

APPENDIX

DEFINITIONS OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE AND HEART FAILURE:

Acute myocardial infarction (ICD-9: 410); unstable and stable angina (ICD-9: 411, 413); chronic ischemic heart disease (ICD-9: 414); unspecified atherosclerotic cardiovascular disease (ICD-9: 429.2); ischemic and hemorrhagic stroke, including subarachnoid hemorrhage, intracerebral hemorrhage, occlusion and stenosis of precerebral arteries, acute but ill-defined cerebrovascular disease and other ill-defined cerebrovascular disease (ICD-9: 430, 431, 433, 436, 437); and peripheral vascular disease, including atherosclerosis and accompanying procedures (ICD-9: 440, 38.1, 39.22, 39.24, 39.25, 39.26, 39.28, 84.1). We defined heart failure as an incident event (ICD-9: 428, 398.91, 402.01, 402.11, 402.91).

Supplementary Table 1. Association of Serum Albumin with Mortality, Atherosclerotic Cardiovascular Disease and Heart Failure, 1986-1996

Level of Albumin, g/dL	Hazard Ratio (95% Confidence Interval)				
	≥4.0	3.5-3.9	3.0-3.4	2.5-2.9	<2.5
Mortality (n=5,055)					
Baseline Albumin					
Demographic Adjusted Model	Ref	1.43 (1.33, 1.54)	1.89 (1.74, 2.05)	2.85 (2.62, 3.09)	3.79 (3.23, 4.45)
Multivariable Adjusted Model	Ref	1.34 (1.24, 1.44)	1.64 (1.51, 1.78)	2.28 (2.09, 2.49)	3.02 (2.56, 3.57)
Time-updated Albumin					
Demographic Adjusted Model	Ref	1.76 (1.59, 1.95)	3.77 (3.42, 4.16)	8.68 (7.92, 9.50)	17.5 (15.7, 19.5)
Multivariable Adjusted Model	Ref	1.59 (1.43, 1.76)	3.06 (2.77, 3.38)	6.25 (5.69, 6.86)	11.7 (10.4, 13.1)
Level of Albumin, g/dL	≥4.0	3.5-3.9	3.0-3.4	<3.0	
Composite Cardiovascular Event (n=182)					
Baseline Albumin					
Demographic Adjusted Model	Ref	1.38 (0.97, 1.97)	1.30 (0.83, 2.04)	1.81 (1.12, 2.92)	
Multivariable Adjusted Model	Ref	1.31 (0.92, 1.87)	1.08 (0.68, 1.70)	1.22 (0.73, 2.04)	
Time-updated Albumin					
Demographic Adjusted Model	Ref	1.16 (0.80, 1.70)	2.07 (1.37, 3.11)	2.26 (1.44, 3.55)	
Multivariable Adjusted Model	Ref	1.12 (0.77, 1.65)	1.83 (1.21, 2.79)	1.74 (1.08, 2.78)	
Level of Albumin, g/dL	≥4.0	3.5-3.9	3.0-3.4	<3.0	
Heart Failure (n=74)					
Baseline Albumin					
Demographic Adjusted Model	Ref	1.04 (0.55, 1.96)	1.91 (0.99, 3.67)	2.94 (1.52, 5.71)	
Multivariable Adjusted Model	Ref	0.95 (0.50, 1.79)	1.44 (0.73, 2.83)	2.00 (0.99, 4.06)	
Time-updated Albumin					
Demographic Adjusted Model	Ref	5.37 (1.99, 14.4)	13.1 (4.90, 35.1)	23.2 (8.72, 61.7)	
Multivariable Adjusted Model	Ref	4.87 (1.80, 13.1)	11.1 (4.09, 29.9)	15.8 (5.81, 42.9)	

Supplementary Table 2. Association of Serum Albumin with Mortality, Atherosclerotic Cardiovascular Disease and Heart Failure, 1997-2007

Level of Albumin, g/dL	Hazard Ratio (95% Confidence Interval)				
	≥4.0	3.5-3.9	3.0-3.4	2.5-2.9	<2.5
Mortality (n=5,634)					
Baseline Albumin					
Demographic Adjusted Model	Ref	1.39 (1.30, 1.48)	2.03 (1.88, 2.19)	3.07 (2.83, 3.33)	5.42 (4.65, 6.32)
Multivariable Adjusted Model	Ref	1.27 (1.19, 1.36)	1.61 (1.48, 1.75)	2.17 (1.98, 2.37)	3.20 (2.72, 3.77)
Time-updated Albumin					
Demographic Adjusted Model	Ref	1.91 (1.74, 2.09)	5.07 (4.63, 5.55)	16.0 (14.7, 17.4)	55.5 (50.5, 61.0)
Multivariable Adjusted Model	Ref	1.56 (1.42, 1.70)	3.12 (2.85, 3.43)	6.88 (6.28, 7.53)	17.5 (15.8, 19.5)
Level of Albumin, g/dL	≥4.0	3.5-3.9	3.0-3.4	<3.0	
Composite Cardiovascular Event (n=901)					
Baseline Albumin					
Demographic Adjusted Model	Ref	0.99 (0.85, 1.15)	1.09 (0.89, 1.34)	1.16 (0.91, 1.48)	
Multivariable Adjusted Model	Ref	0.96 (0.82, 1.12)	0.95 (0.77, 1.18)	0.94 (0.73, 1.23)	
Time-updated Albumin					
Demographic Adjusted Model	Ref	1.36 (1.15, 1.61)	2.49 (2.06, 3.00)	3.81 (3.11, 4.66)	
Multivariable Adjusted Model	Ref	1.40 (1.18, 1.65)	2.47 (2.03, 3.00)	3.59 (2.88, 4.48)	
Level of Albumin, g/dL	≥4.0	3.5-3.9	3.0-3.4	<3.0	
Heart Failure (n=361)					
Baseline Albumin					
Demographic Adjusted Model	Ref	1.24 (0.96, 1.61)	1.90 (1.41, 2.55)	2.24 (1.61, 3.12)	
Multivariable Adjusted Model	Ref	1.15 (0.89, 1.49)	1.41 (1.03, 1.94)	1.40 (0.97, 2.02)	
Time-updated Albumin					
Demographic Adjusted Model	Ref	2.72 (1.90, 3.88)	7.13 (4.98, 10.2)	18.7 (13.3, 26.4)	
Multivariable Adjusted Model	Ref	2.50 (1.75, 3.58)	5.48 (3.80, 7.91)	11.2 (7.71, 16.1)	

Supplementary Table 3. Association of Serum Albumin with Cardiovascular Disease and Heart Failure, 1986-2007, adjusting for competing events

Level of Albumin, g/dL	Hazard Ratio (95% Confidence Interval)				
	≥4.0	3.5-3.9	3.0-3.4	2.5-2.9	<2.5
Composite Cardiovascular Event (n=1,083)					
Baseline Albumin					
Demographic-Adjusted	1.0 (Reference)	1.01 (0.87-1.18)	0.98 (0.79-1.21)	1.02 (0.79-1.31)	-
Multivariable-Adjusted	1.0 (Reference)	0.99 (0.85-1.16)	0.89 (0.71-1.11)	0.88 (0.67-1.16)	-
Time-updated Albumin					
Demographic-Adjusted	1.0 (Reference)	1.26 (1.06-1.49)	2.07 (1.71-2.52)	2.58 (2.08-3.20)	-
Multivariable-Adjusted	1.0 (Reference)	1.29 (1.09-1.52)	2.12 (1.72-2.60)	2.64 (2.08-3.33)	-
Heart Failure (n=435)					
Baseline Albumin					
Demographic-Adjusted	1.0 (Reference)	1.11 (0.78-1.57)	1.47 (0.96-2.25)	2.07 (1.33-3.22)	-
Multivariable-Adjusted	1.0 (Reference)	1.02 (0.72-1.45)	1.12 (0.71-1.76)	1.31 (0.81-2.12)	-
Time-updated Albumin					
Demographic-Adjusted	1.0 (Reference)	3.72 (2.16-6.42)	10.8 (6.30-18.6)	22.7 (13.3-38.8)	-
Multivariable-Adjusted	1.0 (Reference)	3.42 (1.98-5.93)	8.45 (4.83-14.8)	14.6 (8.26-25.7)	-