINE MENTAL HEALTH; PRIOR LIFE THREATENING ILLNESS
SCHNYDER ET AL (2001)	PROSPECTIVE	TRAUMA (121)	BIGRAPHICAL RISK; SENSE OF DEATH THREAT; INTRUSIVE SYMPTOMS; PROBLEM ORIENTATED COPING.
SCRAGG ET AL (2001)	RETROSPECTIVE	BROAD CASE MIX (80)	YOUNGER AGE, 22% LONGER TIME SINCE DISCHARGE. 23%
CREAMER ET AL (2004)	PROSPECTIVE	TRAUMA (307)	REXPERIENCING; AROUSAL SYMPTOMS
RATTRAY ET AL (2005)	PROSPECTIVE	BROAD CASE MIX (60)	INTRUSION 6/12 (24.7%) - AGE/INTRUSION AT DISCHARGE AVOIDANCE 6/12 (30.4%) - AGE/AVOIDANCE AT DISCHARGE INTRUSION 12MTH (38.3%) - AGE/CCTS/INTRUSION AT DISCHARGE AVOIDANCE 12MTH (35.5%) - AGE/CCTS/HTS/APACHE II /AVOIDANCE AT DISCHARGE/FRIGHTENING EXPERIENCE
HAMANAKA ET AL (2006)	PROSPECTIVE	TRAUMA (100)	ASD+/PHYSICAL INJURY SEVERITY/ PERSISTANT PHYSICAL DISABILITY.

- **TABLE 2.4 cont. - PREDICTORS OF PTSD**

AUTHOR	STUDY DESIGN	SAMPLE (SIZE)	PREDICTOR
LIBERZON ET AL (2006)	CROSS SECTIONAL	AAA (109)	YOUNGER AGE/ PRE-OP HYPERTENSION/ PROLONGED INTUBATION.
BOER ET AL (2007)	RETROSPECTIVE	PERITONITIS (61)	FEMALE GENDER/YOUNGER AGE/ILLNESS SEVERITY/ PROLONGED ICU STAY
SAMUELSON ET AL (2007)	CROSS SECTIONAL	BROAD CASE MIX (226)	FEMALE GENDER/ AGITATION AND EXTREME FEAR DURING ICU.
JONES ET AL (2007)	PROSPECTIVE	BROAD CASE MIX (304)	SEDATION/DELUSIONAL MEMORY/PHYSICAL RESTRAINT

Eighteen studies from the systematic review provided evidence of factors associated with the development of later PTSD. However, eight studies conducted only correlation analysis, which would not constitute prediction. Of the ten remaining studies, four (Creamer et al 2004; Hamanaka et al 2006; Boer et al 2007; Samuelson et al 2007) used odds ratios and four (Schnyder et al 2001; Scragg et al 2001; Rattray et al 2005; Liberzon et al 2006) used regression analysis to predict PTSD. One (Michaels et al 1999) study used a path analysis and one (Jones et al 2007) used structural equation modeling to predict PTSD. There were six (Michaels et al 1999; Schnyder et al 2001; Creamer et al 2004; Rattray et al 2005; Hamanaka et al 2006; Jones et al 2007) prospective studies. Two (Scragg et al 2001; Boer et al 2007) studies were retrospective and two (Liberzon et al 2006; Samuelson et al 2007) studies were cross sectional designs.

The most prevalent risk factors for PTSD were traumatic stress symptoms and younger age. Five studies (Michaels et al 1999; Schnyder et al 2001; Creamer et al 2004; Rattray et al 2005; Hamanaka et al 2006) found traumatic stress symptoms predicted PTSD. Similarly, five studies (Michaels et al 1999; Scragg et al 2001; Rattray et al 2005; Liberzon et al 2006; Boer et al 2007) found younger age to be predictive of PTSD.

Although two studies (Boer et al 2007; Samuelson et al 2007) found female gender predicted PTSD, Michaels et al (1999) found male gender, predictive. In two studies (Rattray et al 2005; Boer et al 2007) a prolonged stay in ICU contributed to predictive models for later PTSD symptoms, but Liberzon et al (2006) found that only a prolonged period of ventilation was predictive.

Baseline mental health was associated with later PTSD in Michaels and colleagues study, and Schnyder et al (2001) found pre trauma variables such as biographical risk predicted PTSD. However, Jones et al (2007) found previous psychological problems were only indirectly related to PTSD. Two other pre-trauma variables, pre-operative hypertension (Boer et al 2007) and a prior life threatening illness (Michaels et al 1999) also contributed to a predictive model of PTSD.

Some aspects of the critical care experience, such as fear and extreme agitation were predictive of PTSD in one study (Samuelson et al 2007). Similarly, Rattray and colleagues (2005) found that participants' subjective reports of ICU as a frightening experience, contributed to a predictive model for PTSD. Jones et al (2007) found patient restraint during ICU treatment was predictive of PTSD, although the effect size was small. Effect size was larger for prolonged sedation, in the same study, which was directly associated with PTSD and physical restraint was directly related to this, but with a much larger effect size, which was also indirectly associated with PTSD. Delusional memory was also directly associated with later PTSD in Jones and colleagues' study, although the effect size was small. One further peri-traumatic variable, intentional injury, found by Michaels et al (1999) also contributed to the predictive model for PTSD.

There were also themes around the issue of trauma severity that predicted PTSD in three studies. Two of these (Rattray et al 2005; Boer et al 2007) found baseline APACHE II scores predicted PTSD. Schynder and colleagues (2001) found that subjective death threat for the

trauma predicted later PTSD, and Hamanaka et al (2006) found physical illness severity to be predictive. Some post trauma variables such as permanent physical disability (Hamanaka et al 2006), problem orientated coping (Schnyder et al 2001) and a longer time since critical care discharge (Scragg et al 2001) were also found to be associated with the prediction of PTSD after critical care discharge.

Although there were some universal risk factors for PTSD from the studies examined, the reliability may be questionable. There were a number of methodological differences between the studies such as sample size, study design, the population studied and respective trauma type, the methods used to determine predictive factors, and the timing, type and methods of assessment of PTSD. The strength of the relationship between some predictive factors and PTSD have been found to differ according to whether PTSD assessment was conducted through an interview or by questionnaire, whether dichotomised or continuous measures were used and by study design (Brewin et al 2000; Ozer et al 2003). Prospectively designed studies that included a broad case mix of patients were lacking amongst the critical care literature. Only two (Rattray et al 2005; Jones et al 2007) were reported and both used different measures and methods of assessment. Prediction in one (Jones et al 2007) was through a categorical PTSD diagnosis, according to the PDS (Foa et al 1997) and in the other (Rattray et al 2005) continuous measures according to total scores for intrusion and avoidance on the IES (Horowitz et al 1979).

There is no published evidence to date that has prospectively examined the predictors of PTSD according to a gold standard clinical interview after critical care treatment, by indexing responses early after discharge. This is important as two thirds of ICU survivors will experience significant problems with physical and psychological health and social functioning, and around 13% of survivors will experience severe limitations in their every day life (DOH 2003; Audit Commission 1999). Because this wide array of serious and concerning long-term sequelae interferes with optimal patient-centred outcomes (Angus & Carlet 2002), the detection of vulnerable survivors who present with early traumatic stress symptoms may facilitate improved management of psychological outcomes, as survivors may then be offered the practical, social and emotional support that is currently recommended (NCCMH 2005).

Chapter 3 - Other Outcomes after Critical Care Treatment

3.1 - Introduction

It is only in more recent years that health professionals have gained a better understanding of the full impact of critical illness on the patient and his/her family. Whilst some of our knowledge has been generated by survival research, much has been learned through the provision of follow-up clinics. This has undoubtedly drawn attention to broader patient-centred outcomes after intensive care (Broomhead & Brett 2002).

A lot more is now known about survivors who often face a prolonged recovery period due to weakness, dyspnoea, malnutrition, loss of muscle mass, and cognitive dysfunction (Weinert 2005). Maximum impairment in the quality of life sub-category of physical functioning has been reported in survivors of ARDS, four years after treatment in critical care (Schelling et al 1998) and one to two years following acute lung injury (ALI), health related quality of life has been found to be comparable to that of chronic illness populations (Cooper et al 1999).

The psychological consequence of surviving critical illness has also received much attention, although most of this has been concentrated on post traumatic stress reactions. Despite a number of studies having conducted assessments of the more common reactions of anxiety and depression following the critical care experience in addition to PTSD, they appear to be the "poor relation", when compared to some other outcomes.

The aim of this chapter is to examine the evidence of other outcomes such as anxiety, depression, cognitive function and health related quality of life, as experienced by survivors of critical care treatment. In order to do this a review of the critical care literature was undertaken through the OVID Medline search engine for the years 1996 through to September week one 2008, using the key words anxiety; depression; critical care; intensive care; critical illness; psychological and psychiatric morbidity; health related quality of life and cognitive function; cognitive impairment; and predictors. The identified studies that had used previously validated screening measures to detect the presence of anxiety, depression, health related quality of life and cognitive function after discharge from critical care were selected for inclusion in the review.

3.2 - Anxiety and Depression

Seventeen studies assessed rates of anxiety and/or depression after critical care treatment.

The studies reviewed are shown in Table 3.1

- **TABLE 3.1 - ANXIETY AND DEPRESSION studies**

AUTHOR	NUMBER	AGE (M)	SAMPLE	CLINICAL MEASURE	TIME	ANXIETY	DEPRESSION
EDDLESTON ET AL (2000)	143	49	BROAD CASE MIX	HADS >8	3 MTHS	11.9%	9.8%
SCRAGG ET AL (2001)	80	57	BROAD CASE MIX	HADS >8	3 - 5 YRS	43%	30%
JONES ET AL (2003)	126	58	BROAD CASE MIX	HADS >11	6 MTHS	33%	11%
KRESS ET AL (2003)	32	48	BROAD CASE MIX	STAI/BDI	6 MTHS+	25% STATE 56% TRAIT	59%
RATTRAY ET AL (2005)	109 87 80	55	BROAD CASE MIX	HADS >8	D/C 6 MTH 1 YR	45% 41% 45%	36% 26% 27%
YOUNG ET AL (2005)	20	54	BROAD CASE MIX	HADS >8	3 MTHS	25%	15%
SUKANTARAT ET AL (2007)	51 45	57	BROAD CASE MIX	HADS >11	3 9 MTHS	16% 22%	24% 31%
SAMUELSON ET AL (2007)	226	63	BROAD CASE MIX	HADS >11	2 MTHS	4.9%	7.5%
LIBERZON ET AL (2006)	68	64	AAA	STAI/BDI	6 MTHS - 2 YRS	NR	17%
SCHNYDER ET AL (2001)	106	38	TRAUMA	HADS >7	1 YEAR	17%	9.5%
FRENISEY ET AL (2006)	59	30	SBI/MTI	NRS-R	6-24 MTHS	12% -SBI 28%-MTI	76% - SBI 76% - MTI
JACKSON ET AL (2007)	58	45	TRAUMA	BAI/BDI	1-2 YRS	29.3%	56.7%
WEINERT ET AL (2006)	164	54	ACUTE RESPIRATORY FAILURE	SCID	2 MTHS	-	33%
WEINERT ET AL (1997)	24	40	ALI	CES-D	6-41 MTHS	-	43%
NELSON ET AL (2000)	24	40	ALI	CES-D	6-41 MTHS	-	69%
HOPKINS ET AL (2005)	66 62	46	ARDS	BAI/BDI	1 YR 2 YRS	24% 23%	16% 23%
CHRISTIE ET AL (2006)	79	43	ARDS	BAI/ZDRS	28 MTHS	48%	34%

STAI - SPIELBERGER STATE-TRAIT ANXIETY INDEX; CES-D - CENTER FOR EPIDEMIOLOGICAL STUDIES – DEPRESSION; ZDRS - ZUNG DEPRESSION RATING SCALE; HADS- HOSPITAL ANXIETY AND DEPRESSION SCALE; NRS-R - REVISED NEUROBEHAVIOURAL SCALE; NR - NOT REPORTED; SBI - SEVERE BRAIN INJURY; MTI - MULTIPLE TRAUMATIC INJURIES; ALI - ACUTE LUNG INJURY; ARDS - ACUTE RESPIRATORY DISTRESS SYMDROME

Eight (Eddleston et al 2000; Scragg et al 2001; Jones et al 2003; Kress et al 2003; Rattray et al 2005; Young et al 2005; Sukantarat et al 2007; Samuelson et al 2007) studies reported rates of anxiety and depression in a broad case mix of survivors. Four studies were of survivors of acute lung injury (ALI) (Weinert et al 1997; Nelson et al 2000) and acute respiratory distress syndrome (ARDS) (Hopkins et al 2005; Christie et al 2006). Three (Schnyder et al 2001; Frenisey et al 2006; Jackson et al 2007) studies were of survivors of trauma, one (Weinert et al 2006) following acute respiratory failure and one (Liberzon et al 2006) of survivors of abdominal aortic aneurysm.

The determination of "prevalence" of the disorder was mostly through self-report questionnaires although one (Weinert et al 2006) study used a gold standard semi structured interview (SCID) (First et al 1998) to diagnose depression. Only six of the studies had samples sizes in excess of one hundred participants. The mean age of participants ranged from 30 years to 64 years. There were considerable differences in the rates of anxiety and depression reported across the populations studied.

3.2.1 - Broad case mix

On reviewing the studies that investigated anxiety and depression in a broad case mix of patients, there were a number of differences between the samples. The sizes of samples ranged from 20 (Young et al 2005) to 226 (Samuelson et al 2007). The mean age of the samples varied from 48 (Kress et al 2003) years to 63 (Samuelson et al 2007) years. The earliest assessments conducted, at hospital discharge (Rattray et al 2005), two months (Samuelson et al 2007) and three months (Eddleston et al 2000; Young et al 2005; Sukantarat et al 2007) after discharge from critical care. Others (Kress et al 2003; Sukantarat et al 2007;Rattray et al 2005; Scragg et al 2001; Jones et al 2003) reported morbidity; from six months to five years after discharge. The most frequently used questionnaire was the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith 1983), which was used in seven studies whilst one (Kress et al 2003) used the Spielberger State-Trait Anxiety Index (STAI) (Spielberger 1983) and the Beck Depression Inventory (BDI) (Beck et al 1961) to measure anxiety and depression respectively. Prevalence rates of anxiety and depression in the studies varied considerably, the highest rates reported were 56% for Trait anxiety and

59% for depression (Kress et al 2003) and the lowest rates reported were 4.9% for anxiety and 7.5% (Samuelson et al 2006) for depression.

One probable explanation for the lower rates of anxiety and depression found in Samuelson and colleagues study was the use of a higher cut off score of eleven on the HADS, to denote more probable anxiety and depression. Later experiences with the HADS however has resulted in the questionnaire being used to measure severity of the conditions with four score ranges (Snaith & Zigmond 1994), instead of the original three, as used by Samuelson and colleagues. Subsequently by adopting the higher cut off score, participants with mild anxiety were not included in the overall prevalence rates reported by Samuelson and colleagues.

In most of the studies that used the HADS, a cut off score of eight was used to determine rates of anxiety and depression, however, two (Jones et al 2003; Sukantarat et al 2007) other studies also used the HADS cut off score of 11. In both of these, rates of anxiety and depression were higher than the rates found by Samuelson and colleagues. Although both studies had smaller sample sizes than that of Samuelson et al, the length of time participants spent within critical care was much longer, an objective measure found to be related to negative emotional outcome after critical care discharge (Rattray et al 2005). It is also likely that having had a more prolonged critical care stay, participants in the two studies may have been more physically debilitated, resulting in an overall prolonged hospital stay, which may also have influenced overall rates of anxiety and depression.

Of those studies using the HADS cut off score of eight, Eddleston et al (2000) found lower rates of anxiety and depression compared to the other broad case mix studies. Participants in their study were younger than in the other three studies, but their median critical care stay was only 3.8 days. Participants in the study by Scragg et al (2001) also had short stays within critical care but participants were older, and thus more comparable to the participants of Jones et al and Sukantarat et al. Prevalence of anxiety and depression in Scragg and colleagues study was among the highest rates reported, although this was three to five years after critical care discharge. Rattray et al (2005) found similar high rates of anxiety and depression in a prospective study over a period of one year. Rattray et al also noted a significant reduction in anxiety and depression scores between hospital discharge and the six-month follow up. Participants in their study had longer stays within critical care than those studied by Scragg et al, but not as prolonged as those of Jones et al and

Sukantarat et al. The higher prevalence in this study compared to that of Jones and Sukantarat and their colleagues' can be accounted for by the lower HADS cut off score used.

Young et al (2005) investigated anxiety and depression rates at three months in general ICU patients and their relatives and compared them to those obtained from cardiac surgery patients' and their relatives. Prevalence of anxiety and depression in the general ICU patients was 25% and 15% respectively, but the sample size was very small compared to the other broad case mix studies. The final broad case mix study was that conducted by Kress et al (2003). In this retrospective study, the authors examined the long-term psychological effects of daily sedative interruption on critical care patients, at least six months after treatment. The prevalence rate of depression was the second highest of all the broad case mix studies with 59% of participants found to have depression according to the BDI. The rate of chronic anxiety was also high (56%), whilst acute anxiety was much lower (25%), according to the STAI. The use of different clinical measures to those used in the other studies, in addition to the small sample size makes generalisability of these results somewhat limited.

3.2.2 - ARDS, ALI and other respiratory failure

Only two (Hopkins et al 2006; Christie et al 2006) studies measured anxiety and both used the Beck Anxiety Inventory (BAI) (Beck et al 1998) to quantify this. All four (Weinert et al 1997; Nelson et al 2000; Hopkins et al 2005; Christie et al 2006) studies measured depression. Two (Weinert et al 1997; Nelson et al 2000) used the Centre For Epidemiological Studies – Depression (CES-D) questionnaire, whilst the Beck Depression Inventory (BDI) (Beck et al 1961) was used by Hopkins et al (2006) and the Zung Depression Rating Scale (ZDRS) (Zung 1965) was used by Christie at al (2006).Rates of anxiety and depression were very different.

Two years after discharge, using BAI, Christie et al (2006) found twice the rate of anxiety compared to that found by Hopkins et al (2006), despite similarities in sample size and the ages of participants. There are a number of possible explanations for the higher rates of anxiety in Christie and colleagues' study, in that the participants were recruited through an advertisement on an ARDS support website and thus may have been actively seeking

support because of specific problems. This particular study was considered somewhat limited because of the method of recruitment, because there were no medical records to confirm that participants were in fact survivors of ARDS and subsequently no available baseline data. The method of assessment of participants in the two studies also differed; in one (Hopkins et al), participants returned to a follow-up appointment whilst the in the other study (Christie at al) the assessment was conducted via a telephone interview, which adds potential for misunderstanding or indeed interviewer bias.

A further noteworthy observation was the number of patients with anxiety in Hopkins and colleagues' study increased between the one and two year follow-ups. The restrictions imposed through the use of a screening measure as opposed to a more formal psychiatric interview, makes it impossible to determine if the increase in anxiety was as a result of ARDS or an alternative stressor. Pulmonary function tests following ARDS have generally demonstrated a restrictive ventilatory defect and some impairment of diffusion capacity (Dowdy et al 2006) and given that respiratory threat is considered a specific activator of panic-anxiety responses (Klein 1993), this may explain the increase in anxiety symptoms for some patients, over time.

All reported rates of depression in survivors and these were also diverse, ranging from 16%, one year after ARDS, to 69% in survivors of ALI who had been discharged between six and forty one months previously. The most plausible explanation for the higher rates of depression in the ALI survivors were the small sample sizes, as only 24 participants were included in each of the two (Weinert et al 1997; Nelson et al 2000) studies. Given that ARDS is a more severe sub category of ALI (Davydow et al 2008) one may even expect to see a higher rate of depression in ARDS survivors, but clearly this was not the case. As observed with rates of anxiety, there was also a similar increase in the number of participants reporting depression between the one year and two year follow-ups in Hopkins and colleagues (2005) study. Prolonged critical care stays of 11 days or longer are often "the norm" in ARDS and this is one risk factor thought to contribute to higher rates of psychiatric morbidity in these patients (Davydow et al 2008).

3.2.3 - Trauma participants

Of the three (Schnyder et al 2001; Frenisey et al 2006; Jackson et al 2007) trauma studies reviewed, sample size ranged from 58 to 106 participants and the age of participants from 30 years to 45 years. The follow up of participants also varied, one study (Frenisey et al (2006) assessed symptoms between six months and two years after, one (Schnyder et al 2001) assessed participants at one year and one (Jackson et al (2007) was conducted one to two years after trauma. All three studies used different clinical measures to detect symptoms of anxiety and depression and as a result, generalisabilty of the results is questionable.

The generalisability of studies of psychiatric morbidity after trauma have also been challenged (O'Donnell et al 2004) because many fail to obtain the gender ratios that are considered representative of the overall trauma population. This was not the case in the three critical care studies involving trauma survivors, since they all comprised more male patients, although two (Frenisey et al 2006; Jackson et al 2006) of them had particularly small sample sizes.

Frenisey et al (2006) investigated the outcome of two participant groups; those with severe brain injury (SBI) and those who had sustained multiple traumatic injuries (MTI) but no head trauma. Although the sample sizes were divided equally between the two groups, they were very small. The rates of anxiety were very different but rates of depression were identically high in the two groups. By comparison to the other trauma studies although the rate of anxiety for the MTI patients was similar to that identified by Jackson et al (2007), the rate of anxiety for SBI patients was the lowest prevalence identified of all the studies. Despite using other validated measures of anxiety and depression to determine prevalence, those reported were taken from the Revised Neurobehavioural Rating Scale (NRS-R)(Levin et al 2001) which although validated in three different populations (Levin et al 2001), these did not include MTI survivors or those surviving critical care treatment. This might explain the particularly high rates of depression identified in the study, although participants were younger and had a prolonged mean hospital stay of 126 days.

Jackson et al (2007) investigated the long-term outcomes of survivors of traumatic injuries, of which the majority (71%) were involved in motor vehicle accidents. Although the rate of anxiety, according to the BAI, was similar to that found by Frenisey and colleagues, it was

much higher than that found by Schnyder et al (2001) and those of other psychiatric studies (Melman et al 2001; Mayou et al 2001). The rate of depression in Jackson and colleagues' study, according to the BDI, was also higher than that found by Schnyder and colleagues, in participants of the Trauma Recovery Project (Holbrook et al 1998) and that found by O'Donnell et al (2004). There are possible explanations for this in that the sample size was small and comprised participants with multiple prior mental health issues, of which 48% had a previous history of depressive illness. A prior history of depression has been associated with a greater risk for developing major depression and with reporting more symptoms across time (Shalev et al 1996). Added to this, participants' mean injury severity score (ISS) was much higher than that of either of the two other trauma studies. Schnyder et al (2001) did not find ISS predictive of later clinically relevant psychiatric symptoms, but this may have been a reflection of the particularly low ISS in their sample. The lower rates of anxiety and depression identified in Schnyder and colleagues' study may have been a result of the stringent recruitment criteria, since subjects with prior mental health problems were excluded from participation. In addition to this, only 21% of the sample studied were females and whilst this is said to be typical of the trauma population, it serves to keep the level of psychiatric morbidity low (Schnyder et al 2001).

3.2.4 - Other participants

Of the two (Weinert et al 2006; Liberzon et al 2006) remaining studies reviewed, only rates of depression were reported. The study by Weinert and colleagues was the only study, amongst all those reviewed to have used a gold standard clinical interview to determine rates of depression after critical care treatment. In this study of 164 survivors of acute respiratory failure, 33% were found to have depression at a two-month follow up.
There were high rates of pre admission psychiatric morbidity however in this sample, with 36% reporting some lifetime experience of psychiatric problems, 34% having taken anti depressant medication in the previous six months and 27% taking antidepressants, one week prior to admission. The particularly high rate of pre-admission psychiatric morbidity may explain the particularly high rate of depression found in this sample.
In Liberzon and colleagues' study, 88 survivors of treatment for abdominal aortic aneurysm were investigated between six months and two years after discharge. Interestingly even

though depression has been associated with an increased risk of arteriosclerosis (Musselman et al 1996), only twelve patients recruited to the study had a prior history of major depression. On excluding them from the analysis, the authors found that of those admitted to ICU after surgery, 22% had depression at follow up. Because the authors had included two groups of patients in the study, those who had surgery and those who were treated conservatively, one of the conclusions of the investigation was that exposure to surgery itself may have been associated with the development of psychiatric pathology. Boer et al (2007) reported similar findings in survivors of peritonitis.

Despite the methodological differences between all the studies reviewed and the subsequent disparate prevalence rates of anxiety and depression, there is clearly evidence of significant anxiety and depression after critical care treatment and a need for more prospective longitudinal investigations in order to clarify the symptom trajectories over time.

3.3 - Cognitive function

Seven critical care studies described degrees of impairment of cognitive function after critical care discharge. In all but one (De-Rooij et al 2008) of the studies sample size was relatively small. The timing of follow up also varied with the earliest assessment performed at discharge and the latest at 3.7 years after discharge. Several different clinical measures were used across the studies examined, with some employing a complex battery of screening measures to determine more specific impairment (Jackson et al 2003; Sukantarat et al 2005; Hopkins et al 2005). There were no assessments of validity or reliability in any paper and although one (Nelson et al 2006) study used the Confusion Assessment Method (CAM-ICU), which was a validated ICU version, the telephone version used in the study was validated in a population of subjects recovering from hip fractures only.
Using the CAM-ICU (Ely et al 2001), Nelson et al (2006) assessed brain dysfunction, in relation to coma and delirium, during admission to a respiratory care unit and the CAM-T (Marcantonio et al 1998), three months and six months after discharge. This sample comprised of 85 participants with chronic critical illness, of an average of 45 days duration and with a mean participant age of 72 years. Of the 85 survivors, 58 (68.2%) were too

profoundly impaired to respond to telephone cognitive assessment, and 53 (62.4%) were dependent in all activities of daily living at six months. This profound deterioration in cognitive function in elderly patients is not uncommon, as some studies of medical patients have suggested that pre-morbid insults may influence the rate of cognitive deterioration (Hopkins et al 2007).

Conversely, one year after discharge from a general critical care unit, De-Rooij et al (2008) investigated cognitive function in elderly survivors aged 80 years old. Their carers completed the Informant Questionnaire on the Cognitive Decline short form (IQCODE-SF) (Jorm et al 2000), a global measure of cognitive impairment as rated by a close relative, and the survivors were found to have fair to good cognitive function. The participants in this study however, despite being older than those in Nelson and colleagues study, had a particularly brief stay within critical care.

Frenisey et al (2006) investigated some neuro-behavioural and psychopathological aspects of trauma in severe brain injured patients and survivors of multiple traumatic injuries. The authors found that at six to twenty four months after serious trauma, the multi-trauma survivors suffered from memory troubles (60%), concept disorganization (32%), loss of initiative (36%), irritability (52%), unusual thought content (40%), mood swings (40%), attention difficulties (24%), suspiciousness (48%), and feelings of guilt (36%), according to The Revised Neurobehavioral Rating Scale (NRS-R) (Levin et al 1990). The survivors of severe brain injury were found to have impairments in all domains of the NRS-R.

Cognitive and executive functions were measured using Raven's Progressive Matrices (Raven et al 1998), the Hayling Sentence completion test (Burgess & Shallice 1997) and the Six-Element Test (Burgess et al 1996), by Sukantarat et al (2005) in a broad case mix of patients who had survived a nine-day stay within critical care. At three months, 35% of patients scored at or below a level equivalent to the lowest performing 5% of a normal population, on two or more tests of cognitive function, at nine months only 4% of patients were impaired to this extent.

Jones et al (2006) investigated thirty long stay critical care patients for cognitive dysfunction using the Cambridge Neuropsychological Test Automated Battery (CANTAB), a computerised software programme. One week after critical care discharge, six (20%) patients showed evidence of difficulties with problem solving and fifteen (50%) had memory impairment. At a two month follow-up, five of sixteen (31%) scored below the 25th percentile for memory

and eight of sixteen (50%) for problem solving. Although there appeared to be some improvement in the number of subjects reporting memory problems by the two month follow-up, unfortunately the authors did not provide any information regarding the subjects who dropped out, or if those reporting memory problems at two months had also reported it at the initial assessment.

Hopkins et al (2005) investigated cognitive function in 75 survivors of ARDS, in a longitudinal study over two years. At hospital discharge, 73% of patients were found to have impairment in cognitive function, at one year 46% and at two years 47%, according to a battery of standardised neuro-cognitive tests. A pair wise comparison of mean neuro-cognitive scores suggested that there was an improvement in cognitive function between hospital discharge and the one-year and two year follow ups, although there were no differences between the one-year and two-year scores. Despite some improvement in cognitive function in the first year after discharge, a considerable number of survivors remained cognitively impaired for at least two years after ARDS.

Jackson et al (2003) investigated neuro-psychological outcomes in 41 survivors of medical critical care treatment, six months after discharge. They excluded seven patients because of a prior history of cognitive impairment and of the remaining 34 patients, 11 (32%) were found to be neuro psychologically impaired. The sample size in this study was very small although the authors compared all baseline data collected at the time of hospital discharge between those who took part in the study and those who did not (n=146). Interestingly the mean Mini Mental State Examination (MMSE) (Folstein et al 1975) scores of participants who did not take part in the follow up were significantly lower than in those who did take part, which may suggest that had those patients also participated in the follow-up, the rate of cognitive impairment may have been higher.

It was difficult to draw any firm conclusions from these studies regarding the extent of cognitive impairment after critical care discharge. Sample sizes in the studies examined were mostly small and the measures used to assess cognitive function were all very different and had not been validated within the population. From this brief review, it appears that there may be some improvement in cognitive function over time, although there is clearly a need for more longitudinal studies to confirm this. For some patients who

have a more prolonged stay within critical care, such as survivors of ALI/ARDS they may experience greater cognitive impairment, which may be more prolonged.

Hypoxemia has been previously implicated in the decline of cognitive impairment in sufferers of chronic obstructive pulmonary disease (Stuss et al 1997). This is particularly important given that survivors of ARDS are often younger than a more typical critical care population. In relation to age, in three of the studies, the participants were much older and a degree of memory impairment in those more senior is frequently seen, and probably associated with ageing (Petersen 2004).

The assessment of neuropsychological functioning, was considered to be of limited value in general critical care patients (Hayes et al 2000) with the suggestion that it would be better utilised as a disease specific measure, confined to patients who have suffered a head injury or other central neurological insult. This opinion, is certainly not shared by some (Milbrandt & Angus 2006) who have called for further research to understand the specific mechanisms that contribute to the development of critical illness associated cognitive dysfunction, in order to treat or prevent its occurrence. The usefulness of cognitive tests and functional measures have been otherwise recognised (Petersen 2004), but as with any clinical measures for the screening of conditions, ultimately, the final determination of a diagnosis relies upon the clinician's judgement.

The studies that investigated cognitive function after critical care treatment are shown in Table 3.2.

- TABLE 3.2 - COGNITIVE FUNCTION STUDIES

AUTHOR	NO. OF PARTICIPANTS	AGE	POPULATION STUDIED	CLINICAL MEASURE	FINDINGS OF IMPAIRMENT	TIME OF ASSESSMENT
NELSON ET AL (2006)	98 85	72	PMV	CAM ICU-T RASS	SEVERE - 77% SEVERE - 71%	3 MONTHS 6 MONTHS
FRENISY ET AL (2006)	50	30	TRAUMA	NRSR	ALL DOMAINS	6-24 MONTHS
SUKANTARAT ET AL (2005)	51 45	60	SURGICAL ADMISSIONS	RSPM HSCT SET	35% 4%	3 MONTHS 9 MONTHS
DE-ROOIJ ET AL (2008)	204	81	ELDER	IQCODESF	17% SEVERE	3.7 YEARS
JONES ET AL (2006)	32 16	54	LONG STAY	CANTAB	MEM - 50% PS - 20% MEM- 31% PS 50%	1 WEEK 2 MONTHS
HOPKINS ET AL (2005)	74 66 62	46	ARDS	NEURO COGNITIVE BATTERY	73% 46% 47%	DISCHARGE 1 YEAR 2 YEARS
JACKSON ET AL (2003)	34	53	MEDICAL ADMISSIONS	MMSE mBDRS NEURO PSYCHOLOGICAL BATTERY	31%	6 MONTHS

3.4 - Health related quality of life

Thirty-six critical care studies investigating health related quality of life after discharge were identified. Although study designs differed, the sample sizes in most (23) of the studies exceeded that of 100 participants. There were nine different clinical measures used to assess health related quality of life. The timing of the assessments varied with fifteen studies reporting health related quality of life within 6 months of critical care discharge, eight studies within one year of discharge, three studies conducted one to two years after discharge and eleven examined health related quality of life three years and longer after treatment.

The populations studied were quite diverse. Fourteen (Hurel et al 1997; Ridley et al 1997; Rattray et al 1998; Niskanen et al 1999; Eddleston et al 2001; Granja et al 2002; Kvale et al 2002; Elliot et al 2004; Boyle et al 2004; Cuthbertson et al 2005; Capuzzo et al 2006; Sukantarat et al 2007; Fildidssis et al 2007; Hofhuis et al 2008) comprised a broad case mix of patients. Four studies (Kleinpell et al 2002; Kaarlola et al 2003; Merlani et al 2007; Del-Rooij et al 2008) were of the elderly. Two studies (Coomes et al 2003; Chelluri et al 2004) involved patients who had received prolonged mechanical ventilation and another (Douglas et al 2002) that had compared this to a shorter period of ventilation. Four studies (Weinert et al 1997; Schelling et al 1998; Davidson et al 1999; Déjà et al 2006) were of ALI/ARDS survivors. Four (Michaels et al 2000; O'Donnell et al 2005; Jackson et al 2007; Ulvik et al 2008) were of trauma survivors. One (Kerocec et al 2006) of trauma and sepsis, one (Heyland et al 2000) of sepsis only and one each of survivors of acute pancreatitis (Soren et al 2000), surgical complications (Lamer et al 2004), abdominal sepsis (Haraldsen et al 2003), prolonged surgical ICU stay (Lipsett et al 2000) and multi organ failure (Petilla et al 2000).

Eleven broad case mix studies reported on findings within the first six months after discharge. Hofhuis et al (2008) studied the immediate impact of critical illness on HRQOL and patients' recovery over time. Two hundred and fifty two patients survived to the six month follow up. Although physical functioning (PF), general health (GH), and social functioning (SF) remained significantly lower than pre-ICU admission values, there was a rapid improvement over the six-month period.

There were other similar findings to this, within the broad case mix population, in the first six months after discharge. In one multicentre study comprising 559 survivors, Cappuzzo et al (2006) found more than 60% reported an overall good recovery according to the EuroQol (EuroQol group 1990), at a three-month follow up. Cuthbertson et al (2005) investigated pre-morbid health related quality of life (by proxy during admission) in 300 patients according to the SF-36(Ware et al 2001); participants were then assessed at three, six and twelve months after discharge. Participants' physical composite scores (PCS-36) at three months were significantly lower than the proxy scores at baseline. There was a gradual improvement in PCS-36 over twelve month. PCS-36 at twelve months was significantly higher than the three month PCS-36. Participants' mental composite scores (MCS-36) improved significantly over twelve months. Participants' MCS-36 was equal to or higher than the population norms at twelve months but PCS-36 was lower. Although they found limitations in survivors' physical composite scores, these were equal to the pre-morbid scores.

Three months after critical care discharge, Eddleston et al (2001) assessed 143 survivors at a dedicated critical care follow up clinic. They found that men over the age of 65 years and women younger than 65 years demonstrated significantly better health in some sub domains of the SF36, although 80% of survivors overall were satisfied with their health related quality of life at that time. At six months post discharge, Ridley et al (1997) found that patients with pre existing ill health reported significant improvements in mental health, social functioning, pain levels and vitality and only those admitted following acute pathologies were found to have significant decreases in health related quality of life.

Hurel et al (1997) found health related quality of life for 223 survivors to be fair, according to the Nottingham Health Profile, whereas survivors' subjectively rated satisfaction of their health related quality of life was in fact low. Conversely, for 28 participants in one study conducted by Rattray et al (1998) health was not the main determinant of survivors' health related quality of life and only ranked as fourth most important, in a list of individually nominated factors. On examining chronic pain in survivors, Boyle et al (2004) found this to be a significant issue that affected 28% of participants who subsequently reported reductions in physical function, bodily pain, general health and vitality as a result.

Elliot et al (2004) found significant impairment in health related quality of life at critical care discharge in 34 survivors, however at six months this had returned to near normal values.

Conversely Kvale et al (2002) found health related quality of life for 123 survivors to be significantly lower than normal population scores at six months. Impairment at six months was also reported by Granja et al (2004) who found that health related quality of life for 29% of 275 participants, worse than at pre-admission and that 77% of all participants had one SF12 domain problem.

Among other sub populations of critical care patients followed up within six months of discharge, Lamer et al (2004) found that perceived health related quality of life, according to the NHP in 104 survivors of surgical complications, was similar to a matched control group of patients. However, the critical care patients had significantly more pain and impairment in physical functioning than their counterparts. In a study of 164 elderly patients who survived a critical care admission, Kleinpell et al (2002), found that survivors reported an overall good health related quality of life at 4-6 months post critical care discharge. Similarly, in a sample of 368 patients who had survived a long stay within critical care, Niskanen et al (1999) found that although QOL was found to be lower than that of population norms, survivors reported it to be fairly good.
In a small sample of trauma survivors, Michaels et al (2000) found that the SF36 demonstrated a progressive return toward baseline on all subscales from six to twelve months after traumatic injury, although full recovery was not attained in any of the domains by twelve months. Most impairment was identified in the physical subscales of role and functioning, although those with extremity fractures were impaired in physical function, role-physical, and bodily pain.

Of the eight studies that assessed health related quality of life six months to 1 year after discharge, survivors of multi-organ dysfunction (Petila et al 2000) were found to have the worst outcome at one year. They were found to be significantly impaired in all QOL domains, according to the RAND -36, except for in the domains of bodily pain and mental health. O'Donnell et al (2005) also found that 243 survivors of trauma had impairment in all domains of the WHO-QOL, although not all of the survivors had been admitted to critical care following the injury.
On comparing survivors of prolonged mechanical ventilation (PMV) to that of a shorter mechanical ventilation period (SMV), Douglas et al (2001) found that SMV survivors had

better overall QOL and PMV survivors were found to have impairments in physical functioning, according to the SIP. Chelluri et al (2004) also investigated the outcome of PMV patients and found that they also had impairments in physical functioning in addition to social functioning, according to the SF36. Conversely Lipsett et al (2000) found that in survivors of an acute surgical illness who had a prolonged critical care stay, functional outcome was comparable with a good health related quality of life. Similarly, survivors of acute pancreatitis were found to have a QOL that was reportedly as good as it had been pre-admission (Soren et al 2000).

In one small sample of a broad case mix of survivors, Sukantarat et al (2007) found that PCS according to the SF36 improved with time, but MCS did not. In a broad case mix of 152 elderly patients, Lizanza et al (2001) found that 21% of participants reported their health related quality of life to be worse than prior to admission but only 17% were found to be severely impaired.

Where health related quality of life was assessed more than one year after discharge from critical care, there were fewer reports of positive outcomes. In a broad case mix of survivors, eighteen months after discharge, Fildissis et al (2007) found QOL had improved over time but it was worse than pre-admission. One (Haraldsen et al 2003) small sample of survivors of abdominal sepsis were reportedly found to have regained health and functionality,but this was several years after discharge, In a study (De-Rooij et al 2008) of 189 elderly survivors who had undergone surgery, 76% of them had no severe physical limitations, one to six years after discharge. Conversely, Melani et al (2007) found that 52 elderly survivors of severe abdominal pathologies, had a worse health related quality of life two years after discharge, compared to a matched population, although survivors themselves perceived their critical care stay as positive and 75% stated they would agree to be admitted to critical care again. The sample size was very different between the studies, as were the health related quality of life measures used, which may partly explain the difference. However, the most likely reasons for the difference in health related quality of life, between the two studies was 87% of patients were planned surgical admissions in De-Rooij and colleagues' study , compared to 56% in Merlani and colleagues' study and fewer reported pain (57%) in De-Rooij and colleagues' participants compared to 70% reported by participants in Merlani and colleagues' study.

Studies of survivors of ALI/ ARDS (Weinert et al 1997; Schelling et al 1998; Davidson et al 1999; Hopkins et al 2005; Deja et al 2006) were also found to have significant impairments from one year (Hopkins et al 2005) through to three to six years (Schelling et al 1998). These were described as impairment in all domains (Déjà et al 2006), maximum impairment in physical function and chronic pain (Schelling et al 1998), impairment in physical and pulmonary specific domains (Davidson et al 1999) and severe impairment in PCS, although less severely in MCS (Weinert et al 1997). Hopkins et al (2005) found their ARDS survivors had decreased quality of life physical domains that improved during the first year; little change in role emotional, pain, and general health; and improvement, then subsequent decline, in mental health at 2 years. Even as long as three years after receiving prolonged mechanical ventilation, Coomes et al (2003) found that survivors were impaired in all QOL domains of the Nottingham Health Profile, except for the social isolation domain, when compared to a normal French population. One possible explanation is a delay in adjustment or maladaptive "response shift". Response shift is a change in the meaning of one's self-evaluation of QOL, resulting from changes in internal standards, values and the conceptualization of QOL (Sprangers and Schwartz 1999)

The theoretical model proposed by Sprangers and Schwartz comprises an evolving five-stage process, a catalyst (change in health status); antecedents (socio-demographics, personality, expectations); mechanisms (behavioural, cognitive and affective processes) and perceived health related quality of life. The nature of the acute onset of ARDS and subsequent prolonged period of prolonged mechanical ventilation results in patients leaving the ICU with deficits in physical and cognitive function, leading to a delayed return to work; and often disrupted family lives (Davydow 2008). Because response shift is concerned with maintaining or regaining homeostasis, if an individual were unable to adjust to deterioration and maintained internal standards applicable to pre-illness health, the response shift becomes mal-adaptive. (Spranger &Schwartz 1999). High rates of depression following ARDS/ALI have already been discussed, but perhaps this antecedent impedes the response shift.

Although a number of studies have investigated health related quality of life after critical illness and ICU admission, assessment measures differed considerably and thereby conclusions are tentative. It appeared that for some patients, health related quality of life

was impaired, not as severely as some supposed, but improved with time. However, for some patients, particularly those who had prolonged ICU stays, the improvement in health related quality of life was delayed. There are a lack of relevant validity data for questionnaires for the critical care population and only four measures of health related quality of life have been recommended along with the need for the rigorous assessment of them (Hayes et al 2000).

3.4.1 Factors associated with impaired health related quality of life

Nine of the health related quality of life studies reviewed examined factors associated with impairment after critical care treatment and four different clinical measures were used. Four studies comprised less than 100 participants, and five studies had in excess of 100 with an overall range of 24 to 559 participants. One (Capuzzo et al 2006) study found associations with impairment at three months, three (Michaels et al 2000; Hopkins et al 2004; O'Donnell et al 2005) at one-year, two (Weinert et al 1997; Fildissis et al 2007) between one and two years, and three (Schelling et al 1998; Ulvik et al 2007; Deja et al 2006) three to six years after treatment. The studies consisted of two (Capuzzo et al 2006; Fildissis et al 2007) broad case mixes, three (Michaels et al 2000; O'Donnell et al 2005; Ulvik et al 2008) in survivors of traumatic injury and four (Weinert et al 1997; Schelling et al 1998; Hopkins et al 2004; Deja et al 2006) in survivors of ALI/ARDS.

The predictors of impaired health related quality of life in the two broad case mix studies were very different. Capuzzo et al (2006) conducted a multi- centre international study comprising of 559 patients. The EuroQol (Euroqol Group 1990) questionnaire was administered through a telephone interview 90 days after critical care treatment. Using a logistic regression analysis and the patients subjective report of health status ("good" or "poor") as the independent variables, the authors found that creatinine at critical care admission ≥ 2mg/dl, body temperature at admission ≤ 35°C, presence of metastatic cancer, lowest Ph at admission ≤ 7.25 and unplanned admission all contributed to the predictive model with a variance of 12%. Fildissis et al (2008) investigated the long-term outcome of

116 patients using the Quality of Life - Spanish (QOL-SP) (Fernandez et al 1996) questionnaire. Using multi-linear regression analysis, the authors found that age, length of ICU stay and male sex were important risk factors influencing poor health related quality of life at 18 months after discharge from the ICU.

Four years after traumatic injury, Ulvik et al (2008) found that Injury Severity Score (ISS) (Baker et al 1974) and the Simplified Acute Physiology Score (SAPS-II) (Le Gall et al 1993) were significantly associated with impaired health related quality of life, according to the EuroQol, in 210 survivors. Twelve months after injury, Michaels et al (2000) also found ISS, along with twelve-month physical function, mental health, baseline general health and mental health predicted the SF36 general health score, accounting for 39% of the variance. Baseline mental health and twelve-month PTSD score, depression score, increased substance abuse and pain score predicted SF12 mental health score, accounting for 62% of the variance.

Using structural equation modelling, O'Donnell et al (2005) found that acute psychological response, twelve month role related disability and injury characteristics predicted impairment in health related quality of life, twelve months after serious accidental injury according to the World Health Organization QoL-Bref questionnaire (WHOQoL-Bref) (Harper & Power 1998), in 243 patients. One year after discharge, Hopkins et al (2004) also found psychological factors, namely anxiety and depression, were associated with impairment in all health related quality of life domains, according to the SF36, except physical functioning in sixty-six survivors of ARDS. Statistical analysis however, was restricted to correlations only in this study.

Weinert et al (1997) found a negative correlation between depression scores and the MCS-36 and a negative correlation between age and the PCS-36 of the SF36, in twenty-four survivors, fifteen months after treatment for acute lung injury. In addition to the limitation of correlation analysis, the sample size was very small.

Schelling et al (1998) investigated HRQoL in 80 survivors of ARDS and found that PTSD was associated with major impairments in the mental health domains of the SF36, three to six years after discharge. Similar findings were reported by Déjà et al (2006) in sixty five survivors of ARDS, where fifty seven months after discharge HRQoL was reduced in long-term survivors and was also linked with an increased risk of chronic PTSD with ensuing

psychological morbidity. There was no reference to the type of statistical method used for prediction in the report, Schelling and colleagues and Déjà and colleagues used correlation only to determine a relationship with health related quality of life.

Although from the limited evidence, it would appear that psychological factors might be the most influential in determining impairment in health related quality of life after critical care treatment only five studies used the appropriate regression analysis to determine the predictors. There is a need for more research to clarify this. Whilst studies of predictors of impairment in health related quality of life, years after critical care treatment, have been informative, there is a now a need for more research to identify earlier risk for impairment and to examine this over time. Overall, there was a lack of good prospective studies, which is important if we are, to better understand the natural progression of patients' health related quality of life after critical care admission. When such studies have been conducted, investigators may attempt to reduce the time to improvement by the introduction of early active intervention (Eddleston et al 2001).

The predictive studies are shown in Table 3.3

- **TABLE 3.3 - FACTORS ASSOCIATED WITH IMPAIRED HEALTH RELATED QUALITY OF LIFE**

AUTHOR	POPULATION	NUMBER	QOL MEASURE	TIME OF ASSESSMENT	PREDICTOR/ASSOCIATION
CAPUZZO ET AL 2006	BROAD CASE MIX	559	EUROQOL	3 MTHS	UNPLANNED ADMISSION, HYPOTHERMIA, CREATININE>2MG/DL, PH< 7.25, METASTATIC CA (PREDICTION)
HOPKINS ET AL (2004)	ARDS	66	SF36	1 YEAR	CCTS - PF/RP HLOS TID - RP DEPRESSION ANXIETY- RP/BP/GH V/SF/RE (ASSOCIATION) — MH
O'DONNELL ET AL (2005)	TRAUMA	243	WHOQOL	1 YR	ACUTE PSYCH RESPONSE, DISABILITY (PREDICTION)
MICHAELS ET AL (2000)	TRAUMA	146	SF36	1 YR	GH (B/L) MH (B/L) ISS PF(12mth) MH (12 mth) — GH MH (B/L) PTSD (12 mth) BSI D (12 mths) SA (12 mth) BP - SF36 MH (PREDICTION) — MH
WEINERT ET AL (1997)	ALI	24	SF36	15/12	DEPRESSION/MCS AGE/PCS (ASSOCIATION)
FILDISSIS ET AL (2007)	BROAD CASE MIX	116	QOL-SP	18/12	AGE, CCTS, MALE GENDER (PREDICTION)
SCHELLING ET AL (1998)	ARDS	80	SF36	3-6 YRS	PTSD (NOT KNOWN)
ULVIK ET AL (2008)	TRAUMA	210	EUROQOL	4 YEARS	SAPS ISS (PREDICTION)
DEJA ET AL (2006)	ARDS	65	SF36	57 MTHS	PTSD (ASSOCIATION)

ARDS - ACUTE RESPIRATORY DISTRESS SYNDROME; ALI - ACUTE LUNG INJURY; SF36 - SHORT FORM 36 ; WHOQOL - WORLD HEALTH ORGANISATION QOL BREF; QOL-SP- QUALITY OF LIFE-SPANISH; GH - GENERAL HEALTH; PF - PHYSICAL FUNCTIONING; MH - MENTAL HEALTH; CCTS - CRITICAL CARE TOTAL STAY; SAPS - SIMPLIFIED ACUTE PHYSIOLOGY SCORE; ISS - INJURY SEVERITY SCORE; PTSD - POST TRAUMATIC STRESS DISORDER. GH - GENERAL HEALTH, B/L - BASELINE, MH - MENTAL HEALTH, PF - PHYSICAL FUNCTION, PTSD - POST TRAUMATIC STRESS DISORDER, BSI D - DEPRESSION SCORE, SA - SUBSTANCE ABUSE, BP - BODILY PAIN.

Chapter 4 – Aims

The primary aims of this study were –

1. To investigate what proportion of patients develop traumatic stress symptoms after critical illness admission.

2. To compare the performance of the Davidson Trauma Scale(DTS), a self-report questionnaire to that of the Clinician Administered Posttraumatic Stress Disorder Scale (CAPS), a structured clinical interview, in detecting PTSD after critical illness admission.

3. To compare the performance of the SPAN, a self-report questionnaire to that of the Clinician Administered Posttraumatic Stress Disorder Scale (CAPS), a structured clinical interview, in detecting PTSD after critical illness admission.

4. To identify factors associated with traumatic stress symptoms after critical illness admission.

5. To examine the natural course of traumatic stress symptoms over a six-month period.

6. To investigate the impact of a critical illness admission on levels of anxiety and depression.

7. To investigate the impact of a critical illness admission on cognitive function and health related quality of life

8. To identify factors associated with impaired health related quality of life after critical illness admission.

9. To examine the natural course of depression, anxiety, health related quality of life, cognitive function and sense of coherence over a six-month period.

Chapter 5 - Methods

5.1 – Location of Study and Ethical Approval

The study took place within the critical care directorate, at the University Hospital of Wales, Cardiff. The critical care unit is a tertiary referral unit and comprises 27 beds. The South East Wales Local Research Ethic Committee granted ethical approval for the study.

5.2 – Identification of Subjects

All patients aged 18 years or older who were admitted to the critical care directorate for at least 24 hours between 1 March 2005 and 28 February 2006 were eligible for inclusion in the study.

5.3 – Exclusion criteria

Any patients who satisfied one or more of the exclusion criteria listed below were excluded from the study.

1. Absence of capacity to give consent.
2. Absence of ability to engage fully in the study due to communication difficulty.
3. Residing > 50 miles the from study center

5.4 – Procedure

5.4.1 – Recruitment and Consent

All admissions and discharges within the critical care directorate were monitored by members of the research team. A member of the research team visited the ward to which the patient had been admitted, three–five days following discharge from critical care. A member of the patient care team was approached and informed of the research study. They

were asked to confirm with the patient, that the patient agreed to be approached by a member of the research team. If the patient agreed to this, a member of the research team visited survivors of critical care who were eligible. If patients were thought capable of comprehending information, the study was explained and written information provided. Patients were given up to 24 hours to decide if they wanted to participate in the study and then after answering any questions they had regarding the study, written consent was obtained.

5.4.2 – Initial Assessment

After consent was obtained the patients' medical notes, prescription charts and investigations were reviewed. Either the research assistant or I visited patients seven–ten days after discharge from critical care and the standard questionnaires and a clinical interview were administered.

5.4.3 – Follow-up Assessments

At 1-month, 3-month and 6-months after critical care discharge, all individuals were contacted regarding follow-up interviews. Most follow-up interviews were conducted within the patients' home, a small minority took place within the Department of Psychological Medicine and either the research assistant or I conducted them. Both the research assistant and I had received training in the use of the clinical interview and all questionnaires.

5.4.4 - Clinical Measures

5.4.4.1- Clinician Administered Post traumatic Stress Disorder Scale (CAPS) (Blake et al 1995)

Posttraumatic psychological symptoms were assessed using the Clinician Administered PTSD scale for DSM-IV (CAPS), a 17 item structured interview that may be used as either a dichotomous measure of PTSD (present/absent) or as a continous score of PTSD symptom severity. It allows for quantification of the frequency and intensity of each of the 17 PTSD

symptoms on separate five point scales (0-4), which may be summed to give a nine point scale of symptom severity (0-8).
For the conversion of continuous scores, to obtain a present or absent symptom rating, the severity scores are dichotomised according to the empirically derived 1:2 rule (Blake et al 1990); that is a symptom is considered present if an item is rated with a frequency of 1 and an intensity of 2. The DSM-IV diagnostic algorithm is followed to obtain a diagnosis.

A further scoring rule was to be examined, using the empirically derived 1:2 rule at the item level, the DSM -IV diagnostic algorithm and a cut-off score of 65. This rule was originally proposed, to ensure a significant overall level of PTSD symptom severity and a distribution of symptoms corresponding to DSM-IV diagnostic criteria (Weathers et al 1999).

The CAPS has credible psychometric properties and is considered the gold standard for assessment of PTSD (Weathers et al 2001). It has strong test-retest reliability (range .90-.98), high internal consistency (.94) and good convergent validity with other measures (Bryant & Harvey 2000).

5.4.4.2- Davidson Trauma Scale (DTS) (Davidson et al 1997a)

For comparison of traumatic stress symptoms by self- report to those identified through a structured interview, participants completeted the Davidson Trauma Scale (DTS) (Davidson et al 1997). The DTS is a self-administered questionnaire that measures all 17 primary PTSD symptoms relating to the three main symptom areas with specific criteria for both frequency and intensity. For each item, the subject rates the frequency and intensity over the previous week, on separate five-point scales. The maximum total score is 136. A symptom is considered present if the frequency is one or higher and the intensity is two or higher.

Table 5.1 illustrates the DTS rating scale.

- **TABLE 5.1 - DTS RATING SCALE**

CRITERIA	SCALE 0	SCALE 1	SCALE 2	SCALE 3	SCALE 4
FREQUENCY	NOT AT ALL	ONCE ONLY	2 OR 3 TIMES	4-6 TIMES	EVERY DAY
INTENSITY	NOT AT ALL DISTRESSING	MINIMALLY DISTRESSING	MODERATELY DISTRESSING	MARKEDLY DISTRESSING	EXTREMELY DISTRESSING

At a cut-off score of 40, sensitivity and specificity of the DTS was 0.69 and 0.95, the positive predictive value was found to be 0.92, negative predictive value 0.79 and overall efficiency 0.83, compared to the SCID (Spitzer et al 1990) (Davidson et al 1995).

In addition to the cut off score of 40, three further rules were examined. A DSM-IV criterion only rule with no cut-off score, DSM-IV criteria and a cut-off score of 50 and DSM-IV criteria and a cut-off score of 60

5.4.4.3 – Startle, Physiological Arousal, Anger and Numbness (SPAN) (Meltzer-Brody et al 1999)

Participants were not asked to self-report on the SPAN questionnaire. Instead, the self-reported severity scores were taken from the DTS questionnaire. This method was used in the original derivation of the SPAN questionnaire by Meltzer et al (1999).The Span was derived from the DTS questionnaire and consists of four questions (Items 17, 14, 11 and 5 of the DTS). For each question the intensity of the symptom is rated on a five point scale (0 - 4). Total scores on the SPAN questionnaire are converted to dichotomous scores representing PTSD present or absent where a total score of five or more, as suggested by Meltzer et al (1999), is considered to provide a positive PTSD diagnosis.

At a cut-off score of five, the Span demonstrated an efficiency of .88, a sensitivity of .84 a specificity of .91 and a positive likelihood ratio of 9.1. It is said to have also correlated strongly with the Impact of Events Scale (Horowitz et al 1979), The Sheehan Disability Scale

(Sheehan 1983) and the Structured Interview of PTSD (Davidson et al 1997b) and with a diagnostic accuracy of .88 (Meltzer-Brody et al 1999).

5.4.4.4- The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith 1983)

Symptoms of Anxiety and Depression were measured using the HADS. The HADS was initially designed as an aid to clinicians for use within the general hospital outpatient setting (Zigmond & Snaith 1983). It is a self-administered questionnaire consisting of 14 items and separated into two subscales. Seven items concern anxiety and form the anxiety subscale and seven items concern depression and form the depression subscale. The depression and anxiety subscale scores are determined by adding the numbers in the D and A columns respectively. The subscales were initially established for use as a screening measure with a three-band score range (normal, possible, probable), but later experiences with HADS allowed for its use as a measure of severity of anxiety and depression (Snaith & Zigmond 1994). The four score ranges are now classified as, "normal", "mild", "moderate" and "severe". Cronbach's alpha for the anxiety scale was found to be 0.93 and 0.90 for the depression scale (Moorey et al 1991). The HADS questionnaire is contained in the Appendix along with the interpretation of HADS scores.

5.4.4.5 – The SF-12 Health Survey version 2 (Ware et al 2002)

Survival alone is now regarded as insufficient method of disease management and health related quality of life (HRQOL), a multi- multi-dimensional dynamic concept has developed from the need to estimate the psychosocial impact of diseases (Sajid et al 2008). Health related quality of life is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live, in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships and their relationships to salient features of the environment (WHO QOL-group, 1996).

To determine health- related quality of life, version 2 of the SF-12 Health Survey *(Ware et al 2002)* was used. The SF-12 v2 is a multi-purpose short form self-administered health survey

comprising of 12 questions from the longer SF-36 Health Survey. Questions are based upon the individuals' perception of physical functioning, physical role; bodily pain; general health; vitality; social functioning; emotional role and mental health over the previous four weeks. For each question, there is a five-choice response category.

In scoring of the questionnaire, four item values are reverse scored, all items are computed to obtain a raw scale score and these are transformed to a 0 - 100 scale. Linear t-score transformation is applied to the 0 - 100 scale scores to have a mean score of 50 and a Standard Deviation of 10 in the 1998 general US population. The items are aggregated into Physical Composite and Mental Composite Scores.

Regression methods were used to develop the original SF12 from the SF36 and the resulting Physical and Mental composite scores (PCS, MCS) of the SF12 achieved multiple R Square of 91% and 92% predictions of the SF36 PCS and MCS (Ware et al 1996). On comparing the performance of the SF12 with the SF36, the SF12 was found to be a responsive, valid and reliable measure of health status (Hurst et al 1998). The SF-12 v2 questionnaire is contained in the Appendix.

5.4.4.6 – The Sense of Coherence Questionnaire (SOCQ) (Antonovsky 1987)

Individuals with a high Sense of Coherence total score are likely to perceive stressors as predictable and explicable, have confidence in their capacity to overcome stressors and judge it worthwhile to rise to the challenges they face (Schnyder et al 2001). A low sense of coherence score has been found to correlate with early posttraumatic psychiatric symptoms, in survivors of a critical care admission (Schnyder et al 2000). A self-report questionnaire, the Sense of Coherence questionnaire (SOCQ), was used to determine the individuals' resilience to stress and his or her capacity to deal with it. The SOCQ consists of 29 items with answers based upon a 7-point scale. The scale scores are summed to give a total SOCQ score. The SOCQ has excellent test-retest reliability and internal consistency (Antonovsky 1993).The Sense of Coherence questionnaire is contained in the Appendix.

5.4.4.7 – Revised Addenbrooke's Cognitive Examination (ACE-R) (Mioishi et al 2006)

The ACE-R was used to determine cognitive function and was administered by the research assistant or myself. The Addenbrooke's Cognitive Examination (ACE) (Mathuranath et al 2000), was originally developed to provide a brief test, sensitive to the early stages of dementia and capable of differentiating subtypes of dementia including Alzheimer's disease, fronto-temporal dementia, progressive supra-nuclear palsy and other parkinsonian syndromes. It was revised following extensive clinical and research experience. The ACE-R consists of five sub-scores each one representing a cognitive domain (attention/orientation, memory, fluency, language and visuo-spatial). A validation study of the ACE-R showed very good reliability (alpha coefficient = 0.8), a significant correlation with the Clinical Dementia Scale ($r = -0.321$, $p < 0.001$) and the identification of two cut-offs scores (cut-off of 88: sensitivity = 0.94, specificity = 0.89; cut-off of 82: sensitivity = 0.84, specificity = 1.0) (Mioishi et al 2006). Advice was taken from the authors concerning the most appropriate scoring rule for critical care patients. The cut-off score recommended was 82. A copy of the questionnaire is contained in the appendix.

5.4.4.8 – General Information Questionnaire

A general information questionnaire was used to gather information regarding participant specific characteristics. This included comprehensive, critical care specific data, details of previous medical and psychiatric history, dimensions of the current trauma information and the individuals perception of it, details of any prior trauma,details of familial psychiatric history and other demographic and background information. This is contained in the appendix.

Chapter 6 – Statistical Methods

6.1 - Sample size

The differences in reported "prevalence" rates of PTSD and range of clinical measures used to identify the condition, in conjunction with the exploratory nature of the study suggested that a formal power calculation would prove difficult. A decision was made therefore to aim for a sample size of 150 although it was acknowledged that time limitations meant that recruitment would have to be stopped after one-year even if the target sample size had not been reached.

6.2 – Statistical package

All data collected were coded numerically and entered onto a database, created in the Statistical Package for the Social Services (SPSS version 12.0.1 for Windows). In order to ensure that statistical analysis of the data were appropriate, advice was taken prior to commencing the study and through ongoing supervision from Professor Newcombe, Professor of Statistics, for the duration of the analysis.

6.3 – Data analysis

The primary analysis was based on the main outcome variable (CAPS total score).

1. Cross tabulation with significance tests was used to determine sensitivity and specificity according to the DTS and the CAPS.

2. Cross tabulation with significance tests was used to determine sensitivity and specificity according to the SPAN and the CAPS.

3. Stepwise Linear Multiple Regression Analysis was performed to determine associations of patient characteristics with the main outcome variable (CAPS score).

4. Repeated Measures Analysis was carried out to examine the natural course of PTSD symptoms over time.

The secondary analyses included –

5. Stepwise Linear Multiple Regression Analyses were conducted to determine associations of patient characteristics with the Health related quality of life Measure (SF12).

6. Repeated Measures Analyses were conducted to examine the natural course of anxiety, depression, health related quality of life, cognitive function and sense of coherence over time.

6.3.1 – Sensitivity and specificity

The two scoring rules of the CAPS and the four of the DTS used in the analysis have been described in chapter five and will not be repeated here. The two CAPS scoring rules were compared to the four scoring rules of the DTS. The SPAN Questionnaire was compared to the two CAPS scoring rules. In order to compare the performances of the self-report measures (DTS, SPAN) to that of the main outcome measure (CAPS), continuous scores from the DTS, the SPAN and the CAPS, were converted to dichotomous values indicating the presence or absence of PTSD.
Table 6.1 illustrates the scoring rules and method of comparison. The dichotomous values were determined for all assessment times.

- **Table 6.1- Scoring Rules and Comparisons**

SELF-REPORT MEASURES	CAPS (DSM IV CRITERIA)	CAPS (DSM IV CRITERIA + CUT-OFF SCORE 65)
DTS (DSM IV CRITERIA)	*	*
DTS (DSM IV CRITERIA + CUT-OFF SCORE 40)	*	*
DTS (DSM IV CRITERIA + CUT-OFF SCORE 50)	*	*
DTS (DSM IV CRITERIA + CUT-OFF SCORE 60)	*	*
SPAN (CUT-OFF 5)	*	*

The presence or absence of PTSD at each assessment and according to the scoring rules of the DTS and the SPAN, were cross-tabulated with those of the CAPS scoring rules for the relevant assessment. The diagnostic descriptives were compared in two by two tables and sensitivity and specificity proportions were calculated according to Altman and Bland (1994). In order to determine if the DTS and the SPAN gave the correct diagnosis, positive and negative predictive values were calculated according to Altman and Bland (1994). In light of the relatively small sample, confidence intervals were calculated according to Wilson (1927), to express the possible range within which the true value would lie.

6.3.2 – Stepwise linear multiple regression

6.3.2.1 – PTSD

In order to determine if there were any associations for participant specific characteristics with the main outcome variable (CAPS), nine independent variables were selected for investigation, through Stepwise Linear Regression. Altman (1994) suggested the maximum size of the model should be decided in advance and the number of independent variables should be restricted to minimise the risk of chance findings. The maximum number of independent variables advocated, is the square root of the sample size, or the sample size divided by ten.

The nine independent variables selected for the model were critical care length of stay, therapeutic intervention scoring system at discharge, cognitive examination score, physical composite score, DTS total score, HADS depression score, perceived stress, gender and SOC total score. Factors operating during (Ozer et al 2003; Brewin et al 2000) or after the trauma (Brewin et al 2000) have been found to be the strongest predictors of PTSD and so critical care length of stay, therapeutic intervention Scale Score, perceived stress, depression, cognitive function, physical composite score, were selected as factors most closely resembling these. Gender was included in the model because of it's inconsistency as a risk factor in civilian samples (Brewin et al 2000). Sense of coherence was included because it represents prior psychological adjustment and low resilience in dealing with stress was found to be associated with early posttraumatic stress symptoms in a critical care population

(Schnyder et al 2000). The total score on the DTS was included in the model as it was important to examine if early self-reported symptoms would predict later PTSD. A variable was entered if the significance level of its F-to-enter was less than the entry value of 0.05 and removed if the significance was greater than the removal value of 0.1

6.3.2.2 – Health related quality of life

In order to determine if there were any association for participant specific characteristics with Health related quality of life, the SF12 was selected as the dependent variable and nine independent variables were selected for inclusion in the model, through Stepwise Linear Regression. The nine independent variables selected were, previous psychiatric history, CAPS total scores HADS anxiety and depression scores ACE-R total score, admission and discharge TISS, critical care length of stay and past medical history. The reasons for selecting these variables were based upon findings that psychiatric symptoms persist for longer than physical symptoms after critical care discharge and impaired health related quality of life was associated with persistently high PTSD scores(Déjà et al 2006). Neuro-cognitive sequelae following critical illness is a common, possibly permanent outcome, associated with impairments in daily function, decreased health related quality of life, and an inability to return to work (Hopkins and Jackson 2006). Illness severity and chronic ill health scores are associated with impaired health related quality of life in adult trauma survivors (Ulvik et al 2008). The stepwise criteria for entry and removal of variables were applied as previously described.

6.3.3 – One-way repeated measures ANOVA

6.3.3.1 – PTSD

A one-way repeated measures ANOVA was performed to examine the natural course of PTSD over time in survivors of critical care admission. Time was selected as the independent variable with four levels relating to the assessment sessions. The total scores on the CAPS (CAPSTS1, CAPSTS2, CAPSTS3, and CAPSTS4), were selected as the dependent variables. The natural course of symptoms as measured by the DTS, was similarly performed.

6.3.3.2 – Other outcomes

A one-way repeated measures ANOVA was performed, to examine the natural course of each outcome of anxiety, depression, health related quality of life, cognitive function and sense of coherence over time.

Time was selected as the independent variable with the same four levels of time and the total scores on the respective outcome assessments (anxiety, depression, ACE-R, mini mental state examination (MMSE), SOC, physical and mental composite scores) were selected as the dependent variables.

6.4 – Missing value analysis

6.4.1 - Study attrition

This was carried out to determine if dropout was related to baseline characteristics. All 90 participants had completed the initial assessment and all outcome measures. Dichotomous variables were set up based upon whether or not the subject was "scored" (0) or "not scored" (1) during the assessment session. Independent samples t-tests were conducted to compare baseline values of age, admission TISS, discharge TISS, critical care total stay, number of days ventilated and the outcome measures (CAPS, HADS depression, HADS anxiety, ACE-R, MMSE, SOC, SF12 composite scores) to those at the six-month assessment. Chi-square tests were conducted to examine gender, prior medical history, past psychiatric history and admission type.

6.4.2 -Generalisability to the larger study population

This was carried out to determine if those included in the study were representative of the wider population of ICU survivors. One-way between groups ANOVAs with planned comparisons were conducted to compare age, admission and discharge TISS, duration of ventilation and length of time spent on critical care between non-participants and participants. Cross tabulation with significance tests was used to examine gender differences.

6. 5 - Variable distributions and transformations

In order to improve the distributions of scores for parametric statistical analysis, a number of variables required modification through transformation. Histograms of

the relevant variables were inspected and transformations were conducted according to Pallant (2001; p79).Table 6.2 illustrates the variables and applied transformations.

- **Table 6.2 – Variable Descriptive and Transformations**

VARIABLE	DISTRIBUTION PRE-TRANSFORMATION	TRANSFORMATION	DISTRIBUTION POST-TRANSFORMATION
CRITICAL CARE TOTAL STAY	SKEW 2.9 KURTOSIS 10.4 SD 7.7	LOG 10	SKEW 0.9 KURTOSIS 0.2 SD 0.3
STRESS	SKEW -0.6 KURTOSIS -0.9 SD 3.1	REFLECT + SQRT	SKEW 0.2 KURTOSIS -1.3 SD 0.8
CAPS SCORE	SKEW 1.4 KURTOSIS 2.7 SD 16.9	SQRT	SKEW 0.2 KURTOSIS 0.4 SD 1.7
DTS SCORE	SKEW 1.5 KURTOSIS 2.3 SD 22.8	SQRT	SKEW 0.1 KURTOSIS 0.4 SD 2.2
ACE-R SCORE	SKEW -1.9 KURTOSIS 5.6 SD 7.3	REFLECT + LOG 10	SKEW -0.4 KURTOSIS 0.3 SD 0.3
SF12 – PCS	SKEW 0.6 KURTOSIS 0.1 SD 10.5	LOG 10	SKEW -0.4 KURTOSIS 0.2 SD 0.2
SF12 – MCS	SKEW -0.5 KURTOSIS -0.7 SD 12.3	REFLECT + LOG 10	SKEW 0.2 KURTOSIS 0.5 SD 0.1
HADS ANXIETY	SKEW 0.3 KURTOSIS -0.5 SD 4.5	SQRT	SKEW -0.8 KURTOSIS 0.1 SD 1.0
HADS DEPRESSION	SKEW 0.8 KURTOSIS 0.1 SD 4.2	SQRT	SKEW -0.2 KURTOSIS -0.1 SD 1.0

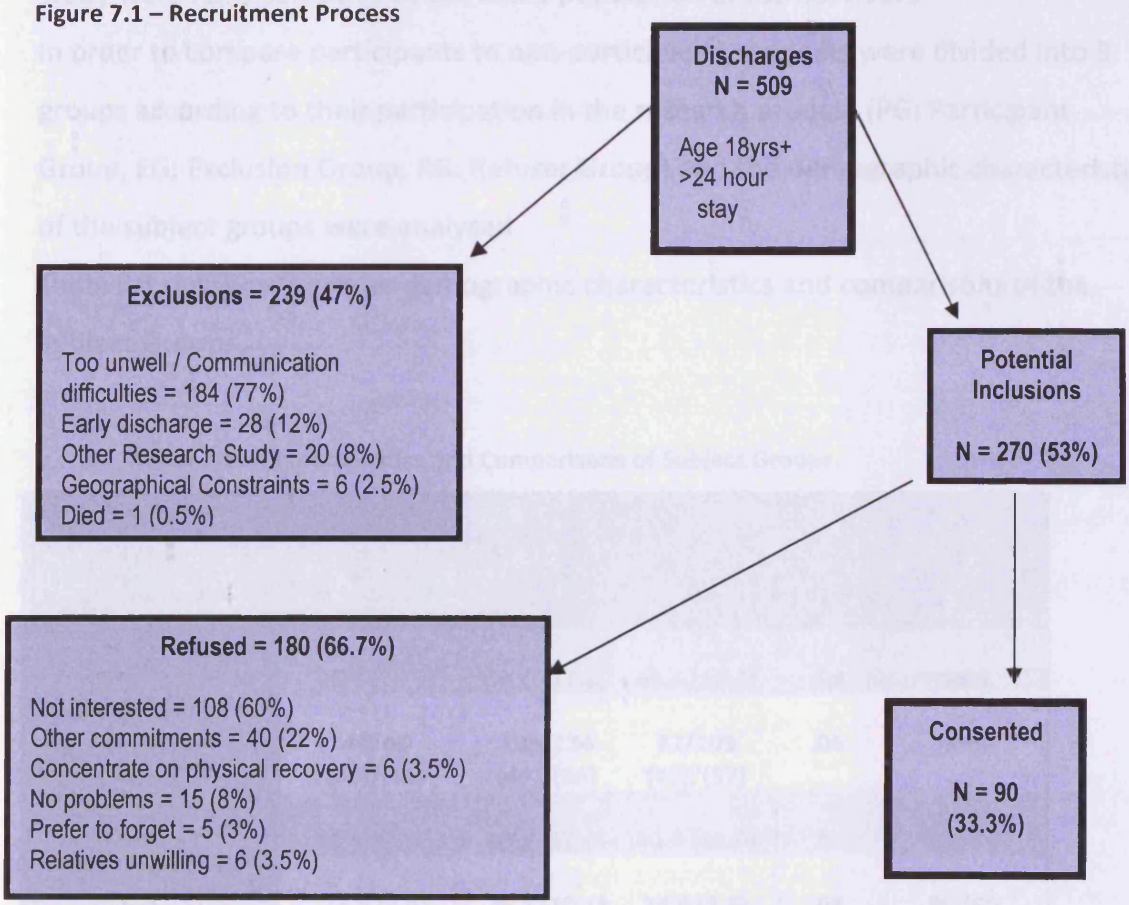
Chapter 7 – Results – Recruitment, Baseline Characteristics and Attrition

7.1 - Recruitment

The recruitment of subjects commenced at the beginning of March 2005 through to the end of February 2006. During this period, 509 consecutively discharged survivors from the critical care unit were eligible for inclusion in the Study.

Figure 8.1 illustrates the recruitment process and reasons for exclusion and refusal.

Figure 7.1 – Recruitment Process



At the initial follow-up visit, three days after critical care discharge, 239 (47%) of the patients were excluded. Of these, one hundred and eighty-four were either too

unwell or had communication difficulties due to the presence of a tracheostomy tube and were unable to participate in the informed consent process. Twenty-eight (12%) patients discharged prior to the recruitment visit did not return phone calls. Twenty (8%) patients were participating in a randomised control trial, six (2.5%) patients lived over 50 miles from the hospital and one (0.5%) patient had died prior to the recruitment visit. Of the remaining 270 (53%) eligible subjects, 180 (66.7%) did not want to participate. The remaining 90 (33.3%) patients consented to take part in the study and completed the initial assessment.

7.2- Population Characteristics and Comparisons

Brief descriptive data for excluded subjects and those who declined participation were obtained from the critical care database to determine if those included in the study were representative of the wider population of ICU survivors

In order to compare participants to non-participants, subjects were divided into 3 groups according to their participation in the research process (PG: Participant Group, EG: Exclusion Group, RG: Refuser Group) and the demographic characteristics of the subject groups were analysed.

Table 7.1 outlines the main demographic characteristics and comparisons of the Subject Groups.

- **Table 7.1 – Characteristics and Comparisons of Subject Groups.**

VARIABLE	PARTICIPANTS (PG)	EXCLUDED (EG)	REFUSED (RG)	P value	GROUP DIFFERENCE
AGE YEARS M (SD)	55.0 (15.1)	58.8 (17.2)	60.1 (16.2)	.69	none
GENDER F/M N (%)	44/46 (49)/(51)	105/134 (44)/(56)	77/103 (43)/(57)	.06	none
ADMISSION TISS M (SD)	44.6 (13.1)	43.5 (13.4)	40.0 (11.9)	.01	RG/EG RG/PG
DISCHARGE TISS (M (SD)	23.6 (8.8)	26.7 (10.1)	24.4 (8.5)	.03	PG/EG
CRITICAL CARE DAYS M (SD)	7.2 (7.7)	8.6 (10.6)	6.4 (7.8)	.05	RG/EG
DAYS VENTILATED M (SD)	3.6 (5.3)	5.4 (9.5)	3.1 (7.2)	.01	RG/EG

There were no significant differences at the p<.05 level for gender (χ^2 = .754 (df 2) p = .69) and no differences at the p<.05 level in mean age (F (df 2) = 2.8, p =.06) between subject groups.

There was a statistically significant difference at the p <.05 level in admission TISS for the three groups (F (2,382) = 4.567, p =.01). Post hoc comparisons using the Tukey HSD test indicated that the mean admission TISS for subjects in the RG (40.0, SD 11.9) was significantly lower that of the EG (43.5, SD13.4) and to that of the PG (44.6, SD13.1).

At the time of discharge from critical care there was a statistically significant difference in discharge TISS between the groups (F (2,380) = 3.6, p = .03). Post hoc comparisons using the Tukey HSD test indicated that the mean discharge TISS for subjects in the PG (23.6, SD 8.8) was significantly lower than that of the EG (26.7, SD 10.1). The RG (24.4 SD 8.5) did not differ significantly from either the PG or the EG.

The duration of stay within the critical care unit was significantly different between the groups (F (2, 384) = 3.10, p = .05). Post hoc comparisons using the Tukey HSD test indicated that the mean length of stay within critical care for the RG (6, 4, SD 7.8) was significantly less than the EG (8.6, SD 10.5). The PG (7.2, SD7.7) did not differ significantly from either the RG or the EG.

The number of days ventilated differed significantly between the groups (F (2.384) = 5.46 p = .01). Post hoc comparisons using the Tukey HSD test indicated that the mean number of days ventilated for the RG (M =3.1, SD7.2) was significantly less than the EG (M =5.3, SD9.5). The PG (M =3.6, SD5.3) did not differ significantly from either the RG or the EG.

7.3 – Recruited subjects

All subjects (90) who consented to participation completed the initial baseline assessment. The main characteristics of participants were collected from the Critical Care Database and through interview at the initial assessment.

Tables 7.2 – 7.4 describe the participant characteristics.

- Table 7.2 Continuous Background and Trauma-related Variables

VARIABLE	N =	MIN	MAX	MEAN	S/D
AGE	90	19	83	55.0	15.1
ADMISSION TISS	84	15	79	44.6	13.1
DISCHARGE TISS	83	6	47	23.6	8.8
CRITICAL CARE DAYS	86	2	48	7.2	7.7
DAYS OF VENTILATION	86	0	28	3.6	5.4
HOW STRESSFUL	90	0	10	6.6	3.1
MMSE	90	21	30	29.0	1.7
ACE-R	90	56	100	91.3	7.3
CAPS	90	0	86	24.6	16.9
DTS	90	0	99	26.7	22.8
SPAN	90	0	15	1.9	3.0
HADS ANXIETY	90	0	17	6.5	4.3
HADS DEPRESSION	90	0	21	7.2	4.8
SF12-PCS	90	10	57.4	28.7	10.5
SF12-MCS	90	19.0	66.3	45.7	12.3

- Table 7.3 – Other participant specific characteristics

VARIABLE	NUMBER	%
GENDER – F/M	44 / 46	49 / 51
PAST MEDICAL HISTORY – Y/N	75/15	83 / 17
PAST PSYCHIATRIC HISTORY – Y/N	24/66	27 / 73
LIVES WITH SOMEONE / LIVES ALONE	67/23	74 / 26
ELECTIVE / EMERGENCY ADMISSION	23/67	26 / 74
MEDICINE / SURGERY	31/59	34 / 66
PERCEPTION OF DEATH THREAT - Y/N	27/63	30 / 70
EXPERIENCE OF PAST TRAUMA – Y/N	51/39	57/ 43
FAMILY PSYCHIATRIC HISTORY – Y / N / NK	27/47/16	30 / 52 / 18

- **Table 7.4 – Description of Trauma**

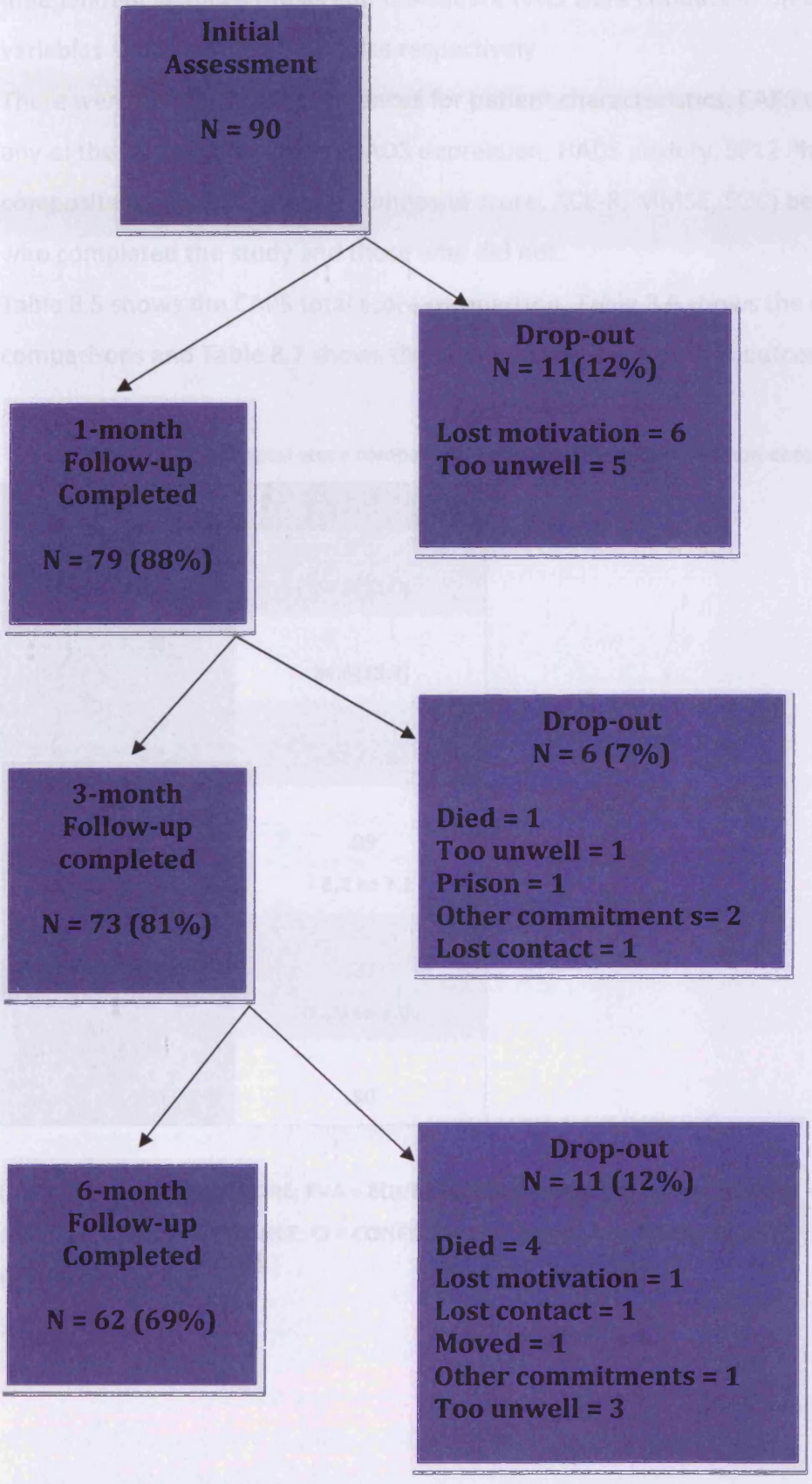
Trauma ID	N / %
DELUSIONAL TRAUMA	19 / 21%
VICARIOUS TRAUMA	22 / 24%
ACTUAL EVENT	16 / 18%
CRITICAL CARE EXPERIENCE	25 / 28%
NON-TRAUMATIC	5 / 6%
REMOVAL OF DRAINS	1 / 1%
INSERTION OF EPIDURAL	1 / 1%
DEBILITATION AFTER CRITICAL CARE	1 / 1%

7.3.1 – Assessment and Attrition

All 90 (100%) participants completed the initial assessment, 2 weeks after discharge from critical care. Follow-up assessment rates were 79 (88%) patients at one-month, 73 (81%) patients at three-months and 62 (69%) patients at 6-months.
At the one-month follow-up, six (7%) patients were no longer interested in taking part and five (5.5%) patients had become too unwell to continue. At the three-month follow-up, one patient (1%) had died and a further five (5.5%) were withdrawn, due to a deterioration in physical condition (one patient), unreturned phone calls (one patient), imprisonment (one patient) and other commitments (two patients). At the six-month follow-up, four (4%) patients had died and a further 7 (8%) patients were lost due to loss of motivation (one patient), unreturned phone calls (one patient), moved out of the area (one patient), other commitments (one patient) and physical illness progression (three patients).

Figure 7.2 illustrates the progression of the research study.

- **Figure 7.2 - Research Study Progression**



7.3.2 - Comparison of completers and non-completers

Independent samples t-tests and Chi-square tests were conducted on continuous variables and categorical variables respectively.

There were no significant differences for patient characteristics, CAPS total score or any of the outcome variables (HADS depression, HADS anxiety, SF12 Physical composite score, SF12 Mental composite score, ACE-R, MMSE, SOC) between those who completed the study and those who did not.

Table 8.5 shows the CAPS total score comparison, Table 8.6 shows the demographic comparisons and Table 8.7 shows the comparisons for the other outcome variables.

- **Table 7.5 - CAPS total score comparison between completers and non-completers**

	CAPS TS
NON-COMPLETERS	
M(SD)	24.3(12.0)
COMPLETERS	
M(SD)	24.8(18.7)
MEAN DIFFERENCES	
EVA/EVNA	-.52 / -.52
SIG. EVA	.89
CI	- 8.2 to 7.2
SIG. EVNA	.87
CI	-7.06 to 6.01
MANN WHITNEY U SIG	.50

(CAPS TS = CAPS TOTAL SCORE; EVA = EQUAL VARIANCE ASSUMED; EVNA = EQUAL VARIANCES NOT ASSUMED; SIG = SIGNIFICANCE; CI = CONFIDENCE INTERVAL; M = MEAN; SD = STANDARD DEVIATION)

- Table 7.6 – Demographic Comparison between completers and non-completers

VARIABLE	COMPLETER	NON-COMPLETER	MD	p =	95% CI
AGE M (SD)	56.0 (15.0)	52.9 (15.5)	-3.1	.4	-9.9 to 3.8
ADTISS M (SD)	44.0 (12.7)	45.9 (14.1)	1.9	.5	-4.2 to 8.0
DISTISS M (SD)	23.6 (8.2)	23.7 (10.1)	.1	1.0	-4.0 to 4.2
CCTS M (SD)	7.3 (7.9)	7.1 (7.4)	.1	1.0	-3.6 to 3.5
VENTD M (SD)	3.6 (5.4)	3.7 (5.4)	.1	.9	-2.4 to 2.6
GENDER M/F (%)	30/32 (33%/36%)	16/12 (18%/13%)	-	.6	-
PMH yes/no (%)	55/7 (61%/8%)	20/8 (22%/9%)	-	.1	-
PPH yes/no (%)	17/45 (19%/50%)	7/21 (8%/23%)	-	1.0	-
ELAD/EMAD (%)	15/47 (17%/52%)	8/20 (9%/22%)	-	.9	-

(MEAN DIFF= mean difference; M = mean; SD = standard deviation; ADTISS = admission TISS; DISTISS = discharge TISS; CCTS = critical care total stay; VENTD = days ventilated; M/F = male/female; PMH = Past Medical History; PPH = Past Psychiatric History; ELAD - Elective Admission; EMAD = Emergency Admission; CI = Confidence Interval)

- **Table 7.7 - Other outcomes total score comparisons between completers and non-completers**

ASSESSMENT OUTCOME	MEAN DIFF	95% CI	SIG
HADS DEPRESSION	.45	-1.7 to 2.6	.68
HADS ANXIETY	-1.14	-3.06 to.79	.24
SF12 PCS	-2.84	-7.57 to 1.90	.24
SF12 MCS	4.14	-1.37 to 9.65	.14
ACE-R	-.78	-4.11 to 2.55	.64
MMSE	.03	-.74 to .81	.93
SOC	5.11	-10.57 to 20.79	.52

Chapter 8 - Results – PTSD Assessment Outcomes.

8.1 – PTSD outcome measure scores

The mean total scores for the follow-up assessments, according to the CAPS, DTS and SPAN are shown in Table 8.1

	2 WEEKS	1 MONTH	3 MONTHS	6 MONTHS
CAPS SCORE M(SD)	24.6 (16.9)	19.1 (14.8)	16.7 (17.1)	14.4 (15.1)
DTS SCORE M(SD)	26.7 (22.8)	19.7 (19.3)	18.2 (23.1)	14.6 (19.1)
SPAN SCORE M(SD)	1.9 (3.0)	1.3 (2.1)	1.7 (3.1)	1.3 (2.3)

- **Table 8.1 - Assessment Outcome scores by Follow-up**

8.2 - Proportion of PTSD according to the CAPS.

The rates of PTSD according to the CAPS lenient and the CAPS stringent at the relevant follow-up assessments are shown in Tables 8.2 and 8.3.

Table 8.2 – PTSD Rates according to a CAPS Lenient Scoring Rule

ASSESSMENT TIME	N	PTSD PRESENT N (%)	PTSD ABSENT N (%)
2 WEEKS	90	9 (10%)	81 (90%)
1-MONTH	79	9 (11%)	70 (89%)
3-MONTHS	73	4 (5.5%)	69 (94.5%)
6-MONTHS	62	4 (6.5%)	58 (93.5%)

- **Table 8.3 – PTSD Rates according to a CAPS Stringent Scoring Rule**

ASSESSMENT TIME	N	PTSD PRESENT N (%)	PTSD ABSENT N (%)
2 WEEKS	90	3 (3%)	87 (97%)
1-MONTH	79	1 (1%)	78 (99%)
3-MONTHS	73	2 (3%)	71 (97%)
6-MONTHS	62	1 (2%)	61 (98%)

According to the CAPS lenient scoring rule, nine subjects were found to have early PTSD symptoms two-weeks after critical care discharge, some symptoms resolved for two participants by the one-month assessment. Two participants, who did not have early PTSD symptoms at two-weeks, were found to have PTSD at the one-month follow-up.

The addition of the cut-off score of 65 (stringent rule) resulted in a lower rate of PTSD, compared to that of having no cut-off (lenient rule). After the one-month assessment, the number of subjects with PTSD declined for both the lenient and the stringent CAPS scoring rules.

8.3 – Proportion of PTSD according to the DTS.

The rates of PTSD at each assessment and according to the respective scoring rule are shown in Tables 8.4 and 8.5

- **Table 8.4 – PTSD Rates according to DTS scores and DSM IV Criteria**

ASSESSMENT TIME	N	PTSD PRESENT N (%)	PTSD ABSENT N (%)
2 WEEKS	90	14 (16%)	76 (84%)
1-MONTH	77	6 (8%)	71 (92%)
3-MONTHS	73	7 (10%)	66 (90%)
6-MONTHS	61	2 (3%)	59 (97%)

- **Table 8.5 – PTSD Rates according to DTS (DSM IV Criteria / Total Severity Score > 40)**

ASSESSMENT TIME	N	PTSD PRESENT N (%)	PTSD ABSENT N (%)
2 WEEKS	90	12 (13%)	78 (87%)
1-MONTH	77	6 (8%)	71 (92%)
3-MONTHS	73	7 (10%)	66 (90%)
6-MONTHS	61	2 (3%)	59 (97%)

Despite the addition of a cut-off score of 40, the number of patients who had PTSD at one-month, three-months and six-months were the same as those fulfilling PTSD DSM IV symptom criteria only. At the 2-week assessment, more patients were found to have PTSD, when the DSM IV symptom criteria only, were used.

8.4 – Proportion of PTSD according to the SPAN.

The SPAN determined PTSD rates at each assessment, are shown in Table 8.6

- **Table 8.6 - Rates of PTSD according to SPAN Questionnaire**

ASSESSMENT TIME	N	PTSD PRESENT N (%)	PTSD ABSENT N (%)
2 WEEKS	90	13 (14%)	77 (86%)
1-MONTH	77	6 (8%)	71 (92%)
3-MONTHS	73	11 (15%)	62 (85%)
6-MONTHS	61	6 (10%)	55(90%)

The number of subjects with PTSD according to the SPAN questionnaire fluctuated somewhat over the study period. Although the number of subjects with PTSD at the one-month assessment had reduced by 46% compared to the two-week assessment, at three-months PTSD had increased by 55% and then at the six-month assessment showed a 55% reduction.

8.5 - PTSD over time

8.5.1 - CAPS scores over time

Ninety (100%) participants completed the initial assessment, two-weeks after critical care discharge. At one-month seventy-nine (88%) participants, at three-month seventy-three (81%) participants and at six-months sixty-two (69%) participants completed the CAPS. The CAPS total scores over time are shown in Table 8.7

OUTCOME MEASURE	NUMBER OF PARTICIPANTS	MIN SCORE	MAX SCORE	MEAN SCORE	STANDARD DEVIATION
CAPS TS time 1	90	0	86	24.61	16.86
CAPS TS time 2	79	0	92	19.06	14.85
CAPS TS time 3	73	0	95	16.73	17.14
CAPS TS time 4	62	0	96	14.40	15.05

- **Table 8.7 – CAPS total scores over time**

There was considerable variation in CAPS total scores at all time points. Although there was a slight increase in the maximum CAPS total score over time, the mean CAPS total scores reduced over the six-month period.

In order to compare scores on the CAPS at time 1, time 2, time 3 and time 4 and examine the effect for differences over time, a one-way repeated measures ANOVA was conducted on $CAPS^{sqrt}$ scores.

There was a statistically significant reduction in $CAPS^{sqrt}$ scores over time -Wilks' Lambda = 0.59, F (3, 59) = 13.86, p = .000, multivariate partial eta squared = 0.413

8.5.2 - DTS scores over time

All participants (100%) completed the initial DTS questionnaire at the two-week assessment. At the one-month assessment seventy-seven (86%) completed the questionnaire, at three-

months seventy-three (81%) and at the six-month assessment sixty-one (68%) participants completed the DTS. Table 8.8 shows the total DTS scores over time.

OUTCOME MEASURE	NUMBER OF PARTICIPANTS	MIN SCORE	MAX SCORE	MEAN SCORE	STANDARD DEVIATION
DTS TS time 1	90	0	99	26.66	22.82
DTS TS time 2	77	0	88	19.73	19.26
DTS TS time 3	73	0	112	18.18	23.13
DTS TS time 4	61	0	86	14.56	19.11

- **Table 8.8 – DTS total scores over time**

There was a fluctuation in the maximum DTS total scores over the course of the study period, but the mean DTS total score showed a gradual reduction over the six-month study period. In order to compare scores on the DTS at Time 1, Time 2, Time 3 and Time 4 and examine the effect for differences over time, one-way repeated measures ANOVA was conducted on DTS^{sqrt} scores.

There was a statistically significant reduction in DTS total scores^{sqrt} over time - Wilks' Lambda = 0.60, F (3, 57) =12.48, p = 0.000, multivariate partial eta squared = 0.40.

Chapter 9 – Results – Comparison of Assessment Measures

9.1 – Comparison of questionnaire performance with CAPS

Two-way cross tabulation procedures were performed to examine the proportion of PTSD according to the CAPS, the DTS and the SPAN. The efficiency of the DTS and the SPAN in confirming a diagnosis of PTSD at each assessment was measured in terms of sensitivity and specificity. Positive (PPV) and Negative predictive values (NPV) were also calculated. Confidence Intervals for single proportions were determined for sensitivity and specificity, according to Wilson (1927). Analysis was based upon the number of completed DTS questionnaires, as two patients at one-month and one patient at six-months, failed to complete the questionnaire.

9.1.2 – DTS performance compared to CAPS lenient scoring rule

Tables 9.1 – 9.4 illustrate the performance of all four scoring rules of the DTS at each assessment time compared to the CAPS lenient scoring rule (DSM IV Criteria).

- **Table 9.1 -TWO- WEEK ASSESSMENT - DTS Performance compared to CAPS Lenient Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	90	16%	77% (45% to 94%)	91% (83% to 95%)	50% (27%-73%)	97% (91%-99%)
RULE 2	90	13%	66% (35% to 88%)	92% (85% to 96%)	50% (25%-75%)	96% (89%-99%)
RULE 3	90	12%	66% (35% to 88%)	93% (86% to 97%)	55% (28%-79%)	96% (89%-99%)
RULE 4	90	9%	55% (27% to 81%)	96% (90% to 99%)	63% (31%-86%)	95% (88%-98%)

- **Table 9.2 -ONE-MONTH ASSESSMENT - DTS Performance compared to CAPS Lenient Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	77	8%	57% (25% - 84%)	97% (90%-99%)	67% (30%-90%)	96% (88%-99%)
RULE 2	77	8%	57% (25% -84%)	97% (90% -99%)	67% (30%-90%)	96% (88%-99%)
RULE 3	77	7%	57% (25%-84%)	98% (92%-99%)	80% (38%-96%)	96% (88%-99%)
RULE 4	77	5%	42% (16%-75%)	98% (92% -100%)	75% (30%-95%)	95% (87%-98%)

- **Table 9.3 -THREE-MONTH ASSESSMENT - DTS Performance compared to CAPS Lenient Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	73	10%	100% (51%-100%)	95% (88%- 98%)	57% (25%-84%)	100% (95%-100%)
RULE 2	73	10%	100% (51%-100%)	95% (88% -98%)	57% (25%-84%)	100% (95%-100%)
RULE 3	73	8%	100% (30% -95%)	97% (90% -99%)	67% (30%-90%)	100% (95%-100%)
RULE 4	73	8%	100% (30% - 95%)	97% (90% -99%)	67% (30%-90%)	100% (95%-100%)

- **Table 9.4 -SIX-MONTH ASSESSMENT - DTS Performance compared to CAPS Lenient Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	61	3%	25% (5% -70%)	98% (91%-100%)	50% (9%-91%)	95% (86%-98%)
RULE 2	61	3%	25% (5%-70%)	98% (91%-100%)	50% (9%-91%)	95% (86%-98%)
RULE 3	61	3%	25% (5% -70%)	98% (91%-100%)	50% (9%-91%)	95% (86%-98%)
RULE 4	61	2%	25% (5% -70%)	100% (94%-100%)	100% (21%-100%)	95% (86%-98%)

The sensitivity of the DTS in detecting PTSD compared to the CAPS varied greatly from 25% for all DTS rules at 6-months, to 100% for all DTS rules at 3-months. Confidence intervals calculated were wide for all rules and assessment time points. Specificity was more consistent with a range of .91 to 1.0 and with narrower confidence intervals. Negative

predictive value ranged from .94 to 1.0, but the positive predictive value varied from .50 to 1.0.

9.1.3 – DTS performance compared to CAPS stringent scoring rule

Tables 9.5 – 9.8 illustrate the performance of all scoring rules of the DTS at each assessment time compared with the CAPS stringent scoring rule.

- **Table 9.5 TWO-WEEK ASSESSMENT - DTS Performance compared to CAPS Stringent Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	90	16%	100% (44%-100%)	87% (79%- 93%)	21% (8%-48%)	100% (95%-100%)
RULE 2	90	13%	100% (44% -100%)	89% (81%-94%)	25% (9%-53%)	100% (95%-100%)
RULE 3	90	12%	100% (44%-100%)	90% (83%-95%)	27% (10%-57%)	100% (95%-100%)
RULE 4	90	9%	100% (44%-100%)	94% (87%-97%)	38% (14%-69%)	100% (96%-100%)

- **Table 9.6 ONE-MONTH ASSESSMENT - DTS Performance compared to CAPS Stringent Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	77	8%	100% (21%-100%)	93% (85%-97%)	17% (3%-56%)	100% (95%-100%)
RULE 2	77	8%	100% (21%-100%)	93% (85%-97%)	17% (3%-56%)	100% (95%-100%)
RULE 3	77	7%	100% (21%-100%)	94% (87%-98%)	20% (4%-62%)	100% (95%-100%)
RULE 4	77	5%	100% (21%-100%)	96% (89%-99%)	25% (5%-70%)	100% (95%-100%)

- **Table 9.7 – THREE-MONTH ASSESSMENT - DTS Performance compared to CAPS Stringent Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	73	10%	100% (34%-100%)	92% (84%-97%)	29% (8%-64%)	100% (95%-100%)
RULE 2	73	10%	100% (34%-100%)	92% (84%-97%)	29% (8%-64%)	100% (95%-100%)
RULE 3	73	8%	100% (34%-100%)	94% (88%-98%)	33% (10%-70%)	100% (95%-100%)
RULE 4	73	8%	100% (34%-100%)	94% (88%-98%)	33% (10%-79%)	100% (95%-100%)

- **Table 9.8 – SIX-MONTH ASSESSMENT - DTS Performance compared to CAPS Stringent Rule**

DTS SCORING RULE	Number	DTS PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
RULE 1	61	3%	100% (21%-100%)	98% (91%-100%)	50% (9%-91%)	100% (94%-100%)
RULE 2	61	3%	100% (21%-100%)	98% (91%-100%)	50% (9%-91%)	100% (94%-100%)
RULE 3	61	3%	100% (21%-100%)	98% (91-100%)	50% (9%-91%)	100% (94%-100%)
RULE 4	61	2%	100% (21%-100%)	100% (94%-100%)	100% (21%-100%)	100% (93%-100%)

Despite a consistent sensitivity of 100% for all scoring rules at all assessment times, confidence intervals were wide. Specificity varied slightly from .87 to 1.0 but with narrow confidence intervals. Negative predictive value was consistent at 1.0 throughout, but the positive predictive value varied considerably with a range of 0.16 to 1.0.

9.1.4 - SPAN performance compared to CAPS

Tables 9.9 and 9.10 illustrate the performance of the SPAN using a cut-off of five, at each assessment time compared with the CAPS lenient scoring rule and stringent scoring rule respectively.

- **Table 9.9 – SPAN Performance compared to CAPS Lenient Scoring Rule**

SPAN ASSESSMENT	Number	SPAN PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
2-WEEKS	90	14%	44% (18%-73%)	89% (80%-94%)	31% (13%-58%)	94% (86%-97%)
1-MONTH	73	8%	29% (8%-64%)	94% (86%-98%)	33% (10%-70%)	93% (85%-97%)
3-MONTH	77	15%	100% (51%-100%)	90% (81%-95%)	36% (15%-65%)	100% (94%-100%)
6-MONTH	61	10%	25% (5%-33%)	91% (81%-96%	17% (3%-56%)	95% (85%-98%)

The sensitivity of the SPAN in detecting PTSD symptoms compared to a CAPS lenient rule varied considerably from 25% at the six-month assessment to 100% at the three-month assessment and with wide confidence intervals throughout. In terms of specificity, there was much less variation and narrower confidence intervals. The NPV of the SPAN was consistently high at all assessments, but PPV was very low throughout.

- **Table 9.10 – SPAN Performance compared to CAPS Stringent Scoring Rule**

SPAN ASSESSMENT	Number	SPAN PTSD	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
2-WEEKS	90	14%	67% (21%-94%)	87% (79%-93%)	15% (4%-42%)	99% (93%-98%)
1-MONTH	73	8%	100% (21%-100%)	93% (86%-97%)	17% (3%-56%)	100% (95%-100%)
3-MONTH	77	15%	100% (34%-100%)	87% (78%-93%)	18% (5%-48%)	100% (94%-100%)
6-MONTH	61	10%	100% (20%-100%)	92% (82%-96%)	17% (3%-56%)	100% (93%-100%)

The sensitivity of the SPAN in detecting PTSD compared to a CAPS stringent rule was lowest at the two-week assessment and consistently high for all others. The confidence intervals however were very wide for all assessment times. Specificity varied very little and confidence intervals were much narrower for all assessments. Although the NPV of the SPAN showed consistently high values, the PPV was very low at all time points.

9.2 - Calculated differences in PTSD proportions

In order to identify any significant differences between the numbers of subjects who had PTSD according to the CAPS rules, to those who had PTSD according to the DTS rules and to that of the SPAN, the proportion of PTSD for the paired differences were calculated according to Newcombe (1998).

9.2.1 - Calculated differences between CAPS lenient scoring rule and DTS rules

Two-way crosstabs' procedures were conducted to examine the rate of PTSD according to a CAPS lenient scoring rule to those according to the DTS Rules and the mean differences and 95% Confidence Intervals between them were calculated. Tables 9.11 to 9.14 show the results of these.

- **Table 9.11 - DTS Rule 1 compared to CAPS Lenient Rule**

ASSESSMENT TIME	CAPS PTSD Number (%)	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	9 (10%)	14 (16%)	6%	-1% to 13%
1-MONTH	7 (9%)	6 (8%)	-1%	-9% to 6%
3-MONTH	4(6%)	7 (10%)	4%	-2% to 11%
6-MONTH	4 (7%)	2 (3%)	-3%	-12% to 5%

- **Table 9.12 – DTS Rule 2 compared to CAPS Lenient Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	9 (10%)	12 (13%)	3%	-4% to 11%
1-MONTH	7 (9%)	6 (8%)	-1%	-9% to 6%
3-MONTH	4 (6%)	7 (10%)	4%	-2% to 11%
6-MONTH	4 (7%)	2 (3%)	-3%	-12% to 5%

- **Table 9.13 – DTS Rule 3 compared to CAPS Lenient Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	9 (10%)	11 (12%)	2%	-5% to 9%
1-MONTH	7 (9%)	5 (7%)	-3%	-10% to 4%
3-MONTH	4 (6%)	6 (8%)	3%	-3% to 9%
6-MONTH	4 (7%)	2 (3%)	-3%	-12% to 5%

- **Table 9.14 – DTS Rule 4 compared to CAPS Lenient Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	9 (10%)	8 (9%)	-1%	-8% to 6%
1-MONTH	7 (9%)	4 (5%)	-4%	-12% to 3%
3-MONTH	4 (6%)	6 (8%)	3%	-3% to 9%
6-MONTH	4 (7%)	1 (2%)	-5%	-14% to 2%

Although the number of subjects who had PTSD according to a CAPS lenient rule differed to those who had PTSD according to all DTS Rules at all time points, none of the differences reached statistical significance.

9.2.2 - Calculated differences between CAPS stringent scoring rule and DTS rules

Two-way crosstabs' procedures were conducted to examine the rate of PTSD according to a CAPS stringent scoring rule to those according to the DTS rules and the mean differences and 95% confidence intervals between them were calculated. These are shown in Tables 9.15 to 9.18

- **Table 9.15 – DTS Rule 1 compared to CAPS Stringent Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	3 (3%)	14 (16%)	12%	5% to 21%*
1-MONTH	1(1%)	6 (8%)	6%	0% to 15%*
3-MONTH	2 (3%)	7 (10%)	7%	0% to 15%*
6-MONTH	1 (2%)	2 (3%)	2%	-5% to 9%

- **Table 9.16 – DTS Rule 2 compared to CAPS Stringent Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	3 (3%)	12 (13%)	10%	4% to 18%*
1-MONTH	1 (1%)	6 (8%)	6%	0% to 15%*
3-MONTH	2 (3%)	7 (10%)	7%	0% to 15%*
6-MONTH	1 (2%)	2 (3%)	2%	-5% to 9%

- **Table 9.17 – DTS Rule 3 compared to CAPS Stringent Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	3 (3%)	11 (12%)	9%	3% to 17%*
1-MONTH	1 (1%)	5 (7%)	5%	-1% to 13%
3-MONTH	2 (3%)	6 (8%)	5%	-1% to 13%
6-MONTH	1 (2%)	2 (3%)	2%	-5% to 9%

- **Table 9.18 – DTS Rule 4 compared to CAPS Stringent Rule**

ASSESSMENT TIME	CAPS PTSD Number	DTS PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	3 (3%)	8 (9%)	6%	0% to 12%*
1-MONTH	1 (1%)	4 (5%)	4%	-2% to 11%
3-MONTH	2 (3%)	6 (8%)	5%	-1% to 13%
6-MONTH	1 (2%)	1 (2%)	0%	-7% to 7%

There were statistically significant differences between a CAPS stringent scoring rule and Rule 1 of the DTS at two-weeks, one-month and three-months, but not at six-months. Statistically significant differences were found at the same time for DTS rule 2. At a total score cut-off of 50 (rule 3) and of 60 (rule 4) on the DTS, there were significant differences for the two-week assessments only but not for the one-month, three-months or six-month assessments.

9.2.3 - Calculated differences between CAPS and the SPAN

Two-way crosstabs' procedures were conducted to examine the rate of PTSD according to the CAPS scoring rules and the rate according to the SPAN questionnaire using a cut-off of five. The mean differences and 95% confidence intervals between the two were calculated and are shown in Tables 9.19 and 9.20

- **Table 9.19 – SPAN Questionnaire compared to CAPS Lenient Scoring Rule**

ASSESSMENT TIME	CAPS PTSD Number	SPAN PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	9 (10%)	13 (14%)	4%	-4% to 13%
1-MONTH	7 (9%)	6 (8%)	-1%	-10% to 7%
3-MONTH	4 (6%)	11 (15%)	10%	2% to 18%*
6-MONTH	4 (7%)	6 (10%)	3%	-7% to 14%

The number of subjects who had PTSD according to a CAPS lenient scoring rule was only statistically significantly different to that of the SPAN questionnaire at the three-month assessment.

- **Table 9.20 – SPAN Questionnaire compared to CAPS Stringent Scoring Rule**

ASSESSMENT TIME	CAPS PTSD Number	SPAN PTSD Number	MEAN DIFFERENCE	95% CI
2 WEEKS	3(3%)	13 (14%)	11%	4% to 20%*
1-MONTH	1(1%)	6 (8%)	6%	0% to 15%*
3-MONTH	2 (3%)	11(15%)	12%	4% to 22%*
6-MONTH	1(2%)	6 (10%)	8%	0% to 18%*

The number of subjects who had PTSD according to a CAPS stringent scoring rule was significantly different at the two-week and three-month assessment, and just significant at the one-month and six-month assessment.

Chapter 10 – Results – Predictors of PTSD

10.1 – Linear regression analysis of participants' data – initial assessment

The independent variables selected were four participant specific characteristics:- discharge TISS, critical care total stay, gender and perceived stress score; and subject data from the initial assessment at two weeks:- cognitive examination score, physical composite score, DTS score, HADS depression score and SOC score. Stepwise linear regression analyses were performed with the nine independent variables, listed in Table 11.1 and the $CAPS^{sqrt}$ total scores as the dependant variables, using the method described in Chapter 5.

- **Table 10.1 – Independent Variables entered in the forward stepwise linear regression analyses**

PRE-TRAUMATIC FACTORS	**GENDER, SENSE OF COHERENCE TOTAL SCORE (2 WEEKS).**
PERI-TRAUMATIC FACTOS	**CRITICAL CARE TOTAL STAY, PERCEIVED STRESS, DISCHARGE TISS,**
POST-TRAMATIC FACTORS	**COGNITIVE EXAM SCORE (2 WEEKS), PHYSICAL COMPOSITE SCORE (2 WEEKS), DTS TOTAL SCORE (2 WEEKS), HADS DEPRESSION SCORE (2 WEEKS).**

10.1.1 – Results for CAPS at 2 weeks.

The first variable to be added was the DTS^{sqrt} at two weeks. This accounted for 77% of the total variance of the $CAPS^{sqrt}$ total score at two weeks. No further variables were added to the results as the predetermined 0.05 limit was reached (i.e. none of the remaining

variables had a p value < 0.05 at that stage. The final results and associated statistics are as shown in tables 10.2, 10.3 and 10.4

- **Table 10.2 - Included Independent Variable**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.664	.038	.88	17.40	.000
(CONSTANT)	1.577	.197		8.009	.000

- **Table 10.3 – Excluded Independent Variables**

Variable	BETA IN	PARTIAL	MIN TOL	T	SIG T
GENDER	.037	.073	.864	.647	.519
DISTISS	.091	.189	.972	1.715	.090
CCTS	.030	.064	.998	.566	.573
STRESS	-.029	-.057	.881	-.505	.615
HADSD0	.021	.036	.664	.317	.752
SOCTS0	.050	.090	.714	.803	.425
PCS0	.064	.134	.998	1.200	.234
ACE-R0	.040	.083	.970	.741	.461

- **Table 10.4 - Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	1	196.314	196.314	302.824	.000
RESIDUAL	88	57.048	.648		

R = .880, R square = 0.775, Adjusted R square = 0.772, Standard Error = .805.

10.1.2 - Results for CAPS at 1-month

The first variable added was DTS^{sqrt} total score at two weeks which accounted for 45% of the total variance of the $CAPS^{sqrt}$ total score at 1-month. No further variables were added to the results as the predetermined 0.05 limit was reached (i.e. none of the remaining variables had a p value < 0.05 at that stage. The final results and associated statistics are shown in Table 10.5, 10.6 and 10.7

- **Table 10.5 - Included Independent Variable**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.518	.064	.678	8.105	.000
(CONSTANT)	1.607	.330		4.867	.000

- **Table 10.6 – Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	-.101	-.128	.864	-1.080	.284
DISTISS	-.007	-.010	.973	-.081	.936
CCTS	.025	.034	.998	.284	.778
STRESSRAT	-.067	-.085	.881	-.714	.478
HADSD	.149	.165	.664	1.399	.166
SOCTS	-.081	-.093	.714	-.781	.437
PCS0	-.105	-.142	.998	-1.204	.233
ACE-R0	.071	.095	.970	.798	.428

- **Table 10.7 - Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	1	104.986	104.986	65.686	.000
RESIDUAL	77	123.068	1.598		

R = 0.678, R squared = 0.46, Adjusted R square = 0.453, Standard Error = 1.26.

10.1.3 - Results for CAPS at 3-months

The first variable to be added was the DTS^{sqrt} total score which accounted for 52% of the total variance of the $CAPS^{sqrt}$ total score at 3-months. The results are shown in table 10.8.

- **Table 10.8 - Step 1 Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.688	.081	.725	8.474	.000
(CONSTANT)	.301	.419		.719	.475

The variable entered on step number two was the critical care total $stay^{log10}$ (CCTS). Along with the DTS^{sqrt} total score this accounted for 58% of the total variance of the $CAPS^{sqrt}$ total score at 3-months. The results are shown in table 10.9.

- **Table 10.9 - Step 2 Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.677	.075	.714	8.994	.000
CCTS	1.745	.512	.270	3.406	.001
(CONSTANT)	-.887	.552		-1.700	.094

The variable added on step number three was the Sense of Coherence score. These three variables together accounted for 61% of the total variance of the $CAPS^{sqrt}$ total score at three months. The results are shown in tables 10.10 and 10.11.

- **Table 10.10 - Step 3 Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.564	.084	.594	6.688	.000
CCTS	1.695	.486	.262	3.489	.001
SOCTS0	-.017	.007	-.223	-2.510	.015
(CONSTANT)	2.064	1.276		1.618	.110

- **Table 10.11 – Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	-.005	-.007	.588	-.052	.958
DISTISS	-.09	-.139	.972	-2.218	.030
STRESSRAT	-.068	-.126	.881	-1.012	.315
HADSD0	.177	.342	.664	2.911	.005
PCS0	.062	.073	.998	.585	.561
ACE-R0	-.009	.073	.970	.585	.561

No further variables were added to the results as the predetermined 0.05 limit was reached. The final results and associated statistics are shown in table 10.12 below.

Table 10.12 - Analysis of Variance

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	3	194.241	64.747	37.425	.000
RESIDUAL	65	112.454	1.730		

R = 0.796, R square = 0.633, Adjusted R Square = 0.616, Standard Error = 1.315

10.1.4 - Results for CAPS at 6-months

The first variable to be added was DTS^{sqrt} total score which accounted for 37% of the total variance of the $CAPS^{sqrt}$ at 6-months. The results are shown in Table 10.13.

- **Table 10.13 - Step 1 Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.593	.102	.620	5.806	.000
(CONSTANT)	.386	.527		.733	.467

The variable entered on step number two was critical care total $stay^{log10}$. Along with DTS^{sqrt} total score this accounted for 46% of the total variance of the $CAPS^{sqrt}$ total score at six months. The results are shown in Table 10.14 and 10.15

- **Table 10.14 - Step 2 Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS0	.580	.093	.607	6.266	.118
CCTS	2.062	.630	.317	3.272	.002
(CONSTANT)	-1.018	.642		-1.586	.823

- **Table 10.15 – Step 2 Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	-.151	-.179	.864	-1.323	.191
DISTISS	-.120	-.150	.972	-1.107	.273
STRESS	.016	.019	.881	.138	.890
HADSD0	.246	.255	.664	1.920	.060
SOCTS0	-.147	-.158	.714	-1.164	.250
PCS0	-.002	-.002	.998	-.016	.987
ACE-R0	.012	.015	.970	.109	..914

No further variables were added to the results as the predetermined 0.05 limit was reached. The final results and associated statistics are shown in Table 10.16.

- **Table 10.16 - Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	2	126.408	63.204	25.860	.000
RESIDUAL	55	134.423	2.44		

Multiple R = .696, R Square = .485, Adjusted R Square = .466, Standard Error = 1.563.

10.2 – Linear regression analysis of participants' data – 1-month assessment

As a secondary analysis stepwise linear regression analyses were performed with the subjects' data, cognitive examination score, physical composite score, DTS score, HADS depression score and SOC score, from the follow-up assessments at one-month post critical

care discharge using CAPS ^{sqrt} as the dependent variable. The participant specific characteristics of gender, critical care total stay, discharge TISS and perceived stress were retained as independent variables. The independent variables selected are listed in Table 10.17.

- **Table 10.17 – Independent Variables entered in the Stepwise Linear Regression Analyses**

PRE-TRAUMATIC FACTORS	**GENDER; SENSE OF COHERENCE TOTAL SCORE (1 MONTH)**
PERI-TRAUMATIC FACTORS	**CRITICAL CARE TOTAL STAY; PERCEIVED STRESS; DISCHARGE TISS**
POST-TRAUMATIC FACTORS	**COGNITIVE EXAM SCORE (1 MONTH), PHYSICAL COMPOSITE SCORE (1 MONTH) DTS TOTAL SCORE (1 MONTH), HADS DEPRESSION SCORE (1 MONTH)**

10.2.1 – Results for CAPS at 1 month.

The first variable to be added was the DTS^{sqrt} total score at one-month (DTSTS1), which accounted for 75% of the total variance of the CAPS^{sqrt} at one-month. No further variables were added to the results as the predetermined 0.05 limit was reached. The final results and associated statistics are shown in Tables 10.18, 10.19 and 10.20

- **Table 10.18 - Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.671	.044	.871	15.373	.000
(CONSTANT)	1.436	.194		7.409	.000

- **Table 10.19 – Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	.077	.140	.791	1.165	.248
DISTISS	.005	.009	.979	.076	.940
CCTS	.010	.021	.998	.169	.866
STRESS	-.070	-.138	.932	-1.147	-.138
HADSDS1	.149	.212	.492	1.793	.077
SOCTS1	-.005	-.009	.646	-.072	.942
PCS1	-.044	-.083	.873	-.689	.493
ACE-R1	.026	.052	.998	.431	.668

- **Table 10.20 -Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	1	168.675	168.675	236.230	.000
RESIDUAL	75	53.532	.714		

Multiple R = .871, R Square = .759, Adjusted R Square = .756, Standard Error = .844

10.2.2 – Results for CAPS at 3-months.

The first variable to be added was DTS^{sqrt} total score at one-month, which accounted for 59% of the total variance of the $CAPS^{sqrt}$ at three-months. The results are shown in table 10.21.

- **Table 10.21 - Step 1-Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	741	.075	.775	9.883	.000
(CONSTANT)	.647	.333		1.944	.056

The variable added on step number two was critical care total stay^{log10} (CCTS). Along with the DTS^{sqrt} at one month, this accounted for 65% of the total variance of the CAPS^{sqrt} total score at three-months. The results are shown in table 10.22.

- **Table 10.22 - Step 2-Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.729	.069	.762	10.585	.000
CCTS	1.692	.465	.262	3.641	.001
(CONSTANT)	-.505	.440		-1.149	.255

The variable added on step number three was Sense of Coherence score total score at one-month (SOCTS1). These three variables together accounted for 68% of the total variance of the CAPS^{sqrt} total score at three-months. The results are shown in tables 10.23 and 10.24

- **Table 10.23 - Step3- Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.609	.081	.637	7.504	.000
CCTS	1.627	.442	.252	3.683	.000
SOCTS1	-.016	.006	-.211	-2.479	.016
(CONSTANT)	2.262	1.192		1.898	.062

- **Table 10.24 – Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	.080	.122	.578	.969	.336
DISTISS	-.114	-.196	.630	-1.570	.122
STRESS	-.109	-.191	.621	-1.531	.131
HADSDS1	.113	.124	.359	.980	.331
PCS1	-.067	-.113	.613	-.893	.375
ACE-R1	.008	.015	.643	.116	.908

No further variables were added to the results as the predetermined 0.05 limit was reached. The final results and associated statistics are shown in table 10.25

- **Table 10.25 -Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	3	213.942	71.314	49.976	.000
RESIDUAL	65	92.752	1.427		

Multiple R = .835, R Square = .698, Adjusted R Square = .684, Standard Error = 1.194

10.2.3 – Results for CAPS at 6-months.

The first variable to be added was DTS^{sqrt} total score at one-month, which accounted for 45% of the total variance of the $CAPS^{sqrt}$ at six-months. The results are shown in Table 10.26

- **Table 10.26 - Step 1-Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.658	.096	.683	6.872	.000
(CONSTANT)	.610	.425		1.436	.157

The variable added on step number two, was critical care total $stay^{log10}$ (CCTS). Along with the DTS^{sqrt} at one month, these accounted for 54% of the total variance of the $CAPS^{sqrt}$ total score at six-months. The results are shown in Table 10.27

- **Table 10.27 - Step 2-Included Independent Variable**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.644	.088	.644	7.339	.000
CCTS	2.011	.592	.309	3.397	.001
(CONSTANT)	-.759	.560		-1.356	.181

The variable added on step number three, was physical composite $score^{log10}$ at one-month. These three variables together accounted for 57% of the total variance of the $CAPS^{sqrt}$ total score at six-months. The results are shown in tables 10.28 and 10.29

- **Table 10.28 - Step 3-Included Independent Variables**

VARIABLE	B	SE.B	BETA	T	SIG T
DTSTS1	.576	.089	.598	6.458	.000
CCTS	1.853	.568	.285	3.264	.002
PCS1	-2.915	1.359	-.200	-2.145	.036
(CONSTANT)	3.982	2.273		1.752	.086

- **Table 10.29 – Excluded Independent Variables**

Variable	Beta In	Partial	Min Tol	T	Sig T
GENDER	-.081	-.114	.696	-.817	.418
DISTISS	-.082	-.122	.834	-.880	.383
STRESS	.066	.095	.791	.685	.497
HADSDS1	.072	.077	.458	.551	.584
SOCTS1	-.076	-.095	.613	-.679	.501
ACE-R1	.068	.106	.853	.761	.450

No further variables were added to the results as the predetermined 0.05 limit was reached.

The final results and associated statistics are shown in table 10.30

- **Table 10.30 -Analysis of Variance**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	3	155.542	51.847	26.591	.000
RESIDUAL	54	105.289	1.950		

Multiple R = .772, R Square = .596, Adjusted R Square = .573, Standard Error = 1.397

Chapter 11 – Results

Other Outcomes and the Effect of Time

In this chapter, the results of the other outcome measures of this study are presented. These refer to anxiety and depression according to the Hospital Anxiety and Depression Scale (HADS); cognitive function, according to the Revised Addenbrookes Cognitive Examination (ACE-R) and the Mini-Mental State Examination (MMSE); physical and mental composite scores (PCS-12; MCS-12) of health related quality of life, according to the Short Form 12 Health Survey(SF12); the individual's orientation to life, according to the Sense of Coherence scale (SOC).

11.1 - HADS - Depression scores

All (100%) participants completed the initial assessment at two weeks, 79 (88%) completed at one month, 73 (81%) at three months and 62 (69%) at six months. Participants' minimum, maximum and mean HADS depression scores at each assessment are shown in Table 11.1

- **Table 11.1 - HADS Depression Scores over time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	0	21	7.2 (4.8)
1-MONTH	79	0	19	5.1 (4.2)
3-MONTHS	73	0	17	4.6 (4.3)
6-MONTHS	62	0	16	4.1 (4.5)

There was a gradual and spontaneous reduction in participants' maximum and mean depression scores over the 6 month study period. A one-way repeated measures ANOVA conducted on the total scores showed that there was a significant effect for time on HADS

depression scores (Wilks' Lambda = .5; f (3,59) = 16.5; p = .000; multi-variate partial eta squared = .5) .

11.1.1 – HADS depression categories

Participants' HADS depression total scores were translated into the four depression subscales of "normal", "mild", "moderate" and "severe". Table 11.2 illustrates these and the number (%) of participants within each category.

- **Table 11.2 – HADS Depression Subscales over time**

ASSESSMENT	NUMBER ASSESSED	NORMAL 0 - 7 N (%)	MILD 8 - 10 N (%)	MODERATE 11 - 14 N (%)	SEVERE 15 - 21 N (%)
2-WEEKS	90	54 (60%)	15 (16.7%)	13 (14.4%)	8 (8.9%)
1-MONTH	79	58 (73.4%)	13 (16.5%)	6 (7.6%)	2 (2.5%)
3-MONTHS	72	56 (77.8%)	6 (8.3%)	9 (12.5%)	1 (1.4%)
6-MONTHS	62	51 (82.3%)	3 (4.7%)	4 (6.5%)	4 (6.5%)

At the first assessment, two weeks after discharge from critical care, 36 (40%) participants were found to have varying degrees of depressive symptoms. By the one month assessment this had reduced to 21 (26.6%) participants, with further reductions at the three month assessment 16 participants (22.2%) and six month assessment 11 participants (17.7%).

Participants classified as having "mild" depression reduced over the six month period with the largest reduction shown at the three month assessment. Those classified as having a "moderate" depression, although reduced by the six month assessment, showed some fluctuation with the largest reduction at the one-month assessment and then an increase at the three-month assessment. Participants with "severe" depressive symptoms showed the largest reduction by the time of the one-month assessment, a further small reduction by the three month assessment and then increased by the time of the six-month assessment.

11.2 – HADS anxiety scores

All (100%) participants completed the initial assessment at two weeks, 79 (88%) completed at one month, 73 (81%) at three months and 62 (69%) at six months. Participants' minimum, maximum and mean HADS anxiety scores at each assessment are shown in Table 11.3

- **Table 11.3 - Mean HADS Anxiety Scores over time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	0	17	6.53 (4.26)
1-MONTH	79	0	20	5.37 (4.48)
3-MONTHS	73	0	16	5.35 (4.49)
6-MONTHS	62	0	18	4.94 (4.92)

The maximum HADS anxiety score showed some fluctuation over the study period. The mean HADS anxiety score however showed a gradual reduction over the six month period. A one-way repeated measures ANOVA conducted on total scores showed there was a significant effect for time on HADS anxiety scores (Wilks' Lambda = .8; f (3, 59) = 5.9; p = .001; multi-variate partial eta squared = .2).

11.2.1 – HADS anxiety categories

Participants' HADS anxiety total scores were translated into the four anxiety subscales of "normal", "mild", "moderate" and "severe". Table 11.4 illustrates the anxiety subscales and the number (%) of participants within each category.

At the first assessment, two weeks after discharge from critical care, 36 (40%) participants were found to have varying degrees of anxiety symptoms. By the one month assessment this had reduced to 24 (30.4%) participants, with further reductions at the three month assessment 20 participants (27.8%) and six month assessment 13 participants (21%). Participants recording "mild" anxiety showed a gradual improvement over the 6 month period, with the largest improvement occurring at the one month assessment. The rate of "moderate" anxiety, although reduced by the time of the six month assessment, showed an

increase at the time of the one month assessment. There was no improvement in the rate of "severe" anxiety over the six month period.

- **Table 11.4 – Anxiety Subscales over time**

ASSESSMENT	NUMBER ASSESSED	NORMAL 0 - 7 N (%)	MILD 8 - 10 N (%)	MODERATE 11 - 14 N (%)	SEVERE 15 - 21 N (%)
2-WEEKS	90	54(60%)	23(25.6%)	9(10%)	4(4.4%)
1-MONTH	79	55(69.6%)	11(13.9%)	10(12.7%)	3(3.8%)
3-MONTHS	72	52(72.2%)	8(11.1%)	9(12.5%)	3(4.2%)
6-MONTHS	62	49(79%)	7(11.3%)	2(3.2%)	4(6.5%)

11.3 – ACE-R scores

All (100%) participants completed the initial assessment at two weeks, 79 (88%) completed at one month, 73 (81%) at three months and 62 (69%) at six months. Participants' minimum, maximum and mean ACE-R scores at each assessment are shown in Table 11.5

- **Table 11.5 - ACE-R Scores over time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	56	100	91.3 (7.3)
1-MONTH	79	71	100	93.5 (5.5)
3-MONTHS	73	72	100	94.4 (5.3)
6-MONTHS	62	64	100	94.7 (5.7)

The minimum ACE-R score showed some fluctuation over time but the maximum ACE-R score remained static. The majority of participants (79 / 88%) at the initial assessment did not display evidence of cognitive impairment using a recommended cut off score of 82 (E.Mioshi - personal communication). At one month, three months and six months, 74 (94%), 70 (96%) and 59 (95%) of participants respectively, had scores above the cut-off for cognitive impairment. Participants' mean ACE-R scores showed a gradual improvement over

the six month study period. A one-way repeated measures ANOVA conducted on total scores showed that there was a significant effect for time for ACE-R scores (Wilks' Lambda = .6; f (3, 59) = 11.8; p = .000; multi-variate partial eta squared = .4).

11.3.1 – Cognitive sub-domain scores

The five cognitive sub-domains of the ACE-R and participants' respective scores are shown in Table 11.6

- **Table 11.6 - Mean Cognitive Domain Scores**

ASSESSMENT	ATTENTION CONCENTRATION M / (SD)	MEMORY M / (SD)	FLUENCY M / (SD)	LANGUAGE M / (SD)	VISUO-SPATIAL M / (SD)
2-WEEKS	17.7 (1.0)	22.3 (3.1)	10.8 (2.3)	25.3 (1.3)	15.2 (1.8)
1-MONTH	17.9 (.5)	23.9 (2.9)	11.0 (1.9)	25.4 (1.1)	15.2 (1.8)
3-MONTHS	17.9 (.3)	24.3 (2.0)	11.4 (2.1)	25.3 (1.3)	15.5 (1.5)
6-MONTHS	17.9 (.4)	24.7 (2.0)	11.3 (2.1)	25.2 (1.3)	15.6 (1.4)

The participants' mean cognitive sub-domain scores were lowest at the two weeks assessment, with exception of the language sub-domain score which was marginally lower at 6 months.

11.3.2 – MMSE scores

The MMSE forms part of the ACE-R total score, the minimum, maximum and mean MMSE scores are shown in Table 11.7.

The minimum scores showed some improvement over the first three assessments but the minimum score at the six month assessment was lower than the one month and six month mean minimum scores. At the initial assessment 82 (91%) participants scored above the normal cut off score of 27 and 8 (9%) scored above the cut off of 20. At the one month assessment, 75 (95%) scored above 27 and 4 (5%) scored above the cut off of 20. At three

months, 70 (96%) scored above the cut off of 27 and 3 (4%) scored above 20. At six months, 60 (97%) scored above the normal cut off of 27 and 2 (3%) scored above the cut off of 20.

- **Table 11.7 - MMSE scores over Time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	21	30	29.0 (1.7)
1-MONTH	79	23	30	29.3 (1.3)
3-MONTHS	73	25	30	29.4 (1.1)
6-MONTHS	62	22	30	29.5 (1.3)

There was very little change in participants' mean MMSE total scores over the study period. One way repeated measures ANOVA was conducted which showed there was no significant effect for time for MMSE total scores (Wilks'Lambda = .90; f (3, 59) = 2.1; p = .11

11.4 - SF12 v2 health related quality of life scores

All (100%) participants completed the initial assessment at two weeks, 79 (88%) completed at one month, 73 (81%) at three months and 62 (69%) at six months. Participants' minimum, maximum and mean physical composite and mental composite scores at each assessment are shown in Tables 11.8 and 11.9 respectively.

- **Table 11.8 – Physical Composite Scores (PCS) over time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	10	57.4	28.7 (10.5)
1-MONTH	79	10.1	56.8	33.3 (10.6)
3-MONTHS	73	13.7	63.1	37.2 (12.6)
6-MONTHS	62	14.9	64.5	39.9(13.3)

Participants' lowest mean PCS, was found at the initial 2 weeks assessment and this showed a gradual improvement over time. A one-way repeated measures ANOVA was conducted on total scores and this showed there was a significant effect for time for PCS scores (Wilks' Lambda = .7; f (3, 59) = 10.2; p = .000; multi-variate partial eta squared = .3).

Table 11.9 – Mental Composite Scores (MCS) over time

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	19.0	66.3	45.7 (12.3)
1-MONTH	79	12.9	65.9	45.7 (12.8)
3-MONTHS	73	17.3	72.0	49.9 (11.9)
6-MONTHS	62	14.1	65.7	50.1 (12.4)

Participants' lowest mean mental composite score was found at the initial assessment and showed gradual improvement over time. A one-way repeated measures ANOVA was conducted on total scores and this showed there was a significant effect for time for MCS scores (Wilks' Lambda = .7; f (3, 59) = 8.2; p = .000; multi-variate partial eta squared = .3)

11.5 – Sense of Coherence Scores (SOC)

All (100%) participants completed the initial assessment at two weeks, 78 (87%) completed at one month, 72 (80%) at three months and 59 (66%) at six months. Participants' minimum, maximum and mean SOC scores at each assessment are shown in Tables 11.10.

- **Table 11.10 - Mean SOC scores over time**

ASSESSMENT	NUMBER	MIN SCORE	MAX SCORE	MEAN SCORE (SD)
2-WEEKS	90	68	196	141.2 (28.0)
1-MONTH	78	76	200	143.1 (27.8)
3-MONTHS	72	82	200	143.2 (27.8)
6-MONTHS	59	90	202	147.8 (28.6)

Participants' minimum, maximum and mean SOC scores increased over the study period. A one-way repeated measures ANOVA was conducted on total scores which showed a significant effect for time for SOC scores (Wilks' Lambda = .8; f (3, 55) = 3.7; p = .016; multi-variate partial eta squared = .2).

Chapter 12 – Results – Predictors of Impaired Health related quality of life after Critical Illness

12.1 Linear regression analysis - initial assessment

Nine independent variables were selected for the regression analysis. These were admission TISS, discharge TISS, critical care total stay, past medical history, past psychiatric history, HADS depression score and HADS anxiety score at two weeks, CAPS total score at two weeks and two weeks' ACE-R total score. Stepwise linear regression analyses were performed with the nine independent variables, the PCS-12 ^{log10} scores and the MCS-12^{reflog10} scores were analysed separately as the dependent variables using the method described in chapter 5. The nine independent variables, are shown in Table 12.1

- **TABLE 12.1 - INDEPENDENT VARIABLES**

	SELECTED VARIABLES
PARTICIPANT SPECIFIC	ADMISSION TISS; DISCHARGE TISS; CRITICAL CARE TOTAL STAY; PMH; PPH.
CLINICAL MEASURES	HADS D; HADS A; CAPS; ACE-R (2-WEEK ASSESSMENT).

12.1.1 - Results for physical composite score at 1-month

The first variable to be added was HADS depression total score at two weeks (HADSDTS0). This accounted for 16% of the total variance (adjusted R square = 0.16) of the PCS total score at one-month. The results are shown in Table 12.2.

- **TABLE 12.2 – STEP -INCLUDED INDEPENDENT VARIABLES OF PCS AT ONE-MONTH**

VARIABLE	B	SE.B	BETA	T	SIG T
HADSDTS0	-.06	.02	-.42	-3.85	.000
(CONSTANT)	1.66	.04		37.39	.000

No further variables were added to the results as the predetermined 0.05 limit was reached (i.e. none of the remaining variables had a p value < 0.05 at that stage. The results and associated statistics, are shown below and in table 12.3.

R = .42, R square = 0.17, Adjusted R square = 0.16, Standard Error = .13

- **TABLE 12.3 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	1	.29	.29	16.09	.000
RESIDUAL	77	1.39	.02		

12.1.2 –Results for physical composite score at 3-months

The first variable to be added was HADS anxiety total score at two weeks (HADSATS0). This accounted for 13% of the total variance (adjusted R square = 0.13) of the PCS total score at three-months. The results, are shown in table 12.4

- **TABLE 12.4 – STEP 1-INCLUDED INDEPENDENT VARIABLES OF PCS AT THREE-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADATS0	-.06	.02	-.38	-3.34	.001
(CONSTANT)	1.68	.05		37.22	.000

The variable entered on step number two was critical care total stay (CCTS). Along with HADSATS0 at two weeks this accounted for 19% of the total variance (adjusted R square = 0.19) of the PCS total score at three-months. The results are shown in Table 12.5

- **TABLE 12.5 – STEP 2- INCLUDED INDEPENDENT VARIABLES OF PCS AT THREE-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADATS0	-.05	.02	-.33	-2.92	.005
CCTS	-.13	.06	-.27	-2.38	.021
(CONSTANT)	1.76	.05		32.69	.000

The variable added on step number three was past psychiatric history (PPH). These three variable together accounted for 23% of the total variance (adjusted R square = 0.23) of the PCS total score at three-months. The results are shown in Table 12.6

- **TABLE 12.6 - STEP 3- INCLUDED INDEPENDENT VARIABLES OF PCS AT THREE-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADATS0	-.07	.10	-.44	-3.62	.001
CCTS	-.12	.05	-.24	-2.14	.036
PPH	-.09	.04	-.25	-2.14	.036
(CONSTANT)	1.94	.10		19.07	.000

No further variables were added to the results as the predetermined 0.05 limit was reached (i.e. none of the remaining variables had a p value < 0.05 at that stage. The results and associated statistics, are shown below and in table 12.7.

R = .52, R square = 0.27, Adjusted R square = 0.23, Standard Error = .14

- **TABLE 12.7 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	3	.48	.16	7.97	.000
RESIDUAL	65	1.30	.02		

12.1.3 –Results for physical composite score at 6-months

The first variable to be added was HADS anxiety total score at two weeks (HADSATS0). This accounted for 11% of the total variance (adjusted R square = 0.11) of the PCS total score at six-months. The results, are shown in table 12.8

- **TABLE 12.8 - STEP 1- INCLUDED INDEPENDENT VARIABLES PCS AT SIX-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADATS0	-.06	.02	-.36	-2.82	.007
(CONSTANT)	1.70	.05		33.94	.000

No further variables, were added to the results as the predetermined 0.05 limit was reached. The results and associated statistics, are shown below and in table 12.9.

R = .36, R square = 0.13, Adjusted R square = 0.11, Standard Error = .15

- **TABLE 12.9 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	1	.21	.21	8.82	.004
RESIDUAL	60	1.40	.02		

12.1.4 –Results for mental composite score at 1-month

The first variable to be added was HADS anxiety total score at two weeks (HADSATS0). This accounted for 30% of the total variance (adjusted R square = 0.30) of the MCS total score at one-month. The results are shown in table 12.10

TABLE 12.10 - STEP 1- INCLUDED INDEPENDENT VARIABLES OF MCS AT ONE-MONTH

VARIABLE	B	SE.B	BETA	T	SIG T
HADSATS0	.05	.01	.56	5.65	.000
(CONSTANT)	1.61	.02		67.01	.000

The second variable to be added was HADS depression score at two weeks (HADSDTS0), which along with HADSATS0 accounted for 34% of the total variance (Adjusted R square = .34) of the MCS at one-month. The results are shown in Table 12.11

- **TABLE 12.11 - STEP 2-** INCLUDED INDEPENDENT VARIABLES **OF MCS AT ONE-MONTH**

VARIABLE	B	SE.B	BETA	T	SIG T
HADSATS0	.04	.01	.39	3.10	.003
HADSDTS0	.03	.01	.27	2.19	.032
(CONSTANT)	1.58	.03		56.82	.000

No further variables, were added to the results as the predetermined 0.05 limit was reached. The results and associated statistics, are shown below and in table 12.12.

R = 0.60, R square = 0.36, Adjusted R Square = 0.34, Standard Error = .08

- **TABLE 12.12 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	2	.28	.14	20.87	.000
RESIDUAL	76	.50	.01		

12.1.5 – Results for mental composite score at 3-months

The first variable, to be added was past psychiatric history (PPH). This accounted for 26% of the total variance (Adjusted R square = 0.26) of the MCS at three-months. The results are shown in Table 12.13

- **TABLE 12.13 -STEP 1- INCLUDED INDEPENDENT VARIABLES OF MCS AT THREE-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
PMH	-.11	.02	-.52	-4.86	.000
(CONSTANT)	1.90	.04		45.30	.000

The variable added on step two, was HADS depression total score at two weeks (HADSDTS0). Along with PMH, these two variables accounted for 34% of the total variance (Adjusted R square = .34) of the MCS at three-months. The results are shown in Table 12.14

- **TABLE 12.14 - STEP 2- INCLUDED INDEPENDENT VARIABLES OF MCS AT THREE-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
PPH	-.09	.02	-.39	-3.63	.001
HADSDTS0	.03	.01	.32	2.98	.004
(CONSTANT)	1.77	.06		30.03	.000

No further variables were added to the results as the predetermined 0.05 limit was reached. The results and associated statistics, are shown below and in table 12.15

R = 0.60, R square = 0.36, Adjusted R Square = 0.34, Standard Error = .08

- **TABLE 12.15 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	2	.25	.12	19.34	.000
RESIDUAL	70	.44	.01		

12. 1.6 –Results for mental composite score at six-months

The first variable to be added, was HADS depression total score at two weeks (HADSDTS0). This accounted for 20% of the total variance (Adjusted R square = 0.20) of the MCS at six-months. The results, are shown in Table 12.16

- **TABLE 12.16 – STEP1- INCLUDED INDEPENDENT VARIABLES OF MCS AT SIX-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADSDTS0	.05	.01	.46	3.81	.000
(CONSTANT)	1.58	.03		47.63	.000

The variable added on step two was past psychiatric history (PPH) Along with HADSDTS0, these two variables accounted for 28% of the total variance (Adjusted R square = .28) of the MCS at six-months. The results, are shown in Table 12.17

- **TABLE 12.17 – STEP 2- INCLUDED INDEPENDENT VARIABLES OF MCS AT SIX-MONTHS**

VARIABLE	B	SE.B	BETA	T	SIG T
HADSDTS0	.03	.01	.34	2.71	.009
PPH	-.07	.03	-.33	-2.64	.011
(CONSTANT)	1.73	.07		25.79	.000

No further variables were added to the results as the predetermined 0.05 limit was reached. The results and associated statistics, are shown below and in table 12.18.

R = 0.55, R square = 0.30, Adjusted R Square = 0.28, Standard Error = .08

- **TABLE 12.18 - ANALYSIS OF VARIANCE**

	DF	SUM OF SQUARES	MEAN SQUARE	F	SIG F
REGRESSION	2	.18	.09	12.88	.000
RESIDUAL	59	.41	.01		

Chapter 13 - Discussion - Recruitment, Baseline Characteristics and Attrition

13.1 - Statement of Principal Findings

Ninety patients admitted to the Critical Care Unit were included in the study. Sixty-two (69%) patients completed the full study. There were no significant differences between completers and non-completers in terms of baseline characteristics or levels of psychological distress.

13.2 - Comparison with other studies

It was difficult to compare this study with other critical care studies for several reasons. To my knowledge, this is the only broad case mix, prospective longitudinal study over a six-month period, to investigate the rate of PTSD early after critical care discharge using a structured clinical interview. Although seven previous critical care studies prospectively investigated PTSD over time, only two (Rattray et al 2005; Jones et al 2007) comprised a broad case mix of survivors, but both used self-report questionnaires to detect PTSD and one (Jones et al 2007) only provided outcome data on one occasion at a three month follow-up.

The other five (Michaels et al1998; Michaels et al 1999; Schnyder et al 2001; Creamer et al 2004; Hamanaka et al 2006) studies were of survivors of accidents or other traumatic injuries. Relative to the main outcome variable in this study, and the recruitment of survivors of accidental injury only, trauma exposure when coupled with physical injury, confers a high risk for the development of PTSD (Zatzick & Byrne 2006). In addition, survivors of trauma admitted to critical care are more likely to be younger males (Schultz et al 2007) and therefore would not be comparable to an over all critical care population, which typically comprises an older age group that is less biased in terms of male gender (Harrison et al 2007). The mean age of participants recruited in the trauma studies was 37 years (range 33yrs - 38 yrs) and male gender ratio was 75%. In comparison, participants

were older (55 years) whilst the male gender ratio was much lower (51%) in this study. In comparison to a typical critical care population, there was a slight gender bias in favour of females in this study, and participants were younger than the average critical care patient.

The mean age of participants in this study was the same as that of Rattray and colleagues, but participants recruited by Jones and colleagues were older (61 years). The gender ratio for males in both studies was higher (58%; 62% respectively) than that recruited in this study. Because individual characteristics such as younger age and female gender are risk factors for PTSD (Brewin et al 2000), the prevalence of PTSD in this study would have been predicted to be higher than that found in both of these studies, but it was in fact lower. The most likely explanation for this was the use of a structured clinical interview to detect PTSD in this study, as opposed to the self-report questionnaires used by Rattray, Jones and their colleagues.

Seven critical care studies quoting PTSD prevalence used clinical interviews to determine PTSD, however only three (Schnyder et al 2001; Creamer et al 2004; Hamanaka et al 2006), were directly comparable to this study, in that they were also prospective, longitudinally designed studies that had recruited consecutive admissions to critical care. Of the remaining five studies, two (Nickel et al 2004; Liberzon et al 2006) were cross sectional and two (Richter et al 2004; Kapfhamammer et al 2004) were retrospective. A problem associated with retrospective studies and PTSD is a tendency for inflated reports of trauma intensity and other post trauma variables, by this method (Brewin et al 2000).

These two retrospective studies and that of Nickel et al (2004) had much smaller sample sizes compared to this study. The other four studies(Schnyder et al 2001; Creamer et al 2004; Hamanaka et al 2006; Liberzon et al 2006) that had used structured clinical interviews, had slightly larger sample sizes. Although the sample size in this study was not large, out of the ten broad case mix studies, it ranks fourth, and ninth compared to all 23 studies that have investigated PTSD prevalence.

The illness severity score of participants in this study proved a further difficult comparison to the existing critical care evidence. The broad case mix studies reported scores for acute physiology and chronic health evaluation (APACHE II) (Knaus et al 1985), the studies of accident injuries reported injury severity scores (ISS) (Baker & O'Neill 1976). In the critical

care unit at this study site, APACHE II scores are only recorded on level 3 patients, but the therapeutic intervention scoring system (TISS) (Keane & Cullen 1983) is recorded daily on all patients. Therefore, TISS scores were used as a marker of illness severity in this study.

Recruitment and the measurement of baseline variables, when engaging with critically ill patients and/or their families, are known to be problematic (Elliot and Leeder 1998). In this study, recruitment was problematic, despite the very broad inclusion criteria. The exclusion criteria in this study, regarding capacity to consent and ability to comply with the constraints in the early part of the study, resulted in the exclusion of a large percentage of survivors who may have been more vulnerable to the development of later PTSD. In longitudinal studies, the main threat to the generalisability of the findings is loss to follow-up (Chaboyer & Elliot 2000). In this study however, it was possible to compare differences between participants and non-participants, and between those who completed and those who did not because of a comprehensive collection of baseline data. By comparison, in the critical care studies, only some studies provided baseline data for participants who completed and those who did not, but generalisability to the larger population was rare.

A knowledge and understanding of the trajectory of symptoms commonly reported by survivors of critical care is important, particularly when planning the appropriate resources necessary to improve patient outcome. This knowledge and understanding is currently haphazard due to the lack of prospective longitudinal studies particularly those comprising a broad case mix. Only one (Rattray et al 2005) broad case mix study provided evidence of outcome early after critical care discharge, the earliest follow up of a broad case mix in the cross sectional studies was two months after critical discharge(Samuelson et al 2007), leaving a considerable gap. The evidence from this study of outcomes two weeks after critical care in addition to that provided over a six-month period after discharge from critical care, fills a gap and adds support to the limited evidence currently available.

13.3 - Strengths and weaknesses of the methodology

There were a number of strengths to this study. It is the first broad case mix study to have used a well validated, and reliable structured clinical interview to detect PTSD. In addition to the CAPS interview, a self-report questionnaire was used and further PTSD scores were

derived from this for a second self-report measure. The multimodal assessment of symptoms has been recommended because it provides converging evidence for PTSD (Weathers et al 2001).

The continuation of the study for a period of six-months provided data at some previously neglected time points regarding several outcomes and their trajectory over time. The absence of major differences between completers and non-completers suggested that the results of this study are likely to be representative for those individuals who originally agreed to take part in it.

Many critical care studies exclude patients with mental health problems from participation in studies of psychological and health related quality of life outcomes. Given that patients with evidence of psychiatric morbidity have been found to have poorer health related quality of life (Davydow et al 2008), the exclusion of such individuals from study participation introduces bias. To avoid this, these patients were included in this study.

Regarding the wider population, patients excluded from the study differed from those who took part because they required a higher level of clinical intervention at the point of discharge from critical care, as shown by the higher TISS score. This may be considered a weakness of the study because those excluded may have been sicker than those who took part in the study. Whilst this confirmed the decisions taken to exclude some patients in accordance with the exclusion criteria, it also suggested potential vulnerability for PTSD amongst the excluded patients. To my knowledge however, there is no evidence to confirm an association between discharge TISS scores and development of PTSD, only findings to suggest that patients discharged with a TISS of ≥ 20 had higher mortality rates (Smith et al 1999).

Another weakness was the small sample size in this study despite extensive efforts made to recruit as many patients as possible. Underpowered studies are ubiquitous in the medical literature and typically lead to a Type I or Type II error (Greenhalgh 2006 p69). In order to counteract a type II error effect in this study, all differences identified were supported by the calculation and inclusion of confidence intervals. One further weakness was the overall attrition rate of 31%, because follow-up rates of 70% or lower are generally considered invalid (Greenhalgh 2006 p71). The attrition rate in this study however, includes those who

died, when this is taken into consideration the follow-up rate in this study was 74%. Although the overall attrition was higher than desired, a problem not uncommon in longitudinal studies, and limit the generalisability of results, the comprehensive comparison of data between participants who completed and those who did not, for which no significant differences were found, is a strength of the study.

13.4 - Summary and conclusions

The recruitment of patients after critical illness can be difficult and measures are necessary to improve the recruitment and retention of participants. The assessment of patients early after critical care discharge often results in the exclusion of patients, usually because they are too unwell or have communication difficulties because of retention of tracheostomy after discharge from critical care. Generalisability of findings may be limited by this but a comprehensive data collection for comparison purposes, helps in the determination of this.

Sample size was modest in this study, although it was larger than over 50% of the critical care studies that have investigated PTSD after critical illness. Small sample sizes are considered unreliable, but some statistical measures may be taken to improve this. This study provides hitherto unavailable evidence of some broad psychological outcomes and the impact of time, from early after discharge from critical care, through to six-months. All clinical measures used in the study were well-validated and the assessment of PTSD was conducted, according to a gold standard.

Chapter 14 - Discussion - PTSD Assessment Outcome and the Effect of Time.

14.1 - Statement of Principal Findings

The rate of PTSD according to a structured clinical interview (CAPS) (Blake et al 1995) at various follow-up times, was lower than that previously identified in all but one of the critical care studies. The rate of PTSD according to a self-report questionnaire (DTS) (Davidson et al 1997), at various follow-up times, was similar to one critical care study, higher than two, but lower than the remaining 12 critical care studies that used self-report questionnaires. Three critical care studies had PTSD rates lower than the SPAN, by follow up time. There was a significant reduction in both the CAPS and the DTS total scores over time.

14.2 - Comparison with other studies

The rates of PTSD according to the lenient CAPS scoring rule were much lower than those according to the CAPS stringent rule. There was no comparison with any of the critical care studies in this respect, but Weathers et al (1999) investigated the effect of nine scoring rules in two samples of Vietnam War veterans. They also found lower rates of PTSD using lenient CAPS scoring rules, compared to the more stringent rules.

Because the stringent CAPS rule utilises a cut off score of 65 in addition to DSM-IV symptom criteria, the lower rate of PTSD in this study, according to this rule, suggested that most participants' had relatively low CAPS total scores. This was interesting particularly since most participants' PTSD remitted over the six-month follow up, and concurs with findings reported by Blanchard et al (1997) where the overall degree of severity and frequency of the 17 symptoms of PTSD at an initial assessment, predicted remission of PTSD at six months.

According to the CAPS, the rates of PTSD in this study were lower than in all the critical care studies that assessed for PTSD at the same time points, except one (Schnyder et al 2001). The rate of PTSD identified by Schnyder and colleagues was 4.7%, according to the CAPS

lenient, two weeks after discharge from critical care. Although this was lower than the rate of 10% identified in this study at two weeks, there were far fewer females in Schnyder and colleagues' study, participants' sense of coherence scores were higher and the critical care stay was shorter (5.9 days). A longer length of stay in critical care was found to be predictive of later PTSD in two critical care studies (Rattray et al 2005; Boer et al 2007), whereas female gender is a known risk factor for PTSD (Brewin et al 2005). A low sense of coherence score has also been found to be associated with PTSD following emergency caesarean section (Tham et al 2007), in survivors of serious accidental injury (Schnyder et al 2000), in survivors of cancer (Black et al 2005), in emergency workers (Jonsson et al 2003) and in firefighters (Dudek et al 2000). Although the differences between this study and Schynyder and colleagues' study can be explained, the most obvious difference was the population studied, as participants were survivors of serious accidents.

Six other critical care studies used structured clinical interviews to determine rates of PTSD after discharge. Three (Nickel et al 2004; Kapfhammer et al 2004; Hamanaka et al 2006) used the Structured Clinical Interview for DSM IV Axis 1 disorder (SCID) (First et al 1997). One (Richter et al 2006) study used the Association for Methodology and Documentation in Psychiatry (AMDP system) (AMDP 1995) and two (Creamer et al 2004; Liberzon et al 2006) used the CAPS.

The study conducted by Nickel et al (2004) was the only study comprising a broad case mix of patients and was comparable to this study. Nickel and colleagues found the point prevalence of PTSD according to the SCID was 9.8%, six months after discharge from critical care. This was slightly higher than the 6.5% identified at six months, in this study. Unfortunately the authors reported very little baseline data, which made comparison with the study difficult although it is probable that the small sample size and particularly high rate of pre-morbid psychiatric problems (41.5%), a known risk factor for PTSD (Brewin et al 2000; Ozer et al 2003), contributed to the higher rate of PTSD in their study.

Kapfhammer et al (2004) investigated PTSD in survivors of ARDS, eight years after critical care discharge. Although psychiatrists only assessed 15 out of 46 patients, the rate of PTSD identified though the SCID, was reported as 24%. The rate of PTSD by the follow up time, could not be compared to this study, but it was interesting to observe that PTSD persisted in

survivors of ARDS many years after treatment, whilst symptoms of PTSD in this study resolved over time. The intensity of symptoms declines in most trauma survivors over time, although some will develop chronic PTSD. Spontaneous recovery from chronic PTSD is unusual and may not occur at all after 6 years of illness (Kessler et al 1995).

Hamanaka et al (2006) found an ASD prevalence of 9% within one month according to the Acute Stress disorder Interview (ASDI) (Bryant & Harvey 2000) and PTSD prevalence of 8.5% according to the SCID at six months. Although ASD was not quantified, the rate of PTSD at six months was lower in this study. Prevalence rates of PTSD after motor vehicle accidents are known to vary considerably from 2% (Schnyder et al 2001) to 32% (Blanchard et al 1995) and are thought to be mostly related to methodological differences between studies (O'Donnell et al 2008). In addition to being survivors of motor vehicle accidents (MVA), participants in Hamanaka and colleagues' study were much younger, than participants in this study and comprised fewer females.

Creamer et al (2004) found a much lower ASD prevalence (2%) eight days after critical care discharge, a PTSD prevalence of 7.4% at three months and 11.6% at twelve months, according to the CAPS. The low rate of ASD identified in the study was very different to that found in survivors of MVA's (Harvey and Bryant 1999) and in survivors of traumatic brain injury (Bryant and Harvey 1998). The criteria for ASD however, although modelled on PTSD in terms of stressor definition, requires fewer symptoms from the intrusive, avoidance and arousal criteria, shorter duration of symptoms and a unique dissociative cluster of symptoms (Bryant & Harvey 2000 p6-7). In this study, the full symptoms of PTSD were assessed at two weeks but it was interesting that the rate of ASD, was much lower in Creamer and colleagues study, despite a similar sample size. The prevalence of PTSD at three months in this study was lower than that found by Creamer and colleagues, but participants in this study were older, which may have contributed to the difference in prevalence. Younger age, has been found to be a risk factor in five (Michaels et al 1999; Scragg et al 2001; Rattray et al 2005; Liberzon et al 2006; Boer et al 2007) critical care studies, and two (Brewin et al 2000; Ozer et al) comprehensive reviews of predictors of PTSD.

Liberzon et al (2006) found a PTSD prevalence of 11%, according to the CAPS, six to twelve months after treatment for abdominal aortic aneurysm. This was almost twice the prevalence identified in this study at six months. A comparison with this study was difficult because they did not provide full details of study participants' characteristics. Furthermore, although the CAPS was used to detect PTSD, no scoring rules were given and these are known to affect overall rates of PTSD (Weathers et al 1999). Fewer participants had pre-morbid psychiatric problems, compared to this study and 73% of the sample, were male, which was higher than in this study. This should have predicted an overall lower PTSD prevalence compared to this study. One possible explanation for the higher prevalence identified by Liberzon and colleagues may be due to retrospective recall of the experiences, as those followed up had been discharged between six months to two years previously. This has been found to inflate the effect of trauma intensity (Brewin et al 2000).

In Richter and colleagues' study, the prevalence of PTSD was 19%, according to the AMDP system interview nearly three years after discharge from critical care. Sample size however, was very small and the AMDP system is not a recognised PTSD gold standard. Although the follow-up in this study did not extend to three years, the rate of PTSD at six months was much lower than that reported by Richter and colleagues. This may have been a result of the sample size, a much longer critical care stay, a higher rate of pre-morbid psychiatric problems and that participants were of a young age group. Furthermore, although the sample comprised participants of trauma and non-trauma, most (78%) were survivors of severe multi-trauma, which was also very different to this study.

This study is the only prospective longitudinal study to have used a structured clinical interview to diagnose PTSD in a broad case mix of critical care patients. Two (Rattray et al 2005; Jones et al 2007) other broad case mix longitudinal studies investigated PTSD, but only one (Rattray et al 2005) provided complete data for prevalence of PTSD at all follow-up assessments. Prevalence of posttraumatic stress symptoms (PTSS) in Rattray and colleagues' study was determined by the Impact of Events Scale, which although recognised as a well-validated measure, cannot be used to diagnose PTSD, because it only documents intrusive and avoidant symptoms. Prevalence of traumatic stress symptoms in the study however were very high compared to that identified in this study through the CAPS and higher than that identified in this study through the self-report DTS questionnaire. Although the IES has

been described as one of the most efficient questionnaires in screening for PTSD (Brewin et al 2005), it may over diagnose between 11% (Neal et al 1994) and 33% (Wohlfarth et al 2003), at a cut off of 35, depending on overall prevalence. At time of hospital discharge, six months and twelve months, the prevalence of PTSS in Rattray and colleagues' study was 32%, 24.5% and 27.5% respectively. Compared to this study, participants in Rattray and colleagues' study were of a similar age, but had a shorter length of stay, and comprised a higher ratio of males, which would theoretically lead to a lower rate of PTSS, than that found in this study. One further possible explanation for the high rate of PTSS was that participants were all emergency admissions, whereas participants in this study comprised elective and emergency admissions, of which 74% were emergency admissions to critical care. However, of the nine patients with PTSD, less the time criterion, at two weeks in this study, eight were emergency admissions. Only one elective admission had a positive diagnosis and at the one-month assessment, symptoms had subsided. Therefore, it is likely that the 100% emergency admission rate in Rattray and colleagues study, impacted on the overall prevalence found.

Only two (Cuthbertson et al 2004; Jackson et al 2007) critical care studies used the DTS questionnaire to screen for PTSD. One (Cuthbertson et al 2004) was a cross sectional study and the other (Jackson et al 2007) was a retrospective study. Cuthbertson and colleagues found that 8 (10%) patients fulfilled DSM-IV criteria for a point prevalence of PTSD according to the DTS questionnaire at a cut-off score of 40, three months after critical care discharge. Although it was a higher prevalence than that of the CAPS in this study, it was the same as that identified through the DTS questionnaire at three months. The authors also provided data for a lower DTS cut off score of 27, at which point 11 (14%) patients had PTSD according to DSM-IV criteria. In this study the rate of PTSD according to DSM-IV criteria only remained unchanged at 10%. Compared to this study, sample size was similar but there were more males in Cuthbertson and colleagues' study, in addition the cohort was slightly older and had a shorter period of mechanical ventilation and subsequent critical care stay, than participants in this study. The higher prevalence of PTSD in Cuthbertson and colleagues' study as compared to that of the CAPS in this study is most likely due to a number of false positive tests. The positive predictive value of the DTS was found to be 79%

(Davidson et al 1997), which suggested that 21% of subjects were incorrectly diagnosed as having PTSD.

Jackson et al (2007) investigated PTSD and other outcomes in a sample of 58 survivors of trauma, without intracranial haemorrhage. They found 22 (38%) patients had PTSD according to the DTS questionnaire at a cut-off score of 40, one to two years after critical care discharge. The rate of PTSD was much higher than that identified in this study at the final follow-up at six months, although participants in their study were younger and had a higher rate of pre-morbid mental health problems, which may partly explain the difference in prevalence. However, the sample studied by Jackson and colleagues, in addition to being very different to this study, had a high rate of skull fractures and concussion. Studies of PTSD after traumatic brain injury have reported prevalence in the region of 17 - 33% (Bryant & Harvey 2000 p149-154) but the studies were conducted within one-year of injury and longitudinal studies of traumatic injury generally point to decreased prevalence over time (O'Donnell et al 2003).

Confounding issues associated with PTSD prevalence in the study were a lack of clarity as to whether DSM-IV criteria were used for diagnosis, as only the cut off score is referred to in the report along with high rates of depression and anxiety because some symptoms may be confused with those of PTSD. Finally, the use of a self-report measure to detect symptoms of PTSD in mild traumatic brain injury (MTBI) may not be the most reliable method of assessment because of the overlap of MTBI symptoms and those of PTSD. Thirty three (56%) participants in the study were found to have cognitive impairment, most pronounced in the domains of attention and executive functioning/verbal fluency, adding further potential for confusion of PTSD symptoms. Traumatic brain injury can result in symptoms of dissociation, neurological disorders and in intrusive imagery. Post concussive symptoms overlap considerably with PTSD symptoms of arousal (Bryant 2001), leading to further diagnostic confusion. It is also possible that PTSD contributed to the cognitive dysfunction of the study participants (McNally 1996).

In Rattray and colleagues' study (2005) symptoms of avoidance and intrusion according to the IES, increased by 4% and 2% respectively, over the twelve month study period in participants with more severe symptoms. Participants with moderate symptoms had a

similar percentage reduction in symptoms; and in those with low PTS symptoms, there was no change. Participants overall scores of intrusion and avoidance, however, showed no significant difference between hospital discharge and the twelve-months follow-up. The findings of O'Donnell et al (2007) showed the symptom trajectories of participants with PTSD at 12 months were a progressive development of the early elevated responses, particularly avoidance symptoms, although these were survivors of traumatic injury and only 33% were admitted to critical care.

In this study, although individual PTSD symptoms were not examined, the overall findings were very different. The number of participants with PTSD at the two weeks assessment according to the CAPS, dropped by 56% by the time of the six-month assessment. The number of patients with PTSD according to the DTS at six months when compared to those who had PTSD at the two weeks assessment, reduced by 83%. Most participants who scored highly on the CAPS at two weeks, as shown in adopting a stringent CAPS scoring rule, did not have PTSD at six months. Both the CAPS and DTS total scores also reduced over time and the reduction was found to be significant for both measures.

Similar reductions in the number of patients who had PTSD at two weeks, were reported by Schnyder et al (2001), although they also found a significant association between measurement points of two weeks and twelve months in respect of a PTSD diagnosis. This was because symptoms had resolved for three participants with PTSD by 12 months and two were subsyndromal. Two subsyndromal participants at two weeks developed full PTSD by the twelve month assessment and six participants without PTSD at two weeks were subsyndromal at 12 months. PTSD status at two weeks therefore, was not predictive of PTSD status at 12 months. In this study, two participants who had full PTSD, less the time criterion, at two weeks were subsyndromal at one month and two subsyndromal participants at two weeks had full PTSD at one-month.

Hamanaka et al (2006) also found some resolution of traumatic stress symptoms at a six-month follow-up, but this was compared to a diagnosis of ASD at one month. The reliability of the predictive ability of the ASD diagnosis however is questionable because findings from other studies have shown, although a high proportion of those with an ASD diagnosis go on

to develop PTSD, a large number of individuals who developed PTSD do not have an ASD diagnosis (Harvey & Bryant, 1999, 2000; Creamer, O'Donnell, & Pattison, 2005).

Symptom trajectories for PTSD in survivors of traumatic injury have been found to increase over time in some studies (Orcutt et al 2004; O'Donnell et al 2007), the lack of prospective longitudinal studies of a broad case mix population of critical care patients however dictates uncertainty in this respect.

14.3 - Strengths and weaknesses of the methodology

The main strengths and weaknesses of this study were discussed in chapter 13 and will not be repeated here. Instead, the strengths and weaknesses as they apply to this part of the methodology will be discussed.

To my knowledge, this is the only prospective study to have examined the longitudinal course of PTSD in a broad case mix of survivors of critical care treatment, using a gold standard measure. The addition of two further self report questionnaires provide converging evidence in determining prevalence and are considered further strengths of the study. The CAPS was administered at the beginning of the assessment and the DTS, was completed by individual participants, at the end of the assessment, after all other clinical measures had been completed. It is possible that the administration of the CAPS prior to the DTS may have influenced some self-reporting on the DTS and it may have been more reliable to have allowed some passage of time between them. An interval of a few days to a week between assessments have been considered the most reasonable (Weathers et al 2001), but time constraints and the logistics of follow up rendered this impractical. In some cases, because of the number of clinical measure used for the assessment, some participants requested that some self-report measures were left with them, to be completed later.

The use of multiple assessors has the potential to introduce bias into the study, however both the research assistant and I had received training in the use of all clinical measures, in addition to piloting our use of them, prior to the commencement of the study. Further to

this both the research assistant and I attended regular clinical supervision sessions for the duration of the study, which was considered a strength.

Participants did not complete the SPAN questionnaire; instead, the scores, were derived from the severity scores of the respective questions from the DTS, as described in the methodology. Whilst this might be a weakness, it was the same method used by the designers of the SPAN (Meltzer-Brody et al 1999) in the development and validation of it.

One further weakness of this study may have been a failure to analyse the individual symptoms of PTSD, in respect of their trajectory over time, as this would have been more directly comparable to the other studies. The study found a significant reduction in PTSD scores over time according to the CAPS and the DTS. It could be argued that the use of a structured interview enabled participants to confront their traumatic experience, with some symptom resolution as a result, of the exposure, although this was not the case in Creamer and colleagues' study (2004), using the same structured clinical interview. Conversely, single session exposure can result in an increase in symptoms for some individuals (Rose et al 2002).

14.4 - Summary and conclusions

The proportion of patients who developed PTSD, according to a structured clinical interview was lower than that previously found, in all but one previous critical care study. There was a reduction in symptoms over time, which was not consistent with other studies. It is likely the prevalent use of self-report questionnaires and studies of some sub-populations, such as survivors of ARDS and traumatic injuries, may contribute to the explanation of these differences.

There is a need to consider the overlap of symptoms commonly reported by survivors of critical care that may be confused with those of PTSD but have another cause. For example symptoms such as difficulties sleeping, concentration problems and numbing of senses may be caused by some prescribed medication, including sedatives, rather than be as a result of PTSD. We only ask patients to be honest about their symptoms, not about what causes them.

Although this study found that symptoms of PTSD reduced over six-months, some studies found that symptoms increased over time. There was a clear lack of prospective longitudinal studies to support these findings.

Chapter 16 - Discussion Predictors of PTSD

16.1 - Statement of Principal Findings

This study found that severity of PTSD within the initial month after critical care treatment was the strongest and most consistent predictor of the Clinician Administered PTSD Scale (CAPS) (Blake et al 1995) total score, at all follow up time points. The DTS score at two weeks independently predicted PTSD at two weeks and one month. Critical care total stay, DTS and low SOQ scores at two weeks contributed to the predictive model at three months. The DTS and critical care total stay formed the predictive model at six months. The DTS score at one month was the sole predictor of one month PTSD. Critical care total stay, the DTS and SOC scores at one month predicted PTSD at three months. Critical care total stay, the DTS and Physical composite score at one month, predicted PTSD at six months.

16.2 - Comparison with other Studies

Evidence (Ozer et al 2003; Brewin et al 2000) from the meta-analysis of studies of traumatic stress suggests that peri-traumatic risk factors and factors operating after the trauma are stronger predictors of PTSD than pre-trauma characteristics. Whilst this study shares some commonalities with this evidence, the findings from this study suggested that severity of PTSD, within one month of discharge from critical care, was the strongest and most consistent contributor to the predictive model at all time points. Although peri-traumatic emotional responses such as fear, helplessness, horror, guilt and shame were examined (Ozer et al 2003), acute emotional distress in the aftermath of the traumatic event was not included in either meta-analysis because of the overlap of the measurement of PTSD (Brewin et al 2000). It has been consistently found that although a high proportion of those with a diagnosis of ASD go on to develop PTSD, many who subsequently develop PTSD do not qualify for the acute diagnosis (Creamer et al 2004). Some of these findings however were discrepant due to procedural variation such as strict exclusion criteria and assessment

tools and several studies found that the majority of people who display ASD subsequently develop PTSD (Bryant 2003).

As discussed in chapter two, ten critical care studies have investigated PTSD prediction. Five (Michaels et al 1999; Schnyder et al 2001; Creamer et al 2004; Rattray et al 2005; Hamanaka et al 2006) of these found the presence of some early traumatic stress symptoms predicted PTSD, but some of the clinical measures used were different to those used in this study.

Schnyder et al (2001) recruited a similar sample size to this study and used the CAPS to determine PTSD. They found the intrusion subscale of the Impact of Events Scale (IES), two weeks after serious accidental injury contributed with other variables to the predictive model that collectively accounted for 34% of the total variance. Although there was good correlation between the IES and the CAPS, only the intrusion subscale score of the IES was entered into the regression equation, whereas in this study the DTS total score was entered which resulted in higher predictive values. Furthermore, unlike this study, the participants recruited were survivors of serious accidental injury and not typical of a critical care population, and prediction was based upon PTSD at a much later follow up of one year. By contrast in this study, predictive data was collected at both two weeks and at a one month assessments in order to determine risk for PTSD at two weeks, one, three and six months.

Creamer et al (2003) conducted an extensive investigation in order to examine the predictive ability of the ASD diagnosis at a mean of seven days after injury, to predict PTSD at three months and twelve months. The authors found that intrusion and arousal predicted a categorical PTSD diagnosis, whilst symptoms of intrusion, avoidance and arousal all contributed to the prediction of PTSD severity. In this study, although predictors were similarly compared to the CAPS total score, the sub scales of intrusion, avoidance and hyper arousal were considered collectively as a predictor, through the DTS total score because generally, continuous measures would be expected to yield larger effect size than a categorical measure which may attenuate it (Brewin et al 2000). The DTS used in this study had been previously validated in different populations, whereas in Creamer and colleagues' study, prediction of symptoms was from a modified version of the CAPS, which had not been validated. This study recruited a broad case mix of patients whereas those who participated in Creamer and colleagues' study were survivors of severe trauma. In this study,

the average age of participants was 55 years and gender distribution was equal amongst males and females. By comparison, Creamer and colleagues recruited mostly male patients who were much younger.

Hamanaka et al (2006) found an ASD diagnosis, within one month of a motor vehicle accident (MVA), predicted PTSD according to the PTSD module of the Structured clinical interview for DSM-IV Axis I disorders (SCID) (First et al 1997), at six months. Although the sample size in this study was similar to that of Hamanaka and colleagues' and PTSD was determined by gold standard structured clinical interviews at six months, the population in this study was more typical of a critical care population. In this study, the total scores of the DTS predicted PTSD, whereas a categorical ASD diagnosis predicted PTSD in Hamanaka and colleagues' study.

The Physical Composite Score (PCS), a sub-category of the SF-12 Health Survey version 2 (Ware et al 2002), as assessed at one month after critical care discharge, was found with other variables to predict PTSD at six months, in this study. Hamanaka et al (2006), reported similar findings of persistent physical disability that was strongly predictive of PTSD at six months, but this is the only evidence from the critical care studies to support this finding. However, in one very large community sample of women, Frayne et al (2004) identified strong associations between physical and mental illness where PTSD alone was associated with a significant 4-point decrease in PCS score and PTSD with co morbid depression was associated with a significant 6.6-point decrease in PCS scores.

The length of time spent within critical care may be either a peri-traumatic or a post-traumatic factor in terms of risk, depending on the timing of the index trauma. Where the index trauma is the experience of critical illness or critical care itself, it might be considered a peri-traumatic factor but in cases where the traumatic event occurred prior to admission, the time spent within critical care may constitute additional life stress in the aftermath of a traumatic event and consequently it would be considered a post traumatic factor. For these reasons and the descriptions of trauma given by participants in this study, critical care total stay was considered both a peri-traumatic and posttraumatic factor and contributed to the predictive model with other predictive variables at three-months and six- months.

The length of time that patients spent within critical care was also found to predict PTSD in two other critical care studies (Deja et al 2007; Boer et al 2007) but these studies were conducted retrospectively at nearly five and four years post discharge, respectively. In Boer and colleagues study, critical care total stay only predicted PTSD when age was controlled for in the regression analysis. The age of patients in this study was very similar to those in Boer and colleagues study and age was not included in the regression model in this study.

One further interesting observation in relation to critical care stay as a predictor of PTSD was in the study by Cuthbertson et al (2004), where although the length of time spent on mechanical ventilation correlated with total DTS scores three months after critical care discharge, the length of time within critical care did not. The authors did not provide an explanation for this although they recommended further investigation in a larger cohort.

Objective measurement of trauma severity using the Therapeutic Intervention scoring system (TISS), (Cullen et al 1974), was not found to be predictive of PTSD in this study. This was somewhat surprising given that Brewin et al (2000) found a small to moderate effect size for trauma severity in civilian samples. Although two critical care studies (Hamanaka et al 2006; Boer et al 2007) found objective measurement of injury and illness severity to be predictive of PTSD, Schnyder et al (2000) did not, although participants' subjective report of accident severity was found to be predictive of PTSD.

Deja et al (2007) found that anxiety experienced whilst on ICU predicted PTSD and Samuelson et al (2007) reported predictors of extreme fear and agitation during ICU stay. In five studies reviewed by Ozer et al (2003), individuals who described having intensely negative emotional responses during or immediately after the index traumatic event, reported much higher levels of PTSD symptoms or rates of current PTSD. In this study however, patients' subjective measures of perceived stressfulness for the trauma were not found to be predictive of PTSD. One possible explanation for this might have been due to the timing of the assessment, which was conducted two weeks after critical care discharge. Asking about trauma intensity early after the event, when individuals still feel numb and unable to appraise what has happened, might produce underestimates of trauma intensity (Brewin et al 2000), although this finding is not consistent (Walters et al 2007).

In this study only two pre-trauma characteristics, gender and sense of coherence (SOC) scores were included in the analysis, but only the SOC score was found to contribute to the predictive models where low scores at both the two week and at one-month assessment were factors among other variables that predicted PTSD at three months. This finding supports that of Schnyder et al (2000) who also found a negative correlation of the SOC score with the CAPS in their study of seriously injured accident victims admitted to ICU.

Four (Girard et al 2007; Samuelson et al 2007; Schnyder et al 2000; Boer et al 2007) critical care studies found female gender to be predictive of PTSD, which was noteworthy considering that two (Schnyder et al 2000; Boer et al 2007) of these studies were biased in favour of male gender. In this study with an equal distribution of males and females in the sample, female gender was not found to predict PTSD. The reliability of the self report questionnaires to detect PTSD in all but one (Schnyder et al 2000) of these studies would have been the most plausible explanation except that effect size for gender, through questionnaire assessment has been found to be lower than that conducted through interviews (Brewin et al 2002). One further suggestion put forward also by Brewin and colleagues is the possibility that effects are mediated by later aspects of the trauma or of the person's response to the trauma and given the large effect size in this study for the DTS scores, gender effect may have become somewhat diluted.

16.3 - Strengths and Weaknesses of the Methodology

The main strengths and weaknesses of the study were discussed in chapter 13 and will not be repeated in this chapter. Instead, the strengths and weaknesses as they apply to this part of the study will be described.

The use of a prospective design, in determining early predictive factors for PTSD is one of the strengths of the study. In examining predictive factors at 2 weeks and one month, evidence for risk for PTSD prior to hospital discharge and later at a follow up clinic may be helpful in terms of informing practice. The recruitment of a broad case mix of patients into this study was more typical of an overall critical care population and adds to a somewhat limited body of evidence that currently exists within the critical care prospective studies.

This is the only study with a broad case mix of patients to have investigated predictors of PTSD, determined by a gold standard structured clinical interview. The overall effect size of all the predictive models in this study was large and therefore may be strongly predictive of PTSD. The main weakness of this study was the sample size, which was modest although larger than 50% of other critical care predictive studies. This modest sample size however does mean there is a risk for false positive association and this, needs to be considered when interpreting the results.

Although the findings in this study for acute emotional distress as a predictor of PTSD concurs with other critical care studies, there were two other potential predictors in the existing critical care evidence of which one, participant age, was not selected for inclusion and the other, gender, was included. The selection of variables for the model, were those most comparable to the findings of Brewin et al (2000) and Ozer et al (2003). A decision to exclude age was determined by the overall number of variables recommended (Altman 1991) for the sample size, and its' weaker association with PTSD than many other independent variables in the meta analyses.

16.4 - Summary

The findings from this study concur with those of other critical care studies for a consistent predictive effect of traumatic stress symptoms, within one month of discharge from critical care, on the development of later PTSD. Prolonged critical care stay and impairment in health related quality of life in the physical composite domain at one-month also contributed to the predictive models in this study. These are consistent with some previous findings in the critical care studies and with the findings of Brewin et al (2000) and Ozer et al (2003).

Chapter 17 - Discussion - Other Outcomes and the Effect of Time.

17.1 - Statement of Principal Findings.

This study found very high rates of depression and anxiety in survivors of critical care, two weeks after discharge. Although the rate of anxiety and depression reduced significantly over time, a large percentage of patients remained affected at six months. Cognitive function was impaired although this improved significantly over time. Health related quality of life for survivors was impaired but improved significantly over time. Despite the improvement, physical functioning summary scores remained lower than that of the 1998 general US population norms (cited in Ware et al 2002, p 82) at six months, but mental health domains were slightly better than the norms at six months.

17.2 - Comparison with other Critical Care Studies.

Our understanding of the full impact of critical illness and admission to critical care for those who survive it is still in its infancy. We have much still to learn. Survival as the main outcome measure of interest is a poor "metric" for describing the impact of critical care (Broomhead & Brett 2002). Psychological issues also influence recovery after critical care and by ensuring that all aspects of a patient's health is cared for we may be able to provide a more optimal environment for recovery.

17.2.1 - Anxiety and Depression

In this study, two weeks after critical care discharge, rates of anxiety and depression as determined through the HADS (Zigmond & Snaith 183) were 40% and 40% respectively. Only one (Rattray et al 2005) of the critical care studies identified had previously reported evidence of anxiety and depression at this time. The rate of anxiety and depression at the two-week follow up in Rattray and colleagues' study was similar to this study, although their sample size was a little larger and participants' stay within critical care was shorter. The

same clinical measure and cut off scores to detect anxiety and depression was used and participants were of a similar age to those who took part in this study.

One month after critical care discharge, the rate of anxiety and depression in this study had reduced to 30% and 27% respectively. No previous critical care studies had reported rates of anxiety or depression at this time, although Samuelson et al (2007) provided rates of anxiety (4.9%) and depression (7.5%) at two months, which were much lower than those found in this study. One possible explanation for the particularly low rate of anxiety in that study may have been the loss to follow up at two months of 15 patients, found to have significantly higher levels of anxiety at discharge, although actual rate at discharge was not reported. Other differences compared to this study were that participants in Samuelson and colleagues' study were older and had a shorter stay within critical care. The shorter stay within critical care, suggests that the physical recovery of survivors may have been faster and the use of a higher cut off score of 11 on the HADS meant that patients with mild anxiety and depression were not included in the overall rates reported. The time difference in symptom assessment between this study and Samuelson and colleagues', suggested some natural resolution of symptoms might have occurred.

Three months after critical care discharge, anxiety and depression in this study reduced to 28% and 22%, respectively. Three (Eddleston et al 2000; Sukantarat et al 2007; Young et al 2005) broad case mix studies reported rates of anxiety and depression at this time. Eddleston and colleagues found lower rates of anxiety (11.9%) and depression (9.8%) than this study, despite the use of the same clinical measure and cut off score. The most plausible explanation for the lower prevalence rate was a shorter stay within ICU, younger age group, higher ratio of male patients and reported high levels of satisfaction for the speed of recovery.

Interestingly, in a later study conducted in the same ICU, Young et al (2005) found a much higher rate of anxiety (25%) and depression (15%), than previously found by Eddleston et al (2000). The rate of anxiety and depression reported was lower than in this study. A full comparison with this study was restricted by the incomplete participant data in their report, although participants were of a similar age, their sample size was smaller and patients with ongoing mental health problems were excluded.

Sukantarat et al (2007) reported rates of 16% and 22% for anxiety and depression respectively, in 51 survivors. By comparison, the rate of anxiety was much lower but the rate of depression was higher, than this study. The use of the higher cut off score of 11 on the HADS suggested rates of anxiety and depression would be higher than reported. By comparison, there were fewer males and the duration of critical care stay was twice that of participants in this study.

The rate of anxiety and depression at six months in this study were 21% and 18%, respectively, which was a further reduction over time. Three (Jones et al 2003, Kress et al 2003; Rattray et al 2005) other critical care studies with a broad case mix of participants had reported psychological morbidity at this time, but only two of these had used the same clinical measure.

The rate of anxiety (33%) and depression (11%) reported by Jones et al (2003) was based upon the higher HADS cut-off score of 11. Using the same HADS cut off score in this study for comparison, the rate of depression (13%) was similar, but anxiety was much lower (10%). Although characteristically participants' in Jones and colleagues' study were similar, they had twice the length of stay in critical care, compared to participants in this study. It is possible that this led to a more protracted recovery, which may have resulted in higher rates of anxiety. However, participants' in the study also had high mean trait anxiety scores (42), which has been associated with perceived vulnerability (Mayall et al 2008) and subsequent development of high levels of anxiety (Beck 1985; Barlow 2002)

The differences and similarities between this study and that of Rattray et al (2005) have already been discussed and will not be repeated here. Despite a number of similarities between the two studies, the high rate of anxiety found by Rattray and colleagues' was twice that found in this study at six months. Participants in Rattray and collegues study were all emergency admissions whereas 26% of participants in this study were electively admitted to critical care. One further possible explanation for the higher rate of anxiety may have been due to individuals' perception of their experiences, since subjective reporting of frightening experiences by participants in Rattray and colleagues' study was associated with higher anxiety scores at six months. By comparison, participants in this study subjectively rated their ICU experience as only moderately stressful. The lower rate of depression found

in this study compared to that found by Rattray et al was noteworthy particularly given that participants in this study had a slightly longer critical care stay, but may be linked to the differences in subjectively rated experiences of the two populations studied. This is further supported by their findings of subjective interpretation of the intensive care experience that emerged as a consistent predictor of adverse emotional outcome, in both the short and the long-term.

The lack of prospective longitudinal studies in the critical care literature limits the opportunity to compare the findings of reduced anxiety and depression over time in this study and others. On examining the outcome of 80 of their survivors over a one-year period, Rattray et al (2005) found a significant effect for time for anxiety and depression, according to HADS scores. This change occurred between hospital discharge and 6 months, but no further reduction was found between 6 months and one year. Although follow up in this study did not extend to one year, our findings echo those of Rattray and colleagues' findings for the first six months.

Hopkins et al (2005) investigated two-year outcomes in survivors of ARDS, using the mental health sub domain of the SF36 (Ware et al 1993), as opposed to specific measures for anxiety and depression. The mental health domain showed an improvement during the first year and then declined to the hospital discharge level at 2 years, which was attributed to decreased life satisfaction and lower health related quality of life. The findings of improvement during the first year was consistent with this study, but raises an interesting question regarding longer term outcome that was not addressed in this study.

17.2.2 - Cognitive Function

Two weeks after critical care discharge, this study found that 11 (12%) participants displayed evidence of cognitive impairment, according to the Addenbrooke's Cognitive Examination (ACE-R) (Mioshi et al 2006). According to the Mini Mental State Examination (MMSE) (Folstein et al 1975) only 8 (9%) participants in this study scored below the normal cut off. This is in stark contrast to Hopkins et al (2005) who found neuro-cognitive impairment in 73% of 74 survivors of ARDS at hospital discharge. Whilst this may be due to prolonged periods of hypoxemia in these patients (Hopkins et al 1999), other contributing factors may

be the prolonged period of intubation (28 days), which most likely entailed longer periods of sedatives and analgesia. The use of benzodiazepines and opioids and the cumulative doses have been previously associated with cognitive impairment (Ersek et al 2004; Stewart 2005).

At a slightly earlier time of one week after discharge from critical care, Jones et al (2006) investigated cognitive function in 30 survivors of a prolonged critical care stay. Using a computerised software programme, they found 6 (20%) participants had difficulties with problem solving and 15 (50%), problems with memory. In this study, although the mean score in the memory sub domain of the ACE-R was 22.3(SD3.1) which was well above the cut off score of 18, nine (10%) patients had memory impairment. This was very much lower than that found by Jones and colleagues. The ACE-R is proficient in terms of memory evaluation because of its ability to investigate both short term and long term memory and because 26 out of 100 total ACE-R points is used to determine this (Tarek 2008). Although the ACE-R does not measure problem solving specifically, it does measure attention and concentration, which is associated with problem solving. In this study, only 5 (5.6%) patients scored below the cut off of 17 for attention and concentration, which again was much lower than that found by Jones and colleagues. The earliest assessment of cognitive impairment in this study was two weeks after critical care discharge. Participants in Jones and colleagues' study were first tested on ICU, but only three days after cessation of all sedatives and analgesics. Some studies have shown that although cognitive dysfunction improved after benzodiazepines were withdrawn, patients did not return to levels of functioning that matched benzodiazepine-free controls (Stewart 2005). Participants in the study had also spent twice the length of time within critical care, compared to participants in this study.

One month after discharge from critical care, the extent of cognitive impairment had improved in this study and only 5 (6%) patients were impaired according to the ACE-R, whilst 4 (5%) scored below the normal cut off according to the MMSE. There were no comparable critical care studies of assessment of cognitive function at this time, although Jones et al (2006) had continued their assessment of long stay patients who were followed up in an outpatient clinic, two months after discharge from critical care. They found that 5 (31%) participants had memory impairment and 8 (50%) had difficulties with problem solving. In this study, only 2 (2.5%) patients scored below the threshold of 18 for memory

impairment and 3 (3.8%) patients scored below the cut off of 17 for impairment in attention and concentration.

Three months after discharge, cognitive function for participants in this study showed further improvement with only 3 (4%) participants found to have cognitive impairment according to the ACE-R and 3 (4%) who scored below the normal MMSE cut off. Two (Sukantarat et al 2005; Nelson et al 2006) studies from the critical care literature assessed cognitive function at this time. Three months after critical care discharge Sukantarat et al (2005) investigated cognitive performance, specifically executive function in fifty-one patients who had undergone major surgery. The authors found that 18 (35%) patients had two or more abnormal tests of cognitive performance. In terms of executive function in this study, participants may have been comparable to some participants investigated by Sukantarat et al, since 8 (17.8%) performed below the cut off of 15 in the visuo-spatial domain of the ACE-R at three month follow up. In tests of executive function, performed by Sukantarat and colleagues, 9 (18%) patients scored at or below the 5% level of normal values in the Six Element Test (Burgess et al 1996). Participants were also considered highly impaired, according to the age-adjusted norms for the Hayling Sentence completion task (Burgess & Shallice 1997).The sample size recruited by the investigators however, was smaller than this study, but participants were only slightly older and critical care stay was longer by two days. The majority of patients (71%) had undergone major surgery and this and anaesthesia has been found to affect cognitive function, particularly in the elderly (Moller et al 1998).

Nelson et al (2006) investigated brain dysfunction in 98 survivors, three months after discharge from a respiratory care unit, using the telephone version of the Confusion Assessment Method (CAM -T) (Marcantonio 1998). The authors found that although 23 (23%) patients were not suffering with delirium, 75 (77%) of them were believed to be too impaired to participate in the interview when contacted. The participants in the study however had considerably extended time in ICU (45 days), as the respiratory care unit was specifically for patients who failed to wean from conventional ventilation and over 60% were admitted for acute or chronic lung conditions.

Six months after discharge from critical care, only 3 (5%) patients were impaired according to the ACE-R, whilst 2 (3%) scored below the MMSE cut off in this study. There were two (Nelson et al 2006; Jackson et al 2003) studies for comparison from the critical care literature that had investigated cognitive function, six months after critical care discharge. As a follow up to the three month, assessment discussed above Nelson et al (2006) conducted the six-month assessment to assess 85 survivors. Using the CAM -T, the authors found that 25 (29%) patients were not delirious and 60 (71%) patients were so profoundly impaired that they were unable to participate in the telephone assessment.

Jackson et al (2003) examined neuro-cognitive function in thirty-four survivors of mechanical ventilation, six months after critical care discharge. They found that 11 (32%) patients were impaired primarily in areas of psychomotor speed, visual and working memory, verbal fluency and visuo-construction. Participants' mean MMSE scores were reported as 24.4. In this study the mean MMSE at six months was much higher than that found by Jackson and colleagues, in fact participants' mean MMSE at two weeks in this study, was higher than that of the "non impaired" in Jackson and colleagues' study at six months. Sample size was very small and although participants were of a similar age, the length of stay in critical care was longer and there was a high rate of participants with respiratory failure, compared to this study.

Comparing the results of cognitive impairment in this study to the other published studies proved difficult mainly because of the diverse selection of clinical measures used in the critical care studies. The most fundamental difference was that participants in this study did not display the extent of cognitive impairment found in the other studies. This in it self is somewhat intriguing. One characteristic difference between this study and that of the five compared, was that participants in this study had a mean critical care stay of 7 days whereas participants in the compared studies had longer mean stays ranging from 9 - 44 days. Although intuitively this may have suggested that patients in this study were less sick, neurocognitive dysfunction observed in survivors of critical illness cannot simply be explained in terms of the degree of acute illness severity (Hopkins et al 2007). Alternatively, one review suggested that there were likely to be multiple mechanisms at work in any given patient (Millbrandt & Angus 2005). One further noteworthy point of that review was for the role of hyperglycaemia in cognitive dysfunction, where the duration of blood glucose

greater than 180mg/dl was found to correlate with worse visuo-spatial tasks, visual memory, processing speed and executive function. This was interesting because the critical care unit that participants were recruited from in this study, has had a stringent "tight glucose control" policy in operation for a number of years, including the time of study recruitment. Finally, one similarity found in this study compared to that reported by Hopkins et al (2005) was that cognitive impairment improved overall over time.

17.2.3 - Health related quality of life

In this study, two weeks after critical care discharge, participants were found to have a mean Physical Composite score (PCS-12) 2.1σ (21 points) and a mean Mental Composite score (MCS-12) 0.37σ (3.7 points) below the norms for the 1998 general US population (cited in Ware et al 2002, p 82). One (Douglas et al 2002) study reported values of health related quality of life after discharge from critical care.

Douglas et al (2002) examined survival and health related quality of life (QOL) in short term (STV) (> 24 hrs / ≤4 days) versus long term ventilated (LTV) (≥5 days) patients, within two weeks of critical care discharge. A precise comparison to this study was not possible because the Sickness Impact Profile (SIP) (Bergner et al 1981) was used to assess QOL. However, participants in this study were most comparable to the STV participants in relation to critical care length of stay, although the participants in this study were much younger (55 years v 66 years). The participants in this study appeared to have been slightly more impaired in terms of physical functioning at two weeks, but 14 (16.7%) STV patients were discharged with oxygen, which suggested otherwise. Two participants in this study were referred for formal rehabilitation, whereas 48% of STV patients required this facility although this was more likely a reflection of the differences in the healthcare systems between the UK and the US. Participants in this study showed a significant improvement in their health related quality of life over six months, whereas STV patients were reported to have improved consistently. There were significant differences between the STV and LTV patients in some aspects of health related quality of life, but whether they improved significantly over time was not reported. It was clear however, that health related quality of life for participants in this study was considerably impaired, two weeks after critical care discharge by comparison to population norms. The provision of formal rehabilitation care as in the US, in terms of improving overall health related quality of life is an interesting one.

One UK randomised controlled study (Jones et al 2003) of a self-help rehabilitation programme, versus follow-up with no rehabilitation, demonstrated an improvement in health related quality of life and depression, for the rehabilitation group compared to the control. Although further psychological care was deemed necessary for both groups, the improvement in health related quality of life through a self-help programme was noteworthy.

At the one-month assessment in this study PCS-12 had improved but was still 1.6σ below the general US population norms, whilst the MCS-12 remained the same as at the two-week assessment. Hofhuis et al (2008) investigated health related quality of life in survivors of admission to critical care of 48 hours and longer. At hospital discharge, survivors were found to lower scores in physical functioning, general health and mental health domains, higher scores in role physical, bodily pain, vitality and social functioning, whereas the role emotional domain was similar to participants in this study. Both the PCS-36 and MCS-36 scores were higher than participants in this study. The differences in scores, may have been due to older age (69 years), a longer period of mechanical ventilation (9 days) and a longer stay in critical care (13 days), compared to participants in this study. However, the mean length of hospital stay for participants in Hofhuis and colleagues' study was 37 days, which meant the discharge assessment took place at least one week later than that of participants in this study. The higher scores in role physical and social functioning were interesting, particularly given that participants in Hofhuis and colleagues' study were still in hospital at the time of the assessment. It is possible that the lower scores of participants in this study were a truer reflection of their limitations because of being at home, whilst the higher scores in physical functioning, general health and mental health domains, may have been influenced by being in their home environment.

Boyle et al (2004) found that participants had profoundly decreased HR-QOL when compared to age- and sex-adjusted Australian population norms. The score for the general health domain was slightly higher (49.2) compared to this study (47.5) but all other domains were lower than this study. Participants in Boyle and colleagues' study had a similar length of stay in critical care, but were slightly older (59 years) than participants in this study (55 years). It would be unlikely that four years would make a significant difference in terms of

health related quality of life, when previously no significant differences were found between participants aged above and below 65 years of age (Ridley et al 1997). Boyle and colleagues' participants differed in relation to male gender (63% v 46%), a shorter period of ventilation (2.4 v 3.6 days), a higher rate of medical admissions (48% v 34%), higher rate of elective surgical admissions (30.3% v 23.3%) and a lower rate of emergency surgical admissions (21% v 53.7%) respectively, compared to this study. Although the investigators used a depression rating scale, prevalence was not reported, but the population mean score ($19.2(_{SD}10.4)$) was in the moderately depressed range (16 - 24) of the subscale score. In addition, 46% of participants reported pain on more than half of the days since discharge. This suggested, in conjunction with a lower mental health domain score compared to participants in this study, that depression and pain may have influenced overall perception of health related quality of life in the study.

At three months in this study, PCS-12 had again improved but remained 1.2σ (12 points) below that of the US population norms. The MCS-12 had also improved at this time and was 0.05σ (0.53 points) above the US population norms. Four (Hofhuis et al 2008; Capuzzo et al 2006; Cuthbertson et al 2005; Eddleston et al 2000) studies had investigated QOL at this time. Unfortunately Capuzzo et al (2006) used the Euroqol (EQ) (Euroqol group 1990) and an additional question to determine outcome and so, only a narrative comparison was possible. According to the additional question, 189(33.8%) participants reported their health as "better", 174 (31.1%) the "same" and 196 (35.1%) "worse", compared to a retrospective assessment of health status, three months prior to admission. The reliance on retrospective recall of health may not be accurate, as it may have been influenced by the health status at that time.

Three months after discharge in Hofhuis and colleagues' (2008) study, both the PCS and MCS scores were similar to those found in participants in this study, which was interesting given participants in this study were younger and had a shorter stay in critical care. Although studies of elderly survivors of critical care are fewer than younger survivors (Merlani et al 2007), older patients have been previously found to adapt well (Mahul et al 1991) and accept a lower level of physical functioning (Carson 2003). This may explain the similarities in the health related quality of life summary scores.

Eddleston et al (2000) used the 36-item short form health survey (SF36) (Ware et al 1992), whereas in this study the shorter generic measure that provides summary information on physical and mental health status was used. In this study, the QOL values are based upon the summarised scores for PCS-12 that comprises the Physical Functioning, Role Physical, Bodily Pain, and General Health domains. The MCS-12 comprises the Vitality, Social Functioning, Role Emotional, and Mental Health domains of the SF12. Although Eddleston and colleagues provided a full profile of scores across the eight domains of the SF36, the use of the same eight dimension summary from the SF-12 was previously not recommended (Jenkinson et al 1997), however the revised version 2 of the SF-12 is comparable (Ware et al 2005, intro p.5). Eddleston and colleagues reported that scores on all domains of QOL were numerically much lower than the general UK population norms except in the mental health domain. In this study, all summary scores except those of emotional role and vitality were lower, than of those reported by Eddleston and colleagues. Patients in their study however were younger and had a shorter stay in critical care, which may explain the differences. They did not calculate the PCS-36 and MCS-36 summarised scores and so comparison between the studies in that respect was more difficult. However although the mental health and social functioning domain scores were higher than in this study, the vitality and role emotional domains that make up the summarised MCS scores were lower. Whilst this suggested that overall mental health of participants in this study may have been better than those in Eddleston and colleagues' study, the more specific measures used to determine anxiety and depression showed that participants in this study had higher rates of anxiety and depression. One possible explanation for this discrepancy may have been in the selection of an acute or standard SF measure. The acute measure asks for a one-week recall and the standard, a one-month recall. The HADS on the other hand asks about symptom occurrence over the preceding week. In this study, the standard questionnaire was used, whereas, this information was not provided by Eddleston and colleagues. This would seem the most rational explanation given participants in Eddleston and colleagues' study, also reported satisfaction in the progress of recovery since their critical care discharge.

Cuthbertson et al (2005) used the SF36 to determine outcome in their study and provided PCS-36 and MCS-36 scores. At three months, participants' mean PCS-36 were lower than

that found in this study, but MCS-36 was higher which suggested that although their participants were more physically impaired, mental health status was better than in participants in this study.

In this study, six months after critical care discharge, PCS-12 was 37.9 and MCS-12 was 50. This represented a further improvement over time in both scores. The PCS however, remained 1.2 σ below the US general population norms, whilst MCS was 0.08 above the norms. At six month follow up Cuthbertson et al (2005) also found that PCS-36 was lower and MCS higher than population norms. By comparison to this study however, their participants PCS-36 scores were lower and MCS-36 scores were higher which again suggested that participants in this study although physically better, were more impaired in terms of mental health. Although participants in Cuthbertson and colleagues' study had spent a similar length of time in critical care, they were older than participants in this study, which may partly explain the differences observed between the studies; however, both samples were small and potentially underpowered.

Ridley and colleagues (1997) unfortunately did not include any of the SF36 values for the six-month assessment in the written report but instead provided a narrative. Having retrospectively assessed participants' premorbid health related quality of life at critical care discharge, they compared this to an assessment conducted at six months and found improvements in mental health, social functioning and vitality domains and also in the bodily pain domain, compared to pre morbid values. In this study, health related quality of life at six months was compared to actual baseline values and not that of pre morbid health related quality of life. So although there were improvements in QOL over time in Ridley's study, this was based upon retrospectively assessed pre-morbid QOL.

Michaels et al (2000) also compared six-month health related quality of life data to that retrospectively assessed for one month prior to admission. All QOL domains were found to be lower than those of the retrospectively assessed QOL. The greatest impairments for their participants were in the role physical and physical function domains of the SF36. The participants in Michaels and colleagues' study differed to participants in this study in that they were all survivors of traumatic injury, of which a number had sustained extremity fractures, which may explain the extent of physical impairments identified.

At the six month follow up, Boyle et al (2004) found significant improvements in four domains of the SF36, whereas general health, bodily pain, role emotional and the mental health domains, were no different compared to the one month assessment. In this study, the scores on the individual domains were higher than those of participants in Boyle and colleagues study, except for the mental health domain which was similar. There was also a significant improvement over time for PCS-12 and MCS-12. Although there were some characteristic differences between the study participants, none was thought particularly significant to account for the differences in health related quality of life. However, 43% of participants in Boyle and colleagues' study reported pain at six months, which was not dissimilar to the one-month assessment. It is possible that lack of improvement in health related quality of life, may have been due to a maladaptive response shift (Sprangers & Schwartz 1999), where the participants, having experienced a life threatening illness, failed to accommodate the change in health status.

At the six-month follow-up to their study, participants in Hofhuis and colleagues' study were found to have lower PCS scores but higher MCS scores, compared to participants in this study. With regards to individual domains at six months, physical functioning, general health and social function were below the population norms, whereas in this study all domains were above the population norms. Over the six-month period of the study Hohuis and colleagues found PCS- 36 had improved significantly, although there was no difference for MCS-36 scores. In this study however, there were significant differences for both summary scores. The differences between the studies were most probably relative to the age of participants.

Some (Pettila et al 2000; Rothenhausler et al 2001; Kapfhammer et al 2001; Heyland et al 2000) studies not discussed in this chapter have suggested a profound decrease of health related health related quality of life, but these are mostly associated with specific critical care patient groups, such as survivors of ARDS, MOD and sepsis. With regards to participants comprising a more broad case mix it was evident from the compared studies and the findings of this study, that physical aspects of health related quality of life were impaired at six months compared to population norms. However, the findings from this

study concur with those of others, in that there is an overall improvement in health related quality of life over a six-month period compared to that identified after discharge from critical care.

17.3 - Strengths and Weaknesses of the Methodology.

The strength and weakness of this study have been described earlier and will not be repeated here, although specific methodological issues that apply to this part of the study will be discussed.

The main strength in this part of the methodology was the full data set at baseline for all outcome measures and no missing data at all follow up assessments for all outcome measures. The use of the HADS was considered a strength of the study because it has been widely used in the critical care studies and was thus comparable to many studies. In addition to this, it was one of only two clinical measures recommended to detect anxiety and depression in survivors of critical care treatment (Hayes et al 2000). The detection of anxiety and depression through a structured clinical interview would be considered a more accurate method for diagnosis, compared to a self-report questionnaire.

The ACE-R has not been validated within the critical care population and this was the first time it has been used. The lack of validation within the population was a weakness, although the questionnaire has been well validated in other populations and is considered a much-improved revision of the original questionnaire (Mioshi et al 2006). The other weakness in terms of the use of the ACE-R was that no other studies had used it and therefore the accuracy of comparison of findings from the other studies may be questionable. However, of the studies compared, all the clinical measures used were different.

The decision to use the SF12 as a health related quality of life measure in this study was mainly based upon the length of the questionnaire and consideration of respondent burden in light of the number of other questionnaires in this study overall. Furthermore, comparisons between the SF-12 and the SF-36 suggests, the SF12 is a reliable, valid and responsible measure that is comparable to the SF-36 and suitable for comparing groups of

patients (Hurst et al 1998). Not all studies used the SF summary scores and there are clear benefits to their use, the main one being that they reduce the risk associated with multiple statistical comparisons between subscales of significant findings arising by chance (Hurst et al 1998). One of the possible strengths of this study therefore, may be that the statistical finding of a significant improvement in summary scores over time may be more reliable than that suggested in some studies.

One of the difficulties in determining health related quality of life in survivors of critical care was not knowing how this compared to participants' health related quality of life prior to admission. A subsequent weakness therefore may have been the lack of a retrospective assessment of health related quality of life, or that acquired through a close relative. A proxy response from a relative or significant other has been considered satisfactory, although they have been found to underestimate physical health domains of HR-QOL and overestimate mental health domains, particularly at the time of the ICU stay (Diaz-Prieto et al 1998). Conversely, retrospective assessments are prone to inaccuracy and often inflated reporting.

One further weakness of the methodology may have been the comparison in this study to that of a general US population. This was done because the values were provided with the Instruction Manual purchased for the study. Given the selection of international studies in the critical care literature and comparisons to many international population norms, this may be a minor weakness only.

17.4- Summary

The findings from this study suggest post discharge burden is indeed high for some patients. Anxiety and depression are considerable problems after discharge from critical care and although symptoms reduce for some patients, a proportion experience enduring symptoms that extend beyond six-months. Cognitive function of participants in this study with a shorter treatment time in critical care was less impaired compared to other studies of survivors who experienced a prolonged critical care stay. Health related quality of life is impaired after critical care treatment and although full function is not attained following a six-month recovery, recovery does occur although progress can be slow. There is a clear

need for more prospective longitudinal studies for all critical care populations and standardisation of clinical measures.

Chapter 18 - Discussion of Predictors of Impaired Health related quality of life after critical illness.

18.1 - Statement of Principal Findings

Two week HADS anxiety and depression scores, critical care length of stay and having a past psychiatric history (PPH) contributed to the predictive models of impairment in the PCS-12. HADS anxiety and depression scores and PPH contributed to predictive models of the MCS-12. The lowest variance was 11% and the highest was 34%. The psychological variables of anxiety and depression made the largest contribution to the predictive models over those of the participant specific characteristics.

18.2 - Comparison with other studies

Five (Hopkins et al 2004; O'Donnell et al 2005 Weinert et al 1997; Schelling et al 1998; Deja et al 2006) studies have previously found associations between psychological factors and impairment in health related quality of life. The findings from this study add to that body of evidence. Most importantly, to my knowledge, this is the first broad case mix study to have found that anxiety and depression predicted impairment in health related quality of life. All the studies so far that have found associations between psychological factors and impaired health related quality of life have been those conducted either after trauma (O'Donnell et al 2005) or after ARDS(Hopkins et al 2004; Schelling et al 1998; Deja et al 2006) or ALI(Weinert et al 1997).

The findings from this study suggested that some psychological factors, namely past psychiatric history (PPH), anxiety and depression, were responsible for the impairment in the physical and mental health summary scores of health related quality of life. Some interesting findings of this study were the absence of an association of traumatic stress symptoms with health related quality of life and the consistent influence of anxiety and

depression over time on impairment, where anxiety, depression or both of these contributed to all the predictive models studied.

18.2 .1 - Anxiety and depression

Anxiety and depression have been previously associated with impaired health related quality of life in survivors of ARDS (Hopkins et al 2004) at a one-year follow up. The authors found significant negative correlations for anxiety and depression with all SF36 domains of health related quality of life, except physical functioning. Unfortunately, only correlation analysis was used to determine these findings and although the associations were large, the correlation method only demonstrates a relationship between the variables.

O'Donnell et al (2005) used structural equation modelling, a multivariate technique combining aspects of multiple regression and factor analysis, to simultaneously estimate the strength of the relationships between variables (Hair et al 1998). They found high levels of acute stress and depression assessed eight days after injury were significant predictors of impaired health related quality of life for survivors at a one-year follow up. Although follow up in this study did not extend to one year, O'Donnell and colleagues' finding for depression severity scores as a predictor, concurs with findings in this study where depression predicted PCS-12 at one-month and MCS-12 at one, three and six months. The findings reported by the authors of acute stress disorder severity as part of the predictive model, contrasts with findings in this study, as CAPS total score did not predict health related quality of life at any follow-up time, although the follow-up in this study did not extend to one-year. Sample size in this study however was relatively small which suggests the possibility of error, can not be ruled out.

There is other evidence of PTSD and depression and association with impairment in functioning and health related quality of life (Roberto et al 2008; Zatzick et al 1997), but the association of acute anxiety and depression with impaired health related quality of life have been similarly identified in other studies (Holbrook et al 1999; Michaels et al 2000). There were, however, a number of other differences between this study and that of O'Donnell et al. The participants in O'Donnell and colleagues' study were younger (36 yrs v 55yrs), comprised a larger male population (75% v 51%) and were mostly survivors of motor vehicle

accidents (74%). The greatest limitation in respect of a comparison with this study was that the model demonstrated by O'Donnell and colleagues was based upon a sample of 363 survivors, of which only 31% were admitted to critical care.

Depression was found to be associated with the MCS-36 in a study of acute lung injury survivors, 15 months after discharge (Weinert et al 1997), but the association was through correlation only. Michaels et al (2000) however, found that depression score at twelve months, with other variables, was predictive of SF36 mental health at twelve months. Although this study did not extend to a twelve-month follow-up, depression was a consistent predictor of MCS-12 at all assessment times. The depression score in Michael and colleagues' regression model was not the strongest predictor (11.6%), but in combination with the other variables, the predictive model accounted for 62% of the variance, which was much larger than in this study. At one month, three months and six months, the models accounted for 34%, 34% and 28% respectively, of the total variance of the MCS-12, in this study. Participants in Michaels and colleagues' study differed however, from participants in this study, in respect of age (37yrs v 55yrs), male gender (73% v 51%), and prior history of mental health problems (19% v 27%). There was also a high rate of alcohol problems (67%) and drug abuse (26%) in their sample and 17% of participants had blood alcohol levels above the legal limit. Although only 19% of the participants' in Micheal and colleagues study admitted to having prior mental health problems, ,which was lower than participants in this study, the rate of drug and alcohol abuse suggested that this may have been much higher, given the prevalence of co morbid substance abuse with mental illness (Tiet & Mausbach 2007).

18.2.2 - Critical care stay

Impairment in physical functioning and the role physical domains were significantly associated with critical care length of stay in survivors of ARDS (Hopkins et al 2004). The significant correlation of critical care total stay with the physical function and role physical domains in Hopkins and colleagues' study, although statistically, only a relationship, were relevant to the findings of this study. Regression analysis conducted for the three-month health related quality of life in this study showed critical care total stay contributed to the

predictive model of impairment in PCS-12, along with other variables, where collectively they accounted for 23% of the total variance of the PCS-12 score.

One (Fildissis et al 2007) other study found similar associations with the critical care total stay and impairment in health related quality of life. Fildissis et al (2007) conducted a multilinear regression analysis to identify the factors that influenced health related quality of life on ICU admission and after ICU discharge. They found strong positive associations with impairment in health related quality of life for critical care length of stay, male gender and age. Age and gender were not included in the regression model in this study, because there was insufficient evidence to support their inclusion. There was a limitation to their findings however, in that the authors used a translated version of the QOL-S (Fernadez et al 1996), but did not validate their translation.

18.2.3 - Past psychiatric history

To my knowledge, PPH has only previously been shown to predict impairment in health related quality of life after critical care treatment in one (Michaels et al 2000) other study. One possible explanation may be that such patients are frequently excluded from participation in psychological research studies. It would be impossible to say if PPH was included as a variable in other regression models because typically, variables included in the analysis in most studies are rarely provided. In Michael and colleagues study (2000), the baseline SF-36 mental health domain score was found with other variables to contribute to the predictive model of the SF-36 general health domain score at twelve months. They also found baseline SF36 mental health domain score, with other variables, accounted for 61% of the total variance of the SF-36 mental health domain score at twelve months. The population differed to this study's however, in that they were all younger survivors of traumatic injuries of which 15% were intentional assaults and, as discussed earlier, they had a higher prevalence of prior mental health problems.

In this study, PPH and HADS depression score at two weeks predicted the MCS-12 score at three months and six months, accounting for 34% and 28% of the total variance, respectively. Along with critical care total stay and HADS anxiety score, at two weeks, PPH was found to predict the PCS-12 score, at three months, accounting for 23% of the variance. Whilst an association with the MCS-12 score may not be atypical, the association of PPH

with the PCS-12 score at three months is compelling. This population is commonly underrepresented in studies of some psychological investigations and past psychiatric history is usually unknown to critical care staff, following the patients' admissions to critical care (Jones et al 2007). Meta-analytical investigations of anxiety disorders found that all types of anxiety disorders were significantly associated with poorer overall health related quality of life (Olatunji et al 2007) and as illnesses that markedly compromise quality-of-life and psychosocial functioning in several functional domains (Mendlowicz & Stein 2000). Similar findings for poorer subjective health and reduced health related quality of life have also been reported for depression in cardiac patients (Norris et al 2007). Poor adherence to treatment regimes, attributed to depression, resulted in increased use of health services and costs by as much as 40%.

18.2.4 - PTSD

One further aspect of psychological morbidity identified after critical care treatment, found to be associated with impairment in health related quality of life in three (Schelling et al 1998; Michaels et al 2000; Deja et al 2006) critical care studies, is that of PTSD. Schelling and colleagues (1998) reported that major impairments in mental health domains of health-related health related quality of life were associated with the development of posttraumatic stress disorder and were a possible result of traumatic experiences during ICU therapy. Unfortunately, no statistical data was provided in the report to support the findings and therefore it was not possible to determine the method or reliability of the findings.

Déjà et al (2006) reported reduced health-related quality of life (HRQoL) in long-term survivors which was linked to an increased risk of chronic PTSD with ensuing psychological morbidity. There were however no regression analyses carried out in the study and the inference that chronic PTSD was linked to HRQoL, appeared only to be due to a significant difference between a "high scoring", "low scoring" and a healthy control group, according to a MANOVA. In this study although PTSD scores were included in the stepwise regression model, they were not found to be predictive of impaired health related quality of life in either of the summary domains. This finding was somewhat surprising given the evidence for impairment (Roberto et al 2008; Magruder et al 2004; Stein et al 1997; Zatzick et al 1997) from other PTSD studies.

A possible explanation for this was the small sample size in this study and the chance finding of no association. However, the two critical care studies that found an association between PTSD and health related quality of life also had small sample sizes but participants were survivors of ARDS and both were retrospectively designed studies, which may have resulted in some over-inflated reporting of symptoms. O'Donnell and colleagues' (2005) and Micheal and colleagues' (2000) findings were based upon survivors of severe accidental injury, all of whom were left with residual physical disabilities. Roberto et al (2008), Magruder et al (2004) and Zatzick, and colleagues' (1997) findings of an association between PTSD and impairment in health related quality of life were conducted in samples of war veterans and these samples were more likely to have chronic PTSD (Brewin et al 2000). The findings from this study were based upon acute symptoms, reported by a broad case mix of critical care patients, which may affect health related quality of life differently. However, all studies including this study, have measured general distress to a degree; despite being represented by discrete measures, the findings from this study of psychological symptoms, being associated with health related quality of life are consistent with other studies.

The prediction of impaired health related quality of life in studies that comprised broad case mixes would be most relevant to the findings in this study and yet only two (Capuzzo et al 2006; Fildissis et al 2007) have carried out this investigation. The absence of psychological predictors in the two studies was noteworthy and may even suggest that after a decade of evidence which has highlighted the prevalence of psychological morbidity during and after critical care treatment, illness characteristics are the more favoured outcomes investigated and appear to dominate many research investigations. This is a somewhat speculative view, but one difficult to prove otherwise and one major criticism of all the reviewed studies was that authors failed to provide full details of the independent variables selected for analysis, or even justify their selections.

18.2.5 - Miscellaneous predictors

Capuzzo et al (2006) reported some very unusual predictors that comprised illness characteristics at admission to critical care. To my knowledge, none were studied previously in relation to health related quality of life in other critical care studies, so it was unclear why

they were selected. One possible explanation for the selected variables wasthat they were meant to represent illness severity. An appropriate predictive analysis was conducted by the investigators, although the variance was found to be very low. In this study, the selection of the independent variables were based upon reported evidence and experience of following up patients after critical care discharge and although there were also some low variances found at some follow ups, the variance exceeded that found by Capuzzo and colleagues. While this suggested the predictors in this study may have been more important than those used by Capuzzo et al, at one month in this study the lowest variance of 23% meant that 77% remained unexplained. This suggested there were other important factors worthy of detection in future studies.

Injury severity score (ISS) (Baker et al 1974) was found to be directly associated with impaired health related quality of life in two (Michaels et al 2000; Ulvik et al 2008) studies and indirectly by O'Donnell et al (2005). The indirect association of injury severity score in O'Donnells' study was through structural equation modelling where injury severity was one of five variables that made up the latent injury variable. The latent injury variable was directly associated with both disability and impaired health related quality of life.
Ulvik and colleagues (2008), performed proportional odds ordinal logistic regressions on six selected variables and found that ISS and severity of illness scores (SAPS II) (Le Gall et al 1993) predicted mobility problems and in addition, SAPS II was related to reported problems in usual activities.
Michaels et al (2000) performed a Linear Regression for the SF36 general health score and found that ISS along with other variables contributed to the predictive model of the SF-36 general health domain score where collectively the variables accounted for 39% of the total variance.
In this study, TISS admission and discharge scores, as surrogates of illness severity, were entered into the regression model but were not found predictive of impairment in health related quality of life. This was a surprising finding, as it was expected that more severely ill individuals would spend a longer period in critical care and be therefore more debilitated, affecting physical aspects of health related quality of life. Discharge and admission TISS previously, has been found to be significantly associated with unfavourable outcomes in survivors of neuro-critical care (Broesnner et al 2007). Compared to this study, Broessnner

and colleagues sample were of a similar age and had a slightly longer critical care stay (9 days v 7 days), but their sample size was much larger than this study (567 v 90 participants). Although their sample comprised survivors of cerebrovascular diseases as opposed to a broad case mix, as in this study, the relatively small sample size meant the chance finding of no association in this study, could not be ruled out. The survivors from the other three critical care studies were survivors of traumatic injury and much younger, which may partly explain the association of illness and injury severity with impaired health related quality of life. Given that more elderly patients are generally more accepting of reduced health related quality of life (Carson 2003).

Although follow up in this study only extended to six months our findings supports the view of others (e.g. O'Donnell et al 2005), that an individual's acute psychological response will tell us much more about their individuals expected health related quality of life, than will the characteristics of their injuries or of hospital admission.

18.3 - Strengths and weaknesses of the methodology

The main strengths and weaknesses of this study have been discussed in an earlier chapter and will not be repeated here. Instead, the specific strengths and weakness that apply to this part of the methodology will be discussed.

Numerous comparisons between the SF-12 and the SF-36 have shown the SF-12 to be strongly correlated and similar to the SF-36. (Ware et al 2002, p164).From a practical perspective the SF12 has been judged more favourably to the SF36 because it incurs far less respondent burden (Jenkinson et al 1997), which was one of the reasons it was selected for this study. A further strength of the study was the use of MCS-12 and PCS-12 as the dependent variables instead of the eight SF12 domains. These summary scores facilitate hypothesis testing in clinical trials and reduce the risk associated with multiple comparisons of between the sub-scales, of significant findings arising by chance (Hurst et al 1998)

The checking of questionnaires completed by participants at each assessment meant that there were no missed questions on any of the SF-12 questionnaires. The capture of full data for all participants was a strength of the study.

Comparison between this study and other critical care studies was limited because although nine had reported associations between specific factors and impaired health related quality

of life, only five had used appropriate predictive analysis and only two studies comprised a broad case mix of participants. Generalisation of findings from this study therefore was somewhat limited and therefore may be a weakness.

One important oversight in this study may have been the exclusion of age as a predictor variable, given that age was associated with impairment in health related quality of life in two critical care studies. However, one of the study findings was based upon correlation analysis only and age as a predictor, has been refuted by others (Ridley et al 1997; Ulvik et al 2008).

18.4 - Summary and conclusions

The findings from this study, for anxiety and depression scores as significant predictors of impaired health related quality of life, supports the evidence from critical care and other studies. There was an existing small body of evidence to suggest the length of stay in critical care may influence health related quality of life and this study's findings add to that evidence. The findings of PPH as a predictor of impaired health related quality of life in this study although supported by only limited evidence from critical care studies, is supported by rigorous evidence from other studies. The prediction of the health related quality of life summary scores did not account for a high proportion of the variance in this study; it confirmed the importance of the role played by the psychological variables. The findings that acute PTSD did not predict impairment in health related quality of life and the consistent performance of anxiety and depression scores in the predictive models, suggested that the detection of them, might be more important, in survivors of critical care.

Chapter 19 -Conclusions and Recommendations for a Model Care Pathway

19.1 - PTSD

The proportion of survivors of critical care treatment who develop PTSD, according to a structured clinical interview, after discharge was modest and lower than that reported previously in most critical care studies. However, the identified proportion of 10% PTSD still represents a significant minority who could potentially benefit from detection and treatment.

The sample size studied was in the middle range of critical care studies, the rate of attrition was 26% and mortality at six months was 5%. Participants differed from those who refused to take part and those who were excluded, with regards admission TISS and discharge TISS respectively. Participants had a significantly higher admission TISS than those who refused to take part, but discharge TISS was significantly lower than in patients who were excluded at recruitment. There were no other significant differences between participants and non-participants. Discharge TISS, as a surrogate for illness severity, was not found to be predictive of later PTSD. Early PTSD symptoms were strongly predictive of PTSD. Other predictors included critical care length of stay, high SOC scores and PCS-12 at one month. The modest sample size means that a Type I error cannot be ruled out.

PTSD reduced significantly over time from 10% at two weeks to 6.5% at six-months. The symptom trajectory is important in determining who may benefit from further treatment and some patients will recover without the need for treatment. One off or brief intervention for every traumatised individual is not recommended (Bisson et al 1997; Sijbrandij et al 2002) and in some cases may even be harmful. In the first month after critical care discharge, when symptoms are mild, watchful waiting as a way of managing the difficulties, is advised with follow-up contact arranged for one-month. The recommendations for severe

PTSD include five sessions of TFCBT, within one-month of the trauma (NCCMH 2005). More attention is required to develop stepped care models of response, which includes immediate practical, social, and emotional support, offered by non-mental health professionals (Bisson 2007a).

The standardisation of clinical measures to detect PTSD has been previously recommended (Tedstone & Tarrier 2003) and the findings from this study support those recommendations. There is a need for further studies to determine the most suitable self-report questionnaire for this population that is brief, simple to complete and score. Consideration should be given to the brief questionnaires that were reviewed by Brewin et al (2005). Any questionnaire considered should be validated against a recognised gold standard, within the given population. The DTS and SPAN questionnaires did not perform as well as anticipated and they may not be suitable for the detection of PTSD in survivors of critical care. Other larger studies may be useful to confirm these findings.

19.2 - Anxiety and depression

The proportion of patients who have anxiety and depression, according to the HADS, after discharge from critical care is high. These are based upon questionnaires and therefore they are likely to over diagnose but, nevertheless a significant minority are likely to suffer with clinically relevant anxiety and/or depression. There was a spontaneous and significant reduction in anxiety and depression scores between two weeks and six-months, with reductions from 40% at two weeks to 21% and 18% respectively, at six-months. The symptom trajectory is important in determining who may benefit from further treatment. These high rates of morbidity suggest, that early detection of such patients is important and further research required, to determine the most effective method for alleviation of symptoms. Participants in this study, identified a need for the integration of greater psychosocial support following Critical Care and the benefits of enhancing communication between staff and patients in Critical Care should be explored (Cuthina et al, *submitted for publication*).

19.3 - Cognitive function

The proportion of patients who have cognitive impairment, according to the ACE-R, after discharge from critical care was much lower than expected although the identified proportion of 12% for cognitive impairment still represents a significant minority of survivors. There was a spontaneous and significant reduction in ACE-R scores between two weeks and six-months and after critical care discharge, cognitive impairment reduced significantly from 12% at two weeks to 5%, at six-months. Although cognitive impairment after critical care discharge has been attributed to multiple factors, the low rate of cognitive impairment in this study suggests that further research into the impact of the practices of altered sedation and tight glucose control may be helpful.

19.4 - Health related quality of life

Impairment in health related quality of life was most pronounced in the physical domains of the SF12. There was a significant improvement in both the PCS-12 and MCS-12 over the six-month study period. The length of stay in critical care, PPH, anxiety and depression contributed to the predictive models of health related quality of life impairment, although with low variance. The recommendation therefore would be for further research into QOL prediction, but highlighted the importance of the role played by the psychological variables in determination of health related quality of life. The consistent performance of anxiety and depression scores in the predictive models suggests that early detection and alleviation of these is important and may improve health related quality of life after critical care discharge.

19.5 -Recommendations for further research

The results of this study and other studies in this field suggests there is a clear need for more research into patient outcomes. There have been a lack of prospective longitudinal studies. Investigations are recommended to examine PTSD, anxiety and depression, health related quality of life and cognitive function, the trajectory of symptoms over time and outcome predictors. The lower rate of PTSD and findings of only mild cognitive impairment

suggests that it might be useful to investigate if the altered sedation practice and the tight glucose control within the critical care unit, contributed to the findings in this study.
There is also a need to standardise outcome measures, although it is recognised some measures were systematically evaluated by Hayes et al (2001). The IES was the only measure for PTSD reviewed by Hayes and colleagues and the measurement properties were found lacking in two critical care studies that had used it. By comparison, the IES was found to perform consistently well, and has been validated with both high and low PTSD prevalence populations in other settings (Brewin et al 2005). The validation of PTSD questionnaires compared to a gold standard and conducted within the critical care population, is therefore recommended.
The high rates of anxiety and depression were high, though self reported, through questionnaires. It would be useful to explore if interventions such as, changes in communication practice could be identified that would reduce anxiety and depression rates.
The results of the PRACTICAL study (Cuthbertson et al 2007) are anticipated to provide evidence for the efficacy of critical care follow-up programmes. With this in sight, a simple questionnaire survey may be helpful to gauge survivor's response to formal follow-up and to examine the potential uptake for a service. Finally, if patients are responsive to formal follow-up, focus group studies of survivors may be useful to "design" this, which could be compared to thoughts/beliefs of what patients need, through focus groups of critical care staff.

19.6 - A Model care pathway

The results of this study and other studies in this field allow a model care pathway for psychological follow-up of critical care survivors to be proposed.
Staff would receive education around aspects of psychological care, including basic counselling skills and risk factors and symptoms of mental health disorders, such as PTSD, other anxiety disorders and depression. They would receive training in all steps of the care pathway, to include pilot sessions and mentoring by the lead nurse.

19.6.1 - Step one

The first step in the care pathway would involve the assessment of vulnerability. After critical care admission, determination of risk factors would be obtained from relatives or

patients' GP, as appropriate. If the patient were awake, aware and orientated, the information would be obtained directly from them. Risk factors for PTSD, such as previous psychiatric history, family psychiatric history, and reported childhood abuse, would be recorded in a discharge care plan. Other influencing factors such as gender, younger age, trauma severity, race, lower level of education, previous trauma, lack of social support and any additional life stress (Brewin et al 2000), in addition to the length of critical care stay, would be determined prior to critical care discharge, and documented in the discharge care plan. At discharge from critical care, the patient would receive the critical care discharge booklet.

Patients' relatives would also be advised to read the booklet and their attention would be drawn to the PTSD information contained in the booklet. Often the optimal way of detecting PTSD and treating most people is to educate those who are most likely to be in contact with them about the recognition of problematic responses (Bisson 2007).

19.6.2 - Step two

One week after discharge from critical care, patients would be visited on the ward, or earlier if discharge is imminent. If it was possible to link in with relatives and the patient agreed to this, this would be encouraged. The patients' condition would be reviewed and any expressed concerns they or family members may have, regarding their time on critical care would be discussed, utilising the information contained in the discharge booklet, if this was applicable. Using this as an opportunity for education, and if the patient's condition allowed, the PTSD information in the discharge booklet would be conveyed. Patients' rarely disclose experiences such as delusional recollections or nightmares experienced during their critical care stay. Normalising these as, something experienced frequently by other patients, along with simple explanations as to why they occur, have been reported by patients as being helpful and reassuring. Patients would not be asked or expected to disclose anything, this is meant to represent an exercise in normalisation and education and not debriefing. Sensitivity and acknowledgement of the patient's condition is paramount and it may be necessary to revisit the patient, in order to complete questionnaires for PTSD, anxiety and depression. After assessments have been conducted, scores would be recorded in the discharge care plan and risks would be re-evaluated. Patients would be informed about the

results of the assessments and advised regarding the management of any symptoms. They would be given a telephone contact number, in order to discuss concerns after hospital discharge and would be encouraged to maintain contact with their GP An expedited critical care discharge letter would be sent to the patient's GP, to ensure that they are fully informed about the patients' condition and of any identified psychological problems. The liaison psychiatry team and admitting consultant would be informed regarding patients presenting with moderately high anxiety and depression symptoms and those who appear to fulfil the criteria for PTSD. If a patient presented with severe PTSD symptoms, a referral would be made to the liason psychiatry team with a view to a formal psychiatric assessment, with the patient's agreement. If the assessment confirmed the presence of early traumatic stress, a practitioner experienced in TFCBT would assess the patients' ability to comply with treatment. If this was considered appropriate and the patient agreed, five sessions of TFCBT would be provided, according to the national guidelines (NCCMH 2005). Patient's, who were not experiencing early symptoms of PTSD, would be given a contact number to call should they require any further information.

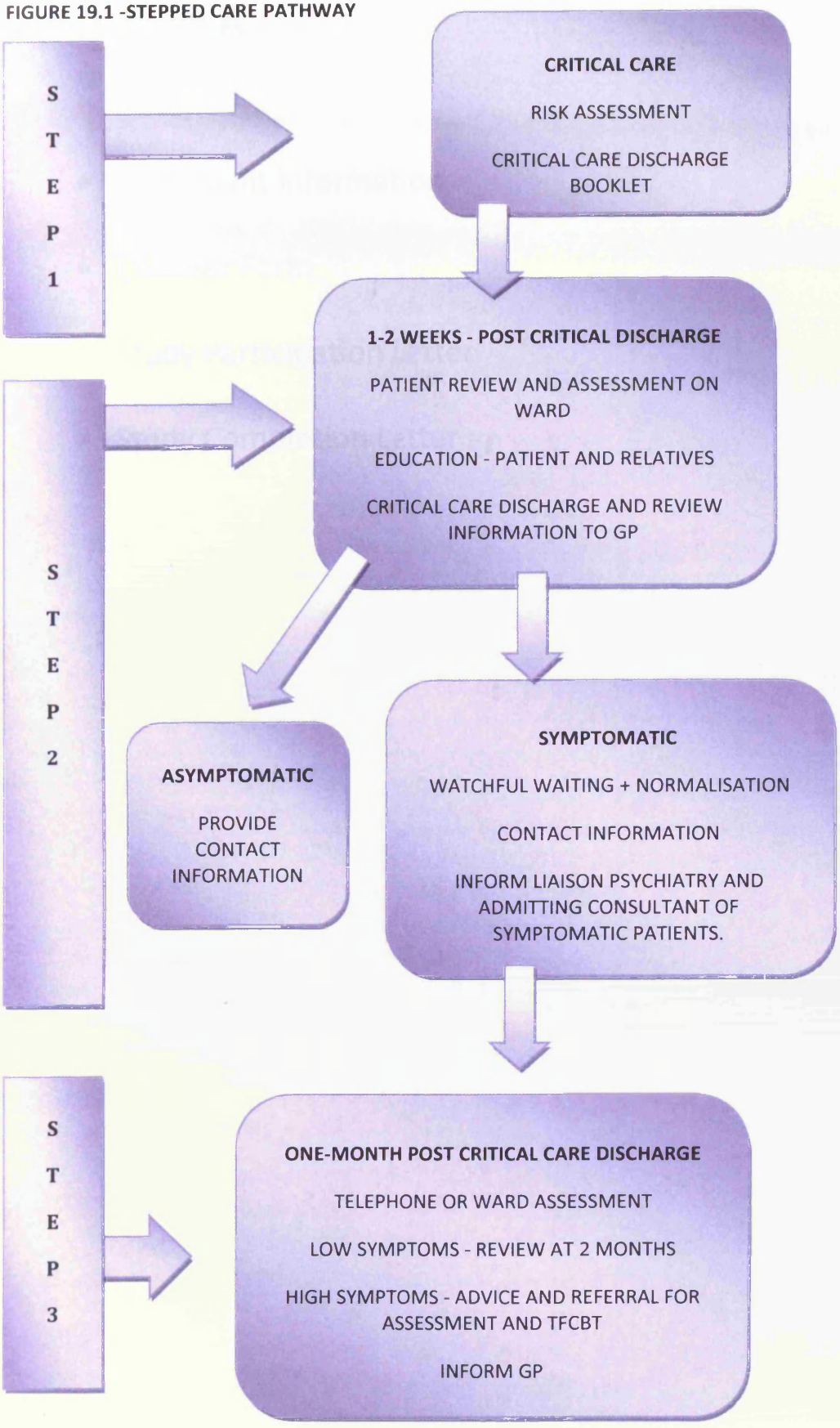
19.6.3 - Step three

One-month after critical care discharge, patients who were previously found to be mildly symptomatic for PTSD, would be contacted by telephone, by a member of the nursing follow-up team who would administer the questionnaires for anxiety, depression and PTSD. If the patient preferred, they would be invited to attend the hospital for an assessment in person. In the event that a patient was still in hospital, an assessment would be carried out on the ward, if the patient's condition allowed this and they agreed to the assessment. The assessment scores would be compared to the scores from the previous assessment. If the scores were lower than those previously reported this would be conveyed to the patient and a review date agreed for one month's time (2 months after critical care discharge). The patient would be advised to use the contact telephone number, if they thought their symptoms were worsening. Any patients, who present with an increased score, would be referred for psychiatric assessment, if they agreed to this. Those patients, who had a confirmed diagnosis of PTSD, would be offered TFCBT, by an experienced practitioner. The

patient's GP would be kept informed of any changes in symptoms or the need for any further treatment.

It is anticipated that this model could be modified if necessary and amalgamated with any planned critical care rehabilitation model, for example the planned NICE guideline for the rehabilitation of critical care patients. The PRACTICAL study (Cuthbertson et al 2007), a randomised controlled trial to examine the provision of critical follow-up clinics, may also shed light on how best to manage individuals, the results of which are expected in January 2009. It is hoped that this model will compliment the findings of that investigation.
The model care pathway is illustrated in Figure 1.1

FIGURE 19.1 -STEPPED CARE PATHWAY



Appendix A

- Participant Information
- Consent Form
- Study Participation Letter
- Study Completion Letter

NHS WALES GIG CYMRU

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sh Health Telephone Network 1872
ct line/Llinell uniongyrchol

Tracey L. Vick - 02920 743084

Patient Information Sheet

"Follow-up after Critical Illness"

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?

The purpose of the study is to find out more about the physical and psychological difficulties that patients experience after being critically ill and admitted to the critical care unit and how this might affect quality of life. We would also like to find out why some patients experience problems, whilst others do not.
Some studies have shown that a significant number of patients experience anxiety, depression and posttraumatic stress disorder after critical illness. We would like to find out how many of our patients, if any, experience any of these problems.

Why have I been chosen?

You have been chosen because you were admitted to the critical care unit. All patients who have been admitted to the critical care unit and who are able to give their consent are being invited to take part in this study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

The study will last for 6 months. If you decide to take part in the study, we will visit you whilst you are in hospital and ask you some questions about your feelings and experiences leading up to when you first became unwell, of your experiences on the critical care unit and since being discharged from critical care. With your permission we will inform your General Practitioner (GP) that you are taking part in the study.
We will need to repeat the interview again, 4 weeks after you have been discharged from critical care. If you are still in hospital, we will carry out the interview on the ward, but if you have been discharged home we can come and visit you or alternatively you can come back to an outpatient appointment.
We will ask you to return to the clinic on 2 further occasions, at 3 months and at 6 months after discharge from the critical care unit, where we will carry out the same interviews. Each appointment will last for approximately 1½ hours.

What do I have to do?

You will need to be prepared to answer our questions, talk about your experiences and how you are feeling. You will also need to attend the Follow-up appointments. If you do not feel well enough to attend the appointments, if you let us know, we can arrange to visit you at home and carry out the interview there. There are no other restrictions

What is being tested?

We are testing to see if any patients have a condition called posttraumatic stress disorder. We will also be testing levels of any anxiety or depression, how you are coping and your quality of life since you became unwell.

What are the alternatives for diagnosis or treatment?

The alternatives for diagnosis would be a formal assessment by a psychiatrist. The psychiatrist would then decide treatment for traumatic stress symptoms, anxiety or depression. If you were found to have symptoms it is possible that the psychiatrist would adopt a "wait and see approach". This would mean that the psychiatrist would wait and see if the symptoms got better without treatment.

What are the side effects?

There are no side effects, although some patients may find talking about their experiences, upsetting. In our experience most patients usually find that talking about problems and feelings is helpful.

What are the possible disadvantages and risks of taking part?

There are no known risks for the study. If traumatic stress symptoms are present you will not normally be offered an intervention until the end of the 6-month follow-up period.

What are the possible benefits of taking part?

There are no benefits in taking part in the study but we hope that the information we get from this study may help us to treat future patients better.

What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the conditions that are being studied. If this happens, the research nurse will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, the research nurse will make arrangements for any necessary care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your research nurse might consider it to be in your best interests to withdraw you from the study. She will explain the reasons and arrange for any necessary care to continue.

What happens when the research study stops?

Further treatment may not be available after the research stops until such time that data collected can be examined. However there are other facilities that can be used such as referral to special clinics that treat patients with traumatic stress symptoms.

What if something goes wrong?

If taking part in this research project harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you.

Will my taking part in this study be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed.

What will happen to the results of the research study?

It is likely that the results of the study will be presented at medical conferences and written up for publication in medical journals. You will not be identified in any report or publication. If you would like a copy of the publication this will be available to you after the study is completed. The research nurse will provide this.

Who is organising and funding the research?

The critical care directorate and liaison psychiatry departments have organised this study. It is being funded by a grant set up by Research and Development, UHW.

Who has reviewed the study?

South East Wales Local Research Ethics Committee has reviewed the study

Contact for Further Information

If you require any further information about this study, please contact the Research Nurse – Tracey Vick, telephone number 02920 743084/743871

You will be given a copy of the information sheet and a signed consent form to keep.

Thank you for taking part in this study.

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cyf/Our ref
sh Health Telephone Network 1872
ect line/Llinell uniongyrchol

Centre :

Patient Identification Number for this trial:

CONSENT FORM

Title of Project: "Follow-up after Critical Illness."

Name of Researcher: **Tracey L. Vick**

Please initial box

1. I confirm that I have read and understand the information sheet dated ———————— for the above study and have had the opportunity to ask questions. ☐

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

3. I understand that sections of any of my medical notes may be looked at by responsible individuals from the research team or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐

Centre :

Patient Identification Number for this trial:

4. I give permission for my GP to be informed of my inclusion in the study. ☐

5. I agree to take part in the above study. ☐

Name of Patient Date.....

Signature .....

Name of Person taking consent (if different from researcher) Date.....

Signature.....

Researcher Date.....

Signature.....

(1 for patient; 1 for researcher; 1 to be kept with hospital notes.)

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Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Date

ext.3084

Dr

Dear Doctor

RE:

The above named patient has agreed to take part in a clinical investigation to determine the prevalence of Posttraumatic Stress symptoms after critical illness

The patient will undergo a structured clinical interview to determine the extent of Posttraumatic Stress symptoms. They will then be asked to complete a number of self-report measures. These measures will determine symptoms of posttraumatic stress, anxiety, depression, quality of life and coping skills. All clinical measures will be repeated three times over a period of 6 months.

Whilst the patient is taking part in the study, no psychological intervention will be offered. If you consider that this is clinically indicated or if you have any concerns regarding the patient's symptoms, please contact me on the above telephone number, so that we may discuss further.

We will advise you of all findings in due course, but should you require any further information, please don't hesitate to contact me.

Yours sincerely

Tracey L. Vick M.A. RGN
Cognitive Behavioural Psychotherapist
Critical Care Directorate / Liaison Psychiatry
University Hospital of Wales

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13/01/05

x 3084

Dr

Dear Dr

Re:

The above named patient previously agreed to take part in a clinical investigation to determine the prevalence of Posttraumatic Stress symptoms after critical illness. All study investigations have now been completed.

At 6-month Follow up, the patient was found to be symptomatic/asymptomatic for Posttraumatic Stress disorder.

The patient has agreed to /declined a further assessment within the Traumatic Stress Clinic.

This appointment has been arranged / Should the patient change his/her mind in the future, we would be happy to receive your referral to the Traumatic Stress Clinic.

Should you wish to discuss any further aspect of the study, please do not hesitate to contact me on the above extension number.

Yours sincerely

Tracey L. Vick M.A. RGN
Cognitive Behavioural Psychotherapist
Critical Care Directorate / Liaison Psychiatry
University Hospital of Wales

Appendix B

- Clinician Administered PTSD Scale (CAPS)
- Hospital Anxiety and Depression Scale (HADS)
- Davidson Trauma Scale (DTS)
- SF 12 v2 Health Survey
- Orientation to Life Questionnaire (SOQ)
- Revised Addenbrookes Cognitive Examination (ACE-R)
- General Information Questionnaire (GIQ)

Clinician-Administered PTSD Scale for DSM-IV (CAPS)

Criterion A

The person has been exposed to a traumatic event in which both of the following were present:

1. the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others;
2. the person's response involved intense fear, helplessness, or horror. Note: in children, this may be expressed instead by disorganized or agitated behavior.

Instructions

I'm going to be asking you about some difficult or stressful things that sometimes happen to people. Some examples of this are being in some type of serious accident; being in a fire, a hurricane, or an earthquake; being mugged or beaten up or attacked with a weapon; or being forced to have sex when you didn't want to. I'll start by asking you to look over a list of experiences like this and check any that apply to you. Then, if any of them do apply to you, I'll ask you to briefly describe what happened and how you felt at the time.

Some of these experiences may be hard to remember or may bring back uncomfortable memories or feelings. People often find that talking about them can be helpful, but it's up to you to decide how much you want to tell me. As we go along, if you find yourself becoming upset, let me know and we can slow down and talk about it. Also, if you have any questions or you don't understand something, please let me know. Do you have any questions before we start?

ADMINISTER CHECKLIST, THEN REVIEW AND INQUIRE UP TO THREE EVENTS. IF MORE THAN THREE EVENTS ENDORSED, DETERMINE WHICH THREE EVENTS TO INQUIRE (E.G. FIRST, WORST, AND MOST RECENT EVENTS; THREE WORST EVENTS; TRAUMA OF INTEREST PLUS TWO OTHER WORST EVENTS, ETC.)

IF NO EVENTS ENDORSED ON CHECKLIST: *(Has there ever been a time when your life was in danger or you were seriously injured or harmed?)*

IF NO: *(What about a time when you were threatened with death or serious injury, even if you weren't actually injured or harmed?)*

IF NO: *(What about witnessing something like this happen to someone else or finding out that it happened to someone close to you?)*

IF NO: *(What would you say are some of the most stressful experiences you have had over your life?)*

NFER-NELSON
Health & Social Care

(CAPS) Checklist

Name: Date: ID:

Interviewer:

Listed below are a number of difficult or stressful things that sometimes happen to people. For each event, check one or more of the boxes to the right to indicate that: (a) it *happened to you* personally, (b) *you witnessed* it happening to someone else, (c) *you learned about* it happening to someone close to you, (d) *you're not sure* if it fits, or (e) *it doesn't apply* to you.

e sure to consider your *entire life* (growing up as well as adulthood) as you go through the list of events.

Event	Happened to me	Witnessed it	Learned about it	Not sure	Doesn't apply
Natural disaster (for example, flood, hurricane, ornado, earthquake)					
Fire or explosion					
Transportation accident (for example, car accident, boat accident, train wreck, plane crash)					
Serious accident at work, home, or during recreational activity					
Exposure to toxic substance (for example, dangerous chemicals, radiation)					
Physical assault (for example, being attacked, hit, slapped, kicked, beaten up)					
Assault with a weapon (for example, being shot, stabbed, threatened with a knife, gun, bomb)					
Sexual assault (rape, attempted rape, made to perform any type of sexual act through force or threat of harm)					
Other unwanted or uncomfortable sexual experience					
Combat or exposure to a war zone (in the military or as a civilian)					
Captivity (for example, being kidnapped, abducted, held hostage, prisoner of war)					
Life-threatening illness or injury					
Severe human suffering					
Sudden, violent death (for example, homicide, suicide)					
Sudden, unexpected death of someone close to you					
Serious injury, harm or death you caused to someone else					
Any other very stressful event or experience					

EVENT NO. 1

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g. event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event – how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ____ other ____]* *Serious injury? NO YES [self ____ other ____]* *Threat to physical integrity? NO YES [self ____ other ____]* *A. (2)* *Intense fear / help / horror? NO YES [during ____ after ____]* *Criterion A met? NO PROBABLE YES*

EVENT NO. 2

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g. event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event – how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ____ other ____]* *Serious injury? NO YES [self ____ other ____]* *Threat to physical integrity? NO YES [self ____ other ____]* *A. (2)* *Intense fear / help / horror? NO YES [during ____ after ____]* *Criterion A met? NO PROBABLE YES*

EVENT NO. 3

What happened? *(How old were you? Who else was involved? How many times did this happen? Life threat? Serious injury?)*	*Describe (e.g. event type, victim, perpetrator, age, frequency):*
How did you respond emotionally? *(Were you very anxious or frightened? Horrified? Helpless? How so? Were you stunned or in shock so that you didn't feel anything at all? What was that like? What did other people notice about your emotional response? What about after the event – how did you respond emotionally?)*	*A. (1)* *Life threat? NO YES [self ____ other ____]* *Serious injury? NO YES [self ____ other ____]* *Threat to physical integrity? NO YES [self ____ other ____]* *A. (2)* *Intense fear / help / horror? NO YES [during ____ after ____]* *Criterion A met? NO PROBABLE YES*

For the rest of the interview, I want you to keep (EVENTS) in mind as I ask you some questions about how they may have affected you.

I'm going to ask you about twenty-five questions altogether. Most of them have two parts. First, I'll ask if you've ever had a particular problem, and if so, about how often in the past month. Then I'll ask you how much distress or discomfort that problem may have caused you.

Criterion B

The traumatic event is persistently re-experienced in one (or more) of the following ways:

KEY: F = Frequency
I = Intensity
Sx = Symptom rated as present or absent (to be present F ≥ 1 and I ≥ 2)

(B-1) recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions.
Note: in young children, repetitive play may occur in which themes or aspects of the trauma are expressed.

Frequency	*Intensity*	*Current*
Have you ever had unwanted memories (EVENT)? What were they like? *(What do you remember?)* [IF NOT CLEAR:] *(Did it ever occur while you were awake, or only in dreams?)* [EXCLUDE IF MEMORIES OCCURRED ONLY DURING DREAMS] How often have you had these memories in the past month? 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	How much distress or discomfort did these memories cause you? Were you able to put them out of your mind and think about something else? *(How hard did you have to try?)* How much did they interfere with your life? 0 None 1 Mild: minimal distress or disruption of activities 2 Moderate: distress clearly present but still manageable, some disruption of activities 3 Severe: considerable distress, difficulty dismissing memories, marked disruption of activities 4 Extreme: incapacitating distress, cannot dismiss memories, unable to continue activities ***QV (specify)*** _____	F ____ I ____ Sx: Y N *Lifetime* F ____ I ____ Sx: Y N

(B-2) recurrent distressing dreams of the event.
Note: in children, there may be frightening dreams without recognizable content.

Frequency	*Intensity*	*Current*
Have you ever had unpleasant dreams about (EVENT)? Describe a typical dream. *(What happens in them?)* How often have you had these dreams in the past month? 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	How much distress or discomfort did these dreams cause you? Did they ever wake you up? [IF YES:] *(What happened when you woke up? How long did it take you to get back to sleep?)* [LISTEN FOR REPORT OF ANXIOUS AROUSAL, YELLING, ACTING OUT THE NIGHTMARE] *(Did your dreams ever affect anyone else? How so?)* 0 None 1 Mild: minimal distress, may not have awoken 2 Moderate: awoke in distress but readily returned to sleep 3 Severe: considerable distress, difficulty returning to sleep 4 Extreme: incapacitating distress, did not return to sleep ***QV (specify)*** _____	F ____ I ____ Sx: Y N *Lifetime* F ____ I ____ Sx: Y N

3. (B–3) acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated).
Note: in young children, trauma-specific reenactment may occur.

Frequency	***Intensity***	***Current***
Have you ever suddenly acted or felt as if (EVENT) were happening again? *(Have you ever had flashbacks about [EVENT]?)* [IF NOT CLEAR:] *(Did this ever occur while you were awake, or only in dreams?)* [EXCLUDE IF OCCURRED ONLY DURING DREAMS] **Tell me more about that. How often has that happened in the past month?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much did it seem as if (EVENT) were happening again?** *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No reliving 1 Mild: somewhat more realistic than just thinking about event 2 Moderate: definite but transient dissociative quality, still very aware of surroundings, daydreaming quality 3 Severe: strongly dissociative (reports images, sounds, or smells) but retained some awareness of surroundings 4 Extreme: complete dissociation (flashback), no awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout) ***QV (specify)*** _____	***Current*** F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

4. (B–4) intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.

Frequency	***Intensity***	***Current***
Have you ever gotten emotionally upset when something reminded you of (EVENT)? *(Has anything ever triggered bad feelings related to [EVENT]?)* **What kinds of reminders made you upset? How often in the past month?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much distress or discomfort did (REMINDERS) cause you? How long did it last? How much did it interfere with your life?** 0 None 1 Mild: minimal distress or disruption of activities 2 Moderate: distress clearly present but still manageable, some disruption of activities 3 Severe: considerable distress, marked disruption of activities 4 Extreme: incapacitating distress, unable to continue activities ***QV (specify)*** _____	***Current*** F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

(B-5) physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.

requency	***Intensity***	***Current***
aive you ever had any physical reactions hen something reminded you of VENT)? *(Did your body ever react in some ay when something reminded you of VENT]?)* **Can you give me some amples?** *(Did your heart race or did your eathing change? What about sweating or eling really tense or shaky?)* **What kinds of minders triggered these reactions? ow often in the past month?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***)escription/Examples***	**How strong were (PHYSICAL REACTIONS)? How long did they last?** *(Did they last even after you were out of the situation?)* 0 No physical reactivity 1 Mild: minimal reactivity 2 Moderate: physical reactivity clearly present, may be sustained if exposure continues 3 Severe: marked physical reactivity, sustained throughout exposure 4 Extreme: dramatic physical reactivity, sustained arousal even after exposure has ended ***QV (specify)*** _____	***Current*** F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

Criterion C

Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

(C-1) efforts to avoid thoughts, feelings, or conversations associated with the trauma.

Frequency	***Intensity***	***Current***
Have you ever tried to avoid thoughts or eelings about (EVENT)? *(What kinds of houghts or feelings did you try to avoid?)* **What about trying to avoid talking with ther people about it?** *(Why is that?)* **How often in the past month?** 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	**How much effort did you make to avoid (THOUGHTS/FEELINGS/CONVERSATIONS)?** *(What kinds of things did you do? What about drinking or using medication or street drugs?)* [CONSIDER ALL ATTEMPTS AT AVOIDANCE, INCLUDING DISTRACTION, SUPPRESSION, AND USE OF ALCOHOL/DRUGS] **How much did that interfere with your life?** 0 None 1 Mild: minimal effort, little or no disruption of activities 2 Moderate: some effort, avoidance definitely present, some disruption of activities 3 Severe: considerable effort, marked avoidance, marked disruption of activities, or involvement in certain activities as avoidant strategy 4 Extreme: drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify)*** _____	***Current*** F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

(C-2) efforts to avoid activities, places, or people that arouse recollections of the trauma.

Frequency	*Intensity*	*Current*
Have you ever tried to avoid certain activities, places, or people that reminded you of [EVENT]? *(What kinds of things did you avoid? Why is that?)* How often in the past month? 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	How much effort did you make to avoid (ACTIVITIES/PLACES/PEOPLE)? *(What did you do instead?)* How much did that interfere with your life? 0 None 1 Mild: minimal effort, little or no disruption of activities 2 Moderate: some effort, avoidance definitely present, some disruption of activities 3 Severe: considerable effort, marked avoidance, marked disruption of activities or involvement in certain activities as avoidant strategy 4 Extreme: drastic attempts at avoidance, unable to continue activities, or excessive involvement in certain activities as avoidant strategy ***QV (specify)*** _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

(C-3) inability to recall an important aspect of the trauma.

Frequency	*Intensity*	*Current*
Have you had difficulty remembering some important parts of (EVENT)? Tell me more about that. *(Do you feel you should be able to remember these things? Why do you think you can't?)* In the past month, how much of the important parts of (EVENT) have you had difficulty remembering? *(What parts do you still remember?)* 0 None, clear memory 1 Few aspects not remembered (less than 10%) 2 Some aspects not remembered (approx. 20-30%) 3 Many aspects not remembered (approx. 50-60%) 4 Most or all aspects not remembered (more than 80%) ***Description/Examples***	How much difficulty did you have recalling important parts of (EVENT)? *(Were you able to recall more if you tried?)* 0 None 1 Mild, minimal difficulty 2 Moderate, some difficulty, could recall with effort 3 Severe, considerable difficulty, even with effort 4 Extreme, completely unable to recall important aspects of event ***QV (specify)*** _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

C–4) markedly diminished interest or participation in significant activities.

equency	*Intensity*	*Current*
ve you been less interested in activities ıt you used to enjoy? *(What kinds of* *ıgs have you lost interest in? Are there some* *ıgs you don't do at all anymore? Why is* *t?)* [EXCLUDE IF NO OPPORTUNITY, PHYSICALLY UNABLE, OR IF VELOPMENTALLY APPROPRIATE [ANGE IN PREFERRED ACTIVITIES] **the past month, how many activities** **ve you been less interested in?** *hat kinds of things do you still enjoy doing?)* **ıen did you first start to feel that way?** *ter the [EVENT]?)*) None Few activities (less than 10%) : Some activities (approx. 20-30%) ; Many activities (approx. 50-60%) { Most or all activities (more than 80%)	**How strong was your loss of interest?** *(Would you enjoy [ACTIVITIES] once you got started?)* 0 No loss of interest 1 Mild: slight loss of interest, probably would enjoy after starting activities 2 Moderate: definite loss of interest, but still has some enjoyment of activities 3 Severe: marked loss of interest in activities 4 Extreme: complete loss of interest, no longer participates in any activities ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Current*** F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N
:scription/Examples		

(C–5) feeling of detachment or estrangement from others.

'equency	*Intensity*	*Current*
ıve you felt distant or cut off from ıer people? What was that like? How ıch of the time in the past month have u felt that way? When did you first ırt to feel that way? *(After the [EVENT]?)*) None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx. 20-30%) 3 Much of the time (approx. 50-60%) 4 Most or all of the time (more than 80%)	**How strong were your feelings of being distant or cut off from others?** *(Who do you feel closest to? How many people do you feel comfortable talking with about personal things?)* 0 No feelings of detachment or estrangement 1 Mild: may feel 'out of synch' with others 2 Moderate: feelings of detachment clearly present, but still feels some interpersonal connection 3 Severe: marked feelings of detachment or estrangement from most people, may feel close to only one or two people 4 Extreme: feels completely detached or estranged from others, not close with anyone ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	***Current*** F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N
escription/Examples		

11. (C–6) restricted range of affect (e.g. unable to have loving feelings).

Frequency	***Intensity***	***Current***
Have there been times when you felt emotionally numb or had trouble experiencing feelings like love or happiness? What was that like? *(What feelings did you have trouble experiencing?)* **How much of the time in the past month have you felt that way? When did you first start having trouble experiencing** (EMOTIONS)? *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx. 20-30%) 3 Much of the time (approx. 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How much trouble did you have experiencing** (EMOTIONS)? *(What kinds of feelings were you still able to experience?)* [INCLUDE OBSERVATIONS OF RANGE OF AFFECT DURING INTERVIEW] 0 No reduction of emotional experience 1 Mild: slight reduction of emotional experience 2 Moderate: definite reduction of emotional experience, but still able to experience most emotions 3 Severe: marked reduction of experience of at least two primary emotions (e.g., love, happiness) 4 Extreme: completely lacking emotional experience ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

12. (C–7) sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span).

Frequency	***Intensity***	***Current***
Have there been times when you felt there is no need to plan for the future, that somehow your future will be cut short? Why is that? [RULE OUT REALISTIC RISKS SUCH AS LIFE-THREATENING MEDICAL CONDITIONS] **How much of the time in the past month have you felt that way? When did you first start to feel that way?** *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx. 20-30%) 3 Much of the time (approx. 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How strong was this feeling that your future will be cut short?** *(How long do you think you will live? How convinced are you that you will die prematurely?)* 0 No sense of a foreshortened future 1 Mild: slight sense of a foreshortened future 2 Moderate: sense of a foreshortened future definitely present, but no specific prediction about longevity 3 Severe: marked sense of a foreshortened future, may make specific prediction about longevity 4 Extreme: overwhelming sense of a foreshortened future, completely convinced of premature death ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

Criterion D

Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

1. (D-1) difficulty falling or staying asleep.

Frequency	*Intensity*	*Current*
Have you had any problems falling or staying asleep? How often in the past month? When did you first start having problems sleeping? *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day Sleep onset problems? Y N Mid-sleep awakening? Y N Early a.m. awakening? Y N Total no. hrs. sleep/night ____ Desired no. hrs. sleep/night ____	How much of a problem did you have with your sleep? *(How long did it take you to fall asleep? How often did you wake up in the night? Did you often wake up earlier than you wanted to? How many total hours did you sleep each night?)* 0 No sleep problems 1 Mild: slightly longer latency, or minimal difficulty staying asleep (up to 30 minutes' loss of sleep) 2 Moderate: definite sleep disturbance, clearly longer latency, or clear difficulty staying asleep (30-90 minutes' loss of sleep) 3 Severe: much longer latency, or marked difficulty staying asleep (90 minutes to 3 hrs of sleep) 4 Extreme: very long latency, or profound difficulty staying asleep (more than 3 hrs loss of sleep) ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

2. (D-2) irritability or outbursts of anger.

Frequency	*Intensity*	*Current*
Have there been times when you felt especially irritable or showed strong feelings of anger? Can you give me some examples? How often in the past month? When did you first start feeling that way? *(After the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***Description/Examples***	How strong was your anger? *(How did you show it?)* [IF REPORTS SUPPRESSION:] *(How hard was it for you to keep from showing your anger?)* How long did it take you to calm down? Did your anger cause you any problems? 0 No irritability or anger 1 Mild: minimal irritability, may raise voice when angry 2 Moderate: definite irritability or attempts to suppress anger, but can recover quickly 3 Severe: marked irritability or marked attempts to suppress anger, may become verbally or physically aggressive when angry 4 Extreme: pervasive anger or drastic attempts to suppress anger, may have episodes of physical violence ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

15. (D–3) difficulty concentrating.

Frequency	*Intensity*	*Current*
Have you found it difficult to concentrate on what you were doing or on things going on around you? What was that like? How much of the time in the past month? When did you first start having trouble concentrating? *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx. 20-30%) 3 Much of the time (approx. 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How difficult was it for you to concentrate?** [INCLUDE OBSERVATIONS OF CONCENTRATION AND ATTENTION IN INTERVIEW] **How much did that interfere with your life?** 0 No difficulty with concentration 1 Mild: only slight effort needed to concentrate, little or no disruption of activities 2 Moderate: definite loss of concentration but could concentrate with effort, some disruption of activities 3 Severe: marked loss of concentration even with effort, marked disruption of activities 4 Extreme: complete inability to concentrate, unable to engage in activities ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

16. (D–4) hypervigilance.

Frequency	*Intensity*	*Current*
Have you been especially alert or watchful, even when there was no real need to be? *(Have you felt as if you were constantly on guard?)* Why is that? How much of the time in the past month? When did you first start acting that way? *(After the [EVENT]?)* 0 None of the time 1 Very little of the time (less than 10%) 2 Some of the time (approx. 20-30%) 3 Much of the time (approx. 50-60%) 4 Most or all of the time (more than 80%) ***Description/Examples***	**How hard did you try to be watchful of things going on around you?** [INCLUDE OBSERVATIONS OF HYPERVIGILANCE IN INTERVIEW] **Did your (HYPERVIGILANCE) cause you any problems?** 0 No hypervigilance 1 Mild: minimal hypervigilance, slight heightening of awareness 2 Moderate: hypervigilance clearly present, watchful in public (e.g., chooses safe place to sit in a restaurant or movie theater) 3 Severe: marked hypervigilance, very alert, scans environment for danger, exaggerated concern for safety of self/family/home 4 Extreme: excessive hypervigilance, efforts to ensure safety consume significant time and energy and may involve extensive safety/checking behaviors, marked watchfulness during interview ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ___ I ___ Sx: Y N ***Lifetime*** F ___ I ___ Sx: Y N

D-5) exaggerated startle response.

equency	***Intensity***	*Current*
ve you had any strong startle ctions? When did that happen? *hat kinds of things made you startle?)* w often in the past month? When did first have these reactions? *(After the ENT]?)* Never Once or twice Once or twice a week Several times a week Daily or almost every day	How strong were these startle reactions? *(How strong were they compared to how most people would respond?)* How long did they last? 0 No startle reaction 1 Mild: minimal reaction 2 Moderate: definite startle reaction, feels 'jumpy' 3 Severe: marked startle reaction, sustained arousal following initial reaction 4 Extreme: excessive startle reaction, overt coping behavior (e.g., combat veteran who "hits the dirt") ***QV (specify)*** _____ *Trauma-related? 1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ____ I ____ Sx: Y N *Lifetime* F ____ I ____ Sx: Y N
scription/Examples		

Criterion E

Duration of the disturbance (symptoms in Criteria B, C and D) is more than 1 month.

onset of symptoms.

NOT ALREADY CLEAR:] When did you first start having TSD SYMPTOMS) you've told me about? *(How long after trauma did they start? More than six months?)*	_____ *total no. months delay in onset* *With delayed onset (≥ 6 months)? NO YES*

duration of symptoms.

URRENT] How long have these TSD SYMPTOMS) lasted altogether? ETIME] How long did these TSD SYMPTOMS) last altogether?		*Current*	*Lifetime*
	Duration more than 1 month?	*NO YES*	*NO YES*
	Total no. months duration	_____	_____
	Acute (< 3 months) or chronic (≥ 3 months)?	*acute chronic*	*acute chronic*

Criterion F

The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

KEY: Symptom rated as present if score ≥ 2

20. subjective distress.

[CURRENT] **Overall, how much have you been bothered by these (PTSD SYMPTOMS) you've told me about?** [CONSIDER DISTRESS REPORTED ON EARLIER ITEMS] [LIFETIME] **Overall, how much were you bothered by these (PTSD SYMPTOMS) you've told me about?** [CONSIDER DISTRESS REPORTED ON EARLIER ITEMS]	0 None 1 Mild: minimal distress 2 Moderate: distress clearly present but still manageable 3 Severe: considerable distress 4 Extreme: incapacitating distress	*Current* _____ *Lifetime* _____

21. impairment in social functioning.

[CURRENT] **Have these (PTSD SYMPTOMS) affected your relationships with other people? How so?** [CONSIDER IMPAIRMENT IN SOCIAL FUNCTIONING REPORTED ON EARLIER ITEMS] [LIFETIME] **Did these (PTSD SYMPTOMS) affect your social life? How so?** [CONSIDER IMPAIRMENT IN SOCIAL FUNCTIONING REPORTED ON EARLIER ITEMS]	0 No adverse impact 1 Mild impact: minimal impairment in social functioning 2 Moderate impact: definite impairment, but many aspects of social functioning still intact 3 Severe impact: marked impairment, few aspects of social functioning still intact 4 Extreme impact: little or no social functioning	*Current* _____ *Lifetime* _____

22. impairment in occupational or other important area of functioning.

[CURRENT – IF NOT ALREADY CLEAR] **Are you working now?** IF YES: **Have these (PTSD SYMPTOMS) affected your work or your ability to work? How so?** [CONSIDER REPORTED WORK HISTORY, INCLUDING NUMBER AND DURATION OF JOBS, AS WELL AS THE QUALITY OF WORK RELATIONSHIPS. IF PREMORBID FUNCTIONING IS UNCLEAR, INQUIRE ABOUT WORK EXPERIENCES BEFORE THE TRAUMA. FOR CHILD/ADOLESCENT TRAUMAS, ASSESS PRE-TRAUMA SCHOOL PERFORMANCE AND POSSIBLE PRESENCE OF BEHAVIOR PROBLEMS] IF NO: **Have these (PTSD SYMPTOMS) affected any other important part of your life?** [AS APPROPRIATE, SUGGEST EXAMPLES SUCH AS PARENTING, HOUSEWORK, SCHOOLWORK, VOLUNTEER WORK, ETC.] **How so?** [LIFETIME – IF NOT ALREADY CLEAR] **Were you working then?** IF YES: **Did these (PTSD SYMPTOMS) affect your work or your ability to work? How so?** [CONSIDER REPORTED WORK HISTORY, INCLUDING NUMBER AND DURATION OF JOBS, AS WELL AS THE QUALITY OF WORK RELATIONSHIPS. IF PREMORBID FUNCTIONING IS UNCLEAR, INQUIRE ABOUT WORK EXPERIENCES BEFORE THE TRAUMA. FOR CHILD/ADOLESCENT TRAUMAS, ASSESS PRE-TRAUMA SCHOOL PERFORMANCE AND POSSIBLE PRESENCE OF BEHAVIOR PROBLEMS] IF NO: **Did these (PTSD SYMPTOMS) affect any other important part of your life?** [AS APPROPRIATE, SUGGEST EXAMPLES SUCH AS PARENTING, HOUSEWORK, SCHOOLWORK, VOLUNTEER WORK, ETC.] **How so?**	0 No adverse impact 1 Mild impact: minimal impairment in occupation/other important functioning 2 Moderate impact: definite impairment, but many aspects of occupational/other important functioning still intact 3 Severe impact: marked impairment, few aspects of occupational/other important functioning still intact 4 Extreme impact: little or no occupational/other important functioning	*Current* _____ *Lifetime* _____

Global Ratings

gglobal validity.

TIMATE THE OVERALL VALIDITY OF RESPONSES. NSIDER FACTORS SUCH AS COMPLIANCE WITH EE INTERVIEW, MENTAL STATUS (E.G., PROBLEMS TH CONCENTRATION, COMPREHENSION OF MS, DISSOCIATION), AND EVIDENCE OF EFFORTS EXAGGERATE OR MINIMIZE SYMPTOMS.	0 Excellent: no reason to suspect invalid responses 1 Good: factors present that may adversely affect validity 2 Fair: factors present that definitely reduce validity 3 Poor: substantially reduced validity 4 Invalid responses: severely impaired mental status or possible deliberate 'faking bad' or 'faking good'

global severity.

TIMATE THE OVERALL SEVERITY OF PTSD MPTOMS. CONSIDER DEGREE OF SUBJECTIVE TRESS, DEGREE OF FUNCTIONAL IMPAIRMENT, SERVATIONS OF BEHAVIORS IN INTERVIEW, AND DGMENT REGARDING REPORTING STYLE.	0 No clinically significant symptoms, no distress and no functional impairment 1 Mild: minimal distress or functional impairment 2 Moderate: definite distress or functional impairment but functions satisfactorily with effort 3 Severe: considerable distress or functional impairment, limited functioning even with effort 4 Extreme: marked distress or marked impairment in two or more major areas of functioning	***Current*** _____ ***Lifetime*** _____

global improvement.

TE TOTAL OVERALL IMPROVEMENT PRESENT CE THE INITIAL RATING. IF NO EARLIER RATING, KNOW THE SYMPTOMS ENDORSED HAVE ANGED OVER THE PAST 6 MONTHS. RATE THE GREE OF CHANGE, WHETHER OR NOT, IN YOUR DGMENT, IT IS DUE TO TREATMENT.	0 Asymptomatic 1 Considerable improvement 2 Moderate improvement 3 Slight improvement 4 No improvement 5 Insufficient information

Current PTSD Symptoms

Criterion A met (traumatic event)?		NO	YES
___ *number of Criterion B symptoms*	*(at least one rating over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
___ *number of Criterion C symptoms*	*(at least three ratings over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
___ *number of Criterion D symptoms*	*(at least two ratings over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
Criterion E met (duration ≥ 1 month)?		NO	YES
Criterion F met (distress/impairment)	*(at least one rating equal to or greater than 2)?*	NO	YES
CURRENT PTSD (Criteria A–F met)?		NO	YES

IF CURRENT PTSD CRITERIA ARE MET, SKIP TO ASSOCIATED FEATURES.

IF CURRENT CRITERIA ARE NOT MET, ASSESS FOR LIFETIME PTSD. IDENTIFY A PERIOD OF AT LEAST A MONTH SINCE THE TRAUMATIC EVENT IN WHICH SYMPTOMS WERE WORSE.

Since the (EVENT), has there been a time when these (PTSD SYMPTOMS) were a lot worse than they have been in the past month? When was that? How long did it last? *(At least a month?)*

IF MULTIPLE PERIODS IN THE PAST: **When were you bothered the most by these (PTSD SYMPTOMS)?**

IF AT LEAST ONE PERIOD, INQUIRE ITEMS 1–17, CHANGING FREQUENCY PROMPTS TO REFER TO WORST PERIOD: **During that time, did you (EXPERIENCE SYMPTOM)? How often?**

Lifetime PTSD Symptoms

Criterion A met (traumatic event)?		NO	YES
___ *number of Criterion B symptoms*	*(at least one rating over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
___ *number of Criterion C symptoms*	*(at least three ratings over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
___ *number of Criterion D symptoms*	*(at least two ratings over the minimum threshold i.e. frequency score equal to or greater than 1 and intensity score equal to or greater than 2)?*	NO	YES
Criterion E met (duration ≥ 1 month)?		NO	YES
Criterion F met (distress/impairment)	*(at least one rating equal to or greater than 2)?*	NO	YES
LIFETIME PTSD (Criteria A–F met)?		NO	YES

Associated Features

uilt over acts of commission or omission.

quency	*Intensity*	*Current*
you felt guilty about anything you didn't do during (EVENT)? Tell me about that. *(What do you feel guilty t?)* How much of the time have you hat way in the past month? None of the time Very little of the time (less than 10%) Some of the time (approx. 20–30%) Much of the time (approx. 50–60%) Most or all of the time (more than 80%)	How strong were these feelings of guilt? How much distress or discomfort did they cause? 0 No feelings of guilt 1 Mild: slight feelings of guilt 2 Moderate: guilt feelings definitely present, some distress but still manageable 3 Severe: marked feelings of guilt, considerable distress 4 Extreme: pervasive feelings of guilt, self-condemnation regarding behavior, incapacitating distress	F ____ I ____ Sx: Y N *Lifetime* F ____ I ____ Sx: Y N
cription/Examples	*QV (specify)* _____	

urvivor guilt [APPLICABLE ONLY IF MULTIPLE VICTIMS].

quency	*Intensity*	*Current*
e you felt guilty about surviving ENT) when others did not? Tell me e about that. *(What do you feel guilty t?)* How much of the time have you that way in the past month? None of the time Very little of the time (less than 10%) Some of the time (approx. 20–30%) Much of the time (approx. 50–60%) Most or all of the time (more than 80%) Not applicable	How strong were these feelings of guilt? How much distress or discomfort did they cause? 0 No feelings of guilt 1 Mild: slight feelings of guilt 2 Moderate: guilt feelings definitely present, some distress but still manageable 3 Severe: marked feelings of guilt, considerable distress 4 Extreme: pervasive feelings of guilt, self-condemnation regarding survival, incapacitating distress	F ____ I ____ Sx: Y N *Lifetime* F ____ I ____ Sx: Y N
scription/Examples	*QV (specify)* _____	

28. a reduction in awareness of his or her surroundings (e.g., ' being in a daze').

Frequency

Have there been times when you felt out of touch with things going on around you, like you were in a daze? What was that like? [DISTINGUISH FROM FLASHBACK EPISODES] **How often has that happened in the past month?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)*

0 Never
1 Once or twice
2 Once or twice a week
3 Several times a week
4 Daily or almost every day

Description/Examples

Intensity

How strong was this feeling of being out of touch or in a daze? *(Were you confused about where you actually were or what you were doing at the time?)* **How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)*

0 No reduction in awareness
1 Mild: slight reduction in awareness
2 Moderate: definite but transient reduction in awareness, may report feeling 'spacy'
3 Severe: marked reduction in awareness, may persist for several hours
4 Extreme: complete loss of awareness of surroundings, may be unresponsive, possible amnesia for the episode (blackout)

QV (specify) _____

Trauma-related? *1 definite 2 probable 3 unlikely*

Current _____ *Lifetime* _____

Current
F ____
I ____
Sx: Y N

Lifetime
F ____
I ____
Sx: Y N

29. derealization.

Frequency

Have there been times when things going on around you seemed unreal or very strange and unfamiliar? [IF NO:] *(What about times when people you knew suddenly seemed unfamiliar?)* **What was that like? How often has that happened in the past month?** [IF NOT CLEAR:] *(Was it due to an illness or the effects of drugs or alcohol?)* **When did you first start feeling that way?** *(After the [EVENT]?)*

0 Never
1 Once or twice
2 Once or twice a week
3 Several times a week
4 Daily or almost every day

Description/Examples

Intensity

How strong was (DEREALIZATION)? How long did it last? What did you do while this was happening? *(Did other people notice your behavior? What did they say?)*

0 No derealization
1 Mild, slight derealization
2 Moderate, definite but transient derealization
3 Severe, considerable derealization, marked confusion about what is real, may persist for several hours
4 Extreme, profound derealization, dramatic loss of sense of reality or familiarity

QV (specify) _____

Trauma-related? *1 definite 2 probable 3 unlikely*

Current _____ *Lifetime* _____

Current
F ____
I ____
Sx: Y N

Lifetime
F ____
I ____
Sx: Y N

depersonalization.

equency	***Intensity***	***Current***
ve there been times when you felt as if u were outside of your body, watching urself as if you were another person? NO:] *(What about times when your body strange or unfamiliar to you, as if it had nged in some way?)* **What was that like? w often has that happened in the past nth? [IF NOT CLEAR:]** *(Was it due to an ess or the effects of drugs or alcohol?)* **hen did you first start feeling that way?** *ter the [EVENT]?)* 0 Never 1 Once or twice 2 Once or twice a week 3 Several times a week 4 Daily or almost every day ***scription/Examples***	**How strong was this feeling of (DEPERSONALIZATION)? How long did it last? What did you do while this was happening?** *(Did other people notice your behavior? What did they say?)* 0 No depersonalization 1 Mild: slight depersonalization 2 Moderate: definite but transient depersonalization 3 Severe: considerable depersonalization, marked sense of detachment from self, may persist for several hours 4 Extreme: profound depersonalization, dramatic sense of detachment from self ***QV (specify)*** _____ ***Trauma-related?*** *1 definite 2 probable 3 unlikely* *Current* _____ *Lifetime* _____	F ____ I ____ Sx: Y N ***Lifetime*** F ____ I ____ Sx: Y N

CAPS Summary Sheet

Name: Interviewer: Date:

A. Traumatic event:

KEY: F = Frequency rating I = Intensity rating F + I = Frequency **plus** Intensity ratings

B. Re-experiencing symptoms	*Current*			*Lifetime*		
	Freq	Int	F + I	Freq	Int	F + I
1. intrusive recollections						
2. distressing dreams						
3. acting or feeling as if event were recurring						
4. psychological distress at exposure to cues						
5. physiological reactivity on exposure to cues						
B subtotals						
Number of Criterion B symptoms (need 1)						

C. Avoidance and numbing symptoms	*Current*			*Lifetime*		
	Freq	Int	F + I	Freq	Int	F + I
6. avoidance of thoughts, feelings, or conversations						
7. avoidance of activities, places, or people						
8. inability to recall important aspect of trauma						
9. diminished interest or participation in activities						
10. detachment or estrangement						
11. restricted range of affect						
12. sense of a foreshortened future						
C subtotals						
Number of Criterion C symptoms (need 3)						

D. Hyperarousal symptoms	*Current*			*Lifetime*		
	Freq	Int	F + I	Freq	Int	F + I
13. difficulty falling or staying asleep						
14. irritability or outbursts of anger						
15. difficulty concentrating						
16. hypervigilance						
17. exaggerated startle response						
D subtotals						
Number of Criterion D symptoms (need 2)						

E. Duration of disturbance	*Current*		*Lifetime*	
19. duration of disturbance at least one month	NO	YES	NO	YES

F. Significant distress or impairment in functioning	*Current*		*Lifetime*	
20. subjective distress				
21. impairment in social functioning				
22. impairment in occupational functioning				
At least one ≥ 2?	NO	YES	NO	YES

)diagnosis	*Current*		*Lifetime*	
PTSD present – all criteria (A-F) met?	NO	YES	NO	YES
ecify: 18. with delayed onset (≥ 6 months delay)	NO	YES	NO	YES
19. acute (< 3 months) or chronic (≥ 3 months)	acute	chronic	acute	chronic

al ratings	*Current*	*Lifetime*
global validity		
global severity		
global improvement		

iated features	*Current*			*Lifetime*		
	Freq	Int	F + I	Freq	Int	F + I
guilt over acts of commission or omission						
survivor guilt						
reduction in awareness of surroundings						
derealization						
depersonalization						

s developed by Blake, Weathers, Nagy, Kaloupek, Charney and Keane
S Department of Veteran Affairs National Center for PTSD in 1990
ed in 1997.

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[illegible]

Name ...

[illegible] emotions play an important part in [illegible] If you [illegible] about these feelings he or she will be able to help you more.

Please read each item and underline the reply which comes closest to how you have been feeling [illegible] Don't take too long over your replies, your immediate reaction to each item will usually be more accurate than a long, thought-out response.

I feel as if I am slowed down
Nearly all the time
Very often
Sometimes
Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach
Not at all
Occasionally
Quite often
Very often

I have lost interest in my appearance
Definitely
I don't take as much care as I should
I may not take quite as much care
I take just as much care as ever

I feel restless as if I have to be on the move
Very much indeed
Quite a lot
Not very much
Not at all

I look forward with enjoyment to things
As much as I ever did
Rather less than I used to
Definitely less than I used to
Hardly at all

I get sudden feelings of panic
Very often indeed
Quite often
Not very often
Not at all

I can enjoy a good book or radio or television programme
Often
Sometimes
Not often
Very seldom

I still enjoy the things I used to enjoy
Definitely as much
Not quite so much
Only a little
Hardly at all

I get a sort of frightened feeling as if something awful is about to happen
Very definitely and quite badly
Yes, but not too badly
A little, but it doesn't worry me
Not at all

I can laugh and see the funny side of things
As much as I always could
Not quite so much now
Definitely not so much now
Not at all

Worrying thoughts go through my mind
A great deal of the time
A lot of the time
From time to time
Almost never

I feel cheerful
Not at all
Not often
Sometimes
Most of the time

I can sit at ease and feel relaxed
Definitely
Usually
Not often
Not at all

Now check that you have answered all the questions

DAVIDSON TRAUMA SCALE

by Jonathan R.T. Davidson, M.D.

Name:_____ Age: _____ Sex: ☐ Male ☐ Female

Date:_____/_____/_____

Please identify the trauma that is most disturbing to you.

_____

_____

Each of the following questions asks you about a specific symptom. For each question, consider how often in the last week the symptom troubled you and how severe it was. In the two boxes beside each question, write a number from 0 - 4 to indicate the frequency and severity of the symptom.

FREQUENCY	SEVERITY
0 = Not At All	0 = Not At All Distressing
1 = Once Only	1 = Minimally Distressing
2 = 2 - 3 Times	2 = Moderately Distressing
3 = 4 - 6 Times	3 = Markedly Distressing
4 = Every Day	4 = Extremely Distressing

		FREQUENCY	SEVERITY
1.	Have you ever had painful images, memories, or thoughts of the event?		
2.	Have you ever had distressing dreams of the event?		
3.	Have you felt as though the event was recurring? Was it as if you were reliving it?		
4.	Have you been upset by something that reminded you of the event?		
5.	Have you been physically upset by reminders of the event? (This includes sweating, trembling, racing heart, shortness of breath, nausea, or diarrhea.)		
6.	Have you been avoiding any thoughts or feelings about the event?		
7.	Have you been avoiding doing things or going into situations that remind you of the event?		
8.	Have you found yourself unable to recall important parts of the event?		
9.	Have you had difficulty enjoying things?		
10.	Have you felt distant or cut off from other people?		
11.	Have you been unable to have sad or loving feelings?		
12.	Have you found it hard to imagine having a long life span and fulfilling your goals?		
13.	Have you had trouble falling asleep or staying asleep?		
14.	Have you been irritable or had outbursts of anger?		
15.	Have you had difficulty concentrating?		
16.	Have you felt on edge, been easily distracted, or had to stay "on guard"?		
17.	Have you been jumpy or easily startled?		

Your Health and Well-Being

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

For each of the following questions, please tick the one box that best describes your answer.

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

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

2. **The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?**

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
b Climbing several flights of stairs	☐ 1	☐ 2	☐ 3

(IQOLA SF-12v2 Standard, English (United Kingdom) 8/02)

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

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. <u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Were limited in the <u>kind</u> of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. **During the <u>past 4 weeks</u>, how much of the time have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. <u>Accomplished less</u> than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Did work or other activities <u>less carefully than usual</u>	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

6. **These questions are about how you feel and how things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the <u>past 4 weeks</u>...**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt downhearted and low?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7. **During the <u>past 4 weeks</u>, how much of the time has your <u>physical health or emotional problems</u> interfered with your social activities (like visiting with friends, relatives, etc.)?**

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

Thank you for completing these questions!

Orientation To Life Questionnaire

Here is a series of questions relating to various aspects of our lives. Each question has seven possible answers. Please mark the number which expresses your answer, with numbers 1 and 7 being the extreme answers. If the words under 1 are right for you, circle 1; if the words under 7 are right for you, circle 7. If you feel differently, circle the number which best expresses your feeling. Please give only one answer to each question.

1. When you talk to people, do you have the feeling they don't understand you?

1 2 3 4 5 6 7
never have this feeling always have this feeling

2. In the past, when you had to do something which depended upon cooperation with others, did you have the feeling that it:

1 2 3 4 5 6 7
surely wouldn't get done surely would get done

3. Think of the people with whom you come into contact daily, aside from ones you feel closest. How well do you know most of them?

1 2 3 4 5 6 7
you feel that they're strangers you know them very well

4. Do you have the feeling that you don't really care about what goes on around you?

1 2 3 4 5 6 7
very seldom or never very often

5. Has it happened in the past that you were surprised by the behaviour of people whom you thought you knew well?

1 2 3 4 5 6 7
never happened always happened

6. Has it happened that people whom you counted on disappointed you?

1 2 3 4 5 6 7
never happened always happened

7. Life is:

1 2 3 4 5 6 7
full of interest completely routine

8. Until now your life has had:

1	2	3	4	5	6	7
no clear goals or purpose at all						very clear goals and purpose

9. Do you have the feeling that you are being treated unfairly?

1	2	3	4	5	6	7
very often						very seldom or never

10. In the past ten years your life has been:

1	2	3	4	5	6	7
full of changes without your knowing what will happen next						completely consistent and clear

11. Most of the things you do in the future will probably be:

1	2	3	4	5	6	7
completely fascinating						deadly boring

12. Do you have the feeling that you are in an unfamiliar situation and don't know what to do?

1	2	3	4	5	6	7
very often						very seldom or never

13. What best describes how you see life:

1	2	3	4	5	6	7
one can always find a solution to painful things in life						there is no solution to painful things in life

14. When you think about your life, you very often:

1	2	3	4	5	6	7
feel how good it is to be alive						ask yourself why you exist at all

15. When you face a difficult problem, the choice of solution is:

1	2	3	4	5	6	7
always confusing and hard to find						always completely clear

16. Doing the things you do every day is:

1 2 3 4 5 6 7
a source of deep pleasure and satisfaction — a source of pain and boredom

17. Your life in the future will probably be:

1 2 3 4 5 6 7
full of changes without your knowing what will happen next — completely consistent and clear

18. When something unpleasant happened in the past your tendency was:

1 2 3 4 5 6 7
'to eat yourself up' about it — to say 'ok that's that, I have to live with it' and go on

19. Do you have very mixed-up feelings and ideas?

1 2 3 4 5 6 7
very often — very seldom or never

20. When you do something that gives you a good feeling:

1 2 3 4 5 6 7
it's certain that you'll go on feeling good — it's certain that something will happen to spoil the feeling

21. Does it happen that you have feelings inside you would rather not feel?

1 2 3 4 5 6 7
very often — very seldom or never

22. You anticipate that your personal life in the future will be:

1 2 3 4 5 6 7
totally without meaning or purpose — full of meaning and purpose

23. Do you think that there will always be people whom you'll be able to count on in the future?

1 2 3 4 5 6 7
you're certain there will be — you doubt there will be

24. Does it happen that you have the feeling that you don't know exactly what's about to happen?

1 2 3 4 5 6 7
very often — very seldom or never

25. Many people- even those with a strong character-sometimes feel like sad sacks (losers) in certain situations. How often have you felt this way in the past?

1 2 3 4 5 6 7
never — very often

26. When something happened, have you generally found that:

1 2 3 4 5 6 7
you overestimated or underestimated its importance — you saw things in the right proportion

27. When you think of difficulties you are likely to face in important aspects of your life, do you have the feeling that:

1 2 3 4 5 6 7
you will always succeed in overcoming difficulties — you won't succeed in overcoming difficulties

28. How often do you have the feeling that there's little meaning in the things you do in your daily life?

1 2 3 4 5 6 7
very often — very seldom or never

29. How often do you have feelings that you're not sure you can keep under control?

1 2 3 4 5 6 7
very often — very seldom or never

ADDENBROOKE'S COGNITIVE EXAMINATION - ACE-R

Final Revised Version A (May 2004)

Name : Date of birth : Hospital no. : *Addressograph*	Date of testing: ..... /..... /..... Tester's name: ..... Age at leaving full-time education: ..... Occupation: ..... Handedness: .....

ORIENTATION

➢ Ask: What is the	Day	Date	Month	Year	Season	[Score 0-5]
	.....	.....	.....	.....	.....	
➢ Ask: Which	Building	Floor	Town	County	Country	[Score 0-5]
	.....	.....	.....	.....	.....	

REGISTRATION

➢ Tell: 'I'm going to give you three words and i'd like you to repeat after me: lemon, key and ball'. After subject repeats, say 'Try to remember them because i'm going to ask you later'. Score only the first trial (repeat 3 times if necessary).

[Score 0-3]

Register number of trials .....

ATTENTION & CONCENTRATION

➢ Ask the subject: ' could you take 7 away from a 100? After the subject responds, ask him or her to take away another 7 to a total of 5 subtractions. If subject fails, ask: 'did you mean __ ?' If subject still makes a mistake, switch to spelling. If subject corrects himself or herself, continue.

[Score 0-5]
(for the best performed task)

Stop after five subtractions (93, 86, 79, 72, 65). ....

➢ Ask: 'could you please spell **WORLD** for me? Then ask him/her to spell it backwards:

....

MEMORY - Recall

➢ Ask: 'Which 3 words did I ask you to repeat and remember?'

[Score 0-3]

....

MEMORY - Anterograde Memory

➢ Tell: ' I'm going to give you a name and address and I'd like you to repeat after me. We'll be doing that 3 times, so you have a chance to learn it. I'll be asking you later'

[Score 0-7]

Score only the third trial

	1st Trial	2nd Trial	3rd Trial
Harry Barnes	....	....	....
73 Orchard Close	....	....	....
Kingsbridge	.....	.....	.....
Devon	.....	.....	.....

MEMORY - Retrograde Memory

[Score 0 -4]

➢ Name of current Prime Minister .....
➢ Name of the woman who was Prime Minister .....
➢ Name of the USA president .....
➢ Name of the USA president who was assassinated in the 1960's .....

ATTENTION & CONCENTRATION | MEMORY | VISUOSPATIAL | LANGUAGE

VERBAL FLUENCY - Letter 'P' and animals

➢ **Letters**

Say: 'I'm going to give you a letter of the alphabet and I'd like you to generate as many words as you can beginning with that letter, but not names of people or places. Are you ready? You've got a minute and the letter is P'

[Score 0 - 7] ☐

0-15 sec	16-30 sec	31-45 sec	46-60 sec		
				>17	7
				14-17	6
				11-13	5
				8-10	4
				6-7	3
				4-5	2
				3-4	1
				<3	0
				total	correct

➢ **Animals**

Say: 'Now can you name as many animals as possible, beginning with any letter?

[Score 0 - 7] ☐

0-15 sec	16-30 sec	31-45 sec	46-60 sec		
				>21	7
				17-21	6
				14-16	5
				11-13	4
				9-10	3
				7-8	2
				5-6	1
				<5	0
				total	correct

LANGUAGE - Comprehension

➢ Show written instruction:

[Score 0-1] ☐☐

Close your eyes

➢ 3 stage command:
'Take the paper in your right hand. Fold the paper in half. Put the paper on the floor'

[Score 0-3] ☐☐

LANGUAGE - Writing

➢ Ask the subject to make up a sentence and write it in the space below:
Score 1 if sentence contains a subject and a verb (see guide for examples)

[Score 0-1] ☐☐

VISUAL-SPATIAL | FLUENCY | LANGUAGE

LANGUAGE - Repetition

[Score 0-2]

➢ Ask the subject to repeat:' **hippopotamus'; 'eccentricity; 'unintelligible'; 'statistician'**
Score 2 if all correct; 1 if 3 correct; 0 if 2 or less.

[Score 0-1]

➢ Ask the subject to repeat: **'Above, beyond and below'**

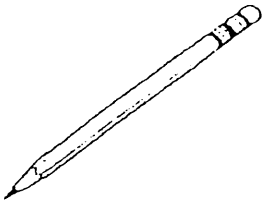
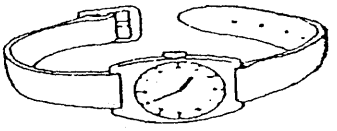
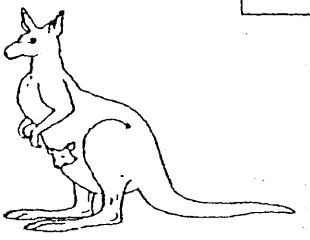
[Score 0-1]

➢ Ask the subject to repeat: **'No ifs, ands or buts'**

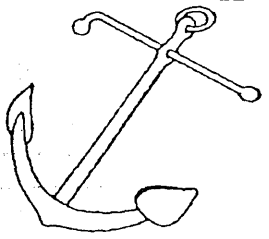
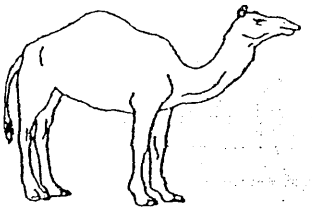
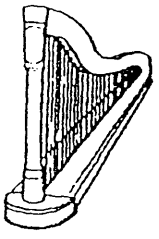
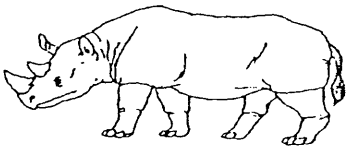
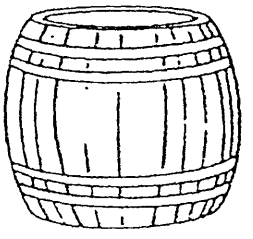
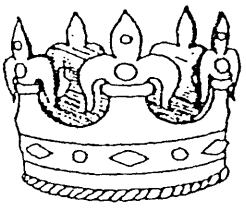
LANGUAGE - Naming

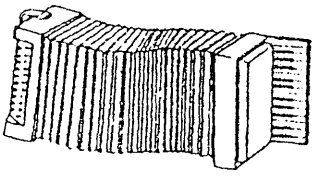
➢ Ask the subject to name the following pictures:

[Score 0-2]
pencil +
watch

[Score 0-10]



LANGUAGE - Comprehension

[Score 0-4]

➢ Using the pictures above, ask the subject to:

- Point to the one which is associated with the monarchy _____
- Point to the one which is a marsupial _____
- Point to the one which is found in the Antarctic _____
- Point to the one which has a nautical connection _____

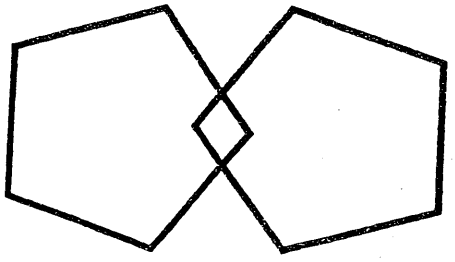
LANGUAGE - Reading

➢ Ask the subject to read the following words: [Score 1 only if all correct] [Score 0-1]

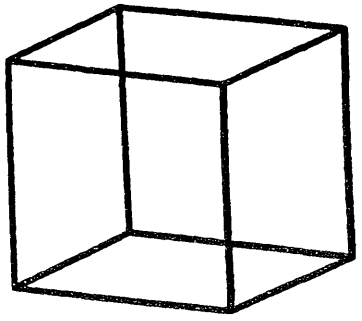
sew
pint
soot
dough
height

VISUOSPATIAL ABILITIES

➢ Overlapping pentagons: Ask the subject to copy this diagram: [Score 0-1]



➢ Wire cube : Ask the subject to copy this drawing (for scoring, see instructions guide) [Score 0-2]

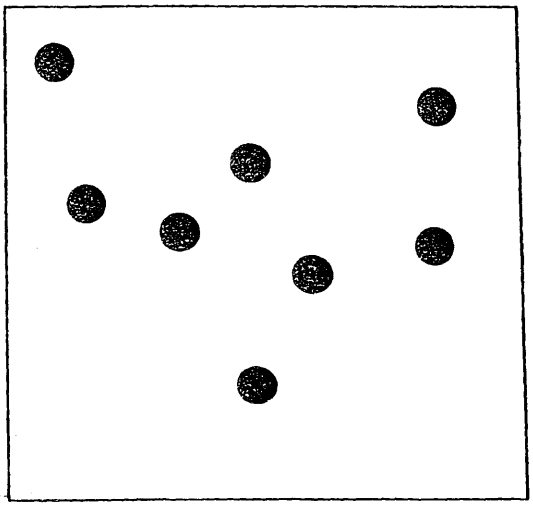


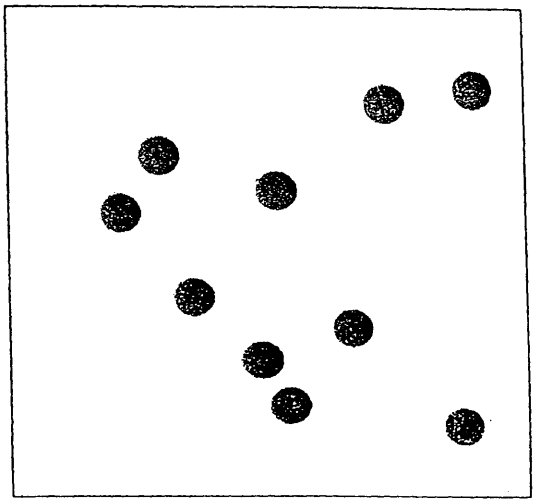
➢ Clock: Ask the subject to draw a clock face with numbers and the hands at ten past five. (for scoring see instruction guide: circle = 1, numbers = 2, hands = 2 if all correct) [Score 0-5]

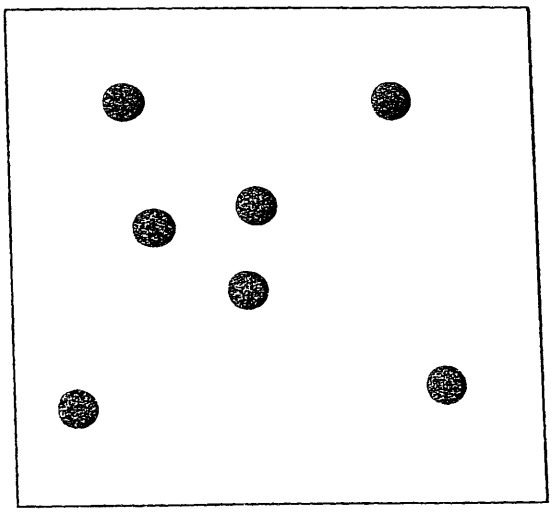
PERCEPTUAL ABILITIES

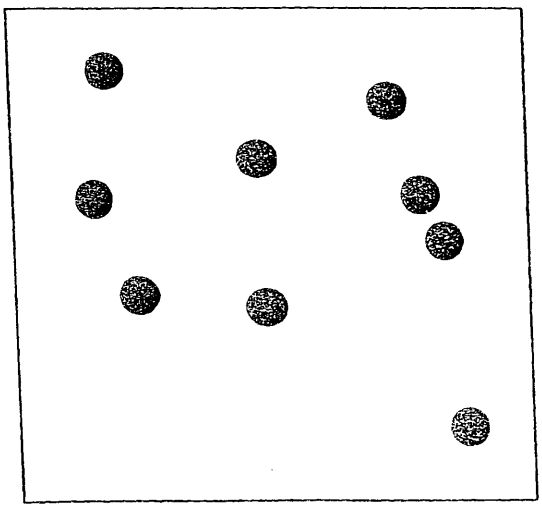
➢ Ask the subject to count the dots without pointing them

[Score 0-4]









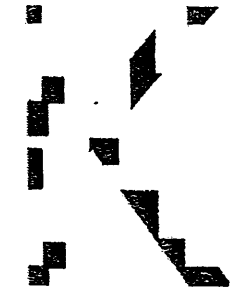
VISUOSPATIAL

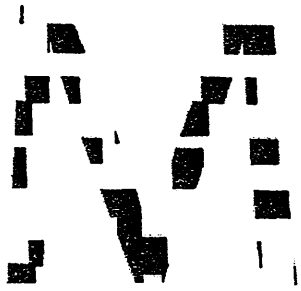
ADDENBROOKE'S COGNITIVE EXAMINATION - ACE-R *Final Revised Version A (May 2004)*

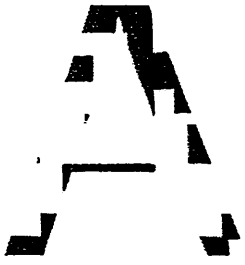
PERCEPTUAL ABILITIES

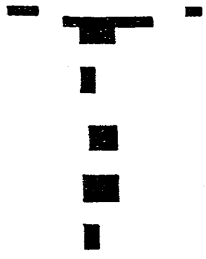
➢ Ask the subject to identify the letters

[Score 0-4]









VISUOSPATIAL

RECALL

➢ Ask "Now tell me what you remember of that name and address we were repeating at the beginning"

Harry Barnes
73 Orchard Close
Kingsbridge
Devon

[Score 0-7]

MEMORY

RECOGNITION

➢ Tick items recalled on the right hand side - shadowed column. For not recalled items, test recognition by reading the 3 alternatives 'was the name X, Y or Z?' and so on. Score 0-5 including items recalled and recognised. If all items were recalled, skip the recognition test, scoring 5 straight away (see instructions guide).

[Score 0-5]

Jerry Barnes		Harry Barnes		Harry Bradford		recalled	
37		73		76		recalled	
Orchard Place		Oak Close		Orchard Close		recalled	
Oakhampton		Kingsbridge		Dartington		recalled	
Devon		Dorset		Somerset		recalled	

General Scores

SCORE

MMSE	/30
ACE-R	/100

Subscores

Attention and Orientation	/18
Memory	/26
Fluency	/14
Language	/26
Visuospatial	/16

GENERAL INFORMATION QUESTIONNAIRE

This questionnaire has been developed to help us gain a better understanding of your experiences following your recent admission to the Critical Care Unit. We would be grateful if you could answer the following questions as honestly as possible. Your answers will be treated in complete confidence.

PART ONE

A. Background Information

Name: _____ Study Number _____

Address:

_____

_____

_____

Telephone Number: _____

Date of Birth: _____

Age: _____

Sex: _____

Marital Status: SINGLE MARRIED DIVORCED SEPARATED WIDOWED

Names and ages of

i. Partner: _____

ii. Children: _____

_____

_____

Occupation: _____

How long have you been in your present job? : _____

1. Have you ever-received treatment for any significant physical illness or injury in the past?

YES NO

Please describe this.

_____

_____

_____

_____

_____

2. Have you ever-received treatment or counselling for any psychological problems in the past?

YES NO

Who was this with?

_____

_____

3. Have you ever been involved in any major traumatic events in the past? (e.g. fires, road traffic accidents, attacks, previous serious illness) YES NO

If yes, please give details

_____

_____

_____

_____

_____

4. Has any relative of yours (please include distant relatives) ever received treatment or counselling for any psychological problems in the past?

YES/NO/DON'T KNOW

If yes, please describe

_____

_____

_____

PART TWO

The next questions concern your level of functioning before your recent (traumatic) experiences. Please circle the number, which best applies to you.

5. Before the experience my work was impaired:

1 2 3 4 5 6 7 8 9 10

Not at All Very Severely

6. Before the experience, my home management (cleaning, shopping, paying bills, looking after children, cooking) was impaired:

1 2 3 4 5 6 7 8 9 10

Not at All Very Severely

7. Before the experience, my social activities with others (parties, outings, sports etc.) were impaired:

1 2 3 4 5 6 7 8 9 10

Not at All Very Severely

8. Before the experience, my private leisure activities (reading, gardening, walking) were impaired:

1 2 3 4 5 6 7 8 9 10
Not at All — Very Severely

9. Before the experience I was content with my life:

1 2 3 4 5 6 7 8 9 10
Not at All — Very Content

10. In the last week, I have felt content with my life:

1 2 3 4 5 6 7 8 9 10
Not at All — Very Content

THE TRAUMATIC EXPERIENCE

11. The most traumatic experience was being a patient on the Critical Care Unit YES/NO

12. Please describe the experience of being a patient on Critical Care.

_____
_____
_____
_____
_____
_____

13. How stressful was your experience of being a patient on the Critical Care Unit?

1 2 3 4 5 6 7 8 9 10
Not at all Stressful — Extremely Stressful

14. What were the most stressful experiences on the critical care unit?

_____
_____
_____
_____
_____

15. Did you think you were?

Going to die? YES NO
Think it was possible you could die? YES NO
Think it was unlikely you would die, but that it could happen? YES NO

16. Did anyone else die? YES NO

17. If yes, who died?

_____

18.Was witnessing other sick patients, distressing for you? YES NO

19. How did you cope with this?

_____

_____

20. During the Critical Care experience were you:

Calm?	YES	NO
Frightened?	YES	NO
Panicky?	YES	NO
Tearful?	YES	NO
Shocked?	YES	NO
"Frozen"?	YES	NO
Acting Rationally?	YES	NO
Unconscious?	YES	NO
No Recollection?	YES	NO

21. If you were unconscious or have no recollection, how have you learnt about your experience?

_____

_____

_____

22. Please describe any other feelings you may have experienced

_____

_____

_____

_____

23. Did you have any previous training or experience, which has helped you cope with the experience?

YES NO

Please describe this.

_____

_____

24. Do you hold anyone or anything as responsible for the incident?

YES NO

If Yes, who/what?

_____

_____

25. Do you feel you are to blame in any way? YES NO

If yes, please explain.

_____

_____

_____

If your most traumatic experience was something other than being a patient on the Critical Care Unit – please answer questions 26 - 40, if not please go to question 41

26. Please describe your traumatic experience?

_____

_____

_____

28.How stressful was your experience of the trauma?

1	2	3	4	5	6	7	8	9	10
Not at all Stressful									Extremely Stressful

29. What were the most stressful experiences?

_____

_____

_____

_____

_____

30. Did you think you were?

Going to die? YES NO

Think it was possible you could die? YES NO

Think it was unlikely you would die, but that it could happen? YES NO

31. Did anyone else die? YES NO

32. If yes, who died?

_____

_____

33.Was witnessing these events, distressing for you? YES NO

34. How did you cope with this?

_____

_____

_____

35. During the experience were you:

Calm?	YES	NO
Frightened?	YES	NO
Panicky?	YES	NO
Tearful?	YES	NO
Shocked?	YES	NO
"Frozen"?	YES	NO
Acting Rationally?	YES	NO
Unconscious?	YES	NO
No Recollection?	YES	NO

36. If you were unconscious or have no recollection, how have you learnt about your experience?

_____

_____

_____

37. Please describe any other feelings you may have experienced below.

_____

_____

_____

_____

38. Did you have any previous training or experience, which helped you cope?

YES NO

Please describe this.

_____

_____

39. Do you hold anyone or anything as responsible for the incident?

YES NO

If Yes, who/what?

_____

_____

40. Do you feel you are to blame in any way? YES NO

If yes, please explain.

_____

_____

_____

Applicable to all patients

41. Do you find yourself often thinking about the experience?

1 2 3 4 5 6 7 8 9 10
Not at all some of the time all of the time

43. If you do have thoughts about the experience, do you deliberately try to avoid thinking about it?

1 2 3 4 5 6 7 8 9 10
Not at all some of the time all of the time

44. Have you found that you feel angry when you have these thoughts?

1 2 3 4 5 6 7 8 9 10
Not at all some of the time all of the time

45. Have you found that you feel guilty, when you have these thoughts?

1 2 3 4 5 6 7 8 9 10
Not at all some of the time all of the time

46. Are you satisfied with the treatment you have had so far?

1 2 3 4 5 6 7 8 9 10
Not at All Very Satisfied

47. How much physical pain are you suffering from at present?

1 2 3 4 5 6 7 8 9 10
None at all Severe pain

48. How do you see the future? GOOD/BAD/UNSURE

49. Since the experience do you feel your mental health has? IMPROVED/DETERIORATED/STAYED THE SAME

50. How much do you expect to recover physically?

1 2 3 4 5 6 7 8 9 10
Not at All Totally

51. How much do you expect to recover mentally?

1	2	3	4	5	6	7	8	9	10
Not at All									Totally

Thank you for completing this questionnaire.

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