Supporting Information

Shenhar-Tsarfaty et al. 10.1073/pnas.1418264112

SI Materials and Methods

Measures. The questionnaire covered background, occupational, psychological, and physical morbidity factors. The respondent's score on each of the indexes was obtained by computing the mean of his or her responses to the items in the index. Means and SDs for the indexes are presented in Tables 1 and 2.

Statistics. Given the multiple components involved we selected the decision tree support tool (1) and PLS analysis (2) to identify those parameters that are the major contributors to residual pulse (the additional pulse compared with that predicted according to age, sex, and BMI). The resultant regression tree is a hierarchical plot presented as a tree-like model (Figs. 1*A* and 2*A*) and highlights parameters that emerged as highly significant predictors of residual pulse. The tree model further offers subdivision of the remaining cohort into "branches" based on the calculated cut-point value of each continuous parameter. The same procedure was done in Fig. 2, where the annual change of calculated residual difference from predicted value (delta-pulse rest) served as the dependent variable.

The explanatory variables were sex, BMI, blood pressure, fitness data, medical history, medication, smoking, waist to hip ratio, sport intensity, inflammatory profile, and psychological scores [Patient Health Questionnaire (PHQ), Shirom-Melamed Burnout Measures (SMBM)], vigor, anxiety, FOT, and perceived control over one's life.

Multivariate data often contain systematic variation that is unrelated to the studied responses and may interfere with predictions based on the analyzed data. To remove such undesirable systematic variation in the data, we used PLS analysis to filter the input signals and achieve a better quantitative relationship between the descriptor and response matrices. Cross-validation was performed to avoid an overfitting situation.

More specifically, FOT was assessed by three items ("Nowadays, I worry about my personal safety." "Nowadays, I feel heightened tension when I am in crowded places." "I am afraid of a terror strike harming me or my family.") (3). For each item, participants checked off one of the following responses: "not at all," "a little bit," "moderately," "quite a bit," and "extremely." The scores on these items were averaged to yield a continuous FOT score (range, 1–5).

Perceived control included items assessing the two major dimensions of control, decision authority and skill discretion, similar to those of the job content questionnaire's decision authority scale (4). It was scored high for participants who reported that they were able to use their initiative and had opportunities to decide how best to use their skills. Sample items are, "My opinions and suggestions influence what happens at work"; "My job enables me to make decisions on my own and to follow them through"; and "I am free to determine how to perform my work."

1. Breiman L, Friedman J, Stone CJ, Olshen RA (1984) *Classification and Regression Trees Wadsworth Statistics/Probability* (Chapman and Hall/CRC, Belmont, MA).
2. Bylesjö M, et al. (2007) Orthogonal projections to latent structures as a strategy for microarray data normalization. *BMC Bioinformatics* 8:207.
3. Melamed S, Shirom A, Toker S, Berliner S, Shapira I (2004) Association of fear of terror with low-grade inflammation among apparently healthy employed adults. *Psychosom Med* 66(4):484–491.
4. Karasek R, Theorell T (1990) *Healthy Work: Stress, Productivity, and the Reconstruction of Working Life* (Basic Books, New York).

Table S1. Population characteristics

Variable	Men (n = 10,972)	Women (n = 6,408)	P
Risk factors			
Age, y (SD)	44.5 (11.3)	45.1 (10.8)	<0.001
BMI, kg/m^2	26.9 (3.8)	25.5 (4.9)	<0.001
Current smokers (%)	16.3	18.3	0.001
Diabetes (%)	3.8	3.1	0.018
Hyperlipidemia (%)	17.6	15.8	0.03
Hypertension (%)	42.8	27.3	<0.001
Systolic blood pressure, mm Hg	124.6 (14.7)	117.3 (16.1)	<0.001
Diastolic blood pressure, mm Hg	78.4 (8.4)	74.2 (8.2)	<0.001
Pulse, beats/min	69.8 (12.1)	72.7 (11.3)	<0.001
Inflammatory biomarkers			
hs-CRP, mg/L (SD)	2.5 (3.9)	3.4 (5.2)	<0.001
ESR, mm/H (SD)	10.7 (8.0)	19.5 (10.4)	<0.001
Fibrinogen, g/dL (SD)	285.2 (59)	313.3 (60.1)	<0.001
WBCC, 10^3/μL (SD)	6.8 (1.7)	6.8 (1.8)	0.699
Medications			
Acetylsalicylic acid, %	8.3	3.6	<0.001
β-Blockers, %	5.4	4.8	0.099
Diuretics, %	2.7	2.3	0.116
ACE inhibitors, %	4.7	2.4	<0.001
HMG-CoA reductase inhibitors, %	11.0	7.8	<0.001
Hypoglycemic (oral) %	2.4	1.4	<0.001
Antidepressants %	1.2	1.9	<0.001

ACE, angiotensin-converting enzyme; HMG-CoA, 3-hydroxy-3-methylglutarylcoenzyme A; WBCC, white blood cell count.

Table S2. Population statistics of full variables list

Variable	Mean or %	SD
Sex, male	63.3	
Age, y	44.5	11.03
Religion (% Jews)	98.9	
Tradition (% secular, traditional, religious, orthodox)	67.8, 24.3, 7.2, 0.7	
Marital status (% married)	76.6	
Education years	15.4	2.9
No. of children	2.5	1.25
No. of children living with you	1.9	1.25
City of birth	NA	
Father/Mother city of birth	NA	
Address	NA	
Height, m	1.7	0.09
Weight, kg	77.26	15.2
Waist, cm	90.7	12.7
Thigh, cm	97.0	8.3
Body temperature, °C	36.4	0.37
Ergometric test	NA	
Fitness scale	NA	
Fitness %	89.2	11.6
Basal heart rate (pulse), beats per min	70.8	12.0
Diastolic blood pressure, mmHg	76.9	8.7
Systolic blood pressure, mmHg	122.0	15.5
METS	11.8	3.2
METS-tool	NA	
Spirometry test scale	NA	
Spirometry indication	NA	
Spirometry severity	NA	
Forced vital capacity (FVC)	101.9	18.8
Forced expiratory volume in 1 s (FEV1)	99.2	15.5
FEV1/FVC ratio	101.6	10.5
Ergometry testing	NA	
Ergometry test duration, min	9.83	2.9
Ergometry test recovery, min	5.5	5.8
Ergometry test pulse peak, beats per min	162.3	12.5
Ergometry test recovery pulse	90.8	11.7
Hemoglobin A1C, %	5.4	0.64
CRP, wide range, mg/L	2.87	5.03
CRP, high sensitive, mg/L	2.8	4.5
Troponin, ng/mL	2.28	3.4
Creatinine, mg/dL	95.1	85.1
ESR, mm/h	14.1	10.0
Fibrinogen, mg/dL	295.0	60.7
Creatinine albumin ratio	0.1169	9.93
Microalbumin, mg/L	12.2	72.0
Urine gravity	1.01	0.00776
Urine pH	6.2	0.85
Red blood cells (RBC)	4.78	0.45
Hemoglobin, g/dL	14.3	1.3
Hematocrit, %	41.8	3.8
MCV, fL	87.5	4.6
MCH, picograms/cell	29.96	1.9
MCH concentration	34.2	0.9
WBC, $10^3/\mu$L	6.83	1.7
Neutrophils, %	59.0	7.8
Neutrophils total	4.1	1.3
Eosinophils, %	2.7	1.9
Basophils	0.5	0.3
Monocytes, %	7.5	7.9
Monocytes total	0.51	0.2
Lymphocytes, %	30.2	7.0
Lymphocyte total	2.0	0.7
Platelets, μL	250.2	58.7
Mean platelets, fL	8.8	1.0

Table S2. Cont.

Variable	Mean or %	SD
RBC total	4.8	0.45
Hemoglobin	14.3	1.3
Glucose, mg/dL	92.7	18.1
Chloride, mEq/L	103.9	2.5
Sodium, mEq/L	141.2	2.6
Potassium, mEq/L	4.4	0.4
BUN, mg/dL	14.4	3.7
Serum creatinine, mg/dL	1.06	0.2
Serum uric acid, mg/dL	5.5	1.3
Total bilirubin, mg/dL	0.76	0.3
GPT, U/L	25.9	14.1
γ-GT, U/L	20.2	19.7
LDH, U/L	309.1	55.9
GOTAST, U/L	23.7	8.7
Serum total protein, g/L	73.8	4.05
Serum total albumin, g/L	45.2	2.5
Serum total globulin, g/L	28.6	3.3
Cholesterol, mg/dL	196.9	37.1
Triglycerides, mg/dL	118.3	73.0
High-density cholesterol, mg/dL	55.1	14.1
Low-density cholesterol, mg/dL	118.5	31.7
Cholesterol/high-density lipoprotein ratio	3.76	1.2
Alkaline, U/L	61.0	18.4
Medication	Use of medication was recorded according to 42 medication-families including statins, α-, β-, and calcium blockers, diuretics, fibrates, anti-PVD, antipsychotic, antihistamine, laxative, bronchodilators, etc.	
S/P diseases	Cardiovascular disease (CVD), hypertension, CVA, diabetes, cancer, ulcer, kidney stones, intestinal disease, neurological disease, chronic pain, dyslipidemia, PVD, chronic fatigue, etc.	
S/P family diseases	Father/mother/brother CVA, CVD, dyslipidemia, hypertension were recorded	
Hospitalization	Hospitalization during last year was logged	
Sport, % yes	62.8	
Sport kind	NA	
Sport hours	0.8	0.8
Sport d/wk	1.9	1.8
Fruits/2 d	2.7	2.3
Vegetables/2 d	3.5	2.6
Fry food	1.0	1.15
Breakfast	NA	
Coffee (cups/d)	2.7	2
Vitamins (%)	5.3	
Fasting hours	12.0	1.64
Smoke (% current, past)	16.8, 24.4	
Count of cigarettes per day	2.3	6.5
Alcohol drinks	37.6	
No. of alcohol drinks/d	1.5	1.1
No. days of alcohol consumption	1.8	1.4
Sleep questionnaire (13 items)	2.2	0.6
Subjective health questionnaire (4 items)	3.7	0.6
Subjective life satisfaction questionnaire (6 items)	5.1	0.98
Financial strain questionnaire (6 items)	1.6	0.66
Self-efficacy questionnaire (8 items)	4.2	0.61
Depression PHQ questionnaire (10 items)	1.3	0.35
Anxiety questionnaire (4 items)	1.8	0.8
FOT questionnaire (3 items)	1.5	0.7
JAWS questionnaire (10 items)	3.4	0.75
Current work description and details questionnaire (30 items)	NA	

Table S2. Cont.

Variable	Mean or %	SD
Job satisfaction questionnaire (10 items)	5.4	0.9
Work load questionnaire (9 items)	2.3	0.8
Support questionnaire (16 items)	4.0	0.6
Perceived control questionnaire (7 items)	3.9	0.9
Burnout questionnaire, SMBM (16 items)	2.2	0.9
Vigor questionnaire (14 items)	5.5	0.9

BUN, blood urea nitrogen; CVA, cerebrovascular accident; GGT, gamma-glutamyl transpeptidase; GOTAST, aspartate aminotransferase, glutamic oxaloacetic transaminase; GPT, glutamate-pyruvate transaminase; JAWS, job-related affective well-being scale; LDH, lactate dehydrogenase; MCH, mean cell hemoglobin; MCV, mean cell volume; METS, metabolic equivalent of task; PVD, peripheral vascular disease; S/P, status/post.