

Supplemental Table 1: Physiological Dysregulation Components Measured in 2000

Biological Markers	Cutoff value <sup>1</sup>
<b>Cardiovascular/metabolic markers</b>	
Systolic blood pressure (the average of the second and third [out of three] seated readings ; mmHg)	≥ 156
Diastolic blood pressure (the average of the second and third [out of three] seated readings mmHg)	≤ 69, ≥ 96
Triglycerides (mg/dL)	≥ 160
Glycosylated hemoglobin (%)	≥ 6.1
Waist-hip ratio	≥ 0.94
Resting pulse rate	≥ 80
Total cholesterol (mg/dL)	≤ 153, ≥ 253
high-density lipoprotein cholesterol (mg/dL)	≤ 37
Fasting glucose (mg/dL)	≤ 84, ≥ 140
<b>Inflammation markers</b>	
White blood cell count (x 10 <sup>9</sup> /L)	≥ 7.4
Neutrophils (%)	≥ 64.9
Interleukin-6 (pg/mL)	≥ 4.5
high sensitivity C-reactive protein (pg/mL)	≥ 0.40
soluble intercellular adhesion molecule-1 (ng/mL)	≥ 318.8
Soluble E-selectin (ng/mL)	≥ 62.3
soluble IL-6 receptor (ng/mL)	≥ 61.7
<b>HPA/SNS Function</b>	
Urinary cortisol (mcg/g creatinine)	≥ 33.4
Epinephrine (mcg/g creatinine)	≤ 0.07, ≥ 5.63
Norepinephrine (mcg/g creatinine)	≥ 29.15
dehydroepiandrosterone-sulfate (mcg/dL)	≤ 34.7
<b>OTHER markers</b>	
insulin like growth factor-1 (ng/mL)	≤ 64.3
Creatinine clearance (mL/min)	≤ 43.56
Albumin (g/dL)	≤ 4.3
Homocysteine (mg/L)	≥ 19.2

<sup>1</sup> Cutoffs were established using the full 2000 biomarker sample.

Supplemental Table 2: Hazard ratios from Cox proportional hazard models of mortality (n=588<sup>a</sup>): Full models

	(baseline)	Models					Model	Model
		(1)	(2)	(3)	(4)	(5)	Footnote c in Table 3	Footnote d in Table 3
Age in 2006	1.06** (0.02)	1.05** (0.02)	1.05** (0.02)	1.04* (0.02)	1.06** (0.02)	1.05** (0.02)	1.06** (0.02)	1.06** (0.02)
Female	0.59 (0.20)	0.51 (0.18)	0.66 (0.22)	0.59 (0.20)	0.49* (0.18)	0.57 (0.20)	0.56* (0.14)	0.62 (0.15)
Years of education	1.04 (0.03)	1.06* (0.03)	1.06* (0.03)	1.08** (0.03)	1.06* (0.03)	1.08** (0.03)	1.03 (0.02)	1.04 (0.02)
Urban residence 2006	0.87 (0.20)	0.88 (0.20)	0.87 (0.20)	0.88 (0.20)	0.87 (0.21)	0.86 (0.20)		
Currently married 2006	0.65 (0.16)	0.65 (0.17)	0.76 (0.19)	0.69 (0.17)	0.61 (0.16)	0.65 (0.17)		
Number of chronic conditions 2006	1.03 (0.06)	0.97 (0.06)	1.00 (0.06)	0.95 (0.06)	0.95 (0.06)	0.92 (0.06)		
Cognitive function score 2006	0.90** (0.03)	0.93* (0.03)	0.94* (0.03)	0.95 (0.03)	0.93* (0.03)	0.95 (0.03)		
Ever smoked 2006	1.39 (0.38)	1.34 (0.38)	1.51 (0.42)	1.45 (0.41)	1.31 (0.38)	1.44 (0.41)		
Physiological dysregulation score 2000		1.28** (0.05)		1.25** (0.05)			1.30** (0.05)	
Frail 2006 (vs. not frail)			3.08** (0.79)	2.43** (0.64)		2.52** (0.66)		3.57** (0.86)
PD subscores 2000								
CV/ metabolic risk (0-7)					1.34** (0.10)	1.30** (0.10)		
HPA/SNS (0-4)					1.22 (0.15)	1.17 (0.15)		
Inflammation (0-6)					1.33** (0.11)	1.31** (0.11)		
OTHER <sup>d</sup> (0-4)					1.10 (0.14)	1.03 (0.14)		
<i>Harrell's C</i>	0.7089	0.7670	0.7483	0.7848	0.7669	0.7833	0.7594	0.7429

\*\* p<0.01, \* p<0.05; <sup>a</sup> Sample of respondents with complete data

CV=cardiovascular; HPA/SNS=Hypothalamic-pituitary-adrenocortical axis and sympathetic nervous system; OTHER biomarkers include: Insulin like growth factor-1 (IGF-1), creatinine clearance, albumin, homocysteine

Supplemental Table 3: Sensitivity Analyses: hazard ratios (Standard Errors) from Cox proportional hazard models of mortality including alternative forms of physiological dysregulation (PD)

	Average Z-Score		High Risk Quartiles		Allostatic Load (10-items)		2006 PD Score	
Age in 2006	1.05**	1.04**	1.05**	1.04**	1.05**	1.05**	1.05**	1.05**
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.01)	(0.01)
Female	0.45*	0.54	0.46*	0.55	0.44*	0.51	0.48*	0.48*
	(0.16)	(0.18)	(0.16)	(0.18)	(0.16)	(0.18)	(0.15)	(0.15)
Years of education	1.05	1.07**	1.05	1.07**	1.03	1.05	1.03	1.04
	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)
Urban residence 2006	0.86	0.87	0.90	0.88	0.89	0.89	0.90	0.90
	(0.20)	(0.20)	(0.21)	(0.20)	(0.21)	(0.20)	(0.21)	(0.21)
Currently married 2006	0.59*	0.64	0.64	0.67	0.68	0.76	0.66	0.68
	(0.15)	(0.16)	(0.16)	(0.17)	(0.17)	(0.19)	(0.17)	(0.18)
Number of chronic conditions 2006	0.96	0.93	0.97	0.94	0.99	0.96	1.01	0.99
	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)
Cognitive function score 2006	0.92**	0.96	0.92**	0.95	0.92**	0.95	0.93*	0.95
	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)
Ever smoked 2006	1.23	1.34	1.28	1.43	1.26	1.36	1.00	1.03
	(0.34)	(0.37)	(0.37)	(0.40)	(0.36)	(0.39)	(0.27)	(0.28)
PD Average Z-score	7.16**	6.51**						
	(2.75)	(2.49)						
PD high risk quartile			1.24**	1.22**				
			(0.05)	(0.05)				
Allostatic Load (10-items)					1.34**	1.32**	1.31**	1.30**
					(0.11)	(0.11)	(0.05)	(0.05)
PD 2006								
Frail 2006 (vs. not frail)		2.83**		2.69**		2.94**		2.07**
		(0.71)		(0.69)		(0.75)		(0.52)
<i>Harrell's C-index</i>	0.7491	0.7743	0.7530	0.7771	0.7361	0.7705	0.8032	0.8072
Observations	588	588	588	588	588	588	936	936

\*\* p<0.01, \* p<0.05