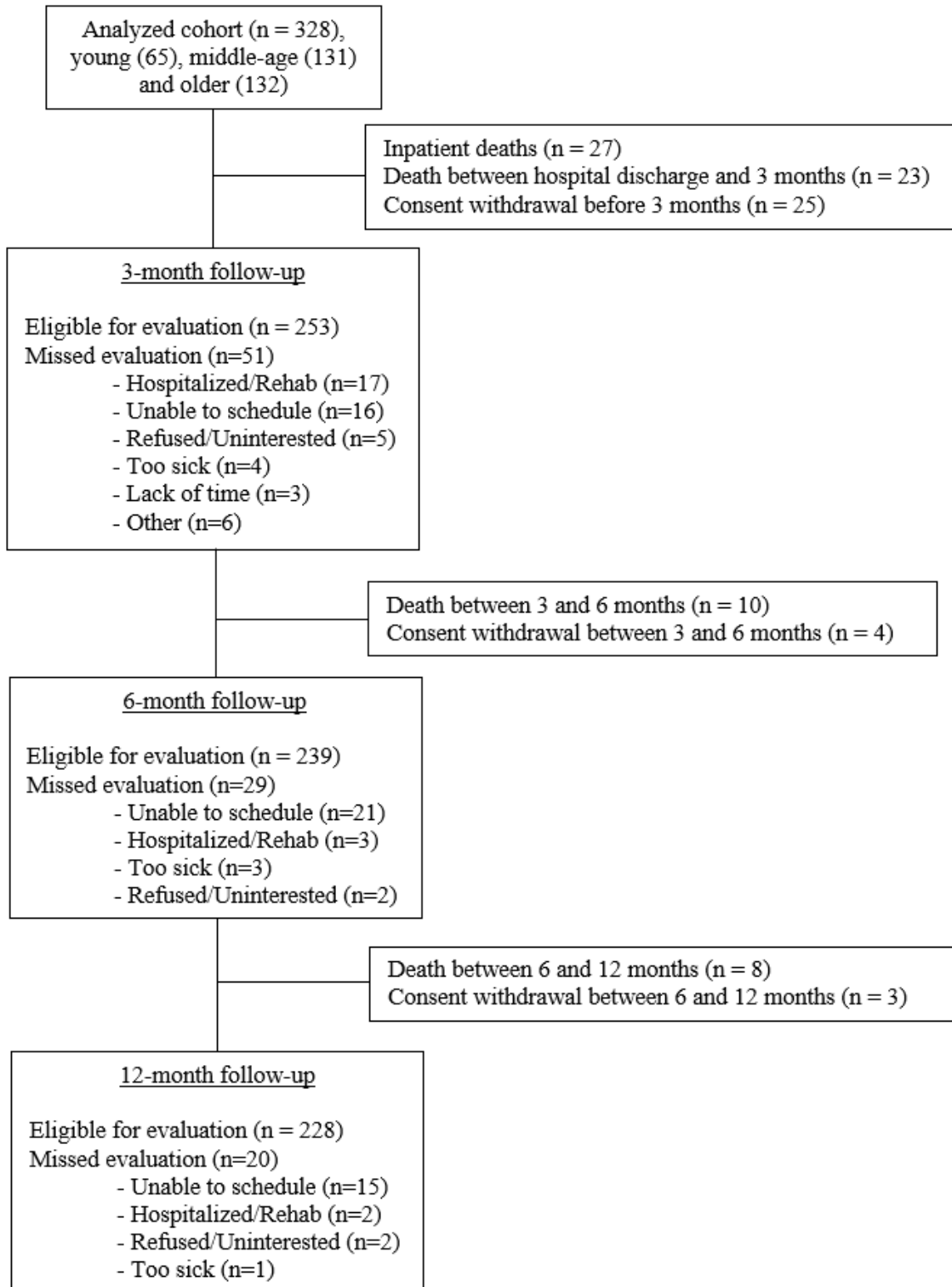
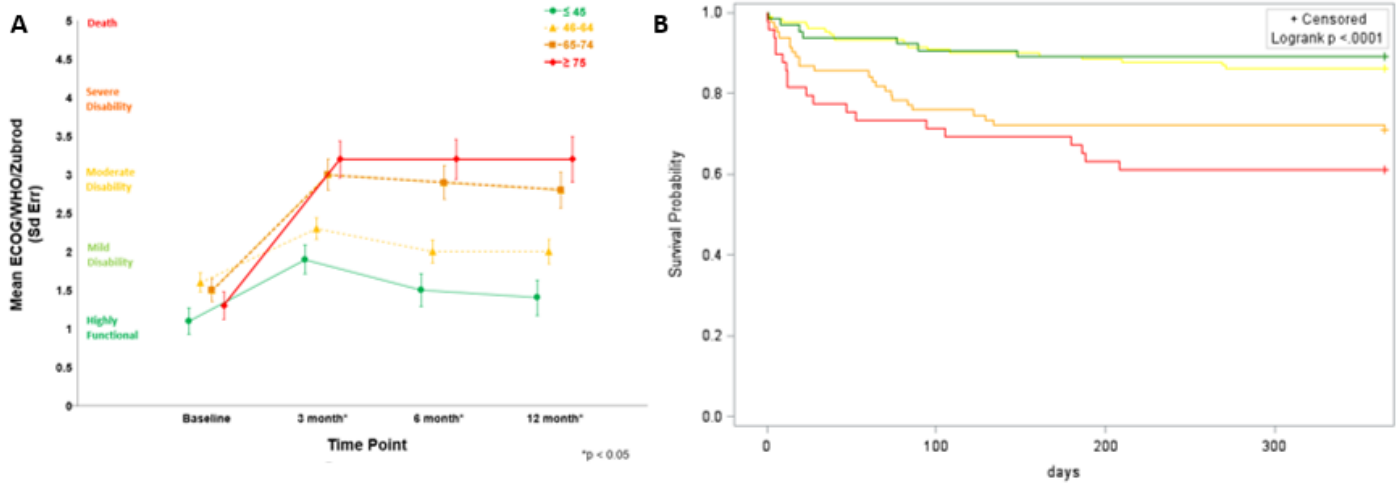


## Supplemental Material

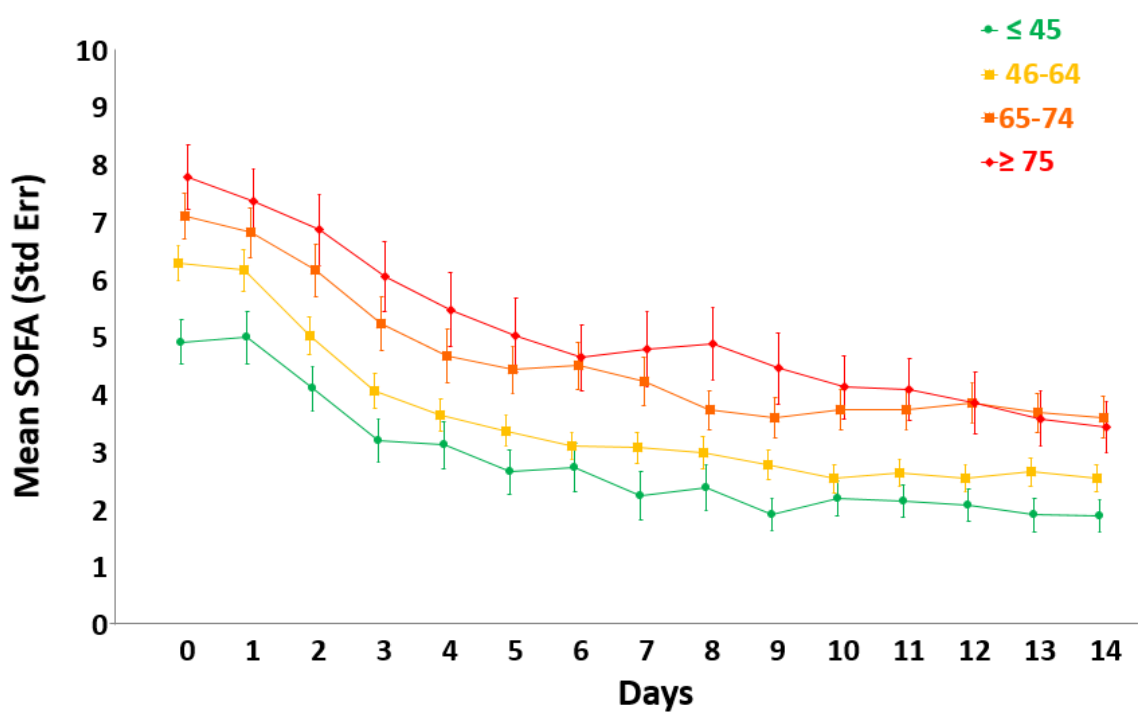
**Supplementary Figure S1.** Consolidated Standards of Reporting Trials (CONSORT) diagram and retention rates of 12-month follow-up.



**Supplementary Figure S2.** 12-month survival estimates (A) and Zubrod Performance Status at baseline and at three, six and 12 month follow-up (B) by age groups, including a breakdown of the older group into 65-74 and  $\geq 75$  years.



**Supplementary Figure S3.** SOFA scores over 14 days by age groups, including a breakdown of the older group into 65-74 and  $\geq 75$  years.



**Supplementary Table S1.** Post-sepsis causes of death by all age groups.

<b>Age Groups n (%)</b>	<b>Young 65 (20%)</b>	<b>Middle-age 131 (40%)</b>	<b>Older 65-74 83 (25%)</b>	<b>Older ≥ 75 49 (15%)</b>
30-day mortality, n (%)	4 (6)	5 (4)	12 (14)	11 (22)
MOF	3 (75)	4 (80)	8 (67)	5 (45)
Respiratory failure/ARDS	0 (0)	0 (0)	0 (0)	2 (18)
Sepsis (recurrent)	1 (25)	1 (20)	0 (0)	3 (27)
End-stage vascular disease	0 (0)	0 (0)	3 (25)	1 (9)
End-stage cancer	0 (0)	0 (0)	0 (0)	0 (0)
Heart failure/MI	0 (0)	0 (0)	1 (8)	0 (0)
>30-day mortality (late deaths)	3 (5)	13 (10)	12 (14)	8 (16)
MOF	0 (0)	3 (23)	2 (17)	3 (38)
Sepsis (recurrent)	0 (0)	1 (8)	2 (17)	2 (25)
End-stage cancer	0 (0)	5 (38)	2 (17)	1 (13)
Heart failure/MI	0 (0)	2 (15)	3 (25)	0 (0)
End-stage vascular disease	1 (33)	1 (8)	1 (8)	0 (0)
Renal Failure	0 (0)	0 (0)	1 (8)	1 (13)
CVA	0 (0)	1 (8)	1 (8)	1 (13)
Unknown	2 (67)	0 (0)	0 (0)	0 (0)

MOF=multi-organ failure, ARDS=acute respiratory distress syndrome, MI=myocardial infarction, CVA=cerebrovascular accident.

**Supplementary Table S2.** Baseline demographics, characteristics of the inciting septic event and predisposition by older age groups.

<b>Age Groups n (%)</b>	<b>Older 65-74 83 (25%)</b>	<b>Older ≥ 75 49 (15%)</b>
Male, n (%)	46 (55)	28 (57)
Age in years, median (IQR 25th, 75th)	69 (67, 72)	79 (76, 83)
Race, n (%)		
Caucasian (White)	76 (92)	45 (92)
African American	5 (6)	4 (8)
American Indian	0 (0)	0 (0)
Asian	1 (1)	0 (0)
Other	0 (0)	0 (0)
Unknown	1 (1)	0 (0)
Ethnicity, n (%)		
Hispanic or Latino	1 (1)	0 (0)
Not Hispanic or Latino	82 (99)	49 (100)
BMI, median (25th, 75th)	28.4 (24.7, 35.6)	26.3 (23.9, 32.3)
Morbid obesity n (%)	13 (16) <sup>a</sup>	0 (0)
Comorbidities, n (%)		
Hypertension	67 (81)	38 (78)
Coronary artery disease	36 (43)	22 (45)
Diabetes	36 (43)	16 (33)
Chronic lung disease	24 (29)	13 (27)
Atrial fibrillation	18 (22)	11 (22)
Chronic renal disease	17 (21)	10 (20)
Heart failure	23 (28)	5 (10)
Peripheral artery disease	18 (22)	10 (20)
Active cancer	15 (18)	7 (14)
Prior Stroke	7 (8)	5 (10)
Substance abuse	8 (10)	0 (0)
Dementia	2 (2)	4 (8)
Liver disease	1 (1)	1 (2)
ESRD	2 (2)	1 (2)
Number of comorbidities (adjudicated), n (%)		
0	4 (5)	1 (2)
1	9 (11)	11 (22)
2	17 (21)	11 (22)
≥3	53 (64)	26 (53)
Reason for Hospital Admission, n (%)		
Planned Surgery	14 (17)	14 (29)
Trauma	6 (7)	4 (8)
Active Infection	52 (63)	27 (55)
Non-Infectious / Chronic Problems	11 (13)	4 (8)
Emergency surgery (within 24 hrs), n (%)	40 (48)	20 (41)
Sepsis present on admission (≤48 hrs), n (%)	49 (59)	25 (51)
Hospital-acquired sepsis (>48 hrs), n (%)	34 (41)	24 (49)
Type of Infection n (%)		
Intra- abdominal	34 (41)	15 (31)
Surgical Site Infection	13 (16)	10 (20)
Pneumonia	13 (16)	10 (20)
Necrotizing Soft Tissue Infection	6 (7)	1 (2)
Urosepsis	10 (12)	9 (18)

Other	6 (7)	3 (6)
Catheter Related Blood Stream Infection	1 (1)	1 (2)
Sepsis severity, n (%)		
Sepsis	21 (25)	10 (20)
Severe Sepsis	32 (39)	22 (45)
Septic Shock	30 (36)	17 (35)
APACHE II Score (24 hrs), median (IQR 25th, 75th)	21 (15, 26)	19 (16, 26)
SOFA score (24 hrs), median (IQR 25th, 75th)		
Culture Negative	33 (40)	23 (47)
Culture Positive	50 (60)	26 (53)
Bacterial – gram positive	16 (32)	6 (23)
Bacterial – gram negative	17 (34)	13 (50)
Fungal	3 (6)	0 (0)
Polymicrobial	14 (28)	7 (27)
Sepsis Source Control Procedure, n (%)	52 (63)	31 (63)
Invasive procedures	40 (77)	24 (77)
Non-invasive procedures	12 (23)	7 (23)

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BMI = Body Mass Index, IQR = Interquartile Range, APACHE II = Acute Physiology + Age + Chronic Health Evaluation, SOFA = the Sequential Organ Failure Assessment. Statistical difference was labeled as <sup>a</sup> older 65-74 vs  $\geq$  75 years old, with statistical significance set at  $p < 0.05$ .

**Supplementary Table S3.** Admission service and types of sepsis source control by all age groups.

	<b>Young 65 (20%)</b>	<b>Middle-age 131 (40%)</b>	<b>Older 65-74 83 (25%)</b>	<b>Older ≥ 75 49 (15%)</b>
<b>Admission Service n, (%)</b>				
Trauma Acute Care Surgery	32 (49)	58 (44)	38 (46)	14 (29)
Vascular	4 (6)	10 (8)	21 (25)	14 (29)
Pancreaticobiliary	5 (7)	14 (11)	6 (7)	5 (10)
Colorectal	2 (3)	6 (5)	2 (2)	2 (4)
Minimally Invasive Surgery	3 (5)	10 (8)	1 (1)	2 (4)
Urology	8 (11)	16 (12)	6 (8)	8 (16)
Otolaryngology	1 (2)	3 (2)	2 (2)	1 (2)
Plastic Surgery	1 (2)	1 (1)	0 (0)	1 (2)
Orthopedic Surgery	2 (3)	1 (1)	4 (6)	1 (2)
Obstetrics / Gynecology	3 (5)	7 (4)	1 (1)	0 (0)
Transplant	2 (3)	3 (2)	0 (0)	0 (0)
Cardiothoracic	0 (0)	2 (2)	1 (1)	1 (2)
Breast Melanoma Sarcoma Endocrine	1 (2)	0 (0)	1 (1)	0 (0)
Oral/Maxillofacial Surgery	1 (2)	0 (0)	0 (0)	0 (0)
<b>Sepsis Source Control Procedure, n (%)</b>				
Invasive procedures	27 (59)	67 (71)	40 (48)	24 (49)
Laparotomy	11 (41)	33 (49)	26 (65)	14 (58)
Laparoscopic intervention	1 (2)	4 (6)	1 (3)	2 (8)
Debridement	11 (41)	25 (37)	4 (10)	2 (8)
Thoracotomy/Sternotomy/VATS	0 (0)	2 (3)	1 (3)	1 (4)
Amputation	0 (0)	1 (2)	2 (5)	0 (0)
Removal of infected implant/device	4 (16)	2 (3)	6 (15)	5 (21)
Non-invasive procedures	19 (41)	28 (29)	12 (15)	7 (14)
Percutaneous drainage	15 (78)	15 (54)	5 (42)	3 (43)
Endoscopic intervention	2 (11)	9 (32)	5 (42)	3 (43)
Incision & drainage	2 (11)	4 (14)	2 (16)	1 (14)

VATS= Video-assisted thoracoscopic surgery.

**Supplementary Table S4.** Characteristics of the hospital and post-discharge outcomes by older age groups.

<b>Age Groups n (%)</b>	<b>Older 65-74 83 (25%)</b>	<b>Older ≥ 75 49 (15%)</b>
Need for mechanical ventilation, n (%)	64 (77)	35 (71)
Ventilator free days (30 days), median (IQR 25th, 75th)	27 (21, 30)	27 (9, 30)
ICU free days (30 days), median (IQR 25th, 75th)	19 (8, 24)	20 (5, 26)
Hospital free days (30 days), median (IQR 25th, 75th)	11 (1, 20)	7 (0, 21)
Secondary infections/patient, mean (SD)	0.7 (0.9)	0.5 (0.8)
Secondary infections/100 hospital days, mean (SD)	2.9 (4)	2.4 (5.5)
AKI, n (%)		
KDIGO Stage 1	22 (27)	12 (25)
KDIGO Stage 2	17 (21)	11 (22)
KDIGO Stage 3	17 (21)	7 (14)
MOF frequency, n (%) – by Denver	17 (21)	12 (25)
30-day mortality, n (%)	12 (15)	11 (22)
Clinical Trajectory, n (%)		
Early Death	6 (7)	3 (6)
Chronic Critical Illness	35 (42)	20 (41)
Rapid Recovery	42 (51)	26 (53)
Discharge disposition, n (%)		
“Good” Disposition	32 (39)	18 (37)
Home	7 (2)	6 (33)
Homecare	14 (44)	10 (56)
Rehab	11 (34)	2 (11)
“Poor” Disposition	51 (61)	31 (63)
Long Term Care Hospital	19 (37)	9 (29)
Skilled Nursing	17 (33)	11 (36)
Another Hospital	1 (2)	0 (0)
Hospice	3 (6)	3 (10)
Death	11 (22)	8 (25)
Number of readmissions, mean (SD)	0.8 (1.3)	1 (1.3)

IQR = Interquartile Range, APACHE II = Acute Physiology + Age + Chronic Health Evaluation, SOFA = the Sequential Organ Failure Assessment., KDIGO = Kidney Disease: Improving Global Outcomes, MOF=multi-organ failure, SD = standard deviation.

**Supplementary Table S5.** Long-term follow-up of physical function and cognitive status for overall and by older age groups.

Age Groups n (%)	Older 65-74 83 (25%)	Older ≥ 75 49 (15%)
<b>Physical function</b>		
Total SPPB, mean (SE)		
3 months	3.8 (1)	3 (1.1)
6 months	4.4 (1)	3.2 (1.2)
12 months	4.8 (1.3)	5.5 (1.4)
Handgrip strength		
3 months	29.3 (6.2)	22.2 (2.7)
6 months	23.6 (1.3)	19.8 (1.3)
12 months	18.5 (2.4)	20.9 (3.4)
<b>Cognitive function</b>		
Hopkins Verbal Learning Test, mean (SE)		
3 months		
Total recall	20 (1)	15.9 (1.6)
Delayed recall	5.8 (0.8)	4.3 (1.2)
Retention	66.9 (7.54)	60.7 (13.6)
6 months		
Total recall	18.8 (2.1)	20.4 (1.41)
Delayed recall	5.3 (0.99)	5.9 (0.95)
Retention	59.8 (10.4)	65.1 (9.56)
12 months		
Total recall	21.1 (1.7)	19.5 (1.7)
Delayed recall	7.1 (0.6)	5.6 (1)
Retention	84.8 (5.5)	63.3 (10.4)
COWA		
3 months	26.8 (2)	32.7 (3)
6 months	25.7 (1.9)	30.5 (1.9)
12 months	26.1 (2.7)	31.2 (2.8)
MMSE		
3 months	83.8 (3.8)	77.4 (5.5)
6 months	77.8 (3)	82.8 (4.3)
12 months	85.3 (2.5)	84.4 (4.4)

SPPB=short physical performance battery, COWA = Controlled Oral Word Association, MMSE = mini-mental state examination, SE=standard error.