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*Crit Care Med.* 2016 August ; 44(8): 1461–1467. doi:10.1097/CCM.0000000000001658.**LONG-TERM QUALITY OF LIFE AMONG SURVIVORS OF SEVERE SEPSIS: ANALYSES OF TWO INTERNATIONAL TRIALS****Sachin Yende, MD, MS<sup>1,2</sup>, Shamly Austin, PhD, MHA<sup>1,3</sup>, Andrew Rhodes, MD, (Res)<sup>4</sup>, Simon Finfer, MD, FCICM<sup>5</sup>, Steven Opal, MD<sup>6</sup>, Taylor Thompson, MD<sup>7</sup>, Fernando A. Bozza, MD, PhD<sup>1,8</sup>, Steven P. LaRosa, MD<sup>9</sup>, V. Marco Ranieri, MD<sup>10</sup>, and Derek C. Angus, MD, MPH<sup>1</sup>**<sup>1</sup>The Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA, USA<sup>2</sup>Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, USA<sup>3</sup>Research and Development, Quality Improvement Department, Gateway Health, Pittsburgh PA, USA<sup>4</sup>Adult Critical Care, St. George's University Hospitals, NHS Foundation Trust, London, UK<sup>5</sup>The George Institute for Global Health, University of Sydney, Sydney, NSW, Australia<sup>6</sup>Infectious Disease Division, Alpert Medical School of Brown University, Pawtucket, RI, USA<sup>7</sup>Pulmonary and Critical Care Division, Massachusetts General Hospital, Boston, MA, USA<sup>8</sup>Evandro Chagas National Institute of Infectious Diseases, Fundação Oswaldo Cruz (FIOCRUZ), Rio de Janeiro, Brazil<sup>9</sup>Beverly Hospital, Lahey Health System, Beverly, MA, USA<sup>10</sup>Department of Anesthesia and Intensive Care Medicine, University Sapienza of Rome, Policlinico Umberto I Hospital, Rome, Italy**Abstract****Objective**—To describe quality of life (QoL) among sepsis survivors.

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**Design**—Secondary analyses of 2 international, randomized clinical trials (ACCESS [derivation cohort] and PROWESS-SHOCK [validation cohort]).

**Patients**—Adults with severe sepsis admitted to the intensive care unit. We analyzed only patients who were functional and living at home without help before sepsis hospitalization (n=1,143 and 987 from ACCESS and PROWESS-SHOCK).

**Measurements and Main Results**—In ACCESS and PROWESS-SHOCK, the average age of patients living at home independently was 63 and 61 years; 400 (34.9%) and 298 (30.2%) died by 6 months. In ACCESS, 580 patients had a QoL measured using EQ-5D at 6 months. Of these, 41.6% could not live independently (22.7% were home but required help, 5.1% were in nursing home or rehabilitation facilities, and 5.3% were in acute care hospitals). Poor QoL at 6 months, as evidenced by problems in mobility, usual activities, and self-care domains were reported in 37.4%, 43.7%, and 20.5%, respectively, and the high incidence of poor QoL was also seen in patients in PROWESS-SHOCK. Over 45% of patients with mobility and self-care problems at 6 months in ACCESS died or reported persistent problems at 1 year.

**Conclusions**—Among individuals enrolled in a clinical trial who lived independently prior to severe sepsis, one third had died and of those who survived, a further one third had not returned to independent living by 6 months. Both mortality and QoL should be considered when designing new interventions and considering endpoints for sepsis trials.

## INTRODUCTION

Severe sepsis is defined as an infection associated with a systemic inflammatory response and acute organ dysfunction (1). It accounts for 10% of all intensive care unit (ICU) admissions, has a 90-day mortality of ~30% (2), and is the leading cause of death in US hospitals (3). Worldwide, best estimates suggest up to 19 million individuals develop severe sepsis each year (4).

Prior studies have shown that severe sepsis survivors incur long-term consequences, including developing new physical, psychiatric and cognitive deficits (5–7). These deficits often limit their mobility and ability to perform day-to-day activities and may impair quality of life (8). As a greater proportion of patients survive hospitalization for severe sepsis, the population that is at risk for these long-term consequences will increase (9).

We sought to determine long-term quality of life among severe sepsis survivors. We addressed 2 key limitations of prior studies. First, prior studies compared quality of life among severe sepsis survivors to age-matched population-based controls (8). However, patients with sepsis often have a high burden of chronic diseases or functional limitations before developing sepsis, and thus long-term impairments in quality of life may be due to sepsis itself or poor health before onset of sepsis. Second, these studies had a small sample size and included patients from a single geographic region. We assessed the quality of life in severe sepsis survivors enrolled in 2 large international clinical trials. We determined the quality of life at 6 months in patients who were functional and self-sufficient before the onset of sepsis. We conducted sensitivity analyses in young patients and those who did not have a chronic disease to assess the independent effect of sepsis on quality of life. Finally, we also examined the predictors of poor quality of life among survivors, particularly

whether it is affected by the severity and type of organ dysfunction during the acute sepsis episode.

## MATERIALS AND METHODS

We conducted a secondary analysis of patients enrolled in 2 clinical trials: A Controlled Comparison of Eritoran and placebo in patients with Severe Sepsis (ACCESS, n=1,984) and PROWESS SHOCK (n=1,697). Details of these trials are published elsewhere (10, 11). The ACCESS and PROWESS-SHOCK trials tested the efficacy of Eritoran, a MD2:toll-like receptor 4 antagonist, and Drotrecogin alfa activated (recombinant human activated Protein C), an anticoagulant and profibrinolytic enzyme, against placebo. In both trials there was no difference in survival in patients who were assigned to receive the active agent or the placebo. We conducted primary and sensitivity analyses and analyzed predictors of reduced quality of life (see Statistical Analysis section) in ACCESS and validated the results of the primary analyses in PROWESS-SHOCK trial.

To minimize the potential effect of pre-existing functional impairment, we restricted analysis in both trials to subjects who were functional and living at home without help prior to hospitalization for severe sepsis (see Online Supplement). All subjects or their legal surrogate gave informed consent and the Institutional Review Board at each site approved the study.

### Patients

The ACCESS trial enrolled patients who were at least 18 years old with early severe sepsis or septic shock and high risk of death. Severe sepsis was defined as documented evidence of infection, at least 3 criteria for systemic inflammatory response syndrome (SIRS), and at least 1 major organ dysfunction. Septic shock was defined as hypotension requiring vasopressors. High risk of death was defined as having an Acute Physiology and Chronic Health Evaluation (APACHE) II score of at least 21 and not greater than 37. The PROWESS-SHOCK trial used similar entry criteria, except included only patients with persistent septic shock and had no enrollment restriction based on APACHE II score. Both trials included patients from North and South America, Europe, Africa, Asia, and Australia. In general, the exclusion criteria were similar and excluded patients who did not want to pursue aggressive care (see Online Supplement).

### Quality of Life

The primary outcome variable was quality of life, assessed over 1 year in ACCESS and 6 months in PROWESS-SHOCK. Quality of life was assessed using a previously validated instrument, EQ-5D (<http://www.euroqol.org/home.html>). It was chosen for both trials because it has been used in patients with sepsis previously (12, 13), it can be completed in a few minutes, and it is available in several languages. The EQ-5D measures the health state in 5 domains: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each domain can take 1 of 3 responses: no problems, some or moderate problems, and extreme problems.

The EQ-5D was obtained by telephone interview either from the patient or proxy. The time window to obtain measures at 6 months was between month 5 and 7 and at 1 year was between month 11 and 13 after enrollment in the original trial.

### Statistical Analysis

We report the clinical characteristics of the subjects prior to and at enrollment and their hospital course in both trials. In the ACCESS cohort, we conducted primary and sensitivity analyses and analyzed patterns of changes in select quality of life measures (mobility and self-care) between 6 months and 1 year, and identified predictors of quality of life at 6 months. We validated the primary analyses in PROWESS-SHOCK.

For the primary analyses, we determined where patients were located (home, acute care hospitals, nursing home, or rehabilitation facilities), whether they needed assistance, and quality of life measures (frequency of patients who had problems with mobility, self-care, and usual activities and who reported pain or discomfort and anxiety or depression).

Patients hospitalized with severe sepsis are often older adults and have chronic diseases, thus they may have reduced quality of life prior to sepsis. We therefore conducted 2 sensitivity analyses in young patients (<45 years) and those who did not have a chronic disease to reduce likelihood of confounding due to these factors. We conducted these sensitivity analyses in the ACCESS cohort and defined a chronic disease as those individuals who reported cardiovascular, kidney, lung, connective tissue diseases, heart failure, diabetes, cancer, AIDS, dementia, and stroke.

We report patterns of changes in mobility and self-care between 6 months and 1 year in the ACCESS trial. We chose these outcomes because impairments in these domains were common and these impairments are likely to affect the patient's functional status. We identified patients with problems in these domains at 6 months and the proportion that had persistent problems (reported some, moderate, or extreme problem), recovered completely (reported no problem), and died.

Finally, we used logistic regression to determine factors prior to and during the acute episode that were associated with poor quality of life in the ACCESS cohort. We constructed 2 models to predict problems with mobility and self-care at 6 months. For each model, covariates included demographic characteristics, chronic disease burden (defined as presence or absence of a chronic disease), and duration of organ failure within the first 28 days, including mechanical ventilation, dialysis, and vasopressor support, as a proxy for the duration and severity of organ failure. We split each organ support variable into individuals who did and did not require the organ support, and among the later, we calculated the odds ratios for increase in organ support in increments of 7 or 14 days. We did not use daily sequential organ failure scores because these data were collected only on select days and require imputation. All analyses were done using SPSS 21 or SAS 9.4.

## RESULTS

### Patient characteristics

Of the 1,984 and 1,697 patients enrolled in ACCESS and PROWESS-SHOCK, 1,143 (57.6%) and 987 (58.1%) patients were fully functional and living at home without help prior to hospitalization with severe sepsis (Figure 1).

For patients in the ACCESS cohort (derivation cohort) and included in this analysis, the mean age was 63.2 years and 454 (39.7%) were women (Table 1). Five hundred and eighty six (51.3%), 340 (29.7%), and 80 (7.0%), 73 (6.4%), 64 (5.6%) were from Europe, North America, Asia, South America, and rest of the world, respectively. Three hundred and forty seven (30.3%), 254 (14.0%), 235 (13.4%), 161 (8.9%), 142 (7.8%), and 58 (3.2%) had diabetes, pulmonary disease, cancer, kidney disease, ischemic heart disease, and heart failure, respectively. Eight hundred and twenty seven patients (72.4%) had at least one or more chronic disease. At enrollment, the illness severity was high (1,269 [64%] had an APACHE II score of 25 or higher and 397 [34.7%], 273 [23.9], and 111 [9.7%] had dysfunction in 2, 3, and 4 or more organ systems, respectively).

In general, the demographic characteristics, chronic disease burden, and illness severity of patients analyzed from the PROWESS-SHOCK cohort (validation cohort) were similar to those analyzed from the ACCESS trial (Table 1). Additional details are provided in the Online Supplement (Section IV).

### Mortality

In the ACCESS trial, 289 (25.3%), 363 (31.8%), and 400 (34.9%) patients died at 28 and 90 days and at 6 months, respectively. In the PROWESS-SHOCK trial, 202 (20.5%), 273 (27.7%), and 298 (30.2%) patients died at the same time points, respectively.

### Quality of life

At 6 months, of the 1,143 patients in the ACCESS trial, 626 (54.7%), 400 (34.9%), and 117 (10.2%) were alive, dead, and lost to follow-up, respectively (Table 1). A quality of life measure was obtained in 580 patients (78%, 580 of the 743 patients who had not died by 6 months, Figure 1). Of these, 58.4% were home and fully functional, 22.7% were home but required help, 5.1% were in nursing home or rehabilitation facilities, and 5.3% were in acute care hospitals (living status was not known for 8.5% patients).

At 1-year, 467 (40.8%), 424 (37.2%), and 252 (22%) were alive, dead, and lost to follow-up, respectively (Table 1). A quality of life measure was obtained for 448 patients (62.3%, 448 of the 719 patients who had not died by 1 year). Of these, 69% of the survivors were at home and fully functional, 17% were at home but required help, 3.1% were in nursing home or rehabilitation facilities, and 3.1% were in acute care hospitals (living status was not known or 7.8% patients).

A large proportion of patients reported a problem with mobility, usual activities, and self-care over 1 year. Of the 580 survivors with an EQ-5D measure at 6 months, more than a third reported problems with mobility (218 patients, 37.5%) and usual activities (254

patients, 43.7%) and 119 (20.5%) patients reported problems performing self-care. Of the 580 responses, 496 (85.5%) were obtained from the patients and proxies reported 84 (14.5%) responses. The proxies included spouse or significant other (36.9%), child (26.2%), parent (7.1%), sibling (3.6%), friends (1.2%), other family members (9.5%), paid caregiver (13.1%), and others (2.4%).

Among the 448 survivors with a quality of life at 1 year, 142 (31.7%), 145 (32.3%), and 66 (14.7%) reported problems with mobility, usual activities, and self-care activities, respectively. A large proportion of patients also reported pain or discomfort and anxiety or depression at 1 year (41.4% and 35.2% reported pain or discomfort; 29.4% and 25% reported anxiety or depression by 6 and 12 months, respectively). Of the 448 responses, 388 (86.6%) were obtained from the patients, proxies reported 52 (11.6%) responses, and data were missing in an additional 8 (1.8%) patients. The proxies included spouse or significant others (42.3%), child (30.8%), parent (5.8%), sibling (7.7%), friends (1.9%), other family members (3.8%), and paid caregiver (5.8%).

Long-term follow-up was limited to 6 months in the PROWESS-SHOCK trial. At 6 months, of the 987 patients, 580 (58.8%), 298 (30.2%), and 109 (11%) were alive, dead, and lost to follow-up, respectively (Table 1). At 6 months, the findings were similar to ACCESS; 61% were home and fully functional, 26.6% were home but required help, 4.1% were in a nursing home or rehabilitation facilities, and 3.6% were in acute care hospitals. The EQ-5D data were available for 580 survivors at 6 months. Of these, 211 (36.4%) patients reported problems with mobility, 242 (41.7%) with performing usual activities, and 119 (20.5%) reported problems performing self-care. Two hundred and seventy six (47.7%) patients reported pain or discomfort and 205 (35.5%) reported anxiety or depression.

### **Sensitivity analyses**

In the ACCESS cohort, the proportion of patients who reported a problem with mobility, usual activities, and self-care were similar among those with and without a chronic disease (Figure 2). The proportion of patients who reported some problem with mobility and self-care was lower among those <45 years (17.9% and 7.7%), but a third (30.8%) were unable to return to usual activities by 6 months.

### **Patterns of quality of life between 6 months and 1 year**

Of the 218 patients in the ACCESS cohort who reported problem with mobility at 6 months, 105 (48.1%) reported persistent problem with mobility, 15 (6.8%) survivors had died, and 45 (20.6%) patients reported no problems with mobility by 1 year (status of an additional 53 patients was unknown). Similarly, of the 119 patients who reported some problem with self-care at 6 months, 42 (35.3%) survivors reported a persistent problem with self-care, 12 (10.1%) had died, and 36 patients report no problems with self-care by 1 year (status of an additional 29 patients was unknown). Thus, most patients who reported problems with mobility or self-care at 6 months had poor subsequent outcomes.

### Predictors of impaired quality of life

Table 2 shows predictors of problems with mobility and self-care at 6 months in the ACCESS cohort; age was an important predictor, but the presence of chronic disease before sepsis was not. Treatment with mechanical ventilation or dialysis for 14 or more days was associated with problems with mobility and self-care, but the duration of vasopressor support was not an important predictor.

## DISCUSSION

Two large international trials independently studying separate treatments for severe sepsis revealed strikingly similar findings. Approximately one third of patients who were functionally independent and residing at home before the onset of sepsis had died by 6 months and a third of the survivors reported problems with mobility and performing self-care or usual activities. Most patients were unable to live at home independently and either required assistance at home, or resided in nursing home or rehabilitation facilities, or they were in acute care hospitals. Furthermore in the ACCESS cohort, half of these patients either died or did not improve by 1 year. The poor quality of life in survivors is less likely to be attributed to advanced age or high burden of chronic diseases, and likely due to persistent critical illness and prolonged treatment with mechanical ventilation or dialysis.

Our findings are consistent with prior studies and have important implications (5, 6, 8). First, there is a need to identify strategies during the hospital course, such as early rehabilitation, or after hospital discharge, such as follow-up clinics (7), to improve quality of life for severe sepsis survivors. Second, currently US Food and Drug Administration recommends using 28-day all-cause mortality as a primary endpoint for sepsis trials. However, using mortality alone would ignore functional impairments that occur among sepsis survivors and affect quality of life. Future sepsis trials should consider a composite endpoint that incorporates mortality and either quality of life or disability measures. These measures are patient-centered outcomes and they are likely to increase caregiver burden. Our findings suggest that quality of life or disability measures obtained at 6 months may be adequate rather than waiting longer because half of patients who reported problems with mobility or self-care either died or did not improve subsequently. Third, consistent with prior studies, our findings showing that a third of sepsis survivors need assistance demonstrate the high societal costs of caring for sepsis survivors. As the incidence of sepsis increases and the short-term mortality decreases, cost of caring for sepsis survivors will likely increase over time.

Our study has several strengths. First, our findings of similar long term outcomes in 2 large, contemporary cohorts strength the inferences that can be drawn from our data. Second, patients were enrolled from various countries, thus our results may be considered widely generalizable. Third, our primary analysis was restricted to those who were functional and living independently prior to hospitalization with severe sepsis and we also conducted sensitivity analysis in young adults and those without chronic diseases; we thus sought to minimize confounding due to advanced age or pre-existing chronic disease. That our findings were similar in the primary and sensitivity analyses, suggests that we succeeded in minimizing such confounding.

Our study has limitations. Although EQ-5D has been widely used, it has not been validated for patients recovering from sepsis. In particular, EQ-5D may not be accurate in individuals with cognitive impairments (14). We also did not calculate quality-adjusted life years because each health state is assigned a value set based on the country of origin and this value set is not available for participants from several countries included in our study. Although we limited our analysis to patients who were living at home without help, quality of life was not available before onset of severe sepsis hospitalization. Thus, we may have overestimated the impairment in quality of life due to severe sepsis. We also did not collect quality of life measures using visual analog scale (EQ-VAS). Finally, data were missing for some patients. Often, these data are missing for those with worse values and we may have underestimated the frequency of some limitations.

## CONCLUSION

Approximately one third of patients who survived hospitalization for severe sepsis had died at 6 months. Another third experienced problems with mobility and self-care and were not able to live independently at this time point. Half of the survivors who had these problems at 6 months had either died by 1 year or had persistent problems. In addition to mortality, future studies should consider persistent functional impairment as an outcome measure and examine strategies to improve both longevity and quality of life in patients who survive severe sepsis.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

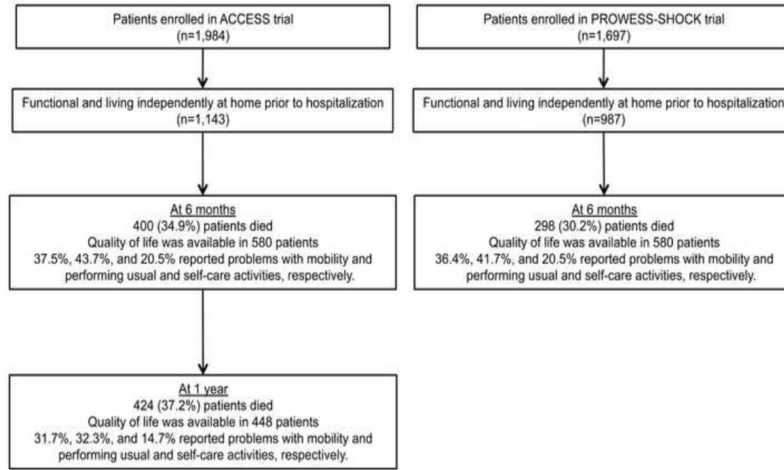
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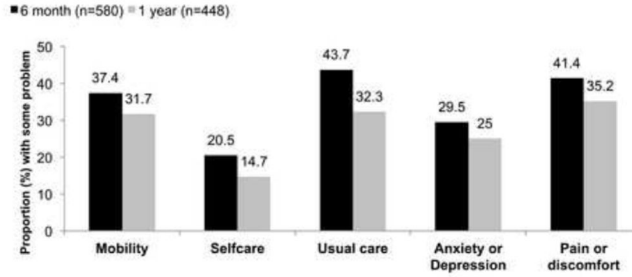


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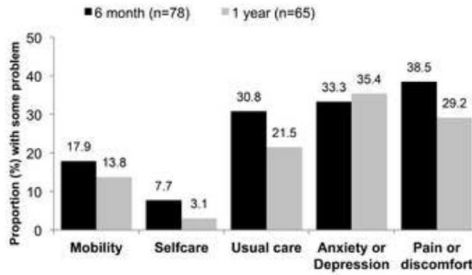


**Figure 1.** Flow chart describing selection of analyses cohorts and number of patients with quality of life measures

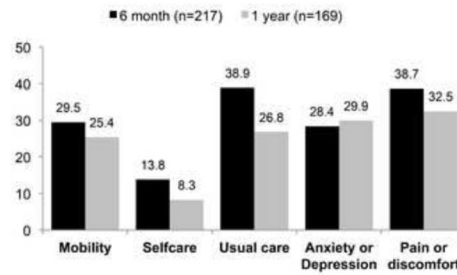
**A. Patients functional and living independently before severe sepsis hospitalization**



**B. Patients less than 45 years**



**C. Patients without chronic disease**



**Figure 2.** Proportion of patients who reported problems with mobility, self-care, and usual activities for all patients (panel A) who were functional prior to onset of severe sepsis and in the subsets that were young (<45 years old, panel B) and without chronic diseases (panel C).

**Table 1**

Clinical characteristics of sepsis survivors who were fully functional prior to hospitalization

Variable	ACCESS cohort (n=1143)	PROWESS-SHOCK cohort (n=987)
Demographics		
Age, mean (SD) y	63.2 (14.6)	61.6 (15.7)
Women, No. (%)	454 (39.7)	414 (41.9)
Race, No. (%)		
White	958 (83.8)	852 (86.3)
Black	55 (4.8)	32 (3.2)
Asian/non-Japanese	29 (2.5)	59 (6.0)
Japanese	71 (6.2)	0 (0)
Others	30 (2.6)	44 (4.5)
Region, No. (%)		
Europe	586 (51.3)	742 (75.2)
North America	340 (29.7)	121 (12.3)
South America	73 (6.4)	34 (3.4)
Asia	80 (7.0)	90 (9.1)
Rest of the world	64 (5.6)	0 (0)
Chronic diseases, No. (%) <sup>a</sup>		
Diabetes	347 (30.3)	225 (22.8)
Chronic pulmonary disease	254 (14.0)	143 (14.7)
Cancer	235 (13.4)	173 (17.5)
Moderate or severe renal disease	161 (8.9)	72 (7.3)
Ischemic heart disease	142 (7.8)	97(9.8)
Heart failure	129 (7.1)	36 (3.6)
Stroke or transient ischemic attack	85 (4.7)	39 (4.0)
Moderate or severe liver disease	58 (3.2)	37 (3.7)
Infection site <sup>a</sup> , No. (%)		
Lung	571 (44.1)	468 (47.4)
Genitourinary	189 (25.2)	98 (9.9)
Abdomen	268 (20.7)	319 (32.3)
Skin/soft tissue	95 (7.3)	69 (7.0)
Primary blood stream	37 (2.9)	163 (16.5)
Catheter-related bacteremia	24 (1.9)	-
Central nervous system	40 (3.1)	15 (1.5)
Other	70 (5.4)	34 (3.4)
Illness severity		
APACHE II score, Mean (SD)	26.8 (4.3)	24.8 (8.0)
With organ dysfunctions, No. (%)		
1	362 (31.7)	15 (1.5)
2	397 (34.7)	122 (12.4)
3	273 (23.9)	326 (33.0)

Variable	ACCESS cohort (n=1143)	PROWESS-SHOCK cohort (n=987)
4	98 (8.6)	385 (39.0)
5	13 (1.1)	139 (14.1)
Type of organ dysfunctions <sup>a</sup> , No. (%)		
Acute lung injury/ARDS	116 (10.1)	773 (78.3)
Thrombocytopenia	95 (8.3)	248 (25.1)
Lactic acidosis	291 (25.5)	460 (47.1)
Shock	551 (48.2)	987 (100)
Acute kidney injury	90 (7.9)	746 (75.6)
Duration of organ support		
Mechanical ventilation, Median (IQR)	7 (2, 15)	6 (2, 15)
Dialysis, Median (IQR)	0 (0, 2)	0 (0, 3)
Vasopressor use, Median (IQR)	3 (2, 7)	4 (2, 7)
Length of stay		
ICU, Median (IQR)	11 (6, 22)	11 (6, 21)
Hospital, Median (IQR)	21(10, 28)	22 (12, 29)
Mortality, No. (%)		
6-month mortality		
Alive	626 (54.7)	580 (58.8)
Dead	400 (34.9)	298 (30.2)
Missing	117 (10.2)	109 (11)
1-year mortality <sup>b</sup>		
Alive	467 (40.8)	-
Dead	424 (37.2)	-
Missing	252 (22)	-

<sup>a</sup>Numbers don't add up to 100% because patients may be part of more than 1 category;

<sup>b</sup>1-yr mortality not available for PROWESS-SHOCK cohort

APACHE – Acute Physiology and Chronic Health Evaluation score; ARDS – acute respiratory distress syndrome; ICU – intensive care unit; IQR - Interquartile range

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**Table 2** Predictors of mobility and self-care at 6 months for sepsis survivors who were at home and functional prior to hospitalization (n=580) in the ACCESS cohort

Variables (Reference Category)	Measures	Mobility			Self Care		
		Unadjusted Model OR (95% CI)	Adjusted Model OR (95% CI)	Unadjusted Model OR (95% CI)	Adjusted Model OR (95% CI)		
Age		1.03 (1.01–1.04) <sup>a</sup>	1.03 (1.02–1.05) <sup>a</sup>	1.04 (1.02–1.05) <sup>a</sup>	1.05 (1.03–1.07) <sup>a</sup>		
Sex (Females)	Males	0.91 (0.64–1.27)	0.75 (0.52–1.09)	1.03 (0.68–1.55)	0.80 (0.51–1.26)		
Race (White)	Blacks	0.97 (0.46–2.04)	1.39 (0.62–3.14)	1.33 (0.58–3.05)	2.92 (1.16–7.34) <sup>a</sup>		
	Others	0.74 (0.41–1.36)	0.71 (0.36–1.39)	1.14 (0.57–2.24)	1.28 (0.59–2.76)		
Chronic disease (None)	Yes	1.74 (1.21–2.49) <sup>a</sup>	1.48 (0.99–2.21)	2.02 (1.28–3.18) <sup>a</sup>	1.64 (0.99–2.71)		
Duration of organ support							
Ventilator (no support)	1–14 support days	1.10 (0.68–1.80)	1.36 (0.81–2.30)	0.92 (0.50–1.68)	0.94 (0.49–1.78)		
	>14 support days	2.07 (1.19–3.58) <sup>a</sup>	2.27 (1.19–4.34) <sup>a</sup>	2.60 (1.36–4.94) <sup>a</sup>	2.56 (1.21–5.41) <sup>a</sup>		
Dialysis (no support)	1–14 support days	0.94 (0.56–1.57)	0.96 (0.55–1.68)	1.49 (0.83–2.67)	1.44 (0.76–2.74)		
	>14 support days	4.97 (2.35–10.53) <sup>a</sup>	5.12 (2.23–11.75) <sup>a</sup>	4.40 (2.21–8.75) <sup>a</sup>	4.33 (1.91–9.83) <sup>a</sup>		
Vasopressor (no support)	1–7 support days	0.45 (0.25–0.80) <sup>a</sup>	0.38 (0.21–0.72) <sup>a</sup>	1.31 (0.59–2.89)	1.28 (0.55–3.00)		
	>7 support days	0.79 (0.40–1.57)	0.44 (0.20–0.98)	2.58 (1.07–6.19) <sup>a</sup>	1.33 (0.49–3.62)		

OR: odds ratio; CI: confidence interval;

<sup>a</sup>Significant at p<0.05