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Life Experiences, Strength of Emotional Response, and Sex-specific
Mortality Risk Zones

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Life experiences, strength of emotional response, and sex-specific mortality risk zones

Abstract

In this paper, we introduce a new operationalization of the concept of allostatic load—the cumulative biological burden exacted on the body through attempts to adapt to life’s demands. We use a recursive partitioning (RP) methodology to specify categories of ‘low’, ‘intermediate’, and ‘high’ risks of later-life mortality. The risk categories are defined in terms of either low or high ranges of values on the biomarkers, each of which has been implicated as an indicator of possible dysregulation in one or more biological systems. We find that the cumulation of positive life experiences is positively related to membership in a low mortality risk zone, thereby supporting our contention that our operationalization of allostatic load is interpretable as a biological signature of adaptation to life challenges. We also find sex differences in risk categories and their corresponding associations with emotional response profiles.

1. Introduction

In the mid-19th century, French scientist Claude Bernard laid the foundation for the scientific analysis of stress by articulating the necessity for the body to maintain a stable internal environment, or *milieu intérieur* (McEwen, 2002a; Wolfe et al., 2000). Walter Cannon fully developed the idea of homeostasis as explicated in his book, *Wisdom of the Body* (Cannon, 1932), having lectured and written extensively on related aspects of the concept (Wolfe et al., 2000; Cannon, 1915). In the 1930s, Hans Selye explored the notion of a generalized stress response by investigating the effects of multiple hormones injected into rats (Selye, 1956; Selye, 1975; Sternberg, 2000). Selye followed by numerous other researchers investigated the relationship between stress and physiological well-being, leaving many questions unresolved (McEwen, 2002a-b). We pursue answers to the following four questions: What are the physiological profiles of mortality risk? Do these profiles differ by sex? How does the accumulation of adverse or advantageous experiences over the life course relate to physiological measures of mortality risk? How does strength of emotional reaction to life events relate to physiological well-being?

To investigate these questions, we present a new operationalization of the concept of allostatic load—the cumulative biological burden exacted on the body through attempts to adapt to life’s demands. We use a recursive partitioning (RP) methodology to specify categories of ‘low’, ‘intermediate’, and ‘high’ risks of later-life mortality. The risk categories are defined in terms of either low or high ranges of values on the biomarkers, each of which has been implicated as an indicator of possible dysregulation in one or more biological systems. We correlate membership in risk zones with life experience and emotional response profiles, thereby supporting the contention that our operationalization of allostatic load is interpretable as a biological signature of adaptation to life challenges.

We propose the following three hypotheses with regard to the questions stated above:

- 1.) Men and women have mortality risk categories/zones defined by different physiological characteristics.
- 2.) People with negative life experience profiles are more likely to belong to a high mortality risk zone. Conversely, those with positive life experience profiles are more likely to belong to a low mortality risk zone.
- 3.) People who have a strong emotional response to life events are more likely to belong to a high mortality risk zone, because they are more likely to show signs of increased physiological dysregulation.

2. Overview of allostatic load

Sterling and Eyer (1988) introduced the term *allostasis*, which means “maintaining stability through change,” to explain how the cardiovascular system adjusts to resting and active states of the body. McEwen and Stellar later applied the term to other biological mediators of stress—such as cortisol and epinephrine—and proposed the concept of *allostatic load* to refer to the wear and tear that the body experiences from continual cycles of turning on and shutting off the biological stress responses (McEwen, 1998; McEwen and Stellar, 1993). That is, allostatic load measures the cost to the body that results from chronic fluctuation of the neuroendocrine system, the autonomic nervous system, and the immune system (McEwen, 2002b; McEwen and Stellar, 1993; Singer and Ryff, 1999). Operationalizations of this concept provide an early warning measure of later-life health consequences (Seeman et al., 1997; 2001; Karlamangla et al. 2002). They also reflect antecedent psychosocial adversity (Singer and Ryff, 1999; Ryff, Singer, Wing and Love, 2001; Seeman et al., 2002).

2.1 Biomarkers of allostatic load

Current operationalizations of the concept of allostatic load include assessments of ten physiological indicators representing various biological systems: the hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic nervous system, the cardiovascular system, and metabolic processes.

The hypothalamic-pituitary-adrenal (HPA) axis plays a vital role in the body's response to environmental stressors and personal challenges. Cortisol and dehydroepiandrosterone (DHEA) levels serve as good indicators of HPA-axis activity. There are adverse health consequences of elevated cortisol, including heightened cardiovascular risk and reduced cognitive functioning (Seeman et al., 1997). DHEA, on the other hand, is negatively associated with heart disease and mortality (Barrett-Connor and Goodman-Gruen, 1995). The protective effect of DHEA is potentially due to its anti-clotting and anti-proliferative properties (Beer et al., 1996).

The sympathetic nervous system (SNS) is a central regulatory system that assists in maintaining the body's physiological integrity when confronted with shifting environmental demands. Thus, it is an additional mechanism through which social and psychological experiences may affect health. Norepinephrine and epinephrine levels, for example, are related to stress and challenge (Seeman and McEwen, 1996). These hormones provide the body with what is needed for the 'fight or flight' responses. As with the HPA axis, SNS activity is beneficial in the short-run, but it is also associated with increased risks for health problems such as hypertension and heart disease if the associated hormone levels are chronically elevated (Crimmins and Seeman, 2001).

Cardiovascular fitness is reliably measured through systolic and diastolic blood pressure. Blood pressure predicts the onset of cardiovascular disease, death rates, and the loss of both physical and cognitive functioning (Kaplan and Keil, 1993). Among older individuals, systolic blood pressure is better than diastolic blood pressure as a predictor of these health outcomes (Crimmins and Seeman, 2001).

Metabolic processes can be assessed by waist/hip ratio, cholesterol levels, and levels of glycosylated hemoglobin. High total serum cholesterol levels are predictive of poor health outcomes such as mortality and cardiovascular disease. In this research, we use two measures of cholesterol: total HDL

cholesterol (a risk factor if too low) and the ratio of the total cholesterol to the HDL cholesterol (a risk factor if too high). Glucose metabolism is another important indicator of metabolic processes. Elevated glucose levels, as measured by glycosylated hemoglobin, are related to insulin resistance and subsequent heart disease (Reaven, 1988), lower cognitive functioning (Craft et al., 1993), and higher mortality (Fried et al., 1998).

2.2 Operationalizations of allostatic load

The original operationalization of allostatic load is called the elevated-risk zone method. Proposed by Seeman et al. (1997), this method counts the number of the biomarkers that are beyond a selected cut-off point. For example, in the MacArthur Study of Successful Aging (MAC Aging), the threshold value for each biomarker is determined by the upper (or lower in the case of DHEA and HDL levels) quartiles, as shown in the far right column of Table 1 (Seeman et al., 2001; Seeman et al., 1997). The summary measure is the total number (between 0 and 10) of the 10 biomarkers that satisfies the stated inequality. The number reflects a cumulative level of dysregulation that serves as a warning sign for adverse downstream health outcomes. The threshold values for this method can vary depending on the characteristics of the population. As shown in Table 1, using the quartile cut points, the younger Wisconsin Longitudinal Study (WLS) sample has threshold values that are in some cases very different (e.g., norepinephrine and epinephrine) than the MAC Aging sample (both samples are described below). On other biomarkers, the cut points are nearly identical (e.g., systolic blood pressure, waist-hip ratio). The difference between the cortisol measures is probably due to measurement differences; cortisol in the MAC Aging sample was assessed via mass spectrometry, and via radioimmunoassay (RIA) in the WLS.

Another method of operationalizing the concept of allostatic load uses canonical correlation analysis (Karlman et al., 2002). Canonical correlation analysis uncovers latent linear relationships between two sets of variables—Karlman et al. use the same 10 biomarkers in Table 1 as one set and functional outcome scores as the second set. Given these two sets of variables, canonical correlation analysis finds a linear combination of the variables from each set, known as a *canonical variable*, such that it maximizes the correlation between the two canonical variables. This maximized correlation,

known as the *canonical correlation*, is at least as big as the multiple correlation between: 1) any predictor variable and all outcome measures, and 2) any outcome measure and all predictor variables.

Table 1 Threshold values identified using the WLS sub-sample and the MAC Aging data, determined by quartile risk cut points

Biological Measures of Mortality Risk	Definitions from WLS Sample (Age 58-59)	Definitions from MAC Aging Sample (Age 70-79)
Systolic Blood Pressure (mm Hg)	≥ 146	≥ 148
Diastolic Blood Pressure (mm Hg)	≥ 85	≥ 83
Waist/hip Ratio	≥ .95	≥ .94
Total Cholesterol/HDL Ratio	≥ 5.2	≥ 5.9
Total Glycosylated Hemoglobin Level (%)	≥ 6	≥ 7.1
Urinary Cortisol Level (mg/g creatinine)	≥ 42.9	≥ 25.7
Urinary Norepinephrine Level (mg/g creatinine)	≥ 37.2	≥ 48
Urinary Epinephrine Level (mg/g creatinine)	≥ 2.9	≥ 5
HDL Cholesterol Level (mg/dl)	≤ 40	≤ 37
DHEA (ng/dl)	≤ 39	≤ 35

Using the MAC Aging data, Karlamangla et al. (2002) conclude that a summary measure of physiological dysregulation is an independent predictor of functional decline in elderly men and women. Further, canonical correlation analysis shows that the four components of the allostatic load biomarkers that reflect hormonal activity (i.e., epinephrine, norepinephrine, cortisol, and DHEA) all contribute directly to functional decline independent of the other six factors, which are cardiovascular risk factors. This research provides support for the inclusion of variables across multiple physiologic systems when determining mortality risk.

There is a need for further refinement of the operationalization of allostatic load. First, current operationalizations of allostatic load fail to account for sex differences when determining health risks (Seeman et al., 2001; Seeman et al., 1997). This is an especially conspicuous gap given that five to seven of the 10 biomarkers commonly used to study allostatic load have mean levels that differ by sex.¹ Second, the original elevated-risk zone method of operationalizing allostatic load allows only one tail of the distribution of a given biomarker to be associated with risk.

¹ The mean value of waist/hip ratio ($p < .0001$), diastolic blood pressure ($p < .001$), total cholesterol/HDL ratio ($p < .05$), urinary norepinephrine ($p < .05$), and urinary epinephrine ($p < .05$) are statistically significantly different by sex in the WLS sample. In the MAC Aging sample, there are statistically significant sex differences in the means of: waist/hip ratio ($p < .0001$), total cholesterol/HDL ratio ($p < .01$), cortisol ($p < .05$), norepinephrine ($p < .05$), epinephrine ($p < .0001$), total HDL ($p < .0001$), and DHEA ($p < .0001$) (values are shown in Tables 3 and 4).

3. *Methods*

3.1 **Data sets**

3.1.1 **MacArthur Study of Successful Aging (MAC Aging)**

MAC Aging is a longitudinal study of 1,189 healthy² people aged 70-79 at baseline, from three sites—East Boston, MA, Durham, NC, and New Haven, CT. The individuals in the sample, who have better cognitive and physical functioning than a nation-wide sample of the same age, have similar social and economic variation as the total US population in the same age range. The original MAC Aging population is 19% black, but we exclude black participants in this analysis because we apply the results of the mortality risk partitions to a white population. For this analysis, we have a usable sample of 291 women and 296 men, because we also exclude individuals with incomplete biomarker records.³ Out of this reduced sample, 13.7% of the women and 28.0% of the men died before the seven-year follow-up.

3.1.2 **Wisconsin Longitudinal Study – Life Histories and Health Study**

Between 1996 and 1999, researchers at the University of Wisconsin collected comprehensive biological information and conducted lengthy interviews with the Life Histories and Health Study sub-sample of the Wisconsin Longitudinal Study (WLS) (46 women and 52 men) who graduated high school in Wisconsin in 1957.

3.2 **Biomarkers**

Assessments of all ten biomarkers were collected for individuals in both the WLS and the MAC Aging sample. The measurements were taken from several sources: direct measurement, blood test, and urine analysis. Systolic and diastolic blood pressure measures are the average of three readings from seated measurement. Waist/hip ratio is the distance around the hips at the iliac crest divided by the distance around the narrowest point of the waist. The hormone levels (epinephrine, norepinephrine, and

² The individuals were screened on the basis of physical and cognitive functioning to identify those in the top third of their age group. The screening criteria were: 1) no self-reported disability on the Katz Activities of Daily Living (ADL) Scale, 2) no more than one disability on the Rosow-Breslau (1966) and Nagi (1976) self-reported scales of disability in physical function, 3) ability to hold a semi-tandem balance test for at least 10 seconds, 4) ability to stand up from a seated position 5 times within 20 seconds, and 5) score of at least 6 on the 9-item Short Portable Mental Status Questionnaire (Pfeiffer, 1975).

³ The recursive partitioning procedure is not as reliable when there is missing data, so we did not include any case in which we had a single missing variable.

cortisol) are measured through urine samples, an integrated measure of 12-hour HPA-axis activity. Total HDL, total cholesterol/HDL, glycosylated hemoglobin, and DHEA levels are measured through blood samples (Crimmins and Seeman, 2001).

3.3 Recursive partitioning for operationalizing allostatic load

Recursive partitioning (RP) is a more sensitive statistical methodology for scoring allostatic load than the techniques in the extant literature (Seeman et al., 1997; Seeman et al., 2001; Karlamangla, et al., 2002; Singer, Ryff, and Seeman, 2003; Zhang and Singer, 1999). RP algorithms begin with a set of candidate predictor variables (e.g., the biomarkers used in the above discussion), and a well-defined outcome (e.g., mortality). The initial step entails having the RP algorithm search among all of the candidate predictor variables to identify the best⁴ single predictor variable – with an accompanying cut point – in a way that individuals on one side of the cut point are predicted to fall in one of the outcome categories and individuals on the other side are predicted to belong in an alternative outcome category. This partitions the original population, or parent node, into two separate groups, or daughter nodes: individuals who score above the cut point on the designated variable and individuals who score below it (Singer, Ryff, and Seeman, 2003). Figure 1a shows the result of this step using the female population of the MAC Aging sample with the 10 biomarkers listed in Table 1. The outcome category is being dead at seven years beyond the baseline biomarker data collection. As shown for the 291 women, systolic blood pressure (SBP) of 141.7 mm Hg splits the population into two groups with different mortality levels. Each terminal node is labeled with a *d* value, which is the percentage of people in that node who died before the 7-year follow-up. Those women with SBP higher than 141.7 mm Hg have a death rate of 25% as opposed to those who fall below it, who have a death rate of 8.5%.

The next step is to repeat the partitioning algorithm with each of the sub-populations separately – i.e., those with SBP less than 141.7 mm Hg and those with SBP greater than 141.7 mm Hg. In Figure 1b, we show that for the low mortality terminal node, norepinephrine at 42.3 mg/g creatinine is the best cut,

⁴ The *rtree.exe* (<http://masal.med.yale.edu/rtree/>) algorithm employs a goodness of split test to rank the variables and associated cut points. The goodness of split statistic is based on maximizing the difference between the two daughter nodes with respect to the outcome variable. It is defined in Appendix 1.

and for the high mortality risk node, the ratio of total to HDL cholesterol at 3.31 is the best cut, resulting in four terminal nodes, each with its own associated mortality rate. In Figure 1c, we refine the partitioning in two of the four terminal nodes. For both of these two splits, the waist/hip ratio serves as the splitting biomarker. Interestingly, on the left-hand side, a low waist-hip ratio increases mortality risk, whereas on the right-hand side a high waist/hip ratio increases mortality risk. It is important to observe that this high-risk condition of having too low a waist-hip ratio is masked in the original elevated-risk zone methodology because the scoring scheme focused entirely on high waist-hip ratio as a risky condition. In the original operationalization there is no systematic strategy that could clearly identify a useful cut point for defining values that are too ‘low’ for the waist/hip ratio. The identification of these types of cut points with RP algorithms is a major advantage of this method over either of the other techniques.

3.4 Life experience pathways

Detailed survey data, interview transcripts, and writing samples of individuals in the Wisconsin Longitudinal Study (WLS) sub-sample were integrated into a taxonomy of life experience pathways through a person-centered approach. The construction of the life experience pathway taxonomy requires a set of organizing principles. Five principles for this research adapted from the work of Singer and Ryff (1998) are as follows:

1. Adversity and its cumulation over time have negative health consequences.
2. Advantage and its cumulation over time have positive health consequences.
3. Reactions to adversity or advantage influence the impact of life experiences.
4. Position in social hierarchies has consequences for health.
5. Social relationships influence the impact of life experiences and enduring conditions.

In addition to these principles, we provide one more:

6. People prioritize different aspects of their lives—one’s relative success or failure within the prioritized domains is more relevant in determining the life pathways than the other domains.

The first five principles are not new to research on healthy aging (Singer and Ryff, 2001).

Using these five guidelines, we use over 200 survey responses to categorize individuals into either positive, neutral, or negative experiences in six domains (1) Family Background and Early Life

Experiences (FBEL), 2) Occupational Experiences (OE), 3) Family Life Experiences (FLE), 4) Mental Health (MH), 5) Physical Health (PH), and 6) Community and Social Networks (CSN) (See Hale, 2003 for more detailed description of this coding process).

In reference to the sixth organizing principle, we use the Emotions Laboratory Stories (ELS) to determine personal priorities of each individual. In the ELS, each individual was asked to write about his or her most positive and most negative emotional experiences in separate paragraphs. This opportunity for free writing is informative of the individual's priorities. We carefully read each paragraph to determine which domain(s)⁵ the person values more heavily than the others. We identify two "prioritized domains" for each paragraph, ultimately allowing for an allocation of 4 prioritized domains per person.⁶ The two priorities for each paragraph need not be from different domains. For example, if an individual wrote about a childhood experience and made no reference to another domain, then both of the weighted prioritized domains for that paragraph would be in the FBEL domain. On the other hand, if a paragraph includes references to both workplace and family life, then the prioritized domains would be both the OE and FLE domains.

To create the final life pathways, we sum the valences assigned to each of the six domains, using a negative valence as -1, a neutral valence as 0, and a positive valence as +1. This results in a score that can range from -6 to 6. In order to weight the experiences in certain domains more heavily, we add the valences of the four priority domains. For example, if an individual prioritized her family life experience domain and her family background and early life domain (two points each), the valences on those domains would be included two additional times each. This summed score, termed the Weighted Life Experience Score (WLES), can range from -10 to 10, because it is the sum of 10 valence scores.

⁵ As described above, the six domains of life are: Family Background and Early Life Experiences (FBEL), Occupational Experiences (OE), Family Life Experiences (FLE), Mental Health (MH), Physical Health (PH), and Community and Social Networks (CSN).

⁶ Two demography graduate students double-checked my coding of these paragraphs, without learning what domains we identified as the most salient. For the negative paragraphs, the percentage of prioritized domains in agreement was .90. For the positive paragraphs, the agreement level was .82. Where there was disagreement (usually in the identification of the second of the two potential prioritized domains), we discussed the discrepancy and came to a consensus.

Figure 1a Step 1 of Sample Recursive Partitioning Tree for Women in the MAC Aging Sample (N=291)
 Systolic Blood Pressure ≥ 141.7 mm Hg

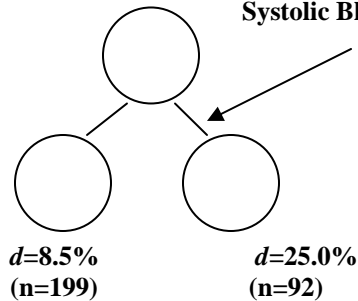


Figure 1b Step 2 of Sample Recursive Partitioning Tree for Women in the MAC Aging Sample (N=291)

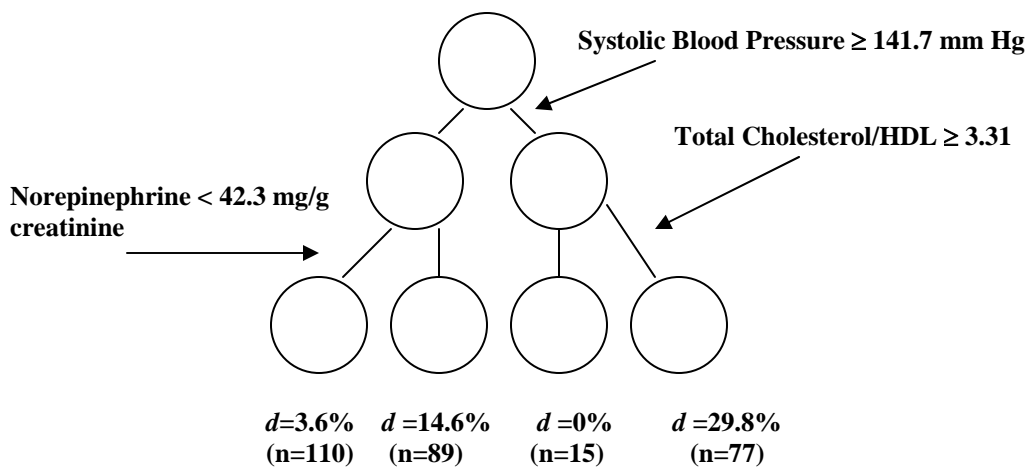
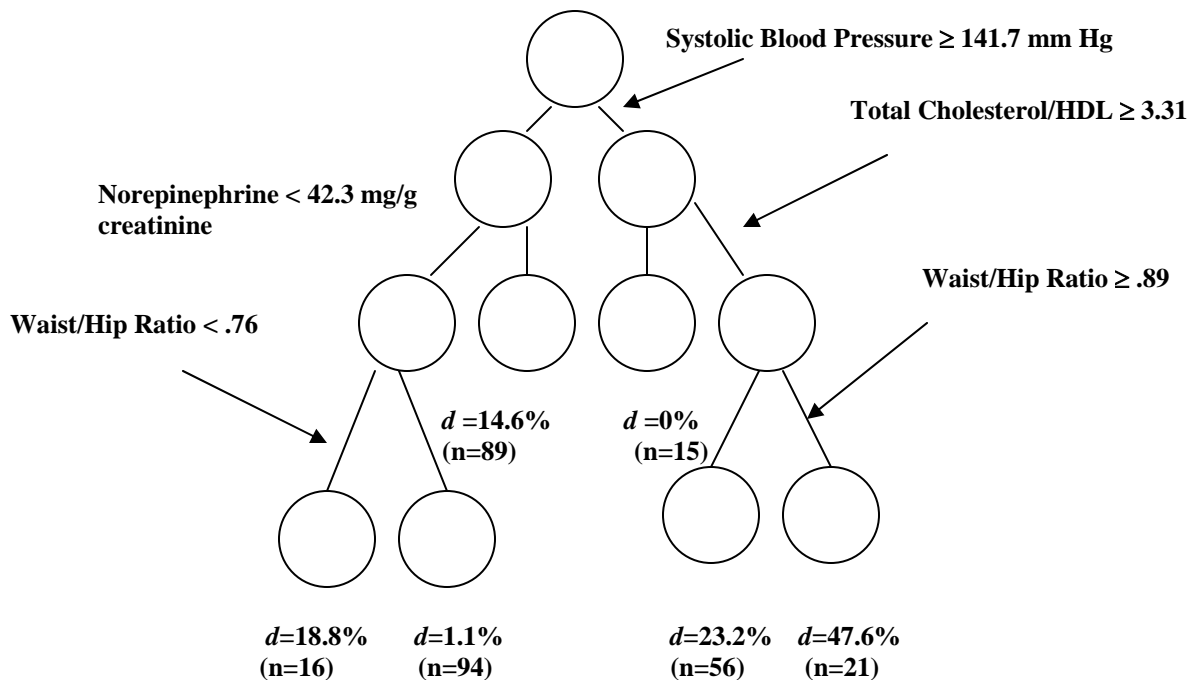


Figure 1c Step 3 of Sample Recursive Partitioning Tree for Women in the MAC Aging Sample (N=291)



3.5 Strength of Emotional Response

We use focused interview transcripts to determine the strength of emotional response (ER) of each participant. For each individual experience, the interviewer asked about the event, the emotion felt at the time, and the strength of the emotion. We summarize this information by calculating⁷ an average emotional response (ER) score. The population is divided into two categories—high ER (ER=1) and low ER (ER=0), as determined by the median value for each sex. Thus, there are 26 high and 26 low emotional responders for men and 23 high and 23 low emotional responders for women.

3.6 Experience-emotion combinations

We classify the sample into eight life experience pathways based on the rules defined in Table 2. There are four life experience pathways multiplied by two emotional response profiles – high and low.

Table 2 Rules for determining the taxonomy of life histories

ID	Life Experience Pathway	Rules (based on Weighted Life Experience Score (WLES) and Emotional Response (ER) score and the valence on the Family Background and Early Life (FBEL) Experiences Domain)	N
1	Positive and an Emotional Responder	$WLES \geq 4$ & $ER = 1$	7
2	Positive, not an Emotional Responder	$WLES \geq 4$ & $ER = 0$	11
3	Mixed with good childhood and an Emotional Responder	$WLES > -4$ & $WLES < 4$ & $ER = 1$ & valence on FBEL = (+)	8
4	Mixed with good childhood, not an Emotional Responder	$WLES > -4$ & $WLES < 4$ & $ER = 0$ & valence on FBEL = (+)	10
5	Mixed without good childhood and an Emotional Responder	$WLES > -4$ & $WLES < 4$ & $ER = 1$ & valence on FBEL = (-) or (0)	24
6	Mixed without good childhood, not an Emotional Responder	$WLES > -4$ & $WLES < 4$ & $ER = 0$ & valence on FBEL = (-) or (0)	19
7	Negative and Emotional Responder	$WLES \leq -4$ & $ER = 1$	10
8	Negative, not an Emotional Responder	$WLES \leq -4$ & $ER = 0$	9

3.7 Composite life experience pathways

To increase the sample size for the analysis, we aggregate the pathways in two ways. First, we group by type of life experiences—i.e., we ignore whether the individual is an emotional responder. The

⁷ This calculation was done using the following scoring scheme for each qualitative answer: No strength = 0, A little = 1, Somewhat = 2, and Extremely = 3. The mean score was then calculated for each individual. The median value for women is 2.64 and the median value for men is 2.46.

population is split into the four types of life experiences: 1) positive life experiences [ID=1 or 2]; 2) mixed life experiences with positive childhood [ID=3 or 4]; 3) mixed life experiences without good childhood [ID=5 or 6]; and 4) negative life experiences [ID=7 or 8]. The second way of splitting the population is into groups of matching emotional responsiveness. We use the following three categories: 1) mostly positive life experiences with high emotional responsiveness [ID=1 or 3]; 2) mostly positive life experiences with low emotional responsiveness [ID=2 or 4]; and 3) mostly negative life experiences [ID=5,6,7 or 8].⁸

4. Results

4.1 Descriptive statistics of biomarkers

The WLS and MAC Aging samples have different mean values for many of the 10 biomarkers. For men, as shown in Table 3, there are statistically significant lower means for diastolic blood pressure ($p < .01$), urinary cortisol ($p < .001$), and DHEA ($p < .01$) in the older MAC Aging population relative to the younger WLS population. In addition, the means of total cholesterol/HDL ratio ($p < .001$), glycosylated hemoglobin ($p < .001$), and norepinephrine ($p < .001$) are higher in the older population than in the younger population. For women, as shown in Table 4, there are statistically significant lower means of cortisol ($p < .001$) and HDL cholesterol ($p < .05$) in the older population relative to the younger population. There are statistically significant higher means for waist to hip ratio ($p < .05$), total cholesterol to HDL ratio ($p < .05$), total glycosylated hemoglobin ($p < .001$), and epinephrine ($p < .001$).

Comparing the means for the biomarkers by sex across Tables 3 and 4, we observe that the means often vary by sex (p-values are summarized in footnote 1). In both samples, the means of cortisol, epinephrine, norepinephrine, and total HDL cholesterol levels are higher in women than in men. Also, in both of the samples, the mean diastolic blood pressure, waist/hip ratio, total cholesterol/HDL ratio, and

⁸ We aggregate these four groups because the proportions of people across the risk zones between the strength of emotional reaction groups with negative life experiences are similar. Also, by grouping these pathways together we increase the size of our comparison group.

DHEA is higher in men than in women. The differences in the means of systolic blood pressure and glycosylated hemoglobin levels are not statistically significant by sex ($p > .05$) in either sample.

Table 3 Summary of the 10 biological assessments of men in the WLS and MAC Aging sample

	WLS (n=52) Age 58-59		MAC Aging (n=296) Age 70-79		
	Mean (μ_{WLS})	St. Dev.	Mean (μ_{MAC})	St. Dev.	
Systolic Blood Pressure (mm Hg)	136.8	16.0	137.6	17.9	
Diastolic Blood Pressure (mm Hg)	81.8	11.3	77.0	10.3	**
Waist/hip Ratio	.94	.05	.94	.06	
Total Cholesterol/HDL Ratio	4.9	1.5	5.4	2.0	***
Total Glycosylated Hemoglobin Level (%)	5.7	.61	6.8	1.8	***
Urinary Cortisol Level (mg/g creatinine)	34.9	27.8	20.9	17.3	***
Urinary Norepinephrine Level (mg/g creatinine)	27.0	10	38.6	24.5	***
Urinary Epinephrine Level (mg/g creatinine)	2.2	1.0	3.5	2.4	
HDL Cholesterol Level (mg/dl)	43.8	9.0	40.9	11.9	
DHEA (ng/ml)	106.8	62.4	80.4	54.5	**

* $p < .05$ ** $p < .01$ *** $p < .001$ ⁹

Table 4 Summary of the 10 biological assessments of women in the WLS and MAC Aging sample

	WLS (n=46) Age 58-59		MAC Aging (n=291) Age 70-79		
	Mean (μ_{WLS})	St. Dev.	Mean (μ_{MAC})	St. Dev.	
Systolic Blood Pressure (mm Hg)	135.6	16.1	137.1	19.0	
Diastolic Blood Pressure (mm Hg)	74.2	10.5	75.8	10.0	
Waist/hip Ratio	.81	.08	.84	.08	*
Total Cholesterol/HDL Ratio	4.3	1.3	4.9	1.7	*
Total Glycosylated Hemoglobin Level (%)	5.87	1.01	6.7	1.6	***
Urinary Cortisol Level (mg/g creatinine)	37.6	22.3	23.9	16.2	***
Urinary Norepinephrine Level (mg/g creatinine)	42.4	46.2	42.9	19.3	
Urinary Epinephrine Level (mg/g creatinine)	2.8	1.6	4.5	2.1	***
HDL Cholesterol Level (mg/dl)	56.8	17	51.4	15.6	*
DHEA (ng/ml)	54.9	36.5	55.0	33.4	

* $p < .05$ ** $p < .01$ *** $p < .001$

4.2 Recursive partitioning (RP) categories

We use mortality after seven years as the outcome and the ten biomarkers discussed above as the explanatory variables in the MAC Aging sample to calculate sex-specific mortality risk partitions. We split the population by sex and create multiple RP trees from each sub-population. A forest of RP trees rather than a single deterministic tree improves the classification and prediction accuracy (Zhang and Yu, 2002; Zhang, Yu and Singer, 2003; Breiman, 2001). We create alternative trees by guiding the RP

⁹ The p-values for Tables 3 and 4 are based upon a t-test for difference in means.

algorithm to select either the second or third best splits at each node rather than using the automated process that always selects the first best split. We developed two small forests of trees through the RP procedure, as graphically depicted in the Appendix 2. We do not include any trees that have fewer than seven people in a terminal node because those trees are less stable.

With the remaining trees, we perform a simultaneous cross validation (SCV)¹⁰ procedure to test how resilient each tree is to minor modifications in the sample. The RP algorithm is run 100 times using a slightly altered sample for each iteration. Each iteration, we modify the sample by dropping two randomly selected individuals—one person who died after the seven-year follow-up and one person who was still alive after seven years. The most resilient trees have no (or very few) differences when the sample changes. A summary of the SCV procedure of the ten trees (five for women and five for men) is shown in Table 5. The trees that are the most resilient for women are trees 1, 3, and 4. For men, the three most resilient trees are trees 1¹¹, 2, and 3. An alternative approach is to create a ‘random forest’ based on a random selection of features to split each node, which Breiman argues produces the lowest error rates (Breiman, 2001).

Table 5 Summary of simultaneous cross-validation (SCV) tests

	Number of Errors Generated
Female Tree 1	0 **
Female Tree 2	3
Female Tree 3	0 **
Female Tree 4	0 **
Female Tree 5	>5
Male Tree 1	4 **
Male Tree 2	0 **
Male Tree 3	0 **
Male Tree 4	>5
Male Tree 5	>5

** trees identified as resilient for each sex

Using the small forest of resilient trees to identify mortality risk partitions for men and women in the MAC Aging sample, we combined trees to identify three mutually exclusive risk pathways, shown in Box 1. This combination improves the categories of any single tree. For women, the ‘high’ risk zone has

¹⁰ We used an adapted version of the Jason Ku’s C++ code for this procedure (Ku, 2002).

¹¹ Although it may not look like the Male Tree 1 is particularly resilient, it has a much lower error rate than the Male Trees 4 and 5 which produce errors in nearly every iteration.

a death rate of 30.0%, the ‘intermediate’ risk zone has a death rate of 12.5%, and the ‘low’ risk zone has a death rate of 1.0%. For men, the ‘high’ risk zone has a death rate at 51.2%, the ‘intermediate’ risk zone has a death rate of 22.0% and the ‘low’ risk zone has a death rate of 14.9%.

To summarize this portion of the analysis, the RP algorithms identify specific physiologic profiles related to mortality risk in both men and women. As shown in Box 1, these profiles differ by sex. For women, systolic blood pressure and total cholesterol/HDL are good predictors of mortality, whereas for men, diastolic blood pressure, DHEA and glycosylated hemoglobin are good predictors. While high epinephrine is a risk factor in both sets of Boolean statements, the cut point for men (61.6 mg/g creatinine) is higher than the cut point for women (42.3 mg/g creatinine).

Using the Boolean statements in Box 1, we assign each woman in the WLS sample into either a ‘high’, ‘intermediate’, or ‘low’ risk zone. Approximately 39% of the women (18/46) in the WLS were assigned to the ‘low’ risk zone, compared to approximately 30% (14/46) who were assigned to each of the ‘intermediate’ and ‘high’ risk zones.

For men, the Boolean statements in Box 1 do not overlay onto the physiological characteristics of the WLS population in three relatively equal-sized groups. In fact, only three men belong to a ‘high’ risk zone using the risk partitions defined in Box 1. This is likely due to the age difference between the two samples. To adjust for this mismatch in biomarker values, we scale each of the male cut points by the ratio of the mean in the WLS population to the mean in the MAC Aging population. For example, rather than using a cut point of 58.3 for diastolic blood pressure to classify people in the WLS sample into risk groups, we used a cut point of 61.9 ($(\mu_{\text{WLS}} / \mu_{\text{MAC}}) * 58.3$). As part of a sensitivity analysis, we find that if we reduce the waist-hip ratio cut point for men from 1.05 to 1.00, we evenly distribute the WLS population into three (‘low’, ‘intermediate’, and ‘high’) risk zones, of 17, 18, and 17 men respectively.

Box 1 Biological profiles of high, medium, and low mortality risk from RP algorithms on MAC Aging sample at a 7-year follow-up

Profiles of High Mortality Risk for Women (% dead in MAC Aging: $d=30.0\%$) (N=90) :

Systolic Blood Pressure ≥ 141.7 mm Hg & (Cholesterol/HDL ≥ 3.3 OR Waist-Hip Ratio $\geq .89$)
OR
Systolic Blood Pressure < 141.7 mm Hg & Epinephrine ≥ 8.3 mg/g creatinine

Profiles of Medium Mortality Risk for Women (% dead in MAC Aging: $d=12.5\%$) (N=96):

Systolic Blood Pressure < 141.7 mm Hg & Epinephrine < 8.3 mg/g creatinine & (Norepinephrine ≥ 42.3 mg/g creatinine OR Waist-Hip Ratio $< .76$)

Profiles of Low Mortality Risk for Women (% dead in MAC Aging: $d=1.0\%$) (N=105):

Systolic Blood Pressure < 141.7 mm Hg & Norepinephrine < 42.3 mg/g creatinine & Waist-Hip Ratio $\geq .76$ & Epinephrine < 8.3 mg/g creatinine
OR
Systolic Blood Pressure ≥ 141.7 mm Hg & (Cholesterol/HDL Ratio < 3.3 & Waist-Hip Ratio $< .89$)

Profiles of High Mortality Risk for Men (% dead in MAC Aging: $d=51.2\%$) (N=84):

Diastolic Blood Pressure < 58.3 mm Hg & DHEA < 76.5 ng/ml
OR
Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA < 76.5 ng/ml & Norepinephrine ≥ 61.6 mg/g creatinine
OR
Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA < 76.5 ng/ml & Norepinephrine < 61.6 mg/g creatinine & Waist Hip Ratio ≥ 1.05
OR
Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA < 76.5 ng/ml & Norepinephrine < 61.6 mg/g creatinine & Waist Hip Ratio < 1.05 & Glycosylated Hemoglobin ≥ 7.55
OR
Diastolic Blood Pressure ≥ 58.3 & DHEA ≥ 76.5 & Norepinephrine ≥ 61.6 mg/g creatinine
OR
Diastolic Blood Pressure ≥ 58.3 & DHEA ≥ 76.5 & Norepinephrine < 61.6 mg/g creatinine & Waist-Hip Ratio < 1.05 & Glycosylated Hemoglobin ≥ 7.55

Profiles of Medium Mortality Risk for Men (% dead in MAC Aging: $d=22.0\%$) (N=118):

Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA < 76.5 ng/dl & Norepinephrine < 61.6 mg/g creatinine & Waist-Hip Ratio < 1.05 & Glycosylated Hemoglobin < 7.55
OR
Diastolic Blood Pressure < 58.3 mm Hg & DHEA ≥ 76.5 ng/ml
OR
Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA ≥ 76.5 & Norepinephrine ≥ 61.6 mg/g creatinine & Waist Hip Ratio ≥ 1.05

Profiles of Low Mortality Risk for Men (% dead in MAC Aging: $d=14.9\%$) (N=94):

Diastolic Blood Pressure ≥ 58.3 mm Hg & DHEA ≥ 76.5 ng/dl & Norepinephrine < 61.6 mg/g creatinine & Waist-Hip Ratio < 1.05 & Glycosylated Hemoglobin < 7.55

4.3 Comparison of RP groups to elevated risk allostatic load method

We use sensitivity and specificity tests to compare RP algorithms to the elevated risk method of calculating allostatic load in the MAC Aging sample in terms of predicting mortality. Sensitivity is the ability of the test to identify correctly those who have a given condition (e.g., dead). It is calculated by dividing the number of true positives by the total number of true positives and false negatives (e.g., actual dead). Specificity is the ability of the test to identify correctly those who do not have a given condition (e.g., not dead). It is calculated by dividing the true negatives by number of true negatives and false positives (e.g., actual not dead). For both of these measures, a higher ratio is better. Figure 2 is helpful in understanding which cases are categorized as a true or false positive and negative.

We calculate the sensitivity and specificity for four types of predictions for death, 1) RP zone \geq ‘intermediate’ risk zone, 2) RP zone = ‘high’ risk zone, 3) elevated risk zone method¹² of allostatic load \geq 3, and 4) elevated risk zone method of allostatic load \geq 4. In Table 6, we show the sensitivity and specificity by the four types of predictions. For both men and women, the sensitivity of RP predictions is higher than (or equal to) the elevated risk prediction method. For women, the specificity is highest using the prediction that death occurs when the allostatic load score is \geq 4 using the elevated risk method of calculating mortality risk. For men, when the prediction of death is defined by membership in the ‘high’ risk zone, the specificity is higher than both of the predictions using the elevated risk summary.

Figure 2 Two-by-two table of actual and predicted values

	Actual Dead	Actual Alive
Predicted Dead	True Positive	False Positive
Predicted Alive	False Negative	True Negative

We also estimate the positive and negative predictive value for the same four predictions found in Table 6. The positive predictive value is the number of true positives divided by the number predicted positive. The negative predictive value is the number of true negatives divided by the number predicted negative. The positive and negative predictive values by each prediction are summarized in Table 7. For

¹² To calculate the elevated risk in this group, we use the MAC Aging cut points defined in Table 1.

women, the positive predictive values are about the same for each method. Yet, for the negative predictive value for women, the RP method is always better than the elevated risk method. For the men, the RP method has consistently better predictive values than for the elevated risk summary.

Table 6 Sensitivity and specificity of RP and elevated risk methods for calculating allostatic load

	Sensitivity	Specificity
WOMEN (N=291)		
RP Summary		
≥ 'Intermediate' Risk Zone	.975	.414
= 'High' Risk Zone	.675	.749
Elevated Risk Summary		
≥ 3	.675	.606
≥ 4	.325	.849
MEN (N=296)		
RP Summary		
≥ 'Intermediate' Risk Zone	.831	.376
= 'High' Risk Zone	.518	.808
Elevated Risk Summary		
≥ 3	.542	.479
≥ 4	.337	.739

Table 7 Positive and negative predictive values of RP and elevated risk methods for calculating allostatic load

	Positive Predictive Value	Negative Predictive Value
WOMEN (N=291)		
RP Summary		
≥ 'Intermediate' Risk Zone	.210	.990
= 'High' Risk Zone	.300	.935
Elevated Risk Summary		
≥ 3	.214	.921
≥ 4	.255	.888
MEN (N=296)		
RP Summary		
≥ 'Intermediate' Risk Zone	.342	.851
= 'High' Risk Zone	.511	.811
Elevated Risk Summary		
≥ 3	.288	.729
≥ 4	.329	.739

4.4 Risk zones by pathways

Table 8 shows the percentage of women in each life experience pathway distributed among the RP risk zones. We use the χ^2 test statistic to test the difference between the distributions across the risk zones between two pathways. We use the distribution of individuals in the negative life experience pathway (Pathway 7 and Pathway 8) as the expected distribution, and compare its distribution to all three

alternative pathways. For women, we find that all three alternative pathways have statistically significant different distributions than the distribution of the negative life experience pathway ($p < .01$ for all). As hypothesized, women with negative life experiences are less likely to belong to the ‘low’ risk zone relative to each of the other life experience profiles (see Figure 3). The distribution in the ‘high’ risk zone is in the hypothesized direction; the highest percentage of women in a ‘high’ risk zone is among those with negative life experiences (40%) (see Figure 4).

In Table 9, we show the distribution of men in each RP risk zone by life experience pathway. According to the χ^2 test statistic, we find that the distribution of men in the negative life experience pathway across the risk zones differs from the distribution in the positive life experience pathways ($p < .05$). With regard to membership in the ‘low’ risk zone, the distribution is in the expected direction. Only 22.2% of men with negative life experiences have a low risk profile as compared to 60.0% of men with positive life experiences (see Figure 3). With regard to membership in the ‘high’ risk zone, the differences are also in the expected direction (see Figure 4), with 44.4% of men in the negative life experiences pathway belonging to the ‘high’ risk zone compared to 10% of the people in the positive life experiences pathway.

Table 8 Cross-tabulation of mortality risk zones by life experience pathways for women (N=46)

ID	Life Experience Pathway	χ^2 test p-value	Low Risk (18/46=.391)	Intermediate Risk (14/46=.304)	High Risk (14/46=.304)
1 & 2	Positive life experiences (N=8)	***	50.0%	25.0%	25.0%
3 & 4	Mixed life experiences with good childhood (N=8)	***	50.0%	37.5%	12.5%
5 & 6	Mixed life experiences without good childhood (N=20)	***	45.0%	20.0%	35.0%
7 & 8	Negative life experiences (N=10)	+	10.0%	50.0%	40.0%
* p<.10		** p<.05	***p<.01	+ Reference group	

Table 9 Cross-tabulation of mortality risk zones by life experience pathways for men (N=52)

ID	Life Experience Pathway	χ^2 test p-value	Low Risk (17/52=.327)	Intermediate Risk (18/52=.346)	High Risk (17/52=.327)
1 & 2	Positive life experiences (N=10)	**	60.0%	30.0%	10.0%
3 & 4	Mixed life experiences with good childhood (N=10)		40.0%	40.0%	20.0%
5 & 6	Mixed life experiences without good childhood (N=23)		21.7%	34.8%	43.5%
7 & 8	Negative life experiences (N=9)	+	22.2%	33.3%	44.4%

* p<.10 ** p<.05 ***p<.01 + Reference group

Figure 3 Percent in Low Mortality Risk Zones by Life Experience Pathways for Women (White, N=46) and Men (Red, N=52) (Source: Tables 8 and 9)

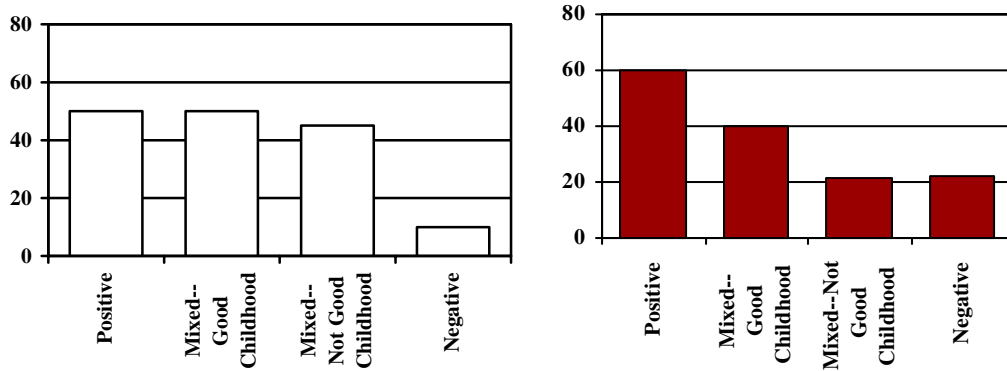
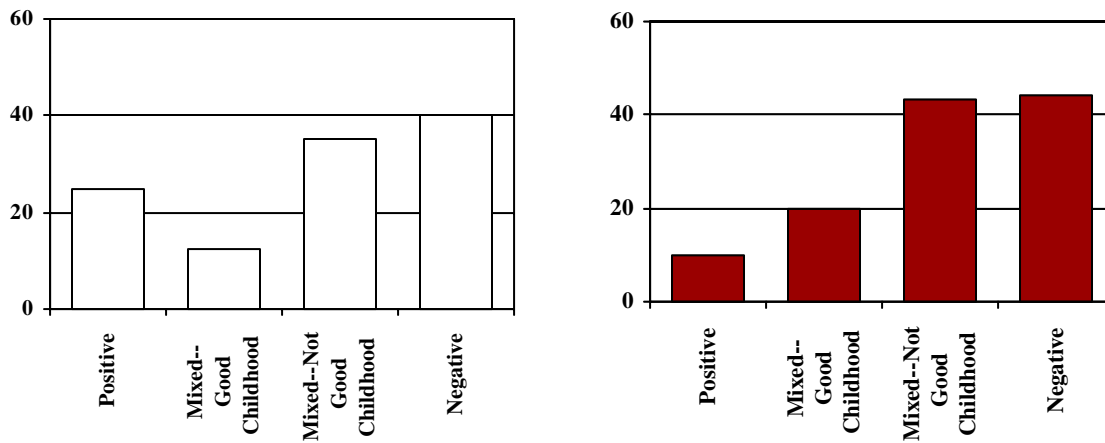


Figure 4 Percent in High Mortality Risk Zones by Life Experience Pathways for Women (White, N=46) and Men (Red, N=52) (Source: Tables 8 and 9)



In Table 10, we show that among the women, those who have mostly positive life experiences and are low emotional responders are more likely to belong to the ‘low’ risk zone than those with mostly negative life experiences, 63.6% vs. 33.3%. The difference between the distributions of these two pathways is statistically significant according to a χ^2 test ($p < .10$). In the ‘high’ risk zone, only 9.1% of non-emotional responders with mostly positive life experiences belong to the ‘high’ risk zone relative to those with mostly negative experiences, 36.7%. These findings suggest that there is a protective effect of not being an emotional responder for women.

Table 11 shows the distribution of membership across the risk zones for men stratified by composite life pathways. A χ^2 test shows a statistically significant difference between the distribution of the mostly negative experiences pathway and the mostly positive experiences and emotional responder pathway across the risk zones ($p < .05$). For men, we observe the unexpected relationship that being an emotional responder is associated with an increased membership in the ‘low’ risk zone and a decreased membership in the ‘high’ risk zone.

It is perplexing that among men with mostly positive life experiences, emotional responders experience a protective physiological health effect, whereas the opposite is true for women. One possibility is that the men in the positive life experience pathway who are emotional are more open to social support than the men who are not emotional. This openness to social support may play a role in the lowered membership in the high mortality risk zone. Another possibility is that men and women have different ways of interpreting the question upon which the indicator was based, i.e., “How <insert emotion felt> did you feel?”

Table 10 Cross-tabulation of mortality risk zones by composite life profiles, splitting the mostly positive experience pathways by emotional reactivity for women (N=46)

ID	Life Experience Pathway	χ^2 test p-value	Low Risk (18/46=.391)	Intermediate Risk (14/46=.304)	High Risk (14/46=.304)
1 & 3	Mostly positive experiences and emotional responder (N=5)		20.0%	40.0%	40.0%
2 & 4	Mostly positive experiences and not emotional responder (N=11)	*	63.6%	27.3%	9.1%
5, 6, 7, & 8	Mostly Negative Experiences (N=30)	+	33.3%	30.0%	36.7%

* p<.10 ** p<.05 ***p<.01 + Reference group

Table 11 Cross-tabulation of mortality risk zones by composite life profiles splitting the mostly positive experience pathways by emotional reactivity for men (N=52)

ID	Life Experience Pathway	χ^2 test p-value	Low Risk (17/52=.327)	Intermediate Risk (18/52=.346)	High Risk (17/52=.327)
1& 3	Mostly positive experiences and emotional responder (N=10)	**	60.0%	40.0%	0%
2 & 4	Mostly positive experiences and not emotional responder (N=10)		40.0%	30.0%	30.0%
5, 6, 7, & 8	Mostly Negative Experiences (N=32)	+	21.8%	34.4%	43.8%

* p<.10 ** p<.05 ***p<.01 + Reference group

Figure 5 Percent in Low Mortality Risk Zones by Life Experience and Emotional Reactivity Pathways for Women (White, N=46) and Men (Red, N=52)

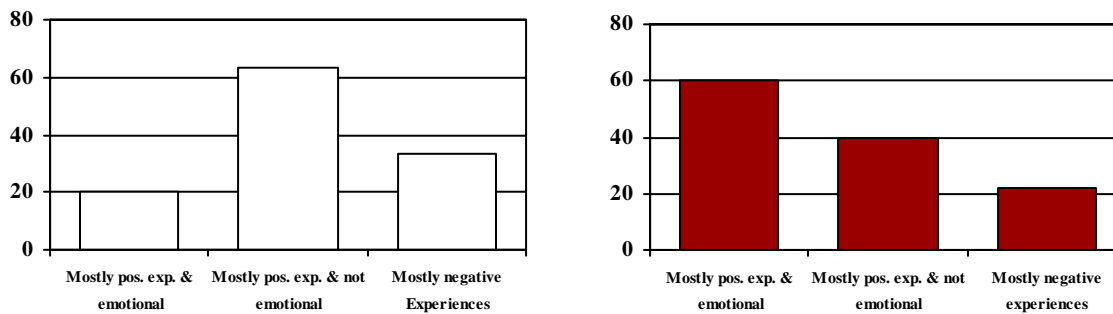
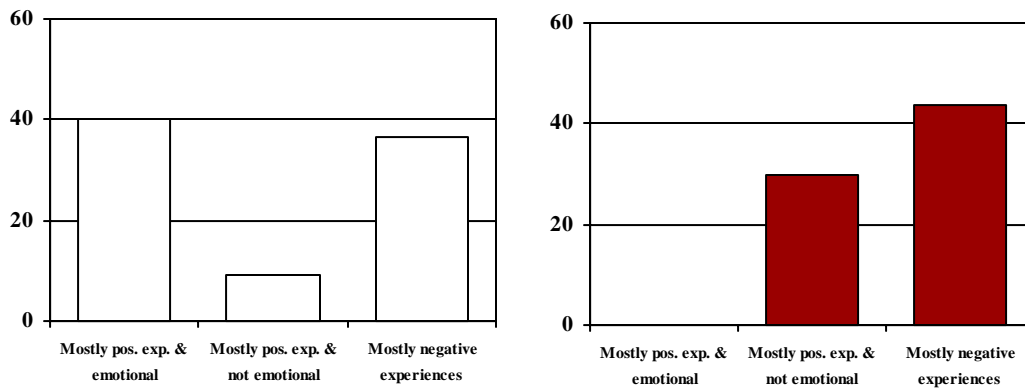


Figure 6 Percent in High Mortality Risk Zones by Life Experience and Emotional Reactivity Pathways for Women (White, N=46) and Men (Red, N=52)



4.5 *Comparison to the elevated risk level allostatic load method*

To see if the previous operationalization of allostatic load provides similar findings to our RP method of operationalizing allostatic load, we compare the results in Tables 8-11 to corresponding results based on the previously described elevated risk method for operationalizing allostatic load. As shown in Table 12, the elevated-risk measure is consistent with the expectation that people with positive life experiences have a low allostatic load and people with negative life experiences have a high allostatic load. People in the mostly positive experiences pathways [ID=1-4] have higher membership in a low allostatic load pathway [AL=0-2] relative to individuals in the mostly negative life experience pathways [ID=5-8]. We are able to combine the sexes because the definitions of risk are the same for both men and women—if the sexes are in separate tables, the numbers are similar but the statistical significance of the difference in the distribution is $p > .05$ (not shown). In addition, when we investigate by the composite life experience/emotional response pathways and sex as done in Tables 8-11, we find no statistically significant differences between the distribution of each pathway across the different allostatic load risk groups (not shown). The lack of statistically significant differences at more detailed levels of analysis contrasts with our findings when we use the RP algorithms to define mortality risk. This reinforces our contention that our operationalization of allostatic load provides a more sensitive way of measuring biological risk.

Table 12 Cross-tabulation of the elevated risk operationalization of allostatic load by mostly positive and mostly negative life experiences (N=98)

ID		χ^2 test p-value	AL = 0-2 (53/98=.541)	AL = 3-4 (38/98=.388)	AL = 4-7 (7/98=.071)
1, 2, 3 & 4	Mostly Positive Experiences (N=36)	**	61.1%	27.8%	11.1%
5, 6, 7 & 8	Mostly Negative Experiences (N=62)	+	50.0%	45.2%	4.8%
* p<.10	** p<.05	***p<.01	+ Reference group		

4.6 Limitations and future research

There are two primary limitations to this research. First, we are limited by sample size, so we have less statistical power to detect differences that exist. Future research should be conducted with larger sample sizes in order to replicate these findings. Second, since the mortality risk factors may vary by age, the use of the MAC Aging sample to identify the risk partitions may not accurately capture mortality risk in the WLS sample. For men, we adjust the cut points for each biomarker to account for this change over time. Another way to correct for this difference in biomarker levels as people age is to apply the risk partitions in Box 1 to an older population that is more comparable with the MAC Aging sample. In the current wave of WLS data collection (2003), the individuals will be in their mid-60s. Physiological data collected at this age will serve as a more appropriate comparison to the MAC Aging risk zones than the data shown in this paper.

Future research into the question of how stress gets under the skin could assess other biological characteristics such as immune system measures (Crimmins and Seeman, 2001; Ridker et al., 2002) or sleep quality measures (Moore et al., 2002). An assortment of measures across multiple systems will best capture warning signs of general dysregulation. The RP algorithms provide a sensitive method of sorting through the indicators to identify which physiological characteristics, and at what levels, place individuals at heightened mortality risk. The RP algorithm could be also used with any number of physiological indicators.

In addition, we re-emphasize the finding that emotional responsiveness plays a role in predicting mortality risk. Since different populations (stratified by race, culture, socioeconomic status) may have varying levels of emotional expressiveness, strength of emotion may account for a portion of the

unexplained social inequalities in health. We suggest that an indicator of strength of emotional response should be used as an explanatory variable in future research on the social determinants of health. While the measure of strength of emotion used in this analysis is fairly simple, future work should be done to refine and develop the theoretical and operational definition of this concept.

5. Conclusions

This analysis supports our contention that the recursive partitioning methodology is a meaningful way of operationalizing the concept of allostatic load. This methodology enhances previous operationalizations in several ways. First, we identify multiple differences between men and women in terms of which physiological indicators predict mortality risk. We underscore this finding because previous studies incorrectly assume that the warning signs of physiological dysregulation are the same for both men and women. A second benefit of the RP methodology is that we identify risks affiliated with having biomarker values that are too high and too low (e.g., hypotension, as shown for men). Thirdly, this methodology is more sensitive in identifying the biomarkers that are predictive of downstream health consequences. We use specificity, sensitivity, positive predictive values, and negative predictive values to show that the RP methods are better than the elevated risk method of calculating allostatic load for predicting mortality. Lastly, our analysis with the WLS sample shows that the RP risk partitions are correlated with antecedent psychosocial experiences in the expected direction.

Specifically, we demonstrate that cumulative life experiences have an observable relationship with mortality risk. As hypothesized, the proportion of men in a 'low' mortality risk partition is lower among people with predominantly negative life experiences than those with predominantly positive experiences. Indeed, the percent belonging to a 'low' risk zone varies from 60.0% to 22.2% in the positive and negative life experience pathways respectively for men and from 50.0% to 10.0% in the positive and negative life experience pathways respectively for women. We find similar results in the reverse direction with regard to membership in the 'high' risk zone.

With regard to strength of emotional response, for women with mostly positive experiences, low strength of emotional response predicts membership in the 'low' risk zone relative to membership in the

group with mostly negative experiences. This finding supports our hypothesis that people who feel strong emotions about life events are more likely to have riskier physiological indicators of mortality risk. Surprisingly, however, for men we find that high strength of emotional reaction (with mostly positive life experiences) provides a protective effect for membership in both the 'high' risk zone and an increased likelihood of membership in the 'low' mortality risk zone. As mentioned above, the men who identify as emotional may be the men who are more willing to seek help and receive support either through friends or therapy. This analysis shows that strength of emotional reaction could play either a harmful or a protective role with regard to one's health, and this may vary by sex. The role of strength of emotional reaction and physiology should be investigated to help individuals learn how to cope with the abundant stressors and emotions associated with life experiences in a way that minimizes physiological damage.

Appendix 1. Goodness of split tests in recursive partitioning trees

Each node in the recursive partitioning tree can be split by any of the predictor variables, x_i , up to $N(x_i)-1$ times where $N(x_i)$ is the number of distinct values that x_i holds. Given that there are $N(x_i)-1$ possible splits, the rtree.exe algorithm uses a goodness of split test to identify the best possible split, as defined by the following example (Zhang and Singer, 1999, p. 10-12).

In the case of x_1 , each potential cut point, c , has an associated table defined by the binary outcome variable, Y , and the left and right nodes, τ_L and τ_R :

		$Y = 0$	$Y = 1$	
Left Node (τ_L)	$x_1 \leq c$	n_{11}	n_{12}	$n_{1.}$
Right Node (τ_R)	$x_1 > c$	n_{21}	n_{22}	$n_{2.}$
		$n_{1.}$	$n_{2.}$	

$IP\{\tau_L\}$ and $IP\{\tau_R\}$ are the probabilities that an individual falls into nodes τ_L and τ_R , or $\left(\frac{n_{1.}}{n_{1.} + n_{2.}}\right)$ and $\left(\frac{n_{2.}}{n_{1.} + n_{2.}}\right)$, respectively.

Entropy impurity in the left daughter node is:

$$i(\tau_L) = -\frac{n_{11}}{n_{1.}} \log\left(\frac{n_{11}}{n_{1.}}\right) - \frac{n_{12}}{n_{1.}} \log\left(\frac{n_{12}}{n_{1.}}\right). \quad (1)$$

Entropy impurity in the right daughter node is:

$$i(\tau_R) = -\frac{n_{21}}{n_{2.}} \log\left(\frac{n_{21}}{n_{2.}}\right) - \frac{n_{22}}{n_{2.}} \log\left(\frac{n_{22}}{n_{2.}}\right). \quad (2)$$

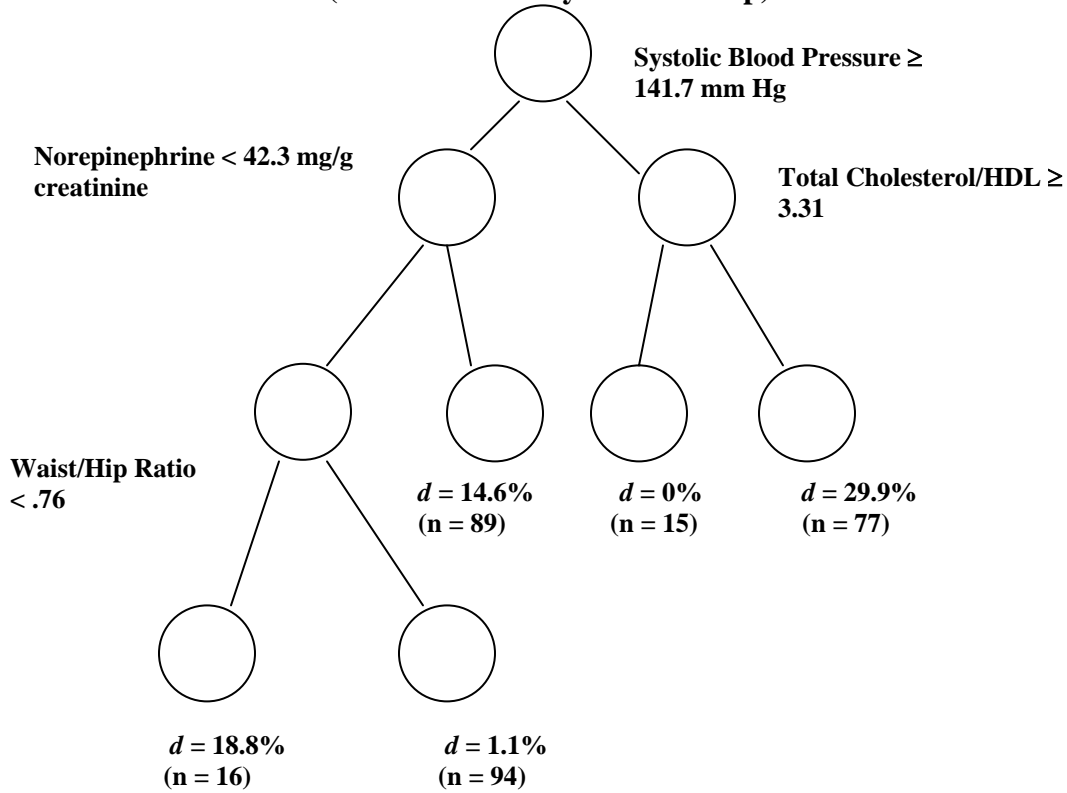
The goodness of split, s , is measured by calculating the degree that the reduction in the impurity changes from going from the parent to the daughter nodes. This change is calculated as follows:

$$\Delta I(s, \tau) = i(\tau) - IP\{\tau_L\}i(\tau_L) - IP\{\tau_R\}i(\tau_R), \quad (3)$$

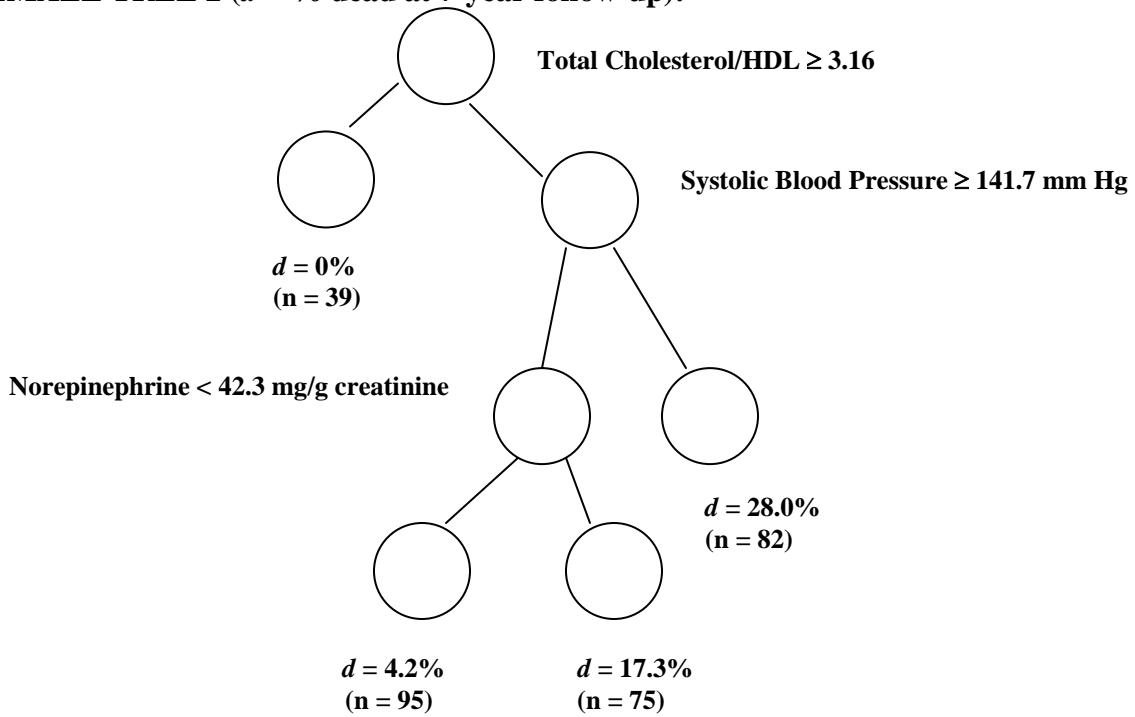
where τ is the parent node of τ_L and τ_R , and $IP\{\tau_L\}$ and $IP\{\tau_R\}$ are the probabilities that a subject falls into nodes τ_L and τ_R , respectively. In selecting the best split, the cut point, c , that produces the largest ΔI provides the best split.

Appendix 2. Diagrams of RP trees

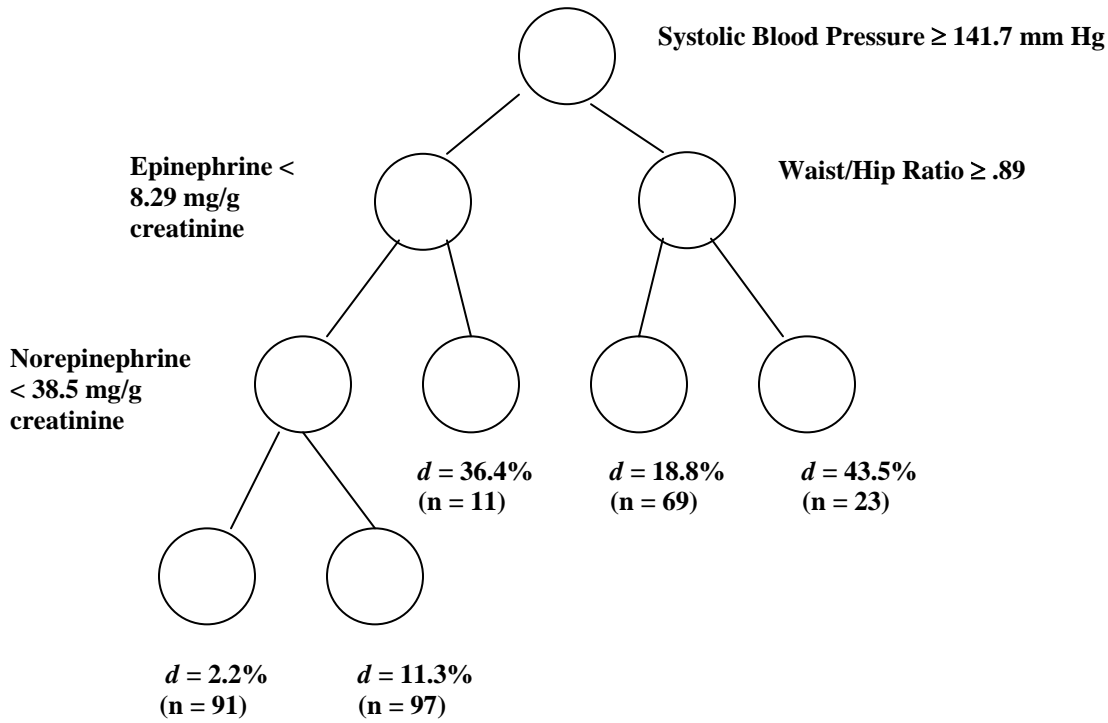
FEMALE TREE 1 (*d* = % dead at 7-year follow-up):



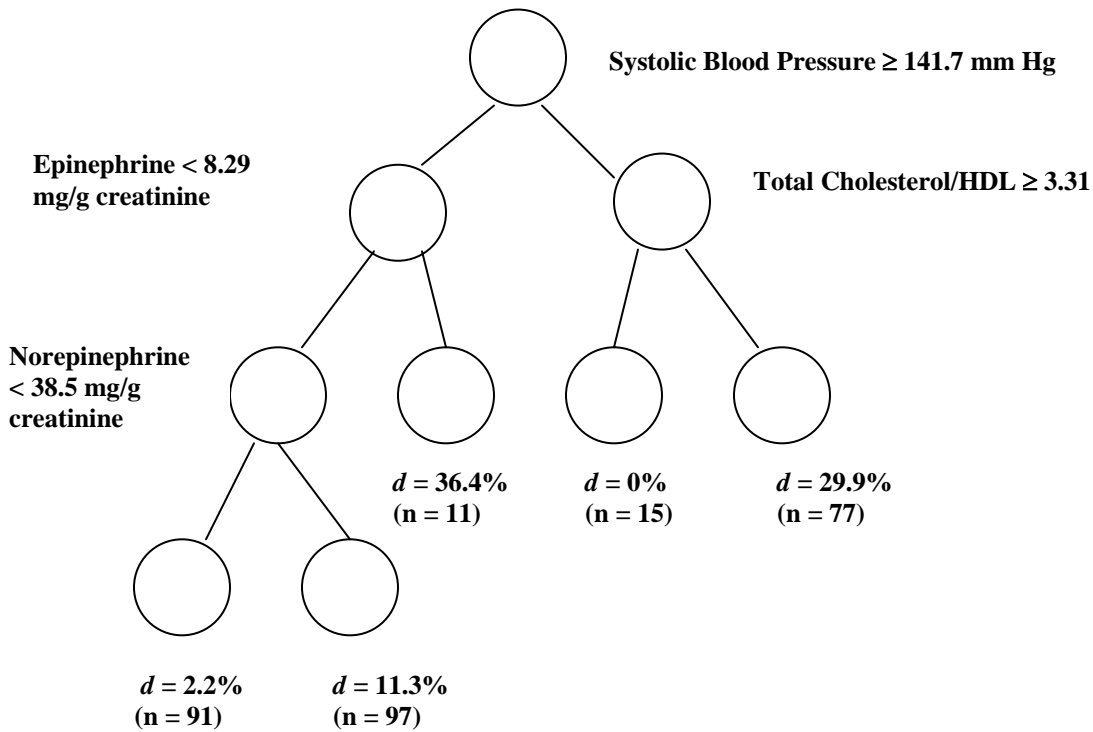
FEMALE TREE 2 (*d* = % dead at 7-year follow-up):



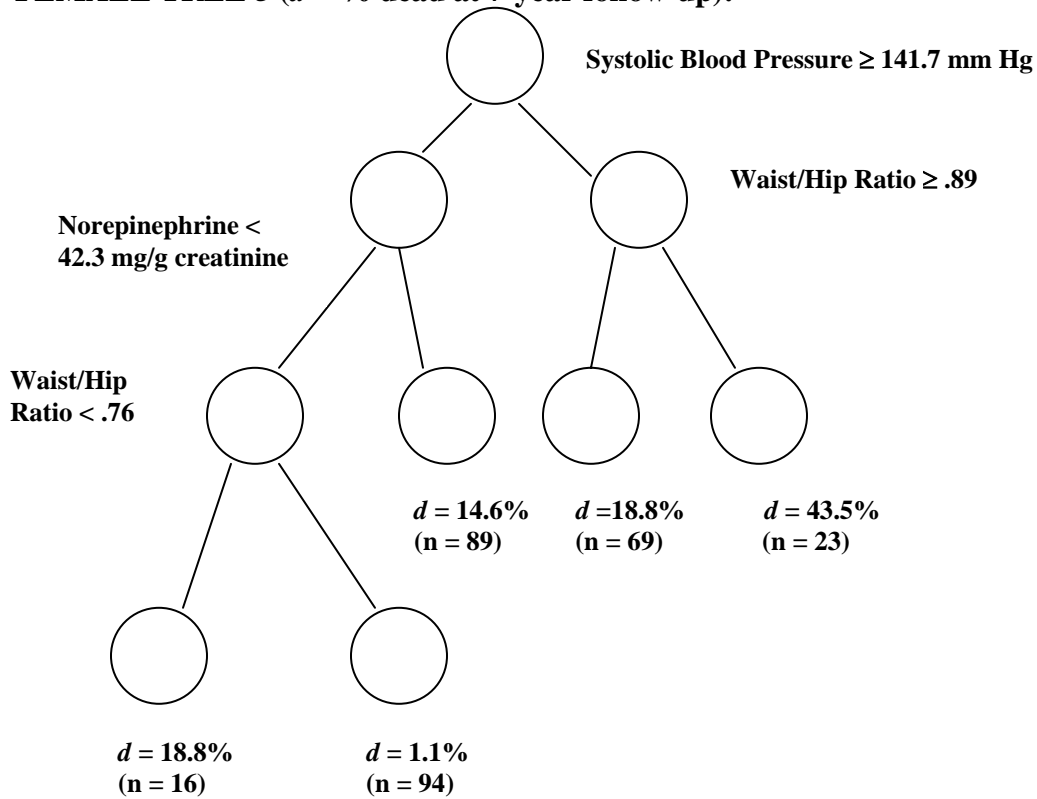
FEMALE TREE 3 (d = % dead at 7-year follow-up):



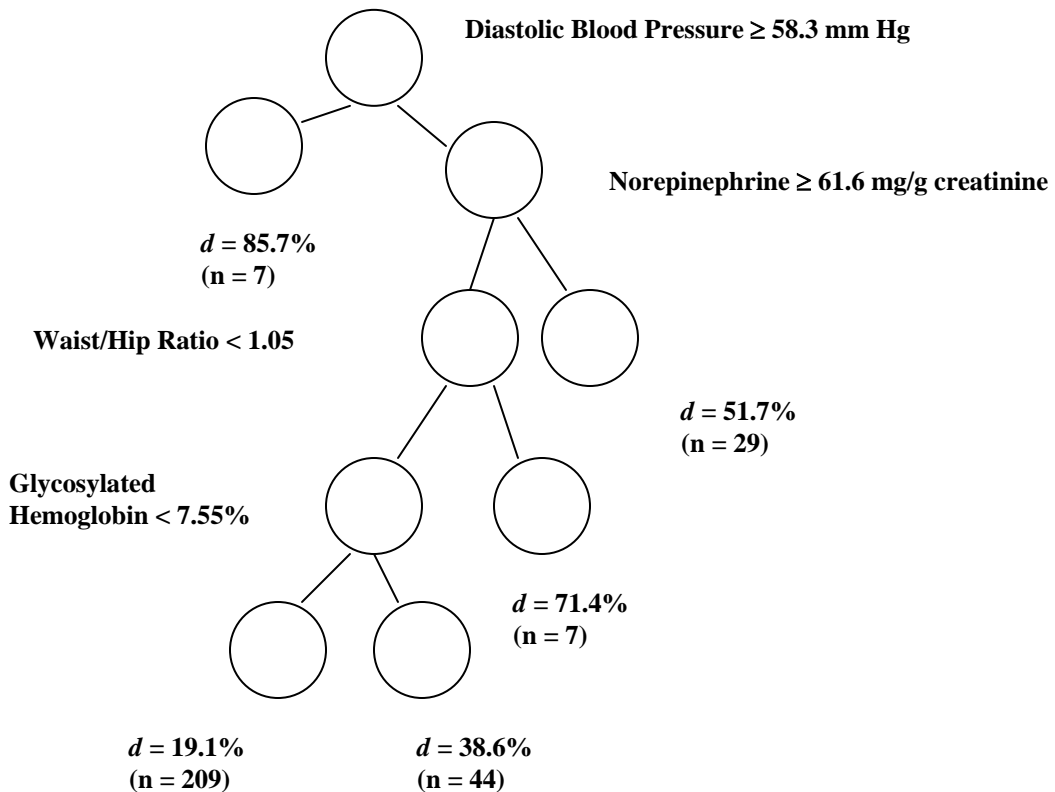
FEMALE TREE 4 (d = % dead at 7-year follow-up):



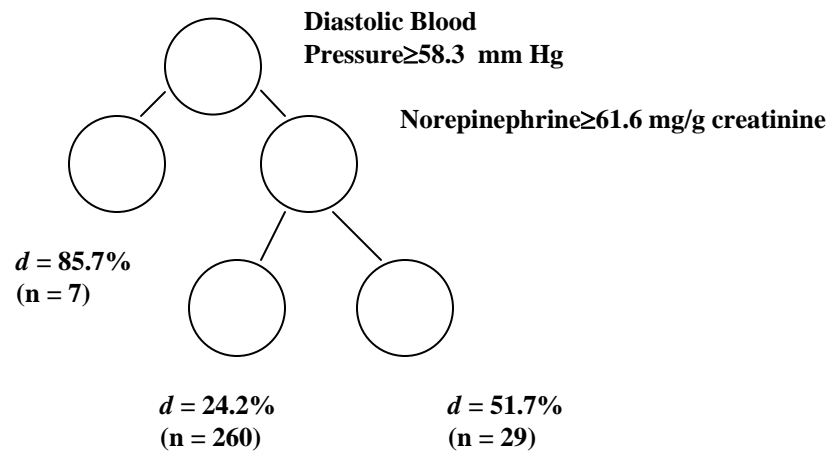
FEMALE TREE 5 (*d* = % dead at 7-year follow-up):



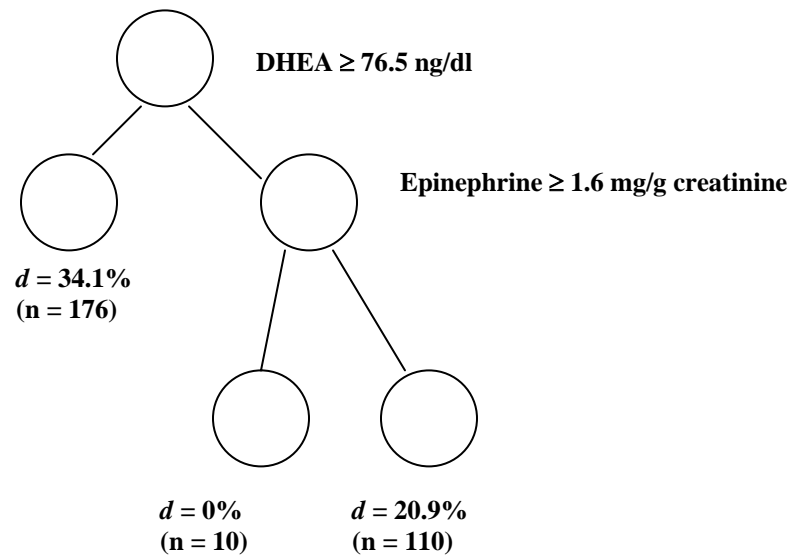
MALE TREE 1 (*d* = % dead at 7-year follow-up):



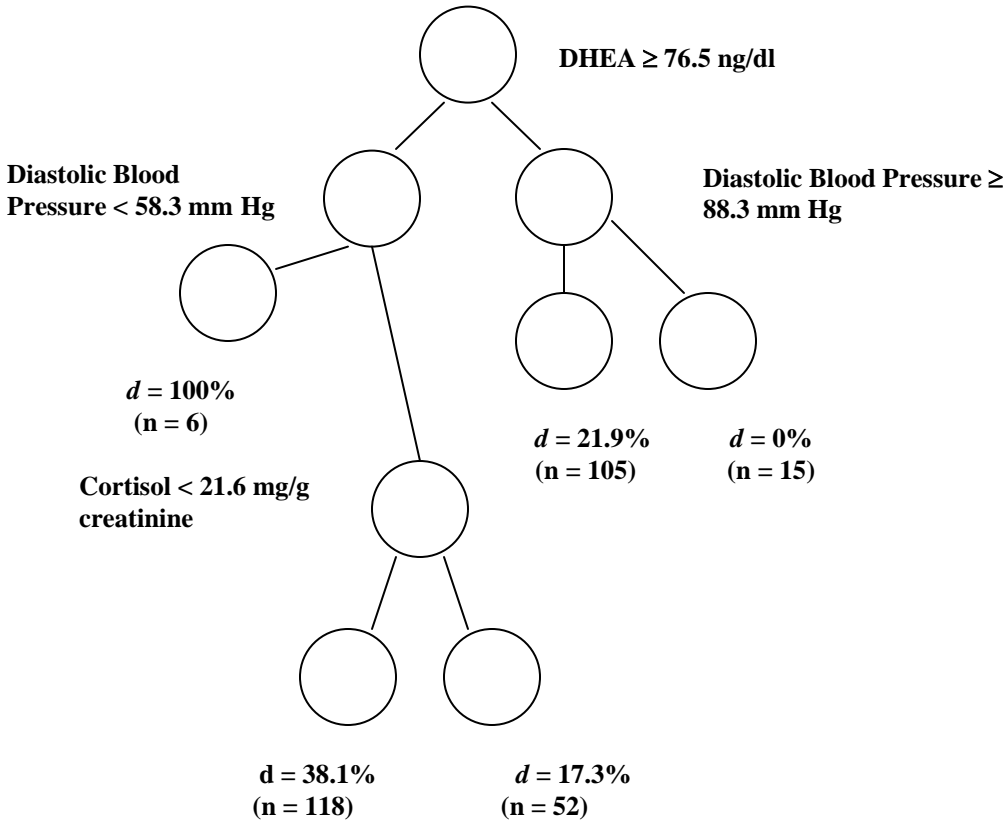
MALE TREE 2 (*d* = % dead at 7-year follow-up):



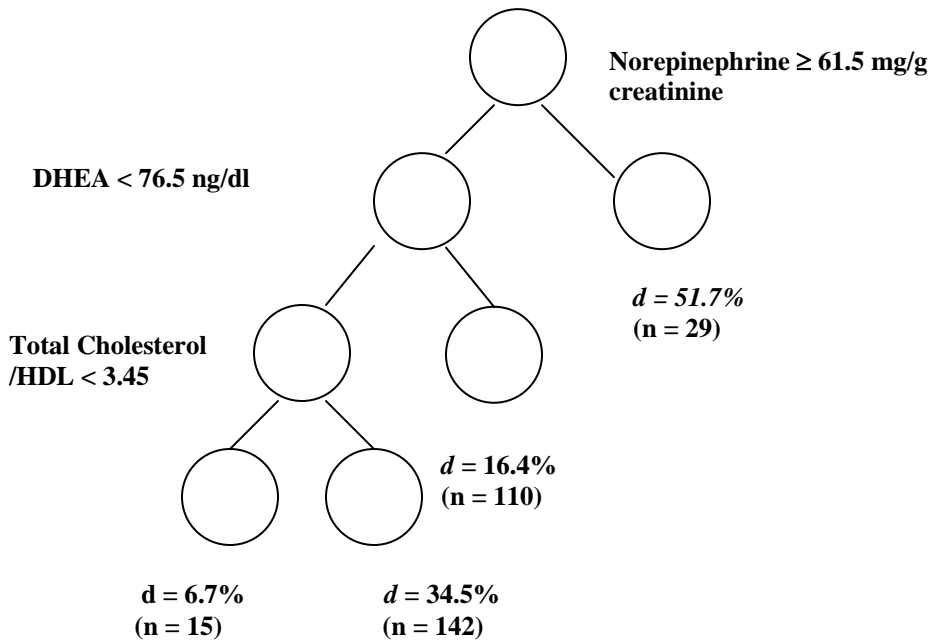
MALE TREE 3 (*d* = % dead at 7-year follow-up):



MALE TREE 4 (*d* = % dead at 7-year follow-up):



MALE TREE 5 (*d* = % dead at 7-year follow-up):



References

- Barrett-Connor, E. and D. Goodman-Gruen. "The epidemiology of DHEAS and cardiovascular disease." *Annals of the New York Academy of Sciences*. 774: 259-270. 1995.
- Beer, N. D. Jakubowicz, D. Matt, R. Beer, and J. Nestler. "Dehydroepiandrosterone reduces plasma plasminogen activator inhibitor type I and tissue plasminogen activator antigen in men." *American Journal of the Medical Sciences*. 311: 205-210. 1996.
- Breiman, Leo. "Random Forests." January 2001.
<ftp://ftp.stat.berkeley.edu/pub/users/breiman/randomforests-rev.pdf>
- Cannon, Walter. *Bodily changes in pain, hunger, fear, and rage; an account of recent researches into the function of emotional excitement*. New York: D. Appleton and Company, 1915.
- Cannon, Walter. *Wisdom of the Body*. New York: W.W. Norton & Company, Inc. 1932.
- Craft, S., S. Dagogo-Jack, B. Wiethop, C. Murphy, R. Nevins, S. Fleischman, V. Rice, J. Newcomer, and P. Cryer. "Effects of hyperglycemia on memory and hormone levels in dementia of the Alzheimer type: A longitudinal study." *Behavioral Neuroscience*. 107: 926-940. 1993.
- Crimmins, Eileen and Teresa Seeman. "Integrating biology into demographic research on health and aging (With a focus on the MacArthur Study of Successful Aging)." In: *Cells and Surveys: Should Biological Measures Be Included in Social Science Research?* Committee on Population. Caleb E. Finch, James W. Vaupel, and Kevin Kinsella, eds. Commission on Behavioral and Social Sciences and Education National Research Council. Washington DC: National Academy Press. 2001.
- Fried, Linda P., Richard A. Kronmal, Anne B. Newman et al. "Risk Factors for 5-Year Mortality in Older Adults: The Cardiovascular Health Study." *Journal of the American Medical Association*. 279(8):585-592. Feb 25, 1998.
- Hale, Lauren. *Healthy Aging: Physiological Correlates of Cumulative Psycho-social Experiences*. Doctoral Dissertation at Princeton University. 2003.
- Kaplan, G. and J. Keil. "Socioeconomic factors and cardiovascular disease." *Circulation*. 88:1973-1988. 1993.
- Karlamangla, Arun S., Burton H. Singer, Bruce S. McEwen, John W. Rowe, and Teresa E. Seeman. "Allostatic Load as a Predictor of Functional Decline: MacArthur Studies of Successful Aging." *Journal of Clinical Epidemiology*. 55: 696-710. 2002.
- Ku, Jason. "Classification of ¹H NMR Spectra Using Recursive Partitioning." Honors Thesis. Princeton University. 2002.
- Low, Carissa. "Life Histories and Affective Style." Honors Thesis. Department of Psychology. University of Wisconsin, 2000.
- McEwen, B.S. *The End of Stress as We Know It*. Washington, DC: John Henry Press. 2002a.
- . "Protective and damaging effects of stress mediators." *New England J. Med.* 338: 171-179. 1998.
- . "Sex, stress and the hippocampus: allostasis, allostatic load, and the aging process." *Neurobiology of Aging*. 23 p. 921-939. 2002b.
- McEwen, B.S. and Stellar, E. "Stress and the Individual: Mechanisms leading to disease." *Arch. Intern. Med.* 153:2093-2101. 1993.
- Moore, Philip, J., Nancy E. Adler, David R. Williams, and James S. Jackson "Socioeconomic Status and Health: The Role of Sleep." *Psychosom Med* 2002 64: 337-344.
- Nagi S.Z. "An epidemiology of disability among adults in the United States. *Milbank Memorial Fund Quarterly*. 6: 492-508. 1976.
- National Research Council (NRC). *New Horizons in Health: An Integrative Approach*. Burton H. Singer and Carol Ryff, eds. Committee on Future Directions for Behavioral and Social Sciences Research at the National Institute of Health. Board on Behavioral, Cognitive, and Sensory Sciences. Commission on Behavioral and Social Sciences and Education. Washington, DC: National Academy Press. 2001.

- Pfeiffer, E. "A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients." *Journal of the American Geriatric Society*. 23: 433-441. 1975.
- Reaven, Gerald M. Banting Lecture 1988: Role of insulin resistance in human disease. *Diabetes* 37: 1595-1607. 1988.
- Ridker, Paul M., Nader Rifai, Lynda Rose, Julie E. Buring, and Nancy R. Cook. "Comparison of C-Reactive Protein and Low-Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events." *The New England Journal of Medicine*. Volume 347 (20): 1557-1565. November 2002.
- Rosow I. and Breslau N. "A Guttman health scale for the aged." *Journal of Gerontology*. 21:556-559. 1966.
- Ryff, Carol. Scales of Psychological Well-Being. University of Wisconsin, Institute on Aging. 608.262.1818.
- Ryff, C. D., B. H. Singer, E. Wing, & G. Love. "Elective affinities and uninvited agonies." In *Emotion, social relationships, and health*. C. D. Ryff & B. H. Singer (Eds.). (pp. 133-175). 2001.
- Seeman, T. E. et al. "Social network characteristics and onset of ADL disability: MacArthur Studies of Successful Aging." *Journal of Gerontology*, 51B:5191-5200. 1996.
- Seeman, Teresa E., Bruce McEwen, John W. Rowe, and Burton Singer. "Allostatic load as a marker of cumulative biological Risk: MacArthur Studies of Successful Aging." *Proceedings of the National Academy of Sciences*. Volume 98, no. 8., 4770-4775. April 10, 2001.
- Seeman, T. E., B. H. Singer, C. D. Ryff, G. Dienberg Love, and L. Levy-Storms. "Social Relationships, Gender, and Allostatic Load Across Two Age Cohorts." *Psychosomatic Medicine*. 64(3): 395 - 406. May 1, 2002.
- Seeman, Teresa E., Burton H. Singer, John W. Rowe, Ralph Horwitz, and Bruce McEwen. "Price of Adaptation—Allostatic Load and Its Health Consequences." *MacArthur Studies of Successful Aging. Arch Intern Med*. Volume 157, October 27, 1997.
- Selye, Hans. *Stress without Distress*. New York: First Signet Printing. 1975
- . *The Stress of Life*, revised edition. New York: McGraw-Hill Book Co. 1956.
- Singer, Burton and Carol D. Ryff. "Hierarchies of Life Histories and Associated Risks." *Annals of New York Academy of Sciences*. Volume 896, 1999.
- Singer, Burton, Carol D. Ryff, and Teresa Seeman. "Operationalizing Allostatic Load." 2003.
- StataCorp. *Stata Statistical Software: Release 7.0*. Stata Press: College Station, TX. 2001.
- Sterling, P. and J. Eyer. Allostatics: A New Paradigm to Explain Arousal Pathology. In Fisher, S. and J. Reason, eds. *Handbook of Life Stress, Cognition and Health*. New York, John Wiley & Sons. 629-649. 1988.
- Sternberg, Esther M. *The Balance Within: The Science Connecting Health and Emotions*. New York: W. H. Freeman & Company. 2000.
- Wolfe, Elin, A. Clifford Barger, and Saul Benison. *Walter B. Cannon: Science and Society*. Cambridge, MA: Harvard University Press. 2000.
- Zhang, Heping and Burton Singer. *Recursive Partitioning in the Health Sciences*. New York: Springer. 1999.
- Zhang, Heping, Chang-Yung Yu, and Burton Singer. "Cell and tumor classification using gene expression data: Construction of forests." *Proceedings of the National Academy of Sciences*. Volume 100. April 1, 2003.