

APPENDIX 1

Hazard of death after sepsis event. Full multivariable Cox regression model for Figure 2.

Characteristic	Hazard Ratio (95% CI)	p-value
<u>FOLLOW-UP TIME</u>		
Year 0.00-1.00	13.07 (10.63-16.06)	<0.001
Year 1.01-2.00	2.64 (1.85-3.77)	<0.001
Year 2.01-3.00	2.18 (1.43-3.33)	<0.001
Year 3.01-4.00	1.97 (1.19-3.25)	0.008
Year 4.01-5.00	2.08 (1.14-3.79)	0.02
Year 5.01+	1.41 (0.67-2.98)	0.36
<u>DEMOGRAPHICS</u>		
Age Decile at Sepsis Event		
<50	Referent	
50-59	1.18 (0.82-1.70)	0.38
60-69	1.92 (1.35-2.75)	<0.001
70-79	3.77 (2.64-5.38)	<0.001
≥80	7.16 (4.98-10.31)	<0.001
Sex (Male vs. Female)	1.84 (1.69-2.01)	<0.001
Race (Black vs. White)	1.13 (1.04-1.23)	0.005
Education		
Less than high school	Referent	
High school graduate	0.90 (0.81-1.01)	0.08
Some college	0.92 (0.83-1.05)	0.22
College or higher	0.87 (0.77-0.99)	0.03
Income		
<\$20k	Referent	
\$20k-\$34k	0.83 (0.75-0.93)	0.001
\$35k-\$74k	0.65 (0.58-0.74)	<0.001
≥\$75k	0.57 (0.48-0.68)	<0.001
Unknown (Refused)	0.83 (0.73-0.95)	0.008
Geographic Region		
Stroke Buckle	0.93 (0.85-1.01)	0.10
Stroke Belt	0.99 (0.89-1.10)	0.85
Non-Belt/Buckle	Referent	
Health Status - Physical Composite Score		
Quintile 1 (≤37.002)	Referent	
Quintile 2 (37.006-46.949)	0.71 (0.64-0.79)	<0.001
Quintile 3 (46.951-52.111)	0.56 (0.50-0.63)	<0.001
Quintile 4 (52.112-55.501)	0.48 (0.42-0.54)	<0.001
Quintile 5 (≥55.502)	0.39 (0.33-0.46)	<0.001
Health Status - Mental Composite Score		
Quintile 1 (≤49.591)	Referent	
Quintile 2 (49.592-55.282)	0.96 (0.86-1.08)	0.52

Quintile 3 (55.282-57.827)	0.87 (0.77-0.99)	0.04
Quintile 4 (57.828-59.872)	0.82 (0.72-0.94)	0.003
Quintile 5 (\geq 59.872)	0.94 (0.84-1.05)	0.28

HEALTH BEHAVIORS

Tobacco Use

Current	2.22 (1.98-2.49)	<0.001
Past	1.19 (1.09-1.30)	<0.001
Never	Referent	

Alcohol Use

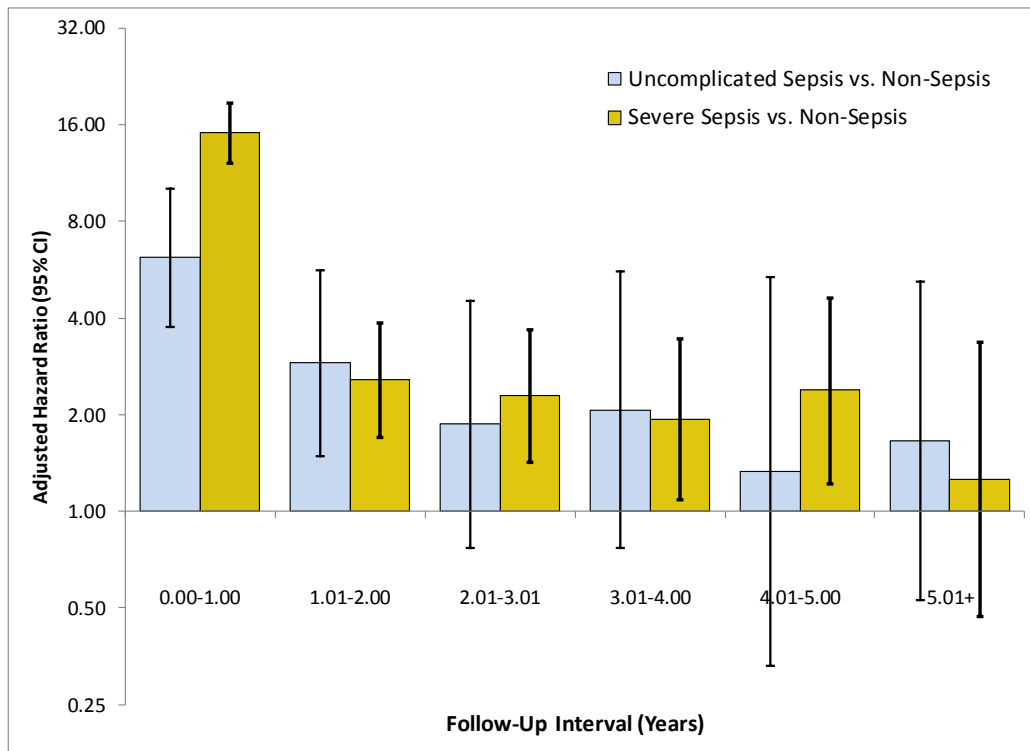
Heavy	1.09 (0.89-1.34)	0.39
Moderate	0.89 (0.81-0.97)	0.01
None	Referent	

CHRONIC MEDICAL CONDITIONS

Atrial Fibrillation	1.40 (1.26-1.56)	<0.001
Cancer History	1.21 (1.09-1.34)	<0.001
Chronic Lung Disease	1.21 (1.08-1.35)	0.001
Chronic Kidney Disease	1.81 (1.65-1.98)	<0.001
Coronary Artery Disease	1.14 (0.99-1.32)	0.08
Deep Vein Thrombosis	0.92 (0.80-1.07)	0.28
Diabetes	1.42 (1.31-1.55)	<0.001
Dyslipidemia	0.84 (0.77-0.91)	<0.001
Hypertension	1.10 (1.01-1.20)	0.03
Myocardial Infarction	1.24 (1.06-1.45)	0.005
Obesity (Elevated Waist Circumference or Body Mass Index \geq 30 kg/m ²)	0.88 (0.81-0.95)	0.001
Peripheral Artery Disease	1.48 (1.24-1.75)	<0.001
Stroke	1.37 (1.22-1.53)	<0.001

APPENDIX 2

Adjusted hazard ratios for associations between uncomplicated sepsis and severe sepsis and long-term survival. Time-dependent effects described using a Cox regression model with all sepsis defined as a time-varying covariate. Analysis censored at 6 years. Each bar reflects the hazard ratio for death among individuals alive at the beginning of that time segment. Graph depicts observation time ≥ 6 months only. Adjusted for age, sex, race, region, health status, smoking, alcohol use, obesity and chronic medical conditions, as reported at the beginning of the REGARDS study.



Follow-up Time Interval (Years)	Adjusted HR (95% CI) for Death Uncomplicated Sepsis vs. Non-Sepsis	Adjusted HR (95% CI) for Death Severe Sepsis vs. Non-Sepsis
0.00-1.00	6.16 (3.75-10.11)	15.07 (12.17-18.66)
1.01-2.00	2.90 (1.49-5.63)	2.57 (1.70-3.86)
2.01-3.00	1.87 (0.77-4.52)	2.29 (1.42-3.68)
3.01-4.00	2.07 (0.77-5.56)	1.94 (1.09-3.45)
4.01-5.00	1.33 (0.33-5.34)	2.38 (1.22-4.61)
5.01+	1.66 (0.53-5.19)	1.26 (0.47-3.37)

APPENDIX 3

Participant characteristics associated with rates of mortality after first sepsis events. Includes individuals experiencing sepsis only. Hospital course data based upon first sepsis episode only.

Characteristic	Hazard Ratio (95% CI)	p-value
<u>DEMOGRAPHICS</u>		
Age at Sepsis Event (HR per year)		
<50	Referent	
50-59	1.31 (0.16-10.72)	0.80
60-69	2.41 (0.32-18.38)	0.40
70-79	2.83 (0.37-21.60)	0.32
≥80	6.15 (0.80-47.17)	0.08
Sex (Male vs. Female)	1.37 (1.002-1.88)	0.048
Race (Black vs. White)	1.28 (0.93-1.76)	0.13
Education		
Less than high school	Referent	
High school graduate	0.70 (0.48-1.03)	0.07
Some college	0.75 (0.50-1.13)	0.17
College or higher	0.79 (0.51-1.24)	0.31
Income		
<\$20k	Referent	
\$20k-\$34k	1.00 (0.69-1.44)	0.98
\$35k-\$74k	1.03 (0.69-1.54)	0.87
≥\$75k	0.96 (0.52-1.77)	0.89
Unknown (Refused)	0.93 (0.55-1.57)	0.79
Geographic Region		
Stroke Buckle	0.90 (0.67-1.23)	0.52
Stroke Belt	1.26 (0.88-1.80)	0.20
Non-Belt/Buckle	Referent	
Health Status - Physical Composite Score		
Quintile 1	Referent	
Quintile 2	0.68 (0.46-1.01)	0.06
Quintile 3	0.55 (0.36-0.84)	0.006
Quintile 4	0.51 (0.33-0.79)	0.002
Quintile 5	0.59 (0.35-0.99)	0.045
Health Status - Mental Composite Score		
Quintile 1	Referent	
Quintile 2	1.62 (1.07-2.46)	0.02
Quintile 3	0.87 (0.55-1.39)	0.57
Quintile 4	1.28 (0.81-2.01)	0.29
Quintile 5	1.16 (0.76-1.78)	0.49

HEALTH BEHAVIORS

Tobacco Use

Current	1.23 (0.81-1.86)	0.33
Past	1.10 (0.80-1.52)	0.55
Never	Referent	

Alcohol Use

Heavy	0.96 (0.69-1.33)	0.80
Moderate	0.60 (0.27-1.34)	0.22
None	Referent	

CHRONIC MEDICAL CONDITIONS

Atrial Fibrillation	1.01 (0.71-1.45)	0.94
Cancer History	1.68 (1.24-2.27)	0.001
Chronic Lung Disease	1.35 (0.97-1.87)	0.07
Chronic Kidney Disease	1.43 (1.05-1.95)	0.02
Coronary Artery Disease	0.84 (0.49-1.42)	0.51
Deep Vein Thrombosis	0.63 (0.38-1.04)	0.07
Diabetes	1.57 (1.17-2.11)	0.003
Dyslipidemia	0.73 (0.55-0.98)	0.04
Hypertension	1.46 (1.07-2.00)	0.02
Myocardial Infarction	1.29 (0.75-2.22)	0.35
Obesity (Elevated Waist Circumference or Body Mass Index ≥ 30 kg/m ²)	0.74 (0.56-0.99)	0.04
Peripheral Artery Disease	1.28 (0.77-2.12)	0.34
Stroke	1.37 (0.93-2.00)	0.11

HOSPITAL COURSE

Infection Type

Lung	Referent	
Kidney	0.80 (0.55-1.17)	0.24
Abdominal	0.48 (0.29-0.78)	0.004
Skin	0.79 (0.43-1.43)	0.43
Sepsis	0.98 (0.58-1.67)	0.96
Other	1.33 (0.72-2.46)	0.37

Admission to Intensive Care Unit	2.02 (1.40-2.91)	<0.001
Sequential Organ Failure Score		

0	Referent	
1	1.10 (0.71-1.71)	0.68
2	1.25 (0.79-2.00)	0.34
3-4	1.66 (1.06-2.58)	0.03
5+	3.62 (2.23-5.88)	<0.001
