SUPPLEMENTARY MATERIAL

associated with

"Beyond Self Reports: Changes in Biomarkers as Predictors of Mortality"

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PREDICTED PROBABILITY OF DYING BY THE END OF FOLLOW-UP

To calculate the AUC using ROC analysis, we use the model coefficients to compute the predicted probability of dying by June 30, 2011 for each respondent, which is then compared with the observed outcome (i.e., whether or not the respondent actually died). The Gompertz proportional hazards model takes the following form:

$$\log \boldsymbol{\lambda}(\boldsymbol{t}) = \boldsymbol{x\beta} + \boldsymbol{\gamma t}\ , \qquad (1)$$

where t represents time measured in age, $\lambda(t)$ is the hazard rate at time t (age), γ denotes the age slope, x represents a covariate, and β is the corresponding regression coefficient. In our case, we fit a model that allows for non-proportional hazards. That is, γ is a function of x (i.e., the covariate x is interacted with age)

$$\boldsymbol{\gamma} = \boldsymbol{\gamma_0} + \boldsymbol{\gamma_1 x} \qquad (2)$$

For this model, the conditional probability of surviving from the date of the survey (t_0) to the end of follow-up (t_1) can be computed as:

$$\boldsymbol{S(t_1|t_0)} = \boldsymbol{exp}\{-\boldsymbol{e^{x\beta}}(\boldsymbol{e^{\gamma t_1}} - \boldsymbol{e^{\gamma t_0}})/\boldsymbol{\gamma}\}\,. \qquad (3)$$

Thus, for each respondent, we: a) calculate the linear prediction ($x\beta$) based on the observed value(s) for the covariate(s) and the model coefficient(s); b) compute γ given the observed value(s) of any covariates that were interacted with time t (age); and c) estimate conditional survival for using equation (3).

The probability of dying between t_0 and t_1 is simply the complement:

$$\boldsymbol{\hat{q}(t_1|t_0)} = \boldsymbol{1} - \boldsymbol{\hat{S}(t_1|t_0)}\,. \qquad (4)$$

Table S1. Biomarker summary score: cutoffs used to define high-risk levels for each biomarker

	Definition of high risk: Clinical cutoffs (where available); Otherwise, high risk quartile[a] (bottom 25% for DHEAS, CrCl, & Albumin; Top 25% for all others)
Cardiovascular/Metabolic	
SBP (mmHg)	>140 (Chobanian et al. 2003, World Health Organization, International Society of Hypertension Writing Group 2003)
DBP (mmHg)	>90 (Chobanian et al. 2003, World Health Organization, International Society of Hypertension Writing Group 2003)
Ratio total/HDL cholesterol	≥5 (AHA website)
HDL (mg/dL)	<40 (National Cholesterol Education Program, National Heart, Lung and Blood Institute 2001)
Triglycerides (mg/dL)	≥200 (National Cholesterol Education Program, National Heart, Lung and Blood Institute 2001)
HbA1c (%)	>6.5 (Rodbard et al. 2007)
BMI	<18.5 or ≥27 (Department of Health (Taiwan) 2002)
Waist circumference (cm)	> 88cm(F)/102cm(M) (World Health Organization (WHO) 2008)
Inflammation	
IL-6 (pg/mL)	>3.69
CRP (mg/L)	>3 (Pearson et al. 2003)
sICAM-1 (ng/mL)	>290.9
sE-selectin (ng/mL)	>56.5
Neuroendocrine	
DHEAS (µg/dL)	≤42.2
Cortisol (µg/g creatinine)	≥28.2
Epinephrine (µg/g creatinine)	≥4.44
Norepinephrine (µg/g creatinine)	≥26.4
Other markers	
CrCl (ml/min)[a]	≤52.6
Albumin (g/dL)	≤4.4
Homocysteine (µmol/L)	≥16.7

Abbreviations: BMI = body mass index; CrCl = creatinine clearance; CRP = C-reactive protein; DBP = diastolic blood pressure; DHEAS = dehydroepiandrosterone sulfate; HbA1c = glycoslyated hemoglobin; HDL = high-density lipoprotein cholesterol; IGF-1 = insulin-like growth factor 1; IL-6 = interleukin-6; SBP = systolic blood pressure; sE-selectin = soluble E-selectin; sICAM-1 = soluble intercellular adhesion molecule 1

[a] Quartile cutoffs are based on the weighted distribution in 2000 among the longitudinal cohort (n=639).

[b] Estimated using the Cockcroft-Gault formula (Cockcroft and Gault 1976).

Table S2. Index of social integration: description and coding of each component

Indicator	Definition	Coding
Network size	Number of friends and relatives with whom the respondent lives or has regular contact	Recoded <5, 5-7, 8-10, 11-14, 15-19, 20-29, 30+.
Network range	Number of types of relationships in social network	One point each for spouse/partner, kids, other relatives, non-relatives; range=0-4.
Married/partner	Dummy indicating that the respondent is married or lives with a companion.	
Household size		
Does not live alone	Dummy indicating that the respondent does not live alone.	
Number of friends	Number of close friends and neighbors with whom the respondent has weekly contact	Recoded 0, 1-2, 3-4, 5-9, 10-19, 20+.
Religious attendance	How often the respondent attends church or temple	Response categories: never, rarely, sometimes, often.
Socializing	How often the respondent socializes with friends, neighbors, or relatives.	Response categories: never, less than once a month, two to three times a month, once or twice a week, nearly daily.
Volunteer work	Dummy indicating that the respondent does volunteer work.	
Participation in social organizations	Whether respondent participates in the following activities/organizations: 1) Group activities (e.g., singing, dancing, tai chi, or karaoke) 2) Neighborhood association (e.g., women's association or arts & crafts classes) 3) Religious organization (e.g., church or temple committee) 4) Occupational associations for farmers, fishermen, or other professional group, civic group, Lion's Club, etc. 5) Political association (e.g., political party) 6) Social service groups (e.g., Lifeline, relief association, benevolent societies, charities, etc.) 7) Village or lineage association 8) Elderly club (e.g., Elderly Association, Evergreen Recreation Club, etc.)	One point for each type of organization in which the respondent participates; range = 0-7.

Table S3. Biomarker summary scores: coefficients from models predicting mortality using social and demographic characteristics, self-reported indicators of health status, and biomarker summary scores

	Model 0	Model 2	Model 3	Model 6
Age slope[a]				
Age	0.11***	0.09***	0.09***	0.06**
Age x Perceived social support	0.04***	0.03**	0.03**	0.04***
Age x Current smoker			0.14**	0.14**
Female	-0.46*	-0.67**	-0.77**	-0.82**
Mainlander	-0.55*	-0.58*	-0.57*	-0.64*
Urban resident	-0.06	-0.18	-0.21	-0.08
Education[b]	0.03	0.12	0.16	0.16
Social integration[b]	-0.14	-0.12	-0.09	-0.09
Perceived social support[b]	-0.96***	-0.82***	-0.81**	-0.98***
Self-assessed health status[b]				-0.18
Index of mobility limitations[b]				0.34*
History of diabetes				0.07
History of cancer				0.11
Number of hospitalizations[b]				0.28***
Former smoker				-0.02
Current smoker				-2.73**
Biomarker risk score in 2006[b]		0.60***	0.80***	0.53***
Change (2006 – 2000) in biomarker risk[b]			-0.35**	
Intercept[c]	-5.13***	-4.83***	-4.77***	-4.35***

[a] The age slope represents the exponential increase in the mortality rate per year of age.
[b] This variable was standardized (Mean=0, SD=1) prior to fitting the model; so, the coefficient represents the effect per SD of the specified variable.
[c] Time was measured in terms of years after age 60. Thus, the intercept represents the mortality rate at age 60.

Table S4. Individual biomarkers: coefficients from models predicting mortality using social and demographic characteristics, social factors, self-reported indicators of health status, and individual biomarkers

	Model 4a	Model 4b	Model 5a	Model 5b	Model 8a	Model 8b	Model 9a
Age slope (γ)[a]							
Age	0.09***	0.08***	0.10***	0.11***	0.07**	0.06**	0.09**
Age x Perceived social support	0.04**	0.04***	0.03*	0.03**	0.05***	0.05***	0.05**
Age x Current smoker					0.14**	0.15**	0.14**
Age x Change in $\sqrt{\text{DHEAS}}$			0.05***	0.04***			0.04***
Female	-0.22	-0.25	-0.37	-0.25	-0.28	-0.21	-0.45
Mainlander	-0.53	-0.54	-0.48	-0.60*	-0.70*	-0.66*	-0.68*
Urban resident	-0.02	-0.12	-0.03	-0.12	-0.10	-0.19	-0.06
Education[b]	0.16	0.19	0.23	0.22	0.23	0.26*	0.33*
Social integration[b]	-0.14	-0.16	-0.08	-0.13	-0.15	-0.14	-0.06
Perceived social support[b]	-1.00***	-1.01***	-0.82**	-0.81**	-1.13***	-1.16***	-1.06***
Self-assessed health status[b]					-0.25	-0.23	-0.19
Index of mobility limitations[b]					0.33*	0.34*	0.35*
History of diabetes					0.19	0.10	0.26
History of cancer					0.49	0.40	0.65
Number of hospitalizations[b]					0.26***	0.25***	0.26***
Former smoker					0.11	0.13	0.06
Current smoker					-2.67*	-2.82**	-2.75*
SBP (log) in 2006[b]	0.18		0.28		0.16		0.26
Change (2006 – 2000) in SBP (log)[b]			-0.11				-0.08
DBP (log) in 2006[b]	0.07		0.04		0.07		0.02
Change (2006 – 2000) in DBP (log)[b]			-0.01				0.03
TC/HDL (log) in 2006[b]	0.19		0.44*		0.32		0.56*
Change (2006 – 2000) in TC/HDL (log)[b]			-0.15				-0.09
HDL (log) in 2006[b]	-0.01	-0.11	-0.01	-0.19	0.07	-0.07	0.05
Change (2006 – 2000) in HDL (log)[b]			-0.07	0.12			-0.01
TG (log) in 2006[b]	-0.15		-0.31		-0.21		-0.39*
Change (2006 – 2000) in TG (log)[b]			-0.08				-0.08
$-1/(\text{HbA1c})^2$ in 2006[b]	-0.06		-0.16		-0.09		-0.25
Change (2006 – 2000) in $-1/(\text{HbA1c})^2$[,b]			0.01				0.09
BMI (log) in 2006[b]	-0.03	-0.04	0.03	-0.14	0.07	-0.08	0.20
Change (2006 – 2000) in BMI (log)[b]			-0.09	-0.13			-0.09
Waist in 2006[b]	-0.03		-0.19		-0.18		-0.40
Change (2006 – 2000) in Waist[b]			-0.10				0.01

	Model 4a	Model 4b	Model 5a	Model 5b	Model 8a	Model 8b	Model 9a
IL-6 (log) in 2006[b]	0.32**	0.32**	0.48**	0.42**	0.40**	0.37**	0.58***
Change (2006 – 2000) in IL-6 (log)[b]			-0.15	-0.22			-0.19
CRP (log) in 2006[b]	0.09	0.06	0.08	0.12	-0.00	-0.00	-0.01
Change (2006 – 2000) in CRP (log)[b]			-0.09	-0.06			-0.08
$\sqrt{\text{sICAM-1}}$ in 2006[b]	0.18	0.18	0.23	0.27*	0.19	0.18	0.26
Change (2006 – 2000) in $\sqrt{\text{sICAM-1}}$ [b]			-0.05	-0.04			-0.06
sE-selectin (log) in 2006[b]	0.13	0.08	0.17	0.10	0.09	0.04	0.21
Change (2006 – 2000) in sE-selectin (log)[b]			-0.03	-0.03			-0.09
$\sqrt{\text{DHEAS}}$ in 2006[b]	-0.18	-0.20	-0.26	-0.20	-0.10	-0.14	-0.21
Change (2006 – 2000) in $\sqrt{\text{DHEAS}}$ [b]			-0.95***	-0.87***			-0.87**
Cortisol (log) in 2006[b]	0.03		0.10		0.04		-0.01
Change (2006 – 2000) in Cortisol (log)[b]			-0.07				0.11
EPI (log) in 2006[b]	0.19		0.11		0.13		0.13
Change (2006 – 2000) in EPI (log)[b]			-0.02				-0.08
NE (log) in 2006[b]	-0.17		0.12		-0.08		0.14
Change (2006 – 2000) in NE (log)[b]			-0.33*				-0.29
CrCl in 2006[b]	-0.01	-0.14	0.13	0.11	0.18	0.11	0.27
Change (2006 – 2000) in CrCl[b]			-0.27	-0.27			-0.24
Albumin (cubed) in 2006	-0.24*	-0.23*	-0.13	-0.11	-0.09	-0.06	-0.04
Change (2006 – 2000) in Albumin (cubed)			-0.04	-0.11			0.01
Hcy (log) in 2006[b]	0.32*	0.32**	0.50**	0.36*	0.46**	0.52***	0.60**
Change (2006 – 2000) in Hcy (log)[b]			-0.24	-0.05			-0.24
Intercept[c]	-5.25***	-5.04***	-5.66***	-5.53***	-4.98***	-4.77***	-5.48***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$

[a] The age slope (γ) represents the exponential increase in the mortality rate per year of age.

[b] This variable was standardized (Mean=0, SD=1) prior to fitting the model; so, the coefficient represents the effect per SD of the specified variable.

[c] Time was measured in terms of years after age 60. Thus, the intercept represents the mortality rate at age 60.

Table S5. Subscores for biomarker clusters: coefficients from models predicting mortality using social and demographic characteristics, self-reported indicators of health status, and biomarker subscores

	Model 7a	Model 7b	Model 7c	Model 7d	Model 7e
Age slope (γ)[a]					
Age	0.08***	0.07***	0.08***	0.05*	0.05*
Age x Perceived social support	0.04***	0.05***	0.05***	0.05***	0.04***
Age x Current smoker	0.12**	0.14**	0.11*	0.11*	0.14**
Female	-0.69*	-0.54	-0.78*	-0.46	-0.71*
Mainlander	-0.60*	-0.64*	-0.60*	-0.67*	-0.65*
Urban resident	-0.03	-0.07	0.02	0.03	-0.07
Education[b]	0.12	0.19	0.11	0.17	0.19
Social integration[b]	-0.10	-0.14	-0.09	-0.10	-0.10
Perceived social support[b]	-0.20	-0.16	-0.20	-0.21	-0.19
Self-assessed health status[b]	0.34*	0.37**	0.38**	0.38**	0.30*
Index of mobility limitations[b]	-0.00	0.23	0.39	0.30	0.02
History of diabetes	0.06	0.17	0.29	0.41	0.06
History of cancer	0.30***	0.27***	0.27***	0.25***	0.24***
Number of hospitalizations[b]	0.06	0.05	0.11	0.14	0.05
Former smoker	-2.08*	-2.71**	-1.99*	-2.10*	-2.67**
Current smoker	-0.20	-0.16	-0.20	-0.21	-0.19
Cardiovascular/metabolic subscore in 2006[b]	0.36**				0.30*
Change (2006 – 2000) in cardiovascular/metabolic subscore[b]	-0.26*				-0.21
Inflammation subscore in 2006[b]		0.49***			0.34**
Change (2006 – 2000) in inflammation subscore[b]		-0.14			-0.06
Neuroendocrine subscore in 2006[b]			0.19		0.24
Change (2006 – 2000) in neuroendocrine subscore[b]			-0.06		-0.19
Other markers subscore in 2006[b]				0.50***	0.41**
Change (2006 – 2000) in other markers subscore[b]				-0.15	-0.14
Intercept[c]	-4.71***	-4.76***	-4.76***	-4.53***	-4.26***
AUC	0.824	0.833	0.823	0.824	0.846
Change in AUC (vs. Model 1)	0.007	0.016	0.006	0.007	0.029*

* $p<0.05$, ** $p<0.01$, *** $p<0.001$

[a] The age slope (γ) represents the exponential increase in the mortality rate per year of age.

[b] This variable was standardized (Mean=0, SD=1) prior to fitting the model; so, the coefficient represents the effect per SD of the specified variable.

[c] Time was measured in terms of years after age 60. Thus, the intercept represents the mortality rate at age 60.