

## 2010 Annual Evidence Update on Critical Illness Rehabilitation

### Introduction



Annual Evidence Updates (AEU) are produced by NHS Evidence and aim to draw together recently published, high quality evidence – focusing particularly on systematic reviews and published guidelines - which it is hoped will inform and enhance the decision making and planning of clinicians, commissioners and others involved in the process of health care.

NICE issued guidance [CG83 Critical illness rehabilitation](#) in March 2009 based on literature published up to June 2008. This AEU intends to highlight any relevant, good quality evidence published subsequently until October 2009.

### Background

The introduction to the [original guideline](#) provides a background to critical illness rehabilitation: More than 110,000 people are admitted into critical care units in England and Wales each year (estimated from the UK Intensive Care National Audit and Research Centre [ICNARC] Case Mix Programme [CMP] Summary Statistics); most of these people (75%) survive to be discharged home. Many of these people experience significant and persistent problems with physical, non-physical (such as psychological, psychiatric or cognitive) and social functioning after discharge from critical care. These problems are frequently unrecognised and, when identified, may not be appropriately assessed or managed.

Rehabilitation strategies during critical care and after discharge from critical care may help to improve patient outcomes. Such strategies may also reduce the length of stay in critical care and hospital stay after discharge from critical care, minimise hospital readmission rates and reduce the use of primary care resources. Furthermore, these strategies could help patients return to their previous level of activities sooner. The time taken to return to the previous level of activities depends on the patient's critical illness and is typically between 9 and 12 months after hospital discharge, or longer.

Currently, rehabilitation strategies after a period of critical illness tend to be disease-specific and served by neuroscience, cardiac services and burns units. For general adult critical care patients who do not fall into the above specialist rehabilitation services, no alternative rehabilitation pathway currently exists.

There is evidence to suggest that multidisciplinary rehabilitation strategies after critical illness can aid physical recovery and help people cope with the physical and non-physical problems associated with critical illness. The availability of rehabilitation after critical illness varies widely across the country and currently lacks coordination. [End of excerpt of original guideline]

### Evidence Update

For this annual evidence update a detailed literature review was undertaken to retrieve any evidence published subsequent to the literature search which formed the basis for the NICE guideline. A total of 29 articles were selected for review and appraisal by a team of critical care practitioners. In this context it has to be noted that the evidence base on the subject is still relatively small. For the original guideline only 12 articles were selected as evidence which addressed the review questions. This evidence update intends to give an indication of encouraging trends within critical illness rehabilitation.

Evidence report and methodology:

- [Methods for retrieving and evaluating the evidence](#)

- [Expert commentary and evidence on critical illness rehabilitation](#)

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## **2010 Annual Evidence Update on Critical Illness Rehabilitation - Methods**

### **Methods for retrieving and evaluating the evidence**

NICE issued guidance on [critical illness rehabilitation](#) in March 2009 based on literature published until June 2008. This update aims to present evidence published between June 2008 and October 2009. The search aimed to identify high quality studies published in English. Due to the paucity of evidence in this subject, the clinical reviewers included lower level evidence when they considered it to be of interest to the critical care community.

#### **Search strategies**

Searches were conducted in Medline, Embase, AMED, CINAHL, the Cochrane Database of Systematic Reviews, CRD and PsycINFO. The search strategies replicated those used in the NICE guideline on Critical Illness Rehabilitation. Due to the length of the search strategies we have not included the individual steps here, for full details please refer to the [appendix to the NICE guideline](#). In total 29 articles were selected based on their abstracts.

#### **Inclusion criteria**

Publication types - guidelines, systematic reviews, health technology assessments, economic evaluations, meta-analyses, case series  
Publication dates - June 2008 - October 2009  
Publication language - English only

## 2010 Annual Evidence Update on Critical Illness Rehabilitation - Reviews

Expert commentary by **Dr Robert Parker**, Specialist Registrar and **Dr John Griffiths**, Consultant and Honorary Senior Clinical Lecturer, Adult Intensive Care Unit, Oxford Radcliffe Hospitals NHS Trust, Oxford, OX3 9DU, United Kingdom

### Introduction

The first NHS Evidence Annual Evidence Update on Rehabilitation after Critical Illness has recently been published. The NHS Evidence team have searched for trials, articles, reviews and guidelines pertaining to the rehabilitation of survivors of critical illness that have published since the National Institute for Health and Clinical Excellence (NICE) clinical guideline on 'Rehabilitation after Critical Illness' (March 2009)<sup>1</sup>. This clinical commentary provides a brief review of the clinical significance of the selected publications, but each publication should be read in full by following the links to the pubmed abstract or free full text where available.

### United Kingdom guidelines

Over one hundred thousand adults are admitted annually to intensive care units (ICUs) in the United Kingdom (UK). Although many patients experiencing ICU treatment make a good and timely recovery, evolving research has demonstrated that a significant number of patients develop long-term physical and psychological sequelae, such as exercise limitation, depression, post traumatic stress disorder (PTSD) and cognitive dysfunction. In the past decade interest in the long-term physical and psychological sequelae suffered by survivors of critical illness has spread beyond a few enthusiasts to the wider critical care community. Few critical care practitioners would argue that survival alone is an appropriate outcome measure for modern day critical care practice.

The 2009 NICE clinical guideline on rehabilitation after critical illness represented a milestone publication for many UK critical care practitioners. It provided a review of the best available evidence, acknowledging that in many areas recommendations were formed from the experience of the guideline development group due to a paucity of prospective randomised trials. The guideline provides a framework of key principles of care and an audit tool for ICUs to assess and provide appropriate physical and non-physical support at all stages of critical illness.

### Clinical intervention trials

An important goal for critical care practitioners interested in the rehabilitation of survivors of critical illness is the development of specific interventions or packages of care that improve the quality of recovery from ICU treatment, and showing the effectiveness of these interventions in rigorous clinical trials. It was good to see the publication of several such trials in 2009.

ICU follow up clinics and post-ICU aftercare are potential mechanisms of extended ICU follow-up and the development of these services has been recommended by previous publications such as 'Comprehensive Critical Care' and 'Quality Critical Care'. Whether structured extended ICU follow-up can improve recovery from ICU treatment was studied in the PRaCTICaL study (Cuthbertson et al)<sup>2</sup>. This was a UK, pragmatic, multicentre randomised controlled trial of nurse led ICU follow up clinics compared with standard care (that provided in primary care and by primary admitting hospital physicians). The aim of the study was to test the hypothesis that a structured ICU follow-up programme is effective and cost-effective at improving physical and psychological quality of life in the first year after ICU discharge. The PRaCTICaL study showed no outcome or cost effectiveness benefit in the primary or secondary outcome measures assessed. Whilst it may be true that certain subgroups may benefit from structured ICU follow up or that a different service model is preferred, this trial should encourage critical care departments to review the structure and function of their ICU follow-up service. The authors of the PRaCTICaL trial suggest that further research is needed to firstly try and determine which specific group of ICU survivors may benefit from structured ICU follow-up, secondly to better characterise the nature and timing of the post-ICU interventions, and thirdly confirm that the assessment tools currently applied are of sufficient sensitivity and specificity.

With respect to the characterisation of nature and timing of a potential rehabilitation intervention, Schweickert et al<sup>3</sup> have recently demonstrated the benefit of a structured exercise and mobility package over standard care in 104 medical ICU patients on two separate units in the USA. Patients in the intervention group had a greater chance of returning to their pre-morbid function, spent less time on the ventilator and had lower rates of delirium. This improvement in physical and non-physical domains was achieved without a significant increase in adverse events. The potential benefit of an ICU structured exercise programme has been reinforced by Burtin et al<sup>4</sup> who studied the value of additional daily lower limb cycling session to standard care in ninety patients in a single Belgian university hospital ICU. At hospital discharge there was a significant improvement in the intervention

group in both the primary outcome measure (6 minute walk distance), and various secondary outcome measures that included quadriceps strength and the physical function component of the SF-36. These two important trials represent a step change in the field of exercise therapies on the ICU. Both are rigorous prospective clinical trials designed to assess the potential benefits of a predetermined rehabilitation intervention. It is our view that current published work in this field confirms that undertaking exercise therapy on ICU is safe and is not associated with significant adverse events. Indeed ICU patients, including those mechanically ventilated, are capable of much more rehabilitation intervention than previously thought. It follows on that the majority of ICU patients should be assessed for and receive an exercise plan in keeping with the NICE guidelines pertaining to rehabilitation after critical illness. Future trials in this field should attempt to clarify the type, timing and dose of such rehabilitation interventions. The fact that the studies of Schweickert et al<sup>3</sup> and Cuthbertson et al<sup>2</sup> were published in high impact general medical journals, outside the critical care literature, underlines how important the study of rehabilitation of survivors of critical illness is to the medical community.

ICU sedation strategy has been widely studied and debated in the critical care literature over the last decade. It is increasingly recognised that ICU sedation strategy, notably the use of benzodiazepenes, can influence longer-term outcome in ICU survivors. Sackey et al<sup>5</sup> followed up patients from their previously published study of isoflurane versus midazolam for sedation on the ICU. At 6-month follow-up they report a non-significant decrease in hallucinations and delusional memory in those patients randomised to isoflurane sedation. There was no difference between the two groups with respect to the other psychological outcome measures assessed. The practicality of delivering sustained sedation with isoflurane may well limit the generalisability of these findings. However, this study adds to the increasing interest in the possible benefits of non-GABA agonist sedation agents. Interventions such as protocolised sedation and daily sedation holding have become best practice on most ICUs. Treggiari et al<sup>6</sup> studied protocolised 'light' versus 'deep' midazolam sedation strategy without sedation holding. Morphine was titrated to analgesic effect in both groups. The major finding was that the light sedation group had reduced length of mechanical ventilation and ICU stay. However, at the prescribed four week assessment, there was no significant difference between the two groups in the primary outcome measures (namely symptoms of anxiety, depression and PTSD). There was a non-significant trend to reduced PTSD symptoms in the light sedation group, in keeping with the reduction of disturbing memories and amnesia for the ICU experience. At its most basic level this study confirms that a 'light' sedation strategy can reduce the time a patient spends on ICU without precipitating long-term psychological ill effects.

In a pragmatic randomised controlled trial, Knowles and Tarrier<sup>7</sup> study the effect of prospective patient diaries detailing the ICU experience on subsequent levels of anxiety and depression. The diary was reviewed at a median of 30 days post-ICU discharge in the presence of an ICU nurse consultant. The use of a prospective ICU diary was associated with a decrease in anxiety and depression scores. However, the short time from intervention to assessment, the small number of recruited patients and the fact that the control group did not have a meeting with the nurse consultant without a diary are legitimate questions of this work. The completed 'multicentre intensive care unit diaries as a therapeutic intervention for post traumatic stress disorder following critical illness (RACHEL II)' has yet to report and should help clarify any potential therapeutic role of patient diaries in the context of an ICU admission.<sup>8</sup>

### **The long-term consequences of critical illness**

#### **Assessment tools**

At the current time the long-term health related quality of life of ICU survivors is commonly assessed through generic tools such as the SF-36 and SF-12 and Euroqol 5D. The application of widely used and well-validated generic assessment tools in the post-ICU population helps ensure rigorous data and allows comparison with other rehabilitation populations. However, a 'disease specific' assessment tool (the disease being "ICU admission") could potentially provide more sensitive and specific outcome data for the post-ICU population. Akerman et al<sup>9</sup> designed such an assessment tool (the '4P' questionnaire) and tested it against the SF-12 in a small group of Swedish ICU survivors. Although the questionnaire was reliable and displayed adequate content and concurrent validity, the sample population was small and further studies are required to confirm its true validity as an assessment tool for survivors of critical illness.

#### **The size, scale and nature of problems experienced after critical illness**

A multitude of studies reporting the prevalence of psychological and physical problems after critical illness continue to be published. Important levels of psychological morbidity have been reported in a

variety of patient groups using a variety of methods. The patient groups studied include survivors of acute lung injury (Dowdy et al)<sup>10</sup>, trauma (Ringdal et al)<sup>11</sup>, and post coronary artery bypass grafting (Panagopoulou et al)<sup>12</sup>. Using questionnaire follow-up, Adhikari et al<sup>13</sup> report increased levels of depressive symptoms between 6 and 48 months post-ICU discharge. In 41% of responders the depression was classified as moderate or severe and it was associated with decreased levels of return to employment. Davydow et al<sup>14</sup> report a PTSD symptomatology prevalence rate of 25% in survivors of trauma admitted to ICU. Potential aetiological factors identified were increased early post-ICU distress, pre-ICU depression and the use of a pulmonary artery catheter. The later factor is likely to represent a surrogate marker for illness severity.

Using well validated and widely used questionnaires (SF-36, HADS and IES), van der Schaaf et al<sup>15</sup> assessed 12-month functional status, anxiety, depression and PTSD symptomatology rates in survivors of at least two days treatment on a general Dutch ICU. Over 50% of patients report functional limitation, 18% PTSD symptomatology and 14% anxiety and depressive symptoms. In the Netherlands, Hofhuis et al<sup>16</sup> undertook a combined qualitative and quantitative assessment of ICU survivors. A number of themes emerged from the qualitative interviews and interestingly the most valued aspect of nursing care was not recognised high levels of knowledge or technical skill but the relief of fear and worry through caring behaviour. In an increasingly specialised and technical discipline such as intensive care medicine, all health care professionals should not forget the core relationship with our patients and their family. Quantitative assessment via a self-report questionnaire underlined the high level of sleep disturbance experienced by ICU survivors, reported by nearly half of respondents. Hauer et al<sup>17</sup> combined the longstanding ICU interest in the adrenal axis with the current interest in PTSD. In long-term survivors of ARDS they found an association between low baseline cortisol levels and increased numbers of traumatic memories. Whilst PTSD symptom scores correlated with traumatic memories, in contrast with previous published work, there was no relation between PTSD scores and cortisol levels. Of note, peak serum cortisol level after corticotrophin stimulation was not significantly different between those patients with low or normal baseline cortisol levels. Given the cyclical love affair of critical care with corticosteroids this may well not be the only paper to be published in this area.

Livingston et al<sup>18</sup> report on the longer-term outcome of patients admitted to the ICU of a US trauma centre after severe injury, including traumatic brain injury. Significant impairment and functional limitation is evident 3 years after ICU discharge and the authors conclude that 'survival, though important, is no longer a sufficient outcome to measure trauma center success'. This is a message that few critical care practitioners would disagree with.

ICU acquired weakness is common and presents a considerable barrier to successful early rehabilitation of critically ill patients. Great effort has been directed at minimising risk. A potentially important risk factor for ICU acquired is corticosteroid use. Hough et al<sup>19</sup> analysed the previously published ARDS Network trial of methylprednisolone use in slowly resolving ARDS<sup>20</sup>. ICU acquired weakness was assessed by chart review and was present in 34% of patients and was associated with prolonged mechanical ventilation and delayed hospital discharge. Interestingly, it was not associated with methylprednisolone use. The limitations of this work are considerable. It was a retrospective analysis of a small subgroup of patients from a bigger trial, and ICU weakness was diagnosed solely on the basis of chart review. Therefore, the association of corticosteroids and ICU acquired weakness warrants further prospective, rigorous investigation.

### **ICU Follow up services**

In addition to the PRaCTICaL study, four papers were selected that provide interesting background reading in this field. Peskett and Gibb<sup>21</sup> describe their experience in setting up a support group to enable patients and carers to share experiences of ICU in a supported environment. This was done for minimal extra financial cost. Two pieces of qualitative research from Engstrom et al<sup>22,23</sup> provide evidence for a therapeutic role of firstly patient diaries detailing an individual patient's ICU experience, and secondly encouraging patients to revisit the ICU during their recovery. A descriptive paper by Storli and Lind<sup>24</sup> details ICU survivors experience of ICU admission and treatment and the post-ICU support that was received.

### **Systematic reviews**

The literature review found three recent systematic reviews, all from Davydow as first author<sup>25,26,27</sup>. The reviews are comprehensive and well conducted and provide insight into the estimated prevalence of anxiety, depression and PTSD in survivors of critical illness. As such they are a good primer for newcomers to this rapidly expanding field.

### **Summary**

Interest in the longer-term consequences of critical illness is still evolving but current evidence confirms that a substantial number of patients experience significant physical and psychological morbidity as they recover from their ICU admission and treatment. It is accepted by most critical care physicians that we have a role to play in preventing, recognising and ameliorating the longer-term morbidity associated with critical illness through multidisciplinary co-operation. The study of the longer-term rehabilitation of ICU survivors remains in its infancy and deserves further consideration from the critical care community as highlighted by the recently published NICE guideline. A particular emphasis would be the conduct of rigorous randomised controlled trials of interventions or packages of care that are designed to try and improve the longer-term outcome of survivors of critical illness.

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The following articles were also individually evaluated by our clinical reviewers and deemed to merit inclusion.

Title	Author(s)	Clinical Reviewer's Commentary
Depression in general intensive care unit survivors: a systematic review	Davydow et al <a href="#">[abstract]</a>	Systematic Review. Description of prevalence, it has value - the intention was not to describe therapy. Studies were included if > 1M post ICU discharge and excluded survivors of ARDS/ALI published in 2008 - since it accompanies this paper it probably should be included here, despite being outside the search dates. Point prevalence of 28% "clinically significant depression" and clinician diagnosed 33%. Risk factors remain elusive and hard to define - sex, age, severity illness NOT.
Psychiatric Morbidity in Survivors of the Acute Respiratory Distress Syndrome: A Systematic Review	Davydow et al <a href="#">[abstract]</a>	This is a systematic review of the prevalence of psychiatric syndromes in patients following Acute Lung Disease (ALI) and Acute Respiratory Distress Disorder (ARDS). After sifting out many articles the authors deemed that 10 were suitable for inclusion, these were from the USA and Germany. The authors make explicit the limitations of the original work. The main findings show that Post Traumatic Stress Disorder (PTSD) remains high at 1 year post ALI/ARDS and can still be present at 8 years. Not surprisingly duration of sedation, mechanical ventilation and ICU length of stay may be risk factors for depression and/or PTSD after ALI/ARDS. The presence of depression and PTSD were associated with lower Quality of Life (QoL). It is not certain if the risk factors identified are causally linked to PTSD or if these factors reflected medical management of ICU delirium. Clarification of this could help prevention in future patients and identify patients at risk of psychiatric morbidity. It is uncertain whether the results of the review are specific to ALI/ARDS or critical illness in general because the morbidity may be related to inflammatory cytokines which are present in most causes of critical illness. It is likely that patients with the above risk factors should have follow up and rehabilitation. This is an interesting and useful review paper.
Cognitive, Functional, and Quality-of-Life	De Rooij et al <a href="#">[abstract]</a>	This paper highlights the fact that given high intensity care in ICU, elderly patients do very well in terms of quality of life and cognitive functions. However, most of the patients in the study were planned



<p>Outcomes of Patients Aged 80 and Older Who Survived at Least 1 Year After Planned or Unplanned Surgery or Medical Intensive Care Treatment</p>		<p>surgery and not "critically ill level III patients on multiple organ support". The care of these patients would be provided in a High Dependency Unit (HDU) in UK rather than in ICU. It highlights the importance of HDU after planned surgery in over 80s.</p>
<p>Developing and setting up a patient and relatives intensive care support group</p>	<p>Peskett et al <a href="#">abstract</a></p>	<p>This paper is of general interest to patient groups and clinicians alike. This paper highlights the way in which support groups can successfully be set up for patients and relatives of Intensive Care survivors.</p>
<p>A fate worse than death? Long-Term outcome of trauma patients admitted to the surgical intensive care unit</p>	<p>Livingston D et al <a href="#">abstract</a></p>	<p>US paper. Follow up rate actually low- 100/ 241 patients. Helpful, as it looks at &gt;10 days ICU stay with trauma: 79% tracheostomy and 50% brain injury. At 3.3 years 81% had essentially full independence and 49% back to work. 33 died during follow up: most due to sever brain injury. They identified age being correlated with tolerating greater levels of disability and perceiving a "good outcome". Makes strong recommendation that outcome studies need to include longer follow up.</p>
<p>Are intensive care factors associated with depressive symptoms 6 months after acute lung injury?</p>	<p>Dowdy et al <a href="#">abstract</a></p>	<p>US paper at &gt;6M post ICU discharge, after acute lung injury (ALI). N= 184 and 26% were scored as depressed, although mean/ medians of 5's are below this threshold. They found (weak) associations with surgical ICU, midazolam doses, and organ dysfunction (SOFA score)</p>
<p>Evaluation of negative emotional care experiences in burn care</p>	<p>Wikehult et al <a href="#">abstract</a></p>	<p>This article studies burn injured patients in Sweden. Sample size is small, N=42, but authors report that the number of participants represented 67% of all eligible adult admissions. Negative emotional experiences were uncommon. Despite this fear was a common reaction reported by patients. Fear is associated with Post Traumatic Stress Disorder (PTSD). Nurses should minimise moments of fear and pay extra attention to verbal and non-verbal cues of fear. Fear in this study was mainly associated with not making it. Although the authors make explicit the limitations of research I would suggest the relationship between fear and PTSD is important in the prevention of PTSD. How many times have any of us walked into an ICU and seen terror in patients' eyes. This an interesting article which has limitations but also has important implications for nurses and other practitioners regarding minimisation of frightening experiences during ICU stay.</p>
<p>Experiences of intensive care unit diaries: 'touching a tender wound</p>	<p>Engstrom et al <a href="#">abstract</a></p>	<p>This qualitative research study aimed to describe the experiences of former patients of their personal diaries written whilst they were in the critical care unit. The findings of the study should be utilised with caution but several important issues are highlighted. The use of diaries are common in many ICUs but this study reminds us that the reading of diaries by former patients is not without emotional and psychological consequences. Nurses need to be aware of this when implementing diaries and perhaps they should always be used in conjunction with ICU follow up. Former patients particularly appreciated the parts of the diaries written by close relatives whilst those sections written by nurses tended to be about treatment. Diaries helped former patients make chronological sense of their illness. Interesting paper that will be useful to those considering implementing patient diaries especially if no follow up is available.</p>
<p>Experiences of critically ill patients in the ICU</p>	<p>Hofhuis et al <a href="#">abstract</a></p>	<p>This is a small study from the Netherlands exploring patients' experiences during ICU stay. It concentrated specifically on perceptions of patients regarding nursing care, support and psychological problems. Data was collected both by semi-structured interviews with patients after discharge from ICU but whilst still in hospital, and by questionnaire three months after hospital discharge. The key theme which emerged from the</p>

		<p>interviews was support which was described as a continuum from being supported to not being supported. Three important factors emerged in relation to supporting patients:</p> <ul style="list-style-type: none"> <li>• Providing patients with information and explanation</li> <li>• Placing the patient in a central position i.e. seeing them as a human being.</li> <li>• Personal approach by nurses</li> </ul> <p>The questionnaire sample size was N=100. Only half of the sample had memories of their ICU stay. Pain and noise were the main complaints. Psychological problems reported after ICU stay included fear, inability to concentrate, depression and hallucinations. Interesting study which reminds practitioners of the importance of information giving and seeing the patient as a human being. These fundamental elements of support may get forgotten about in the hi-tech environment of the ICU.</p>
<p>Health care costs, long-term survival, and quality of life following intensive care unit admission after cardiac arrest</p>	<p>Graf et al <a href="#">abstract</a></p>	<p>This is a detailed study of health care costs for long term surviving patients who receive cardio-pulmonary resuscitation and are discharged from hospital. It is complex reading but does point out the fact that those patients who suffer cardiac arrest and are discharged from ICU/hospital without neurological sequelae costs per quality life year gained were comparable to other ICU survivors e.g. sepsis or many non-ICU patients.</p>