

# A Comparison of Cook-Medley Hostility Subscales and Mortality in Patients With Coronary Heart Disease: Data From the Heart and Soul Study

JONATHAN M. WONG, MD, NANCY L. SIN, PhD, AND MARY A. WHOOLEY, MD

**Objective:** Hostility is associated with adverse outcomes in patients with coronary heart disease (CHD). However, assessment tools used to evaluate hostility in epidemiological studies vary widely. **Methods:** We administered nine subscales of the Cook-Medley Hostility Scale (CMHS) to 656 outpatients with stable CHD between 2005 and 2007. We used Cox proportional hazards models to determine the association between each hostility subscales and all-cause mortality. We also performed an item analysis using logistic regression to determine the association between each CMHS item and all-cause mortality. **Results:** There were 136 deaths during 1364 person-years of follow-up. Four of nine CMHS subscales were predictive of mortality in age-adjusted analyses, but only one subscale (the seven-item Williams subscale) was predictive of mortality in multivariable analyses. After adjustment for age, sex, education, smoking, history of heart failure, diabetes, and high-density lipoprotein, each standard deviation increase in the Williams subscale was associated with a 20% increased mortality rate (hazard ratio = 1.20, 95% confidence interval = 1.00–1.43,  $p = .046$ ), and participants with hostility scores in the highest quartile were twice as likely to die as those in the lowest quartile (hazard ratio = 2.00, 95% confidence interval = 1.10–3.65,  $p = .023$ ). **Conclusions:** Among nine variations of the CMHS that we evaluated, a seven-item version of the Williams subscale was the most strongly associated with mortality. Standardizing the assessment of hostility in future epidemiological studies may improve our understanding of the relationship between hostility and mortality in patients with CHD. **Key words:** hostility, Cook-Medley, psychosocial, coronary heart disease, outcomes, mortality.

CMHS = Cook-Medley Hostility Scale; CHD = coronary heart disease; CI = confidence interval; CV = cardiovascular; HR = hazard ratio; MI = myocardial infarction.

## INTRODUCTION

More than 50 years ago, Friedman and Rosenman (1–4) reported that patients with coronary heart disease (CHD) and a “Type A behavior pattern” had worse cardiovascular (CV) outcomes than did those without the Type A behavior pattern. Subsequent work identified hostility and anger as the key elements of the Type A behavior pattern that were responsible for its connection with CHD (5–7). Since then, multiple observational studies have demonstrated that anger and hostility are associated with an increased risk of both incident CHD and adverse outcomes among patients with existing CHD (8).

Hostility is typically defined as a negative attitude toward others and encompasses cynicism, anger, mistrust, and aggression (9). The most commonly used measure of hostility is the Cook-Medley Hostility Scale (CMHS), a 50-item true/false questionnaire derived from the Minnesota Multiphasic Personality Inventory (8,10). However, the 50-item CMHS is too long for administration in many epidemiological studies. Various investigators have validated subscales of the CMHS, with the goal of more efficiently defining the hostility domains measured (5,9,11). However, there is no standardized assessment tool for hostility, and the instruments used in epidemiological studies

continue to vary widely, leading to unintended confusion and inconsistencies across studies (8).

Information on which subscales of the CMHS are most strongly predictive of adverse CV outcomes may be useful for future researchers who are deciding how best to measure hostility in epidemiological studies. Therefore, we sought to evaluate several previously defined subscales of the CMHS as predictors of mortality in a prospective cohort of 656 patients with stable CHD. Our aim was to compare the strength of association between previously studied CMHS subscales and mortality.

## METHODS

We evaluated participants from the Heart and Soul Study, a prospective cohort study originally designed to determine how psychological factors influence the outcomes of patients with stable CHD. A detailed description of the recruitment process has been previously described (12). Briefly, 1024 patients with stable CHD were recruited in 2000 to 2002 from two Veterans Affairs Medical Centers (San Francisco and Palo Alto), one university medical center (University of California, San Francisco), and nine public health clinics in the Community Health Network across San Francisco. In 2005 to 2007, after 5 years of follow-up, 667 participants (>80% survivors) completed a follow-up examination that included the CMHS. Our protocol was approved by the following institutional review boards: the Committee on Human Research at University of California, San Francisco; the Medical Human Subjects Committee at Stanford University; the Human Subjects Committee at the Veterans Affairs Palo Alto Health Care System; and the Data Governance Board of the Community Health Network of San Francisco. All participants provided written informed consent.

## Hostility Subscales

The CMHS is a 50-item true/false questionnaire derived from the Minnesota Multiphasic Personality Inventory. We administered 42 questions from the original CMHS and combined responses to the individual items to create all subscales. Seven items were omitted because they were previously determined to have no clear common underlying psychological content (9). After a thorough literature review, we identified nine subscales of the CMHS that were included in our analysis.

Williams and colleagues (5) found that in patients suspected of having CHD, those with scores greater than 10 on the full 50-item CMHS were more likely to have a significant coronary occlusion as measured by angiogram. They empirically identified nine items that were endorsed by at least 20% more participants in patients with high hostility than in those with low hostility. We administered a seven-item version of the Williams subscale (Box 1) because we

From the School of Medicine (J.M.W.), University of California, Irvine, California; Doris Duke Clinical Research Fellowship Program (J.M.W.) and Departments of Medicine (N.L.S., M.A.W.) and Epidemiology & Biostatistics (M.A.W.), University of California, San Francisco, California; and Veterans Affairs Medical Center (M.A.W.), San Francisco, California.

All correspondence and requests for reprints should be addressed to Mary A. Whooley, MD, Department of Veteran Affairs Medical Center, 4150 Clement St (111A1), San Francisco, CA. E-mail: mary.whooley@ucsf.edu

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were concerned that two of the items (“A large number of people are guilty of bad sexual conduct” and “When a man is with a woman he is usually thinking about things related to her sex”) might offend some participants.

### **Box 1. Modified Seven-item Williams Subscale**

Read each statement and decide whether it is true or false as applied to you.

1. I have often had to take orders from someone who did not know as much as I did.
2. I have often met people who were supposed to be experts who were no better than I.
3. I have frequently worked under people who seem to have things arranged so that they get credit for good work but are able to pass off mistakes onto those under them.
4. Some of my family has habits that bother and annoy me very much.
5. I would certainly enjoy beating a crook at his own game.
6. I have at times had to be rough with people who were rude or annoying.
7. I do not try to cover up my poor opinion or pity of a person so that he won't know how I feel.

Barefoot et al. (9) used an a priori analysis of the content of the CMHS to develop subsets based on psychological dimensions. These subsets included hostile attributions, cynicism, hostile affect, aggressive responding, and social avoidance. They performed a survival analysis, finding that cynicism, hostile affect, and aggressive responding were all predictive of mortality. The combination of these three subscales (27 items) was more predictive than any individual subscale or the entire 50-item CMHS. Barefoot et al. (7) and Boyle et al. (13,14) have used a 39-item composite of Barefoot's subscales (hostile attributions, cynicism, hostile affect, aggressive responding) to perform survival and CV event analyses. Some investigators have chosen to study Barefoot's 13-item cynicism subscale separately. Chaput et al. (15) found that the association between cynicism subscores and CHD events was as strong as the entire CMHS, but other investigators failed to find this association (7,16). We evaluated all of these subscales excluding one item (“When a man is with a woman he is usually thinking about things related to her sex”) because we were concerned it might offend some participants.

The nine-item “Cynical Distrust” subscale (11,17) was created empirically by factor analysis and has been found previously to predict progression of atherosclerosis (18). The subscale has been validated and shown to predict CV events. Among 2125 men who completed the nine-item Cynical Distrust scale as part of the Kuopio Ischemic Heart Disease Risk Factor Study, those with scores in the top quartile had more than twice the risk of myocardial infarction (MI) and CV death as compared with those who had scores in the lowest quartile (19).

### **Other Patient Characteristics**

Demographic information and medical history were determined by self-reported questionnaire. Socioeconomic status was measured by whether the participant attained at least a high school education. To assess the presence of major depression within the past month, a trained research assistant administered the Computerized National Institute of Mental Health Diagnostic Interview Schedule. The Computerized National Institute of Mental Health Diagnostic Interview Schedule is a computerized version of the Diagnostic Interview Schedule, a structured measure designed to assess for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition psychiatric illnesses (20). Study participants who met the criteria for major depression were informed of their results, encouraged to discuss their symptoms with their primary care provider, and provided a list of additional local resources for treatment. We measured alcohol use with the Alcohol Use Disorders Identification Test Consumption questionnaire, with a score of 4 or higher indicating regular use (21). We assessed smoking using the question, “Do you currently smoke cigarettes?”

We measured height and weight to calculate body mass index (in kilograms per meter squared). We measured high-density lipoprotein and calculated low-density lipoprotein from fasting blood samples drawn at the baseline study appointment. To measure cardiac disease severity, left ventricular ejection fraction

was obtained by echocardiography using an Acuson Sequoia Ultrasound System (Mountain View, CA) with a 3.5-MHz transducer.

### **Mortality**

The primary outcome variable was time to death. After the hostility assessment, study participants (or their proxy) were contacted annually by telephone and were asked about hospitalization for “heart trouble.” For any reported event, medical records, electrocardiograms, death certificates, and coroner's reports were retrieved and reviewed by two independent blinded adjudicators. If the adjudicators agreed, their classification was binding. Death was confirmed by death certificates and coroner's reports.

### **Statistical Analyses**

The goal of this study was to evaluate the association of different CMHS subscales with mortality in patients with stable CHD. Six patients missing more than 25% of items from one or more subscales were excluded from the analysis. There were four additional patients who were missing 25% or less of subscale items; for these, subscale scores were calculated by dividing the sum score by the proportion of items completed. An additional five patients were lost to follow-up, leaving 656 patients for analysis. Baseline characteristics between those who died and those who were still alive during the follow-up period were compared using Student's *t* tests for continuous variables and  $\chi^2$  tests for dichotomous variables. Pearson coefficients were calculated to assess correlations between each subscale of the CMHS. We estimated the risk of mortality associated with each subscale entered both as a categorical variable (quartiles) and as a continuous variable (per standard deviation increase) using Cox proportional hazard models. To test for linear trend across quartiles of each subscale, we used an age-adjusted log-rank test. Age, sex, and any baseline covariates that changed the strength of association between hostility (39-item subscale) and mortality by 5% or greater in Cox regression models were included in multivariate analyses. Finally, we estimated the risk of mortality associated with each individual CMHS item using logistic regression analysis, adjusting for age and sex. All analyses were performed using STATA version 12.0 (College Station, TX).

### **RESULTS**

A total of 136 deaths occurred during an average (standard deviation) of 3.7 (1.2) years of follow-up. As compared with participants who were alive at the end of follow-up, those who died were more likely to be older, to be male, and to have a history of MI, congestive heart failure, stroke/transient ischemic attack, or diabetes at baseline (Table 1). Those who died also had a lower resting left ventricular ejection fraction, a lower level of high-density lipoprotein, and a lower body mass index and were more physically inactive.

We used logistic regression analyses to analyze each of the 42 items from the CMHS. After adjustment for age and sex, four items were significant predictors of mortality (Table S1 in Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A121>). Three of these four items were also part of the Williams subscale (“I have often met people who were supposed to be experts who were no better than I,” “I have frequently worked under people who seem to have things arranged so that they get credit for good work but are able to pass off mistakes onto those under them,” and “I do not try to cover up my poor opinion or pity of a person so that he won't know how I feel”), and one item was not part of the Williams subscale (“I am sure I am being talked about”). An additional item from the Williams subscale was marginally associated with mortality (“I have often had to take orders from someone who did not know as much as I did”;  $p = .079$ ).

Nine subscales of the CMHS were compared (Table 2). All nine subscales were positively correlated with each of the other

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TABLE 1. Characteristics of 656 Participants with Coronary Heart Disease, by Death

	Dead (n = 136)	Alive (n = 520)	p
Demographics			
Age, y	75.0 (10.4)	70.1 (9.9)	<.001
White	82 (60.3%)	309 (59.4%)	.85
Male sex	126 (92.7%)	414 (79.6%)	<.001
Married	50 (37.3%)	227 (44.1%)	.16
High school education	113 (83.1%)	464 (89.2%)	.050
Body mass index, kg/m <sup>2</sup>	27.6 (5.4)	28.9 (5.7)	.010
Current smoking	21 (15.7%)	68 (13.6%)	.53
Regular alcohol use <sup>a</sup>	35 (25.9%)	147 (28.4%)	.56
Comorbid diseases			
Hypertension	111 (83.5%)	420 (83.0%)	.90
Myocardial infarction	89 (70.1%)	296 (60.3%)	.042
Heart failure	46 (37.7%)	105 (23.0%)	.001
Diabetes mellitus	57 (42.5%)	146 (29.5%)	.004
Stroke/TIA	37 (30.1%)	90 (18.4%)	.004
Current depression (past month) <sup>b</sup>	13 (9.6%)	54 (10.4%)	.77
Cardiac disease severity			
Left ventricular ejection fraction, %	56.3 (12.2)	61.0 (9.9)	<.001
Low-density lipoprotein, mg/dl	93.5 (31.7)	97.0 (38.3)	.33
High-density lipoprotein, mg/dl	44.0 (12.3)	48.0 (15.9)	.002

TIA = transient ischemic attack.

<sup>a</sup> Assessed by the Alcohol Use Disorders Identification Test Consumption.

<sup>b</sup> Assessed by the Computerized National Institute of Mental Health Diagnostic Interview Schedule.

subscales ( $p < .001$ ). Cynical distrust and Barefoot's cynicism subscales were highly intercorrelated, with a Pearson correlation coefficient greater than 0.80. The Williams scale correlated most strongly with Barefoot's 27-item subscale ( $r = 0.78$ ) and Barefoot's aggressive responding subscale ( $r = 0.68$ ). The mean scores for each subscale among study participants who died were compared with participants who remained alive during the follow-up period (Table 3). Four subscales were significantly predictive

of mortality: the Williams subscale, the cynicism subscale, and Barefoot's 27- and 39-item composite subscales.

The Williams, cynicism, and Barefoot composite scales were further analyzed in multivariate Cox proportional hazard models. When entered as continuous variables, four subscales (Williams, cynicism, and both Barefoot composite scales) were significantly associated with an increased risk of mortality in age-adjusted models (Fig. 1). The Williams subscale was associated with a

TABLE 2. Correlations Between Seven Cook-Medley Hostility Subscales

Subscale <sup>a</sup>	No. Items	Cynical Distrust	Williams Subscale	Cynicism	Hostile Attribution	Hostile Affect	Aggressive Responding	Social Avoidance
Cynical distrust <sup>b,c</sup>	8	—						
Williams subscale <sup>b,d,e</sup>	7	0.494	—					
Cynicism <sup>d,f</sup>	12	0.915	0.629	—				
Hostile attribution <sup>f</sup>	12	0.663	0.611	0.641	—			
Hostile affect <sup>f</sup>	5	0.494	0.550	0.473	0.560	—		
Aggressive responding <sup>f</sup>	9	0.424	0.675	0.431	0.487	0.431	—	
Social avoidance <sup>f</sup>	4	0.406	0.379	0.407	0.414	0.390	0.373	—

<sup>a</sup> Pairwise Pearson correlation coefficients between each Cook-Medley hostility subscale. All  $p$  values <.001.

<sup>b</sup> Original subscale included the additional item "When a man is with a woman, he is usually thinking about things related to her sex."

<sup>c</sup> Greenglass and Julkunen (11).

<sup>d</sup> Original subscale included the additional item "A large number of people are guilty of bad sexual conduct."

<sup>e</sup> Williams et al. (5).

<sup>f</sup> Barefoot et al. (9).

TABLE 3. Mean Baseline Scores of Cook-Medley Hostility Subscales, by Death

CMHS Subscale	No. Items	(Dead) Mean Score (SD)	(Alive) Mean Score (SD)	Increase in Mean Score (Dead Versus Alive), %	<i>p</i> -Value ( <i>t</i> Test)
Cynical distrust subscale <sup>a</sup>	8	3.1 (2.2)	2.8 (2.3)	11.9	.13
Williams subscale <sup>a,b</sup>	7	3.7 (1.9)	3.2 (1.8)	15.7	.006
Barefoot subscales					
Cynicism <sup>a</sup>	12	5.5 (2.8)	4.8 (2.8)	14.8	.009
Hostile attribution	12	3.7 (2.8)	3.3 (2.6)	12.3	.13
Hostile affect	5	1.9 (1.3)	1.8 (1.4)	4.4	.51
Aggressive responding	9	4.2 (2.1)	3.9 (1.9)	8.1	.13
Social avoidance	4	1.4 (1.2)	1.5 (1.1)	− 5.5	.49
Barefoot composite scales					
27-item <sup>a,c</sup>	26	11.6 (4.9)	10.5 (4.9)	10.7	.02
39-item <sup>a,d</sup>	38	15.3 (7.2)	13.8 (7.1)	10.8	.03

CMHS = Cook-Medley Hostility Scale; SD = standard deviation.

<sup>a</sup> Original subscale included the additional item “When a man is with a woman, he is usually thinking about things related to her sex.”

<sup>b</sup> Original subscale included the additional item “A large number of people are guilty of bad sexual conduct.”

<sup>c</sup> Twenty-seven-item Barefoot composite scale is an aggregate of cynicism, hostile affect, and aggressive responding.

<sup>d</sup> Thirty-nine-item Barefoot composite scale is an aggregate of cynicism, hostile attribution, hostile affect, and aggressive responding.

1.25-fold increase in mortality risk with each standard deviation increase (age-adjusted hazard ratio [HR] = 1.25, 95% confidence interval [CI] = 1.06–1.47,  $p = .008$ ). High school education, current smoking, history of heart failure, history of diabetes mellitus, and high-density lipoproteins levels were included in multivariate Cox proportional hazard models because these variables significantly changed the strength of association between hostility (39-item scale) and mortality (Table S2 in Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A122>). Only

the Williams subscale remained predictive of mortality in multivariate analyses when the subscale was entered as a continuous variable (Table 4).

When comparing the highest versus lowest quartiles of each hostility subscale score, the Williams (age-adjusted HR = 2.06, 95% CI = 1.19–3.59,  $p = .010$ ) and 39-item Barefoot composite subscales (age-adjusted HR = 2.09, 95% CI = 1.24–3.55,  $p = .006$ ) were significantly associated with increased mortality (Fig. 1). After multivariable adjustment, these CMHS subscales

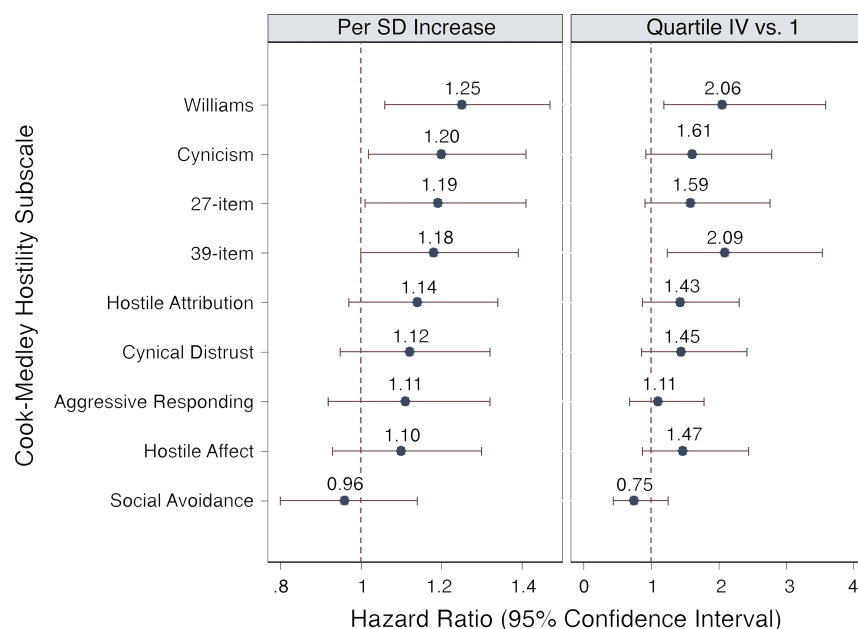


Figure 1. Association between Cook-Medley Hostility Subscales and Mortality. The numerical values are point estimates for the age-adjusted hazard ratio of each hostility subscale, with the horizontal bars representing 95% confidence intervals. The left plot “Per SD Increase” refers to the hazard ratio per SD increase in hostility score (statistically significant hazard ratios included 39-item, 27-item, Williams, and Cynicism subscales). The right plot “Quartile IV vs. I” refers to the hazard rate of the highest compared with the lowest quartile of hostility score (statistically significant hazard ratios included 39-item and Williams subscales). SD = standard deviation.



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**TABLE 4. Association Between Cook-Medley Hostility Subscales and Mortality, With Multivariate Adjustment**

CMHS Subscale	Quartile IV Versus I		Per SD Increase	
	Hazard Ratio (95% CI)	<i>p</i>	Hazard Ratio (95% CI)	<i>p</i>
Williams				
Model 1 (base model <sup>a</sup> )	2.06 (1.19–3.59)	.010	1.25 (1.06–1.47)	.008
Model 2 (final model <sup>b</sup> )	2.00 (1.10–3.65)	.023	1.20 (1.00–1.43)	.046
Cynicism (Barefoot)				
Model 1 (base model <sup>a</sup> )	1.61 (0.93–2.79)	.087	1.20 (1.02–1.41)	.032
Model 2 (final model <sup>b</sup> )	1.26 (0.70–2.30)	.44	1.12 (0.94–1.33)	.21
27-item				
Model 1 (base model <sup>a</sup> )	1.59 (0.92–2.76)	.097	1.19 (1.01–1.41)	.039
Model 2 (final model <sup>b</sup> )	1.37 (0.76–2.49)	.30	1.11 (0.93–1.33)	.26
39-item				
Model 1 (base model <sup>a</sup> )	2.09 (1.24–3.54)	.006	1.18 (1.00–1.39)	.046
Model 2 (final model <sup>b</sup> )	1.82 (1.03–3.22)	.039	1.09 (0.92–1.30)	.33

CMHS = Cook-Medley Hostility Scale; SD = standard deviation; CI = confidence interval.

<sup>a</sup> Model 1 adjusted for age only.

<sup>b</sup> Model 2 adjusted for covariates that changed the strength of association (% change in age-adjusted log hazard ratio) between the 39-item CMHS and mortality by at least 5%. Covariates included age, male, high school education, current smoking, heart failure, diabetes mellitus, and high-density lipoprotein.

remained significantly associated with mortality (Table 4). The results of the age-adjusted linear test for trend across quartiles for each of the four subscales were as follows: Williams,  $p = .033$ ; cynicism,  $p = .046$ ; 39-item Barefoot,  $p = .059$ ; and 27-item Barefoot,  $p = .11$ ).

## DISCUSSION

In 656 patients with stable CHD, we compared nine previously defined CMHS subscales and found that a 7-item version of the Williams subscale and the 39-item Barefoot composite subscale were significantly predictive of mortality in multivariate models. As compared with study participants in the lowest quartile of hostility, those in the highest quartile had more than twice the rate of mortality. These findings confirm that self-reported hostility is associated with future mortality in patients with stable CHD and demonstrate that some CMHS subscales are similarly associated with death. They also suggest that multiple components of hostility (cynicism, aggressive responding, hostile affect, and hostile attribution) contribute to adverse health outcomes.

We are not aware of any other study that has compared the strength of association between CMHS subscales and death in patients with stable CHD. The CMHS is the most commonly used measure of self-reported hostility in CV outcomes studies. Although some prior investigators have found positive associations between CMHS subscales and CV outcomes (6,7,13–15,22), others have found no association (19,23,24). Our results offer one possible explanation for these incongruent findings: not all CMHS subscales are equally associated with death in patients with CHD.

Barefoot observed that, although hostility has multiple components, grouping components together better predicted mortality than any individual hostility domain (9). Our findings are

consistent with these observations, as all CMHS subscales, except social avoidance, were associated with an increased risk of death. Although only seven items in length, the Williams subscale contains questions from four separate hostility constructs, including two items for cynicism, three items for aggressive responding, one item for hostile attribution, and one item for hostile affect. Likewise, Barefoot's 39-item subscale contains questions from the same four constructs and was the only other subscale associated with mortality after multivariable adjustment. These constructs are fundamentally different: cynicism and hostile attributions contain items of belief and reflect an individual's mistrust of another person; hostile affect contains items of negative emotions like anger or impatience; and aggressive responding contains items of hostile behavior. Consistent with this hypothesis, none of the subscales that measured only one hostility construct were found to be associated with mortality. Moreover, the results from our item analysis seem to show that CMHS items involving specific hostile interactions with other people were more strongly predictive of mortality compared with items involving general opinions or statements about the environment or general population.

Despite prior prospective studies that have shown a significant association between self-reported hostility and poor health outcomes, the mechanisms that explain this association are still not well understood. One potential explanation is the health behavior model, which suggests that hostile people are at greater risk for disease because of poor health habits that may include smoking, medication nonadherence, and physical inactivity (19,25). Indeed, our results suggest that smoking may have attenuated the association between hostility and mortality in all CMHS subscales, except social isolation. Another potential explanation is that hostility may exert direct physiological effects that ultimately lead to poor health outcomes. One possible physiological effect is an enhanced adrenergic activation (26–28), leading to increased

blood pressure (29–31), coronary vasoconstriction (32), inflammation (33), and platelet activation (34,35). Hostile individuals tend to experience more frequent anger outbursts, which could act as a triggering event for a nonfatal MI or CHD death (36). Alternatively, hostility may act as a marker for disease severity. However, we attempted to control for disease severity by adjusting for comorbid conditions and left ventricular ejection fraction.

There are a number of study limitations to consider. First, the study cohort consisted of primarily male patients, which may limit generalizability to women. It is important to note that the mechanisms linking hostility with health problems in the general population may be different than the mechanisms linking hostility with a poor prognosis in patients with existing CHD. Second, our study had a relatively short follow-up time with a maximum of 5.6 years for any participant. Despite the short follow-up period, a large difference was still observed in the association between two subscales and mortality. Longer follow-up periods would be expected to only enhance this difference. Third, we measured hostility only with CMHS subscales and therefore could not compare other measurements of anger/hostility and their associations with mortality risk. Other scales used to measure anger/hostility in prior CHD populations include the Spielberger anger expressions scale, the Spielberger trait anger scale, and the Karolinska scales of personality. We also used a binary item response format, which may have limited the variance in participant scoring. Lastly, observed hostility was not measured. Recent evidence suggests that observed hostility may be more strongly associated with CV outcomes than self-reported hostility in patients without CHD (37).

In summary, this study contributes important new data highlighting the differences in mortality risk across CMHS subscales. A 7-item version of the Williams subscale—which contains items representing four different hostility constructs (cynicism, hostile attribution, hostile affect, and aggressive responding)—and the 39-item Barefoot composite subscale were found to be significantly associated with mortality in this cohort and may serve as a useful measurement tools of hostility for future research.

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