Review
Clinical review: Intensive care follow-up – what has it told us?
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Abstract

The majority of intensive care practitioners, until comparatively recently, was content to discharge surviving patients to the care of referring primary specialty colleagues who would undertake subsequent inpatient and outpatient care. With the exception of mortality statistics from clinical studies, the practitioners were thus denied the opportunity of understanding the full impact of critical illness on a patient and their family. The concept of the intensive care follow-up clinic has developed more recently, and is run commonly on multidisciplinary lines. These clinics serve a number of purposes, but importantly have drawn attention to broader patient-centred outcomes after intensive care. Investigators are just beginning to identify, and in some cases quantify, the postdischarge burden on patient and family; additional useful data have also come from follow-up of specific disease states. The purpose of the present review is to highlight some of the important issues that impact on recovery from critical illness towards an acceptable quality of postdischarge life. We have concentrated on the adult literature, and specifically on studies that inform us about the more general effects of critical illness. Head and spinal injury are thus largely ignored, as the effects of the primary injury overwhelm the effects of 'general' critical illness.

Keywords critical illness, follow-up studies, neuropsychology, outcome assessment (healthcare), quality of life

The impact of critical illness on life expectancy

The attrition imposed on health reserve by a critical illness is highlighted by a number of long-term follow-up studies. The 5-year mortality rate for intensive care unit (ICU) survivors is reported to be more than threefold higher than for the general population. Actuarial survival curves for ICU survivors only run parallel to the general population around 2–3 years after hospital discharge. However, marked differences occur depending on the diagnostic category [1–3]. Medical patients requiring a period in ICU have an estimated hospital mortality of 23.2% compared with 14.1% for surgical patients [4]. The difference between medical patient survival and surgical patient survival appears to be sustained beyond the ICU period. In one investigation, the median survival period for medical patients was reported as 40 days post-ICU admission compared with more than 900 days for other patients [5].
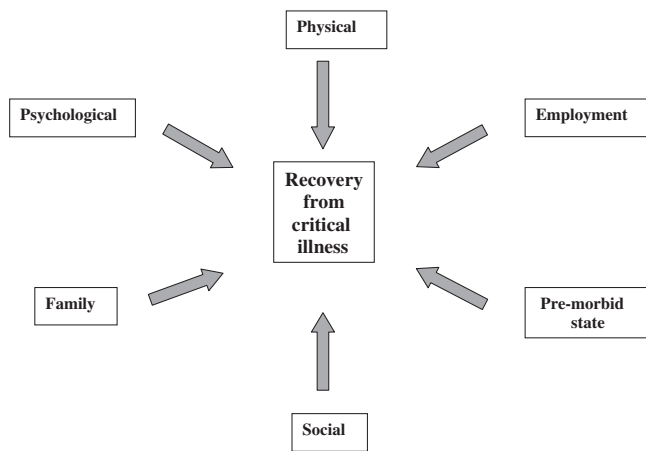
The physical impact of critical illness

Patients often find themselves unable to accomplish even simple physical tasks without exhaustion after a period of critical illness. A variety of aspects of physical status may contribute to impaired physical functioning, and this may have an important impact on quality of life (Table 1).

Nutrition

One invariable consequence of a period of critical illness is weight loss. Losses of 2% lean body mass per day [6] have been reported, which can leave the patient with a formidable energy and protein deficit. Keys *et al*. demonstrated that even healthy volunteers required longer than 1 year to recover lean body mass following a period of prolonged starvation [7]. Weakness, depression, breathlessness and altered taste perception are likely to reduce a patients' appetite and therefore to slow recovery of body mass.

ARDS = acute respiratory distress syndrome; HRQL = health-related quality of life; ICU = intensive care unit; PTSD = post-traumatic stress disorder; SF-36 = Medical Outcomes Study Short Form (SF-36) instrument.

Figure 1

Factors impacting on recovery from the intensive care unit.

Table 1

Common physical problems following a period in the intensive care unit

Weakness	Insomnia
Weight loss	Impotence
Fatigue	Skin and nail changes
Poor appetite	Hair loss
Painful joints	Pruritis
Peripheral neuropathy	Amenorrhoea
Voice and taste changes	

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The inter-relationships between tissue loss and physiological function are complex and depend on the setting within which malnutrition arises [8]. There are few published data regarding long-term nutritional follow-up of general ICU patients. Glutamine supplementation during the acute phase of illness appears to have a beneficial effect that is measurable at 6 months [9]. In addition, a number of patients suffer mechanical difficulties in swallowing specifically related to healing tracheostomy sites [10,11].

Neuropathy

Critical illness neuropathy is a well-recognized axonal neuropathy occurring in ICU patients [12]. Although recovery can be anticipated within a few months in milder cases, more severe forms can have devastating consequences. In a recent 2-year follow-up of 19 patients suffering severe critical illness neuropathy (characterized by quadriplegia or quadraparesis) associated with sepsis and multiple organ failure, two patients died within 2 months, 11 patients recovered completely, four patients remained quadriplegic, and two patients remained quadraparetic [13]. In that study, three parameters correlated with poor recovery: longer length of stay in the ICU, longer duration of sepsis, and greater weight loss [13]. The cause of critical illness neuropathy remains obscure. Numerous factors have been implicated but, as yet, insufficient evidence is available to attribute cause [14], and no information is available regarding its prevention or treatment.

Respiratory consequences

Breathlessness is a common symptom reported by ICU survivors [10]. The possible causes of breathlessness include muscle weakness, neuropathy, pulmonary fibrosis, progression of premorbid respiratory and cardiac disease, and also psychological factors.

One of the best-characterized ICU diseases is acute lung injury and its severe manifestation, the acute respiratory distress syndrome (ARDS). Follow-up studies have included physiology [15–19], radiology [15], quality of life [20], and psychological consequences [21]. Davidson *et al.* suggested that ARDS did not increase a patient's risk of death beyond discharge from hospital [22]; the long-term mortality of ARDS patients correlated with age, underlying risk factors, and comorbidity.

In another study, Davidson *et al.* used the Medical Outcomes Study Short Form (SF-36) instrument (a generic quality-of-life instrument) and the St George's Respiratory Questionnaires (a pulmonary-specific tool) [20]. They assessed 73 ARDS patients matched with control patients having equal severity of disease or injury. Davidson *et al.* concluded that, 2 years after ICU admission, ARDS survivors had clinically significant reductions in health-related quality of life (HRQL) that appeared to be caused exclusively by ARDS and its sequelae. The reductions were primarily noted in physical functioning and pulmonary disease-specific domains [20]. Continuing respiratory dysfunction thus appears to be associated with a broad impact on well-being, and this observation is unlikely to be specific to ARDS.

Most ARDS survivors have abnormal pulmonary function tests in the first 3 months of recovery; this reaches a plateau over the following 3–9 months [16,17]. Pulmonary function tests following ARDS generally demonstrate a restrictive ventilatory defect and some impairment of diffusion capacity. Alteration of lung parenchymal compliance has been documented using whole body plethysmography and measurement of transpulmonary pressure [18]. However, the number of patients followed up in this way is small and the significance of the residual restrictive deficit remains to be clarified. Reduction in diffusion capacity may be more significant in explaining reduced exercise tolerance in these individuals, some of whom desaturate during exertion.

Persistent radiographic changes in survivors of ARDS have been reported. Desai *et al.* examined computerized tomography scans of 27 survivors of ARDS [15]. Follow-up scans were performed 110–267 days (mean ± standard deviation, 196.2 ± 41.3 days) after the initial scan performed during ICU admission. The most frequent persistent abnormality, in 23 patients (85%), was a course reticular pattern with an anterior distribution. The extent of this fibrotic appearance was up to 31% of the lung field. A ground glass appearance, which was taken to indicate either oedema or fine fibrosis below the resolution of the scanner, was observed in 17 survivors; the extent ranging up to 56%. The variation in extent of these changes may partly explain the variation in pulmonary function [16–18]. The importance of these radiological changes to function remains unclear.

Cardiac consequences

Although the cardiovascular system often requires support with inotropes and vasopressors, it is assumed that there are no long-term cardiac sequelae in the absence of infarction. Using a canine model of peritoneal sepsis, Cunnion and Parrillo found that cardiac function returned to normal within a few days of recovery from a septic episode [23]. There are no documented adverse effects of general intensive care on cardiac function or on potential symptomatic problems in the post-ICU period but data are very scarce. Postural hypotension [10], possibly due to a residual autonomic neuropathy, can be problematic; the resulting dizziness decreases mobility and independence.

Other physical problems

Reduced mobility in survivors of intensive care is multifactorial: there is reduction in muscle mass, muscle weakness, joint stiffness, and poor balance. These problems are generally recognized and the appropriate physiotherapy provided.

Less obvious physical problems such as swallowing difficulties may go unnoticed. Weakness and lack of coordination of the pharyngeal musculature can initially be significant, requiring persistent effort by the patient to retrain the muscles. The presence of a tracheostomy physically impedes swallowing. A late complication of percutaneous tracheostomy, tethering of the skin to the trachea, can cause a distressing sensation when swallowing and may need surgical intervention [11].

There are few long-term follow-up studies of percutaneous tracheostomy. Those available suggest a favourable outcome, with a very small incidence of significant complications [24–26]. The results of long-term follow-up studies are awaited. Interestingly, in a comment relating to his experience of patients attending his follow-up clinic, Griffiths suggests that significant tracheal stenosis is more commonly associated with repeated intubations [26].

Table 2

Common psychosocial problems following a period in the intensive care unit

Depression	Irritability
Anxiety	Poor memory
Panic attacks	Poor concentration
Post-traumatic stress disorder	Social isolation
Guilt	Marital difficulties
Lack of confidence	Financial difficulties
Loss of libido	

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Sexual dysfunction

Withdrawal from sexual intimacy can have detrimental effects on relationships and an individual's sense of well-being. Quinlan *et al.*, reporting on the follow-up of 62 patients, found that 26% reported sexual dysfunction at 2 months, 19% at 6 months, and 16% at 1 year [27]. The reasons given by patients for their poor sex life in that study and a subsequent study were having no desire, suffering impotence despite desire, shortness of breath, surgical disfigurement, and concern that sex might precipitate a relapse of illness [28].

Neuropsychological outcomes

The ICU is a stressful and noisy environment with little differentiation between night and day [29]. Patients are often sedated with psychoactive drugs during at least part of their stay, the long-term effects of which are uncertain. Approximately one-third of the patients attending our own follow-up clinic complains of impaired memory, poor concentration, and/or mental slowing 3 months after ICU discharge (unpublished observation). How these symptoms relate to ICU stay is currently uncertain (Table 2).

Delirium

The true incidence of delirium in the ICU is unknown. Various terms have been used in the literature to describe this condition, including 'intensive care syndrome' and ICU psychosis. The lack of an evaluative tool that could be used by ICU staff to diagnose the condition in patients who are unable to communicate has hampered the collection of useful data. Estimates reported in the literature suggest that the incidence of delirium within surgical intensive care patients is 40% [30]; the incidence may be as high as 60% in older patients [31]. Our knowledge of the long-term effects of delirium is extremely limited. The diagnosis of delirium, in all but the most obvious cases, may not be straightforward; apparent quiet withdrawal may be a manifestation as much as agitated confusion. Ely and colleagues have recently developed and validated a tool for the bedside assessment of delirium in ICU

patients [32], which should prove valuable in future long-term studies.

Delirium is accompanied with profound amnesia of events occurring during and preceding the confusional state. The amnesia results in patients' memories of their stay in the ICU being fragmented and frequently distorted. Slow wave sleep is reduced in patients in the ICU [33], which is known to be important for the integration of factual memories [34]. Patients may enter a hypnagogic state during treatment in the ICU, in which control of the boundary between internally generated fantasy and the experience and recognition of external reality is impaired [35]. This state between sleep and wakefulness predisposes to hallucinations and creates a mental environment favouring the development of paranoid delusions.

During the immediate post-ICU period, the patient begins to become aware of the physical changes to their body with little conscious awareness of what has brought them to this state [36]. They may have only vague memories of pain and uncomfortable procedures [37–39]. Nightmares, dreams and hallucinations have all been described during recovery [40]. The recall of delusional memories may predominate and there is some evidence that delusional memories, without factual recall, are highly associated with the early development of stress disorders in ICU patients [41]. The lack of memory of the illness producing physical weakness appears to be a cause of subsequent frustration.

Affective disorders

Symptoms of anxiety and depression are common. In a postal questionnaire study of general intensive care survivors, Scragg *et al.* [42] reported that 38 out of 80 respondents (47%) reported clinically significant anxiety and depression as measured by the Hospital Anxiety and Depression scale [43]. Nelson *et al.* investigated depression in survivors (median period, 15 months) after intensive care for acute lung injury. Sixty-nine percent of patients without a pre-existing history of depression had clinically relevant depressive symptoms [44], which correlated with the days of sedation and the use of neuromuscular blockade.

In a study of a more varied case mix of ICU patients at 3 month follow-up, Eddleston *et al.* found a lower prevalence of psychological distress (Hospital Anxiety and Depression scale score >8): anxiety, 11.9%; depression, 9.8% [45]. Jones *et al.* reported clinically significant Hospital Anxiety and Depression scale scores in ICU patients; notably, those who could not recall any factual memory of events during their ICU stay but who retained delusional thoughts [41].

Stress disorders

Post-traumatic stress disorder (PTSD) is a condition that occurs in individuals who have experienced a traumatic event. In this condition, a 'traumatic' event is characterized by its capacity to provoke fear, helplessness, or horror in response to the threat of injury or death [46]. Symptoms include distressing 'flash backs' (re-experiencing of the event), avoidance of situations reminding the individual of the event, increased arousal, and psychological numbing. The incidence of PTSD in patients following an ICU stay varies; patients who have survived ARDS and younger patients appearing to be particularly vulnerable [45,47].

Schelling and colleagues found that memories of adverse experiences correlated with subsequent PTSD symptoms, and were also related to poor general quality of life scores [21]. By contrast, Jones *et al.* [41] found that factual memories seemed in some way protective and that delusional memories without factual recall was a situation more associated with early stress symptoms at 8 weeks. The Schelling *et al.* study did not attempt to differentiate factual from delusional memories and was undertaken years after discharge. These two important studies are thus complementary rather than contradictory.

In Scragg *et al.*'s postal study [42], 30 survivors (38%) reported symptoms of PTSD, as assessed by the Trauma Symptoms Checklist 33 [48] and the Impact of Events Scale [49]. Using the Experience after Treatment in Intensive Care 7 Item Scale, an additional questionnaire designed specifically for their study, Scragg *et al.* were able to show that intensive care treatment contributed to the causation of post-traumatic stress [42].

Patients may experience symptoms of an acute stress disorder during the early phase of their recovery. This condition is a recent diagnostic category, being defined for the first time in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* in 1999 [50]. Acute stress disorder is characterized by the early development of symptoms similar to PTSD, with the inclusion of dissociative symptoms such as detachment, depersonalization, derealization, and dissociative amnesia. Although the description of this condition as a distinct disorder from severe acute PTSD has been questioned [51], its recognition allows early psychological intervention to facilitate a patient's resolution of the traumatic experience [52].

Disorders of cognitive function

In a landmark study of ARDS survivors, Hopkins and colleagues reported that 100% of survivors experienced cognitive impairment at hospital discharge [53], including problems of memory, attention and concentration. Although they demonstrated improvements at 1 year follow-up, 30% of patients were still globally impaired and 78% were impaired in one or all of the domains assessed. Hopkins *et al.* associated the deficits with hypoxaemic episodes periods in the ICU. This added to earlier work, which had demonstrated the relation between hypoxic brain injury, hippocampal atrophy, and memory deficit [54].

Rothenhäusler *et al.* investigated cognitive performance in ARDS patients at a median time of 6 years after ICU dis-

charge [55]. These investigators found that 75% of ARDS survivors did not display signs of cognitive impairment. Of the remaining 25%, the impairment was either subthreshold or mild in the vast majority. The residual mild cognitive impairments demonstrated were found in subtests relating to attention. Although the impairments were described as mild, all patients with cognitive dysfunction were classified as disabled, compared with 22.9% of those without cognitive impairment. The investigators also found that 58.7% of survivors returned to work. These figures, similar to those published by McHugh *et al.* (56%) [19] and Schelling *et al.* (61.3%) [21], indicate a significant critical care achievement. The corollary of this, however, is that there remained a significant proportion of survivors whose employment status was significantly impaired, implying a negative social outcome.

Social and family consequences

During the patient's stay in intensive care the family members, and especially the spouse, have been shown to exhibit significant degrees of anxiety and depression [56]. After the patient has been discharged from hospital this anxiety and depression may manifest itself in overprotective behaviour that, coupled with unrealistic expectations that the patient may have of their capabilities, leads to frustration and conflict [40]. Survivors may experience guilt as they become aware of the strain placed on their family, which adds to their psychological burden predisposing them to affective disorders [39,40].

The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment investigators collected data to assess the impact of critical illness on the family [57]. They reported that 34% of patients required considerable care-giving assistance. A family member needed to give up work or make major life changes to provide care for their relative in 20% of the total. It is possible that multidisciplinary intensive care follow-up needs to address the needs of the family during the rehabilitation phase [58].

Quality of life

People with the same health status may not necessarily enjoy the same quality of life. Health and well-being are multidimensional, and they include aspects such as individuals' subjective values and preferences that make the direct measurement of quality of life difficult [59]. Item measurement theory proposes that true quality of life can be measured indirectly via a series of questions (items), each of which is a measure of the same concept or construct. The answers are assigned numerical scores that may be combined to provide 'scale' scores (e.g. physical functioning, symptom, distress, or well-being scales). These scores may then be further combined to give 'domain' scores (e.g. physical, psychological, work performance). HRQL measures potentially provide a holistic measure of the impact of critical illness on the patient, a measure of the contribution of disease-specific changes in health to overall patient well-being, and a means to evaluate

the health economic impact of intensive care medicine (e.g. the Quality Adjusted Life Year estimates).

Kutsogiannis and Noseworthy have comprehensively reviewed the available HRQL instruments [60], highlighting the complexity of creating and using HRQL instruments appropriately. By way of a caution, Ridley has recommended that the psychometric properties of questionnaires, which may not have been designed specifically for critically ill patients, should be tested and validated in critically ill patients before the results are presented [61].

Mata *et al.* have published the results of a quality-of-life questionnaire-based study. The questionnaire was completed by patients or a proxy at the time of admission to the ICU, and was compared with the results of the same questionnaire completed by the survivors 12 months later (444 of the initial 606 patients). The quality of life was reduced in 50% of survivors, remained the same in 23% and improved in 27%. A decreased quality of life was most evident in those older than 75 years of age. The pre-ICU quality of life and age were the factors with the greatest influence on post-ICU quality of life [62]. This original seven-item Quality of Life – Spanish questionnaire has since been modified to create a 15-item quality-of-life questionnaire specifically for critically ill patients [63].

Konopad *et al.* used Spitzer's Quality of Life Index, which examines the activity level, the activities of daily living, health, support, and outlook [64]. Of the original group of 504 general ICU patients who completed a baseline questionnaire at ICU admission, 293 completed a 12-month follow-up questionnaire. A significant decrease in the level of activity score and the activities of daily living score occurred at 12 months, and these scores were more significant in the older age group [64].

Using their own quality-of-life questionnaire administered to 238 patients 16 months after discharge, Brooks *et al.* found that survivors have more health problems, are more anxiously depressed, are more dependent on others, and engage in less sexual activity than a random community sample [65].

A number of investigators have used the SF-36 instrument [21,45,47], which consists of 36 questions covering eight domains and has been validated in the intensive care setting [66,67]. Compared with age-matched and gender-matched controls, Schelling *et al.* report that survivors of ARDS, at a median follow-up interval of 4 years, experienced a 25% reduction in physical function and described their general health as 15% lower. Mental health dimensions of the SF-36 were also significantly impaired, although to a lesser degree (4% reduction in mental health, 15% reduction in vitality, 10% reduction in social function) [21]. In that and a more recent study by Eddleston *et al.*, which examined a broader ICU case mix, the SF-36 scores of younger survivors were found to be worse; particularly in physical and emotional role

limitation, and in social functioning [45]. A report by Flaatten and Kvåle on survivors 12 years after ICU treatment described a similar global reduction in SF-36 scale scores, with reductions in six of the eight scale scores [68]. The pattern and scores of the SF-36 in these studies were similar to those described by Ridley *et al.* [47], who were also able to show that the quality of life of patients admitted to their ICU was not the same as the normal population. Patients who enjoyed a normal quality of life before admission suffered significant decreases following their illness. Those with pre-existing morbidity showed some improvement in their quality of life 6 months after intensive care admission, principally by improvements in mental health, vitality and social functioning.

Final remarks

What have ICU follow-up studies shown us overall? Survival curves do not run parallel to those of the average population until 2–3 years post-ICU discharge. 'Survival', however, is a poor metric for describing the impact of critical illness. We as yet have an inadequate understanding of how events in the ICU impact on recovery. The physical and psychological consequences can be significant and unanticipated.

The neuropsychological picture is beginning to emerge; a subject that warrants much further study. The burden carried by families or future caregivers is potentially great and, as yet, we have little data concerning the fiscal impact of ICU survival. Increasing knowledge in these areas will provide us with the potential to modify our approach inside the ICU to improve patient-centred outcomes in the long term.

Competing interests

None declared

References

1. Niskanen M, Kari A, Halonen P: **Five-year survival after intensive care — comparison of 12,180 patients with the general population. Finnish ICU Study Group.** *Crit Care Med* 1996, **24**:1962-1967.
2. Ridley S, Plederleith L: **Survival after intensive care. Comparison with a matched normal population as an indicator of effectiveness.** *Anaesthesia* 1994, **49**:933-935.
3. Moreno R, Agthe D: **ICU discharge decision-making: are we able to decrease post-ICU mortality?** *Int Care Med* 1999; **25**:1035-1036.
4. Intensive Care National Audit and Research Centre: *Data Analysis from the Case Mix Programme Database*, issue 4. Intensive Care National Audit and Research Centre; 2000.
5. Lam S, Ridley S: **Critically ill medical patients, their demographics and outcome.** *Anaesthesia* 1999, **54**:845-852.
6. Plank LD, Connolly AB, Hill GL: **Sequential changes in the metabolic response in severely septic patients during the first 23 days after onset of peritonitis.** *Ann Surg* 1998, **228**:146-158.
7. Keys A, Brozek J, Henschel A, *et al.*: *The Biology of Human Starvation*. Minneapolis, MN: University of Minnesota Press; 1950.
8. Vernon DR, Hill GL: **The relationship between tissue loss and function: recent developments.** *Curr Opin Clin Nutr Metab Care* 1998, **1**:5-8.
9. Griffiths RD, Jones C, Palmer TE: **Six-month outcome of critically ill patients given glutamine-supplemented parenteral nutrition.** *Nutrition* 1997, 13:295-302.
10. Griffiths RD, Jones C: **ABC of intensive care: recovery from intensive care.** *BMJ* 1999, **319**:427-429.
11. Griffiths RD: **Nutrition after intensive care.** In *Intensive Care Aftercare.* Edited by Griffiths RD, Jones C. Oxford: Butterworth-Heinemann; 2002:48-52.
12. Bolton CF, Laverty DA, Brown JD, Witt NJ, Hahn AF, Sibbald WJ: **Critically ill polyneuropathy: electrophysiological studies and differentiation from Guillain-Barre syndrome.** *J Neurol Neurosurg Psychiatry* 1986, **49**:563-567.
13. de Seze M, Petit H, Wiart L, Cardinaud JP, Gaujard E, Joseph PA, Mazaux JM, Barat M: **Critical illness polyneuropathy. A 2-year follow-up study of 19 severe cases.** *Eur Neurol* 2000, **43**:61-69.
14. Hund EF, Fogel W, Krieger D, DeGeogia M, Hacke W: **Critical illness polyneuropathy: Clinical findings and outcomes of a frequent cause of neuromuscular weaning failure.** *Crit Care Med* 1996, **24**:1328-1333.
15. Desai SR, Wells AU, Rubens M, Evans TW, Hansell DM: **Acute respiratory distress syndrome: CT abnormalities at long-term follow-up.** *Radiology* 1999, **210**:29-35.
16. Peters JI, Bell RC, Prihoda TJ: **Clinical determinants of abnormalities in pulmonary function in survivors of adult respiratory distress syndrome.** *Am Rev Respir Dis* 1989, **139**:1163-1168.
17. Ghio AJ, Elliot CG, Crapo RO: **Impairment after adult respiratory distress syndrome: an evaluation based on American Thoracic Society recommendations.** *Am Rev Respir Dis* 1989, **139**:1158-1162.
18. Aggarwal AN, Gupta D, Behera D, Jindal SK: **Analysis of static pulmonary mechanics helps to identify functional defects in survivors of acute respiratory distress syndrome.** *Crit Care Med* 2000, **28**:3480-3483.
19. McHugh LG, Milberg JA, Whitcomb ME, Schoene RB, Maunder RJ, Hudson LD: **Recovery of function in survivors of the acute respiratory distress syndrome.** *Am J Respir Crit Care Med* 1994, **150**:90-94.
20. Davidson TA, Caldwell ES, Curtis JR, Hudson LD, Steinberg KP: **Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients.** *JAMA* 1999, **281**:354-360.
21. Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, Lenhart A, Heyduck M, Polasek J, Meier M, Preuß U, Bullinger M, Schüffel W, Peter K: **Health-related quality of life and posttraumatic stress disorder in survivors of acute respiratory distress syndrome.** *Crit Care Med* 1998, **26**:651-659.
22. Davidson T, Gordon D, Rubenfeld ES, Caldwell LD, Hudson LD, Steinberg KP: **The effect of Acute Respiratory Distress Syndrome on long-term survival.** *Am J Respir Crit Care Med* 1999, **160**:1838-1842.
23. Cunnion RE, Parrillo JE: **Myocardial dysfunction in sepsis.** *Crit Care Clin* 1989, **5**:99-118.
24. Steele APH, Evans HW, Afaq MA, Robson JM, Dourado J, Tayar R, Stockwell MA: **Long-term follow-up of Griggs percutaneous tracheostomy with spiral CT and questionnaire.** *Chest* 2000, **117**:1430-1433.
25. Walz MK, Peitgen K, Thürauf N, Trost HA, Wolfhard U, Sander A, Ahmadi C, Eigler FW: **Percutaneous dilatational tracheostomy — early and long-term outcome of 326 critically ill patients.** *Int Care Med* 1998, **24**:685-690.
26. Jones C, Griffiths RD: **Physical and psychological recovery.** In *Intensive Care Aftercare*. Edited by Griffiths RD, Jones C. Oxford: Butterworth-Heinemann; 2002:56.
27. Quinlan J, Waldmann C, Fawcett D: **Sexual dysfunction after intensive care.** *Br J Anaesth* 1998, **81**:809.
28. Quinlan J, Gager M, Fawcett D, Waldman C: **Changes in sexual function after intensive care.** *Br J Anaesth* 2001, **87**:348.
29. Biley FC: **Effects of noise in hospitals.** *Br J Nurs* 1994, **3**:110-112.
30. Smith S, Garnett P, Buckley P: **Delirium in the critically ill.** *Care Crit Ill* 1997, **13**:175-178.
31. Inouye SK, Bogardus ST, Charpentier PA: **A multi-component intervention to prevent delirium in hospitalized older patients.** *N Engl J Med* 1999, **340**:669-676.
32. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, Speroff T, Gautam S, Bernard G, Inouye SK: **Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).** *Crit Care Med* 2001, **29**:1370-1379.
33. Aurell S, Elmqvist D: **Sleep in the surgical intensive care unit: continuous polygraphic recording of sleep in nine patients**

receiving post-operative care. *BMJ* 1985, **290**:1029-1032.

34. Stickgold R: **Sleep: off-line memory reprocessing.** *Trends Cogn Sci* 1998, **2**:484-492.

35. Schacter DL: **The hypnagogic state: a critical review of the literature.** *Psychol Bull* 1976, **83**:452-481.

36. Compton P: **Critical illness and intensive care: what it means to the client.** *Crit Care Nurse* 1991, **11**:50-56.

37. Tosch P: **Patients recollections of their post traumatic coma.** *J Neurosci Nurs* 1989, **20**:223-228.

38. Hewitt PB: **Subjective follow-up of patients from a surgical intensive therapy ward.** *BMJ* 1970, **4**:669-673.

39. Turner JS, Briggs SJ, Springhorn HE, Potgieter PD: **Patients'recollection of intensive care unit experience.** *Crit Care Med* 1990, **18**:966-968.

40. Jones C, Griffiths RD, Macmillan RR, Palmer TEA: **Psychological problems occurring after intensive care.** *Br J Intensive Care* 1994, **2**:46-53.

41. Jones C, Griffiths RD, Humphris G, Skirrow PM: **Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care.** *Crit Care Med* 2001, **29**:573-580.

42. Scragg P, Jones A, Fauvel N: **Psychological problems following ICU treatment.** *Anaesthesia* 2001, **56**:9-14.

43. Zigmund AS, Snaith RP: **The Hospital Anxiety and Depression Scale.** *Acta Psychiatr Scand* 1983, **67**:361-370.

44. Nelson BJ, Weinert CR, Bury CL, Marinelli WA, Gross CR: **Intensive care unit drug use and subsequent quality of life in acute lung injury patients.** *Crit Care Med* 2000, **28**: 3626-3630.

45. Eddleston JM, White P, Guthrie E: **Survival, morbidity, and quality of life after discharge from intensive care.** *Crit Care Med* 2000, **28**:2293-2299.

46. Yehuda R: **Current concepts: post-traumatic stress disorder.** *N Engl J Med* 2002, **346**:108-114.

47. Ridley SA, Chrispin PS, Scotton H, Rogers J, Lloyd D: **Changes in quality of life after intensive care: comparison with normal data.** *Anaesthesia* 1997, **52**:195-202.

48. Briere J, Runtz M: **The Trauma Symptoms Checklist (TSC-33): early data on a new scale.** *J Interpersonal Violence* 1989, **4**: 151-163.

49. Horowitz M, Wilner N, Alvarez W: **The Impact of Event Scale: a measure of subjective stress.** *Psychosom Med* 1979, **41**:209-218.

50. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition. Washington, DC: American Psychiatric Association; 1999.

51. Marshall RD, Spitzer R, Liebowitz MR: **Review and critique of the new DSM-IV diagnosis of Acute Stress Disorder.** *Am J Psych* 1999, **156**:1677-1685.

52. Bryant RA, Harvey AG: *Acute Stress Disorder: A Handbook of Theory, Assessment and Treatment.* Washington, DC: American Psychological Association; 2000.

53. Hopkins RO, Weaver LK, Pope D, Orme JF, Bigler ED, Larson-Lohr V: **Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome.** *Am J Respir Crit Care Med* 1999, **160**:50-56.

54. Hopkins RO, Kesner RP, Goldstein M: **Item and order recognition memory in subjects with hypoxic brain injury.** *Brain Cogn* 1995, **27**:180-201.

55. Rothenhäusler H-B, Ehrentraut S, Stoll C, Schelling G, Kapfhammer H-P: **The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: results of an exploratory study.** *Gen Hosp Psychiatry* 2001, **23**:90-96.

56. Pochard F, Azoulay E, Chevret S, Lemaire F, Hubert P, Canoui P, Grassin M, Zittoun R, le Gall J-R, Dhainaut JF, Schlemmer B: **Symptoms of anxiety and depression in family members of intensive care unit patients: ethical hypothesis regarding decision-making capacity.** *Crit Care Med* 2001, **29**:1893-1897.

57. Covinsky KE, Goldman L, Cook F, Oye R, Desbiens N, Reding D, Fulkerson W, Connors AF, Lynn J, Phillips RS: **The impact of serious illness on patients families.** *JAMA* 1994, **272**:1839-1844.

58. Lange P: **Family stress in the intensive care unit.** *Crit Care Med* 2001, **29**:2025-2026.

59. Testa M, Simonson D: **Current concepts: assessment of quality-of-life outcomes.** *N Engl J Med* 1996, **334**:835-840.

60. Kutsogiannis DJ, Noseworthy T: **Quality of life after critical care.** In: *Outcomes in Critical Care.* Edited by Ridley S. Oxford: Butterworth-Heinemann; 2002.

61. Ridley S: **Survival and quality of life after intensive care.** *Clin Intensive Care* 1999, **10**:117-123.

62. Mata AV, Fernandez RR, Carmona AG, Delgado-Rodriguez M, Pugnaire AR, De Hoyos EA: **Factors related to quality of life 12 months after discharge from an intensive care unit.** *Crit Care Med* 1992, **20**:1257-1262.

63. Fernandez RR, Cruz JJ, Mata GV: **Validation of a quality of life questionnaire for critically ill patients.** *Intensive Care Med* 1996, **22**:1034-1042.

64. Konopad E, Noseworthy T, Johnston R, Shustack A, Grace M: **Quality of life measures before and one year after admission to an intensive care unit.** *Crit Care Med* 1995, **23**:1653-1659.

65. Brooks R, Kerridge R, Hillman K, Bauman A, Daffurn K: **Quality of life outcomes after intensive care.** *Intensive Care Med* 1997, **23**:581-586.

66. Welsh CH, Thompson K, Long-Krug S: **Evaluation of patient-perceived health status using the Medical Outcomes Survey Short-Form 36 in an intensive care unit population.** *Crit Care Med* 1999, **27**:1466-1471.

67. Chrispin PS, Scotton H, Rogers J, Lloyd D, Ridley SA: **Short Form 36 in the intensive care unit: assessment of acceptability, reliability and validity of the questionnaire.** *Anaesthesia* 1997, **52**:15-23.

68. Flaatten H, Kvåle R: **Survival and quality of life 12 years after ICU. A comparison with the general Norwegian population.** *Intensive Care Med* 2001, **27**:1005-1011.