
Survival as an Outcome for ICU Patients

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Introduction

Why is 'survival' an important outcome? As intensive care unit (ICU) clinicians, it is important for us to obtain a clear understanding of the natural history of the critical illness we treat. While we would like to know how long a patient is likely to stay in the ICU or hospital, their probable future functional status and quality of life, the likelihood of their surviving their critical illness is of paramount interest. Understanding the impact of critical illnesses on survival allows us to share this information with patients and family and guide resource allocation more appropriately. The time interval over which a patient remains at increased risk of death varies among the critical illnesses we treat. For example, patients who become septic have a greater than expected mortality for a number of months beyond the onset of illness [1, 2], while patients surviving overdoses or multiple trauma have shorter time intervals of increased risk. Understanding the time intervals of risk can guide the design of interventional trials. These trials would ideally include a follow-up period that is comparable to the time interval of risk.

Survival is also the most important outcome we have in benchmarking ICU practice. While randomized controlled trials (RCTs) remain the gold standard for identifying effective new technology, benchmarking outcomes among a network of ICUs may reveal differences in survival. Further scrutiny will determine whether these differences are likely real and, if so, related differences in practice may be isolated. Global implementation of these best practices using a systematic approach has the potential to improve overall outcome.

In this chapter, we will briefly address short-term survival (all time-intervals up to ICU survival) for patients admitted to the ICU. Our main focus, however, will be survival beyond the ICU stay. What happens to patients after they are discharged from the ICU? How likely are they to survive their hospital stay or return to the ICU, and what happens once they leave hospital? To address these questions we searched the published literature using MEDLINE and the keywords 'intensive care units' or 'critical care' and 'survival' or 'mortality' or 'outcome'. We also searched 'related articles' for those citations considered most relevant. While RCTs add information and are remarkable in their survival intervals chosen, we have focused primarily on observational studies as they are less likely to be affected by the selection bias of many RCTs. As future chapters of this volume will be devoted

exclusively to the natural history of elderly and pediatric critically ill populations we did not include studies specifically dealing with these patient populations.

Short-term Mortality

Mortality for patients admitted to the ICU is high compared to that for patients cared for in non-critical care units. While the literature on short-term outcomes during ICU stay is too vast to review in detail, three important issues emerge. First, the time interval selected for short-term mortality varies. The selection of intervals as low as 10 [3] to 14-days [4–7] for RCTs has been rationalized on the basis that either the therapy will only influence outcome during the period in which it is being applied (prone positioning) or that the disease process of interest (sepsis or ventilator associated pneumonia) has an attributable mortality that is restricted to the first 14-days. While it is true that for patients with sepsis most attributable mortality occurs early, studies have clearly demonstrated that the impact of sepsis on mortality extends well beyond the first 2 weeks [1, 2], suggesting that selection of a 14-day endpoint may be misleading for sepsis trials. Similarly, selecting a time interval for analysis of mortality to reflect the time interval during which the new treatment or technology is applied is potentially concerning. It is possible that such treatments may just delay death, an outcome that is clearly not desirable. The more commonly used 28-day endpoint in RCTs appears to be more reasonable but still does not fully address the longer-term impact of critical illness. In designing a RCT, one is faced with a trade-off in choosing the time interval for mortality. On the one hand, sensitivity is increased by choosing a shorter time interval to measure the effect of a new technology on survival, a period during which death is more likely to arise from the disease process of interest. As the time interval for study is extended, deaths will be increasingly due to factors other than the disease process of interest, this added ‘noise’ making it more difficult to demonstrate a true ‘signal’. On the other hand, patients are most interested in surviving an event, in this case ICU stay and, more importantly, hospitalization (see Fig. 1).

Second, ICU survival appears to be improving over time despite the fact that advances in medicine have resulted in a greater population of sicker, immunosuppressed patients at risk of critical illness and an increasing proportion of our population being elderly. This improvement in outcome has been well documented. For example, a marked reduction was found in the mortality for the control groups of two trials on patients with acute respiratory distress syndrome (ARDS) of extracorporeal oxygenation [8] and extracorporeal carbon dioxide removal [9], with similar inclusion criteria, published 15 years apart (9 % versus 39 %, respectively). Similarly, the Seattle group demonstrated a reduction in mortality for patients with ARDS over time within their center in a carefully conducted study using similar definitions of ARDS over a 10-year period [10]. Finally, a number of recent landmark studies have demonstrated efficacy of treatments for sepsis [11], ARDS [12], and sedation protocols [13, 14] that establish new benchmarks for short-term outcome.

Lastly, despite this promising trend, there is evidence suggesting that some patient groups may not benefit from life support measures despite the apparent

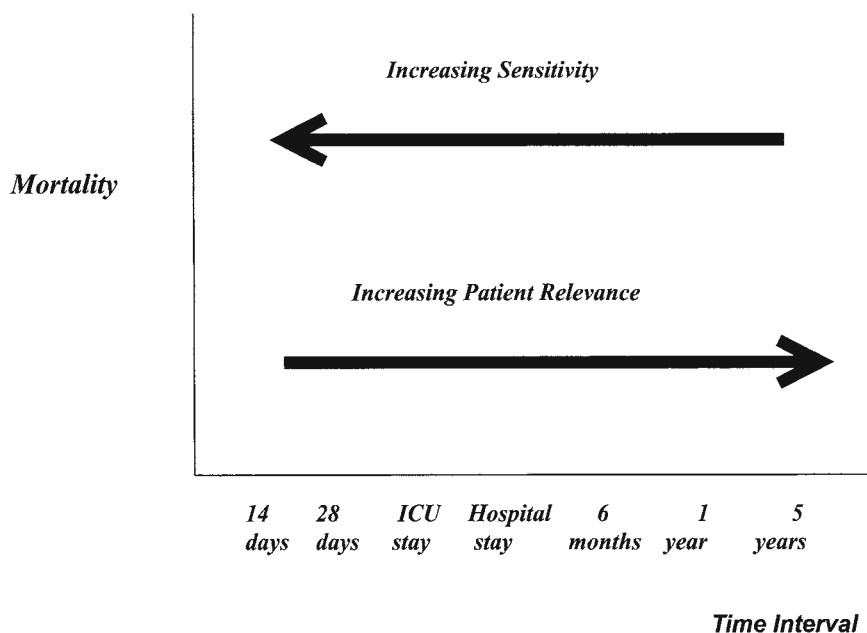


Fig. 1. This figure illustrates the potential trade-off facing designers of a randomized controlled trial in choosing their interval for survival.

need for such measures for immediate survival. For example, there has been an ongoing evaluation of the potential usefulness of ICU admission for patients who have human immunodeficiency virus (HIV) infection. This has become necessary as the introduction of new treatment regimens has radically altered their long-term outcome. While once considered poor candidates for ICU care, a case-by-case approach is warranted in these groups [15, 16]. Patients with underlying malignancies are a heterogeneous group but subpopulations such as patients who develop respiratory failure after bone marrow transplant remain a group with extremely high short-term mortality [17, 18]. Finally, there are other disease processes that appear to have such a poor short-term outcome that serious consideration should be given to avoiding ICU admission in these patients. For example, patients who have idiopathic pulmonary fibrosis who require mechanical ventilation have a very high hospital mortality [19–21]. We need more data on the outcomes, both short and longer-term, for these and other patient groups that may not benefit from ICU admission.

Long-term Mortality

If my patient were to survive her ICU stay, what is the probability that she will die before leaving hospital? If she survives hospitalization, what is the probability that she will die by 6 months, one year, or longer? Less literature exists that describes

these important outcomes for patients admitted to the ICU who survive ICU stay. We will first summarize estimates and determinants of hospital mortality for ICU survivors and then summarize similar descriptors for long-term mortality.

Hospital Mortality

It is clear that a significant proportion of patients discharged from the ICU do not survive hospitalization. The proportion dying in hospital after discharge from the ICU varies among studies from a few percent for observational studies on surgical ICU patients to greater than an additional 10 % for some studies of patients requiring mechanical ventilation or renal replacement therapy (Fig. 2).

The cause of these additional deaths can be divided into those that are expected and those that are not. The former would be comprised of patients who are discharged from the ICU following withdrawal of life support or with express instructions not to have life support reintroduced should they deteriorate further. Other patients may die due to a new, unexpected problem arising on the general ward or due to a worsening of the underlying disease process. Some of these patients may be readmitted to the ICU prior to their death. From the growing literature addressing readmission to the ICU [22–30], well summarized in a review by Rosenberg and Watts [31], patients are readmitted to ICU for the same reason as their initial admission from 19 to 53 % of the time. Readmission rates vary from 4 to 14 % and these patients have prolonged length of stay and marked increase in hospital mortality (1.5 to 10 times that of other ICU patients).

Mortality after Hospitalization

Survival beyond hospitalization for patients requiring an admission to the ICU is an outcome of utmost importance to patients and family. The literature addressing

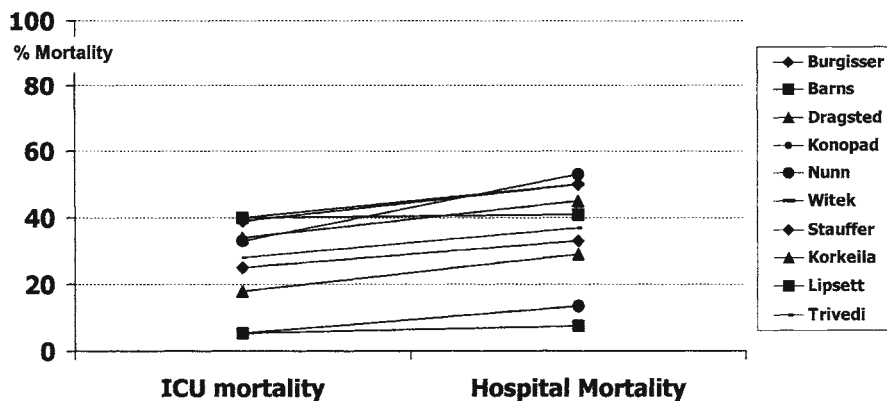


Fig. 2. This figure summarizes the respective ICU and hospital mortality for a representative group of cohort studies that also provided follow-up beyond hospitalization.

long-term survival is comprised of three different study designs. The most common are observational studies describing survival of a single cohort of ICU patients after hospitalization over time without a comparison group. In some studies, variables that distinguish survivors from non-survivors have been determined, most often using univariable analysis, less frequently reporting the more robust use of multivariable analysis. The population studied may either be consecutive patients admitted to a specific ICU, most often a general ICU, or a subset of ICU patients. Table 1 demonstrates wide variation in outcome among studies of 'general' ICU populations with a one-year mortality ranging from 18 to 56 % [32–50].

These studies vary in time of publication, country of origin and number of centers, most being single-centers while one study includes all ICU admissions in a specific health care region [50].

While these single-cohort observational studies provide insight into the apparently poor long-term prognosis of ICU patients who survive hospitalization, they include the expected high hospital mortality rate and do not account for this by comparing survival over time beyond hospitalization to a control group. To address this, a second study design adopted by a number of investigators includes a comparison of survival rates between their patient cohort and the general population [38], matched for age and gender [42, 44, 49, 50]. In the first of these studies, conducted over one-year at a single center, Zaren and Bergstrom found that survival beyond hospitalization, one-year after admission, was 96% of that predicted by comparing it to the general population [38]. However, four subsequent studies, most larger, and two multi-centered, have all documented a significantly greater long-term mortality among ICU patients compared to the general population matched for age and gender [40, 42, 47, 48]. Niskanen and colleagues reported a 5-year mortality rate for 12,180 patients admitted to 25 ICUs in Finland in 1987 that was 3.3 times that of Finland's general population [44]. They also noted that the difference between survival curves occurred over the first 2 years with the curves paralleling each other beyond that. Flaaten and Kvale also found that survival beyond 2 years after hospitalization paralleled that of the general population of Norway [49]. In a single center study in Glasgow, enrolling all patients over 4 years, Ridley and Plenderleith [42] found that the survival curve for ICU patients was significantly worse than that for an age and gender-matched general population. In this study, however, survival curves did not parallel each other until the fourth year. We also found that patients who required ICU admission fared worse than the general population in a study of all ICU admissions during a 3-year period in British Columbia [50]. This difference in survival persists over the three years of follow-up data available to us, although the ratio of observed to expected deaths declined from 6.47 during the first year to 3.10 in the third (Fig. 3).

Patients who require ICU admission differ from the general population, having more co-morbid disease on average prior to their acute event. As such, one would expect their outcome to be worse than that of the general population even without hospital admission. To understand the effect that exposure to an ICU has on long-term outcome, one should choose a comparison group more similar to those patients requiring ICU admission than the general population. The final study design found in the literature uses other hospitalized patients as controls. Parno and associates compared 2-year survival rates between 558 ICU patients and 124

Table 1. Long-term outcome (mortality) of general ICU population

Study	Patients	ICU	Hospital	3 months	6 months	1-yr	2-yrs	3-yrs	4-yrs	5-yrs	12-yrs
Thibault et al. (1980) [32]	2693		10 %			25 %*					
Parno et al. (1982) [33]	558		17.3 %				35.6 %				
Le Gall et al. (1982) [34]	228	34 %			50 %	51 %					
Burgisser et al. (1982) [35]	330	25 %	33 %				15.1 %	50 %			
Barns et al. (1985) [36]	238	5.4 %	7.5 %								
Jacobs et al. (1988) [37]	313	24 %			39 %	42 %					
Zaren et al. (1989) [38]	980	9.6 %				26.4 %					
Dragsted et al. (1989) [39]	1308	18 %	29 %			44 %					
Mundt et al. (1989) [40]	1545				6 %**						
Ridley et al. (1990) [41]	513	24 %					48 %				
Ridley et al. (1994) [42]	1168					35 %	38 %	43 %	45 %	47 %	
Konopad et al. (1995) [43]	504	5.4 %	13.5 %		21 %	25 %					
Niskanen et al. (1996) [44]	12,180	10 %				28 %	30 %	32 %	33 %	33 %	
Capuzzo et al. (1996) [45]	260					17.6 %					
Short et al. (1999) [46]	2268		35 %			56 %					
Eddleston et al. (2000) [47]	370	29 %		39 %	41 %	43 %					
Pettila et al. (2000) [48]	591	15 %				36 %					
Flaatten et al. (2001) [49]	219				30 %	34 %	37 %				58 %
Keenan et al. (2002) [50]	27,103		14 %			24 %	28 %	32 %			

* the "cumulative mortality over a mean of 15 months of follow-up"

** 200 patients lost to follow-up

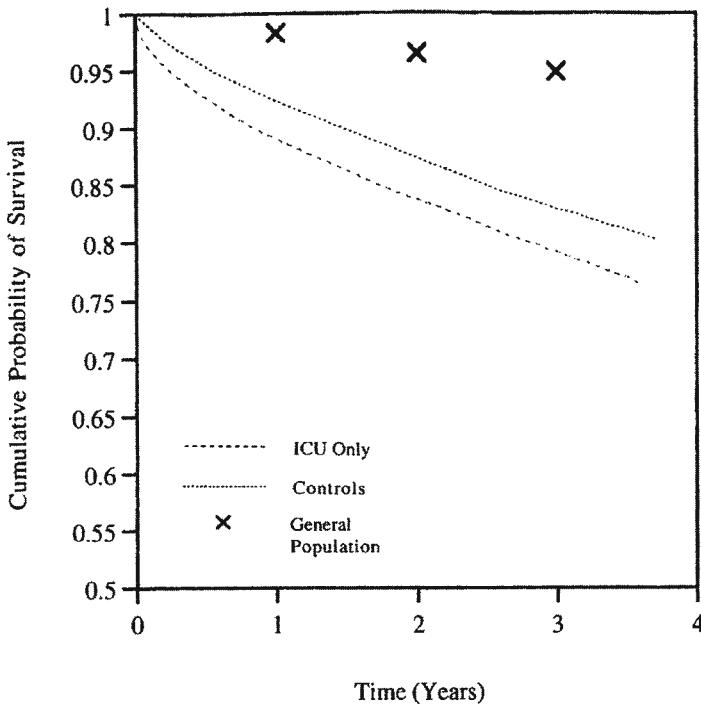


Fig. 3. Unadjusted survival curves for 2 groups of patients surviving hospitalization, one of which was admitted to the ICU during their stay. For comparison, yearly survival for a sample of the general population, adjusted for age and gender has been included (from [50] with permission).

non-ICU patients and while the 2-year mortality was considerably worse for the ICU group (35.6 versus 14.8 %), this was due largely to higher in-hospital mortality [51]. In fact, survival after hospital discharge was very similar, 83.3 versus 89.1 % at 2 years for ICU and non-ICU patients, respectively [51]. In our retrospective study of all ICU admissions in the province of British Columbia, we compared mortality after hospital discharge of ICU patients to that in a random sample of patients who required hospitalization but were not admitted to the ICU [50]. From Figure 3 it is clear that, while the unadjusted survival curve for ICU patients who survived to hospital discharge appears less favorable than that of the control group of hospitalized non-ICU patients, both groups fared considerably worse than a general population, matched for age and gender. Furthermore, after controlling for other prognostic factors we found that the difference in long-term mortality between ICU patients and hospitalized, non-ICU patients, bordered on negligible (see Table 2). This would suggest that after controlling for hospitalization, the difference in long-term mortality between ICU patients and the general population is due more to whatever leads patients to be hospitalized rather than admitted to the ICU.

Table 2. Factors associated with mortality beyond index hospitalization. From [50] with permission

Variable	Hazard Ratio (95% CI)		Wald Chi-square *
Age (per decade)	1.60	(1.58-1.62)	5093
Comorbidity	1.28	(1.27-1.29)	3321
Major Clinical Category (MCC)			
Lymphoma/Leukemia	4.00	(3.59-4.46)	624
HIV	20.99	(16.46-26.77)	602
Respiratory Disorders	1.63	(1.54-1.71)	331
Musculoskeletal Disorders	0.75	(0.69-0.81)	54
Neurological Disorders	1.21	(1.13-1.30)	30
Blood Disorders	1.56	(1.31-1.85)	25
Burns/Multiple Trauma	0.65	(0.47-0.90)	7
Sex (M vs F)	1.22	(1.17-1.26)	92
ICU admission	1.21	(1.17-1.27)	85
Prior Hospital admission	1.02	(1.01-1.02)	72
Prior ICU admission	1.07	(1.04-1.10)	20
Median Income (per \$10,000)	0.99	(0.98-0.99)	19
Residence (urban vs rural)	1.06	(1.01-1.11)	5
Tier (1 to 7) **	0.99	(0.97-1.00)	4

* As all $p < 0.001$, the Wald Chi-square has been reported to illustrate which variables are most significant

** The negative coefficient denotes that there is a decreased risk of death after discharge from hospital in patients who were admitted to ICUs at higher Tier number hospitals which are actually smaller hospitals, i.e., a given ICU patient is more likely to survive after hospital discharge from a smaller hospital.

Studies of general ICU populations like those in Table 1 provide average estimates for long-term mortality. Trying to prognosticate for an individual patient from these studies is more difficult. It is possible to make more precise estimates by considering additional variables that have been shown within these studies to influence mortality. These factors can be divided into patient or non-patient related variables. The patient-related variable that has been most consistently demonstrated to have a major influence on long-term mortality is age (Tables 3 and 4). As the effect of age on outcome is the subject of another chapter in this volume, we will not address it further here. In addition to age, male gender, worse pre-morbid functional status, greater degree of co-morbid disease, organ dysfunction and severity of illness during hospitalization, and reason for ICU admission (diagnosis) are among those demonstrated to increase long-term mortality in specific studies (Tables 3 and 4).

In our recent study, we identified increasing age, male gender, number of prior hospitalizations, major clinical category (diagnosis) and, to a lesser degree, socio-economic factors to be associated with mortality after an index hospitalization [50].

Table 3. Factors associated with poorer long-term survival using univariate analysis

Study	N	Age	Male gender	Comorbidity	Diagnosis	Severity of illness	Organ dysfunction	Pre-morbid functional status
Nunn et al. (1979) [52]	100	✓			✓			
Le Gall et al. (1982) [34]	228	✓					✓	✓
Parno et al. (1984) [51]	558	✓			✓			
Witek et al. (1985) [53]	100	✓						
Spicher et al. (1987) [55]	240	✓						✓
Dragsted et al. (1989) [39]	1308	✓						
Ridley et al. (1990) [41]	513	✓			✓	✓		
Stauffer et al. (1993) [58]	383	✓			✓			
Capuzzo et al. (1996) [45]	260				✓			
Carson et al. (1999) [60]	133	✓						✓
Short et al. (1999) [46]	2268	✓				✓		

Table 4. Factors associated with poorer long-term survival using multivariate analysis

Study	N	Age	Male gender	Comorbidity	Diagnostic group	Severity of illness
Ridley et al.* (1990) [41]	513	✓				✓
Niskanen et al.* (1996) [44]	12,180	✓	✓	✓	✓	
Keenan et al.* (2002) [50]	27,103	✓	✓		✓	

Major clinical categories associated with the highest long-term mortality included patients with HIV, lymphoma, leukemia, other blood disorders, respiratory disorders, or neurological disorders while multiple trauma or burn patients surviving to hospital discharge had a relatively low long-term mortality [50]. Of interest, while non-HIV infection was associated with a marked increased hospital mortality, it was not associated with mortality after the index hospitalization. These findings are consistent with that described by Niskanen and colleagues [44] who reported the highest long-term mortality for patients with cancer and a relatively high mortality for patients with cardiovascular, respiratory or gastroenterological diseases. Diagnostic categories that represent chronic progressive disorders, malignant or otherwise, appear to be those that are of greatest importance in determining a poor long-term outcome regardless of whether patients are admitted to the ICU or not. In contrast, patients admitted to the ICU because of an acute, self-limiting process such as drug overdose, accidental acute intoxication, or multiple trauma, who survive their hospitalization generally have a good recovery with little impact on long-term outcome arising as a result of their admission. Sepsis is an interesting entity as it appears that there is an ongoing increased mortality for a number of years despite the acute nature of this disease process [1, 2].

Differences in patient-related variables also explain some of the differences in mortality rates evident among studies. Lower mortality rates tend to be recorded by large multi-center studies that include ICUs of varying size that likely reflect a population with an average lower severity of illness and degree of organ dysfunction than single center studies at tertiary care centers. Case-mix may also vary among studies and the influence of this factor is clearly demonstrated in the higher mortality levels seen in patients requiring mechanical ventilation [52–60] (Table 5) or specific subgroups such as septic patients or bone marrow transplant patients who require ICU admission [1, 15, 17, 18, 61–78] (Table 6). From studies on chronic obstructive pulmonary disease (COPD), however, it is clear that factors other than diagnosis are of importance, including the stage of disease and severity of the exacerbation, particularly whether mechanical ventilation is required or not [71–78].

Variables that are independent of patients include ICU structure (available technology and personnel) and ICU model used (organizational factors, including the use of clinical practice guidelines and degree of training of attending staff). As these variables are potentially easier to modify than patient-related variables, there has been growing interest in determining whether these variables affect outcome. In the case of guidelines or protocols, there is an expanding literature demonstrating a positive effect on short-term outcomes [14, 15, 79–81], but relatively little on long-term outcomes. In addition, there are few published data on the effect of differences in ICU structure. The possible exception may be the use of non-invasive ventilation in patients with COPD. Two studies, using historical controls have demonstrated that COPD patients who presented with an acute exacerbation and who were treated with non-invasive positive pressure ventilation had a better 1-year survival rate than those who do not receive non-invasive ventilation [76, 77]. Admission policies to ICU that may be related to availability of ICU or other high-dependency beds may also explain some of the differences found among studies.

Table 5. Long-term outcome (mortality) of patients receiving mechanical ventilation

Study	Patients*	ICU	Hospital	3 months	6 months	1-yr	2-yrs	3-yrs	4-yrs	5-yrs	12-yrs
Nunn et al. (1979) [52]	100 > 4 hours	33%	53%					70%			
Davis et al. (1980) [53]	100 > 48 hrs		56%				72%				
Schmidt et al. (1983) [54]	137 > 48 hrs		64%			70%		72%			
Witek et al. (1985) [55]	100	40%	50%			67%					
Spicher et al. (1987) [56]	250 > 10 days		61%			71%	77%				
Gracey et al. (1992) [57]	104 > 29 days		42%			61%		68%			
Stauffer et al. (1993) [58]	383 > 1 hour	39%	50%			70%					
Douglas et al. (1997) [59]	57 > 5 days		44%		58%						
Carson et al. (1999) [60]	133 LTAC**		50%			77%					

* number of patients and minimal duration of mechanical ventilation

** LTAC long-term acute care hospitals providing care for prolonged critical illness

Table 6. Long-term outcome (mortality) of specific ICU patient groups

Study	Patients	ICU	Hospital	3 months	6 months	1-yr	2-yrs	3-yrs	4-yrs	5-yrs	12-yrs
Frutiger et al. (1991) [61]	233 severe trauma		18 %				24 %				
Crawford et al. (1992) [18]	348 ventilated BMT patients		96 %		97 %						
Huaringa et al. (2000) [17]	60 ventilated BMT patients	82 %			95 %						
Staudinger et al. (2000) [62]	414 cancer patients	47 %				77 %					
Sasse et al. (1995) [63]	153 septic patients		51 %		65 %	72 %					
Quartin et al. (1997) [1]	1505 septic patients 607 sepsis 674 severe sepsis 224 septic shock					46 % 71 % 80 %					
Trouillet et al. (1996) [64]	116 cardiac surgery & organ failure	23.3 %									31 % [#]
Bashour et al. (2000) [65]	142 Cardiac surgery > 20 days ICU		33 %					64 %*			
Nickas et al. (2000) [15]	394 HIV patients		37 %			73 %	82 %	87 %	89 %		
Korkkela et al. (2000) [66]	62 RRT	34 %	45 %		55 %					65 %	
Lipsett et al. (2000) [67]	128 SICU pts > 6 days in ICU	40 %	41 %		54 %						
Trivedi et al. (2001) [68]	186 medical patients	28 %	37 %			41 %					

Table 6. (Continued)

Study	Patients	ICU	Hospital	3 months	6 months	1-yr	2-yrs	3-yrs	4-yrs	5-yrs	12-yrs
Schelling et al. (1998) [69]	192 ARDS	38 %				54 %					
Davidson et al. (1999) [70]	207 ARDS due to Sepsis (119) Trauma (88)		30 % 43 % 14 %	34 %							
Gottlieb et al. (1973) [71]	30 COPD					70 %					
Martin et al. (1982) [72]	36 COPD						28 %				
Menzies et al.* (1989) [73]	95 COPD					62 %					
Seneff et al. (1995) [74]	362 COPD		24 %	42 %	48 %	52 %					
Connors et al. (1996) [75]	1,106 COPD		11 %		33 %	42 %	49 %				
Confalonieri et al. (1996) [76]	24 COPD CMV NPPV		25 % 18 %		46 % 29 %	50 % 29 %					
Vitacca et al. (1996) [77]	29 COPD CMV NPPV		26 % 23 %	48 % 23 %		63 % 30 %					
Costello et al. (1997) [78]	85 COPD		20 %			39 %	54 %			73 %	

* over median follow-up of 30.6 months, # mean follow-up 81 months (range 70-93 months), CMV - conventional mechanical ventilation, NPPV - noninvasive positive pressure ventilation, RRT - renal replacement therapy, COPD - chronic obstructive pulmonary disease, ARDS - acute respiratory distress syndrome, BMT - bone marrow transplant

Conclusion

Patients admitted to the ICU have a high short-term mortality rate compared to patients who receive alternate levels of care. Over time there has been an improvement in survival as a result of both the introduction of innovative pharmacological and technological therapies and the improved organization of delivery of care. Survival after discharge from the ICU depends upon a number of patient factors; age, premorbid co-morbidity and diagnosis are the most important. While it is clear that ICU patients who survive hospitalization have a higher long-term mortality than the general population, it appears that this is not related so much to their ICU admission but rather to their need for hospitalization.

The studies and trials that have added to the literature on survival of ICU patients in general have high internal validity, describing an endpoint that is easily measured in a well-defined group of patients. However, there is a greater problem with external validity, or how others may try to use the results from these studies in their own setting; this arises from the heterogeneity of patients included that exists among studies. There is a need for large, multi-center, multi-national, prospective studies on *a priori* defined homogeneous populations of ICU patients. Data collected would include not only baseline demographics and severity of illness but also specific information on ICU and hospital interventions, complications, length of stay and discharge destination. These large cohorts would provide more useful information for families and clinicians. While this may appear daunting at first blush, the burgeoning field of informatics has provided the technology to proceed and groups such as Project IMPACT, sponsored by the Society of Critical Care Medicine in the United States, as well as ICNARC (Intensive Care National Audit and Research Center) in the United Kingdom are already collecting large amounts of data on many ICUs prospectively. With time, we will hopefully have the data on long-term survival, and more importantly associated quality of life, to be able to confidently discuss long-term prognosis with our patients and their families and make informed decisions regarding the institution, continuation, and withdrawal of life support measures.

References

1. Quartin AA, Schein RMH, Kett DH, et al (1997) Magnitude and duration of the effect of sepsis on survival. *JAMA* 277:1058–1063
2. Perl TM, Dvorak L, Hwang T, et al (1995) Long-term survival and function after suspected gram-negative sepsis. *JAMA* 274:338–345
3. Gattinoni L, Tognoni G, Pesenti A, et al (2001) Effect of prone positioning on the survival of patients with acute respiratory failure. *N Engl J Med* 345:568–573
4. McCloskey RV, Straube RC, Sanders C, et al (1994) Treatment of septic shock with human monoclonal antibody HA-1A. *Ann Intern Med* 121:1–5
5. Angus DC, Birmingham MC, Balk RA, et al (2000) E5 murine monoclonal antiendotoxin antibody in gram-negative sepsis. *JAMA* 283:1723–1730
6. Fagon J, Chastre J, Wolff M, et al (2000) Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. *Ann Intern Med* 132:621–630

7. Reeves JH, Butt WW, Shann F, et al (1999) Continuous plasma filtration in sepsis syndrome. *Crit Care Med* 27:2096–2104
8. Zapol WM, Snider MT, Hill JD, et al (1979) Extracorporeal membrane oxygenation in severe acute respiratory failure. *JAMA* 242:2193–2196
9. Morris AH, Wallace CJ, Menlove RL, et al (1994) Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO₂ removal for adult respiratory distress syndrome. *Am J Respir Crit Care Med* 149:295–305
10. Milberg JA, Davis DR, Steinberg KP, Hudson LD (1995) Improved survival of patients with acute respiratory distress syndrome: 1983–1993. *JAMA* 273:306–309
11. Bernard GR, Vincent JL, Laterre PF, et al (2001) Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 344:699–709
12. The Acute Respiratory Distress Syndrome Network (2000) Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 342:1301–1308
13. Brook AD, Ahrens TS, Schaiff R, et al (1999) Effect of nursing-implemented sedation protocol on the duration of mechanical ventilation. *Crit Care Med* 27:2609–2615
14. Kress PJ, Pohlman RN, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 342:1471–1477
15. Nickas G, Wachter RM (2000) Outcomes of intensive care for patients with human immunodeficiency virus infection. *Arch Intern Med* 160:541–547
16. Afessa B, Green B. (2000) Clinical course, prognostic factors, and outcome prediction for HIV patients in the ICU. *Chest* 118:138–145
17. Huaranga AJ, Leyve FJ, Giralt SA, et al (2000) Outcome of bone marrow transplantation patients requiring mechanical ventilation *Crit Care Med* 28:1014–1017
18. Crawford SW, Peterson FB (1992) Long-term survival from respiratory failure after marrow transplantation for malignancy. *Am Rev Respir Dis* 145:510–514
19. Stern J, Mal H, Groussard O, et al (2001) Prognosis of patients with advanced idiopathic pulmonary fibrosis requiring mechanical ventilation for acute respiratory failure. *Chest* 120:213–219
20. Blivet S, Pihit F, Sab JM, et al (2001) Outcome of patients with idiopathic pulmonary fibrosis admitted to the ICU for respiratory failure. *Chest* 120:209–212
21. Fumeaux T, Rothmeier C, Jolliet P (2001) Outcome of mechanical ventilation for acute respiratory failure in patients with pulmonary fibrosis. *Intensive Care Med* 27:1868–1874
22. Baigelman W, Katz R, Geary G (1983) Patient readmission to critical care units during the same hospitalization at a community teaching hospital. *Intensive Care Med* 9:253–256
23. Franklin C, Jackson D (1983) Discharge decision-making in a medical ICU: characteristics of unexpected readmissions. *Crit Care Med* 11:61–66
24. Snow W, Bergin KT, Horrigan TP (1985) Readmission of patients to the surgical intensive care unit: patient profiles and possibilities for prevention. *Crit Care Med* 13:961–964
25. Rubins HB, Moskowitz MA (1988) Discharge decision-making in a medical intensive care unit: identifying patients at high risk of unexpected death or unit readmission. *Am J Med* 84:863–869
26. Durbin CG, Kopel RF (1993) A case-control study of patients readmitted to the intensive care unit. *Crit Care Med* 21:1547–1553
27. Kirby EG, Durbin CG (1996) Establishment of a respiratory assessment team is associated with decreased mortality in patients re-admitted to the ICU. *Respir Care* 41:903–907
28. Cooper GS, Sirio CA, Rotondi AJ, et al (1999) Are readmissions to the intensive care unit a useful measure of hospital performance? *Med Care* 37:399–408
29. Chen LM, Martin CM, Keenan SP, et al (1998) Patients readmitted to the intensive care unit during the same hospitalization: clinical features and outcomes. *Crit Care Med* 26:1834–1841
30. Rosenberg AL, Hofer TP, Hayward RA, et al (2001) Who bounces back? Physiologic and other predictors of intensive care unit readmission. *Crit Care Med* 29:511–518
31. Rosenberg AL, Watts C (2000) Patients readmitted to ICUs: a systematic review of risk factors and outcomes. *Chest* 118:492–502

32. Thibault GE, Mulley AG, Barnett GO, et al (1980) Medical intensive care: indications, interventions, and outcomes. *N Engl J Med* 302:938–942
33. Parno JR, Teres D, Lemeshow S, Brown RB (1982) Hospital charges and long-term survival of ICU versus non-ICU patients. *Crit Care Med* 10:569–574
34. Le Gall JR, Brun-Buisson C, Trunet P, Latournerie J, Chantereau S, Rapin M (1982) Influence of age, previous health status, and severity of acute illness on outcome from intensive care. *Crit Care Med* 10:575–577
35. Burgisser C, Ritz R (1982) Follow-up of intensive medical care patients. *Schweiz Med Wochenschr* 112:1283–1286
36. Bams JL, Miranda DR (1985) Outcome and costs of intensive care: a follow-up study on 238 ICU-patients. *Intensive Care Med* 11:234–241
37. Jacobs CJ, van der Vliet JA, van Roozendaal MR, van der Linden CJ (1988) Mortality and quality of life after intensive care for critical illness. *Intensive Care Med* 14:217–220
38. Zaren B, Bergstrom R (1989) Survival compared to the general population and changes in health status among intensive care patients. *Acta Anaesthesiol Scand* 33:6–12
39. Dragsted L, Qvist J (1989) Outcome from intensive care. III. A 5-year study of 1308 patients: activity levels. *Eur J Anaesthesiol* 6:385–396
40. Mundt DJ, Gage RW, Lemeshow S, Pastides H, Teres D, Avrunin JS (1989) Intensive care unit patient follow-up: mortality, functional status, and return to work at six months. *Arch Intern Med* 149:68–72
41. Ridley S, Jackson R, Findlay J, Wallace P (1990) Long term survival after intensive care. *Br Med J* 301:1127–1130
42. Ridley S, Plenderleith L (1994) Survival after intensive care. *Anaesthesia* 49:933–935
43. Konopad E, Noseworthy TW, Johnston R, Shustack A, Grace M (1995) Quality of life measures before and one year after admission to an intensive care unit. *Crit Care Med* 23:1653–1659
44. Niskanen M, Kari A, Halonen P for the Finnish ICU Study Group (1996) Five-year survival after intensive care: comparison of 12,180 patients with the general population. *Crit Care Med* 24:1962–1967
45. Capuzzo M, Bianconi M, Contu P, Pavoni V, Gritti G (1996) Survival and quality of life after intensive care. *Intensive Care Med* 22:947–953
46. Short TG, Buckley TA, Rowbottom MY, Wong E, Oh TE (1999) Long-term outcome and functional health status following intensive care in Hong Kong. *Crit Care Med* 27:51–57
47. Eddleston JM, White P, Guthrie E (2000) Survival, morbidity, and quality of life after discharge from intensive care. *Crit Care Med* 28:2293–2299
48. Pettila V, Kaarlola A, Makelainen A (2000) Health-related quality of life of multiple organ dysfunction patients one year after intensive care. *Intensive Care Med* 26:1473–1479
49. Flaaten H, Kvale R (2001) Survival and quality of life 12 years after ICU: a comparison with the general Norwegian population. *Intensive Care Med* 27:1005–1011
50. Keenan SP, Dodek P, Chan K, et al (2002) Intensive care unit admission has minimal impact on long-term mortality. *Crit Care Med* 30:501–507
51. Parno JR, Teres D, Lemeshow S, Brown RB, Avrunin JS (1984) Two-year outcome of adult intensive care patients. *Med Care* 22:167–176
52. Nunn JF, Milledge JS, Singaraya J (1979) Survival of patients ventilated in an intensive care unit. *Br Med J* 1:1525–1527
53. Davis H, Lefrak SS, Miller D, Malt S (1980) Prolonged mechanically assisted ventilation: an analysis of outcome and charges. *JAMA* 243:43–45
54. Schmidt CD, Elliott CG, Carmelli D, et al (1983) Prolonged mechanical ventilation for respiratory failure: a cost-benefit analysis. *Crit Care Med* 11:407–411
55. Witek TJ, Schachter EN, Dean NL, Beck GJ (1985) Mechanically assisted ventilation in a community hospital: immediate outcome, hospital charges, and follow-up of patients. *Arch Intern Med* 145:235–239
56. Spicher JE, White DP (1987) Outcome and function following prolonged mechanical ventilation. *Arch Intern Med* 147:421–425

57. Gracey DR, Naessens JM, Krishan I, Marsh HM (1992) Hospital and posthospital survival in patients mechanically ventilated for more than 29 days. *Chest* 101:211–214
58. Stauffer JL, Fayter NA, Graves B, Cromb M, Lynch JC, Goebel P (1993) Survival following mechanical ventilation for acute respiratory failure in adult men. *Chest* 104:1222–1229
59. Douglas SL, Daly BJ, Brennan PF, Harris S, Nochomovitz M, Dyer MA (1997) Outcomes of long-term ventilator patients: a descriptive study. *Am J Crit Care* 6:99–105
60. Carson SS, Bach PB, Brzozowski L, Leff A (1999) Outcomes after long-term acute care: an analysis of 133 mechanically ventilated patients. *Am J Respir Crit Care Med* 159:1568–1573
61. Frutiger A, Ryf C, Bilat C, et al (1991) Five years follow-up of severely injured ICU patients. *J Trauma* 31:1216–1225
62. Staudinger T, Stoiser B, Mullner M, et al (2000) Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. *Crit Care Med* 28:1322–1328
63. Sasse KC, Nauenberg E, Long A, Anton B, Tucker HJ, Teh-wei H (1995) Long-term survival after intensive care unit admission with sepsis. *Crit Care Med* 23:1040–1047
64. Trouillet JL, Scheimberg A, Vuagnat A, Fagon JY, Chastre J, Gilert C (1996) Long-term outcome and quality of life of patients requiring multidisciplinary intensive care unit admission after cardiac operations. *J Thorac Cardiovasc Surg* 112:926–934
65. Bashour CA, Yared JP, Ryan TA, et al (2000) Long-term survival and functional capacity in cardiac surgery patients after prolonged intensive care. *Crit Care Med* 28:3847–3853
66. Korkeila M, Ruokonen E, Takala J (2000) Cost of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. *Intensive Care Med* 26:1824–1831
67. Lipsett AP, Swoboda SM, Dickerson J, et al (2000) Survival and functional outcome after prolonged intensive care unit stay. *Ann Surg* 231:262–268
68. Trivedi M, Ridley SA (2001) Intermediate outcome of medical patients after intensive care. *Anaesthesia* 56:841–146
69. Schelling G, Stoll C, Haller M, et al (1998) Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Crit Care Med* 26:651–659
70. Davidson TA, Rubenfeld GD, Caldwell ES, Hudson LD, Steinberg KP (1999) The effect of acute respiratory distress syndrome on long-term survival. *Am J Respir Crit Care Med* 160:1838–1842
71. Gottlieb LS, Balchum OJ (1973) Course of chronic obstructive pulmonary disease following first onset of respiratory failure. *Chest* 63:5–8
72. Martin TR, Lewis SW, Albert RK (1982) The prognosis of patients with chronic obstructive pulmonary disease after hospitalization for acute respiratory failure. *Chest* 82:310–314
73. Menzies R, Gibbons W, Goldberg P (1989) Determinants of weaning and survival among patients with COPD who require mechanical ventilation for acute respiratory failure. *Chest* 95:398–405
74. Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA (1995) Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease. *JAMA* 274:1852–1857
75. Connors AF, Dawson NV, Thomas C, et al (1996) Outcomes following acute exacerbation of severe chronic obstructive lung disease. *Am J Respir Crit Care Med* 154:959–967
76. Confalonieri M, Parigi P, Scartabellati A, et al (1996) Noninvasive mechanical ventilation improves the immediate and long-term outcome of COPD patients with acute respiratory failure. *Eur Respir J* 9:422–430
77. Vitacca M, Clini E, Rubini F, Nava S, Foglio K, Ambrosino N (1996) Non-invasive mechanical ventilation in severe chronic obstructive lung disease and acute respiratory failure: short- and long-term prognosis. *Intensive Care Med* 22:94–100
78. Costello R, Deegan P, Fitzpatrick M, McNicholas WT (1997) Reversible hypercapnia in chronic obstructive pulmonary disease: a distinct pattern of respiratory failure with a favorable prognosis. *Am J Med* 1997; 103:239–244

79. Ely EW, Baker AM, Dunagan DP, et al (1996) Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 335:1864–1869
80. Kollef MH, Shapiro SD, Silver P, et al (1997) A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. *Crit Care Med* 25:567–574
81. Marelich GP, Murin S, Battistella F, et al (2000) Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory care practitioners and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. *Chest* 118:459–467