Hopelessness and Risk of Mortality and Incidence of Myocardial Infarction and Cancer

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We examined the relationship among low, moderate, and high levels of hopelessness, all-cause and cause-specific mortality, and incidence of myocardial infarction (MI) and cancer in a population-based sample of middle-aged men. Participants were 2428 men, ages 42 to 60, from the Kuopio Ischemic Heart Disease study, an ongoing longitudinal study of unestablished psychosocial risk factors for ischemic heart disease and other outcomes. In 6 years of follow-up, 174 deaths (87 cardiovascular and 87 noncardiovascular, including 40 cancer deaths and 29 deaths due to violence or injury), 73 incident cancer cases, and 95 incident MI had occurred. Men were rated low, moderate, or high in hopelessness if they scored in the lower, middle, or upper one-third of scores on a 2-item hopelessness scale. Age-adjusted Cox proportional hazards models identified a dose-response relationship such that moderately and highly hopeless men were at significantly increased risk of all-cause and cause-specific mortality relative to men with low hopelessness scores. Indeed, highly hopeless men were at more than three-fold increased risk of death from violence or injury compared with the reference group. These relationships were maintained after adjusting for biological, socioeconomic, or behavioral risk factors, perceived health, depression, prevalent disease, or social support. High hopelessness also predicted incident MI, and moderate hopelessness was associated with incident cancer. Our findings indicate that hopelessness is a strong predictor of adverse health outcomes, independent of depression and traditional risk factors. Additional research is needed to examine phenomena that lead to hopelessness.

Key words: hopelessness, depression, mortality, myocardial infarction, cancer.

INTRODUCTION

The importance of hope or optimism has long been recognized (1, 2). Conversely, a lack of hope or "giving up" is generally believed to have a negative impact on psychological well being and physical health (3). Although various researchers have sought to quantify hope (1, 4) and/or hopelessness (5) and have discussed these constructs in terms of their effects on physical and mental health, empirical examinations of the consequences of hopelessness have been fairly limited.

One line of research has focused on the role of hopelessness in predicting survival from cancer. Although not unequivocal (6, 7), there is evidence to suggest that hopelessness is associated with greater disease progression and earlier death among cancer patients (8–10). No well designed, population-based studies have specifically examined the association between hopelessness and cancer incidence or mortality, however, so the potential role of hopelessness in the etiology of cancer is unknown.

Recently, Anda and colleagues (11) found that hopelessness, assessed by one question from a 4-item scale measuring depressed affect, significantly predicted fatal and nonfatal ischemic heart disease (IHD) in a cohort of more than 2800 initially healthy men and women from the National Health Examination Follow-Up Survey (NHEFS). In that study, depressed affect also was found to be a significant predictor of fatal and nonfatal IHD; however, the single item measuring hopelessness was more strongly related to the outcomes than the complete 4-item depression scale. To our knowledge, the NHEFS is the first and only study to show an association between hopelessness per se and increased IHD morbidity and mortality. Other lines of research provide supportive evidence for this relationship, however. For example, a positive association between depressive symptoms and increased

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risk of cardiovascular morbidity and mortality has been demonstrated in both coronary patients and population samples (12–16). Also, the growing literature on "vital exhaustion," a mental state characterized by excessive fatigue, irritability, and feelings of demoralization and hopelessness, has identified a positive association between this characteristic and manifestations of coronary disease in both men and women (17–19).

Hopelessness also has been importantly related to various psychopathological conditions, including alcoholism, suicide, and, most commonly, depression (20–23). It is important to note, however, that hopelessness and depression are not identical constructs. Indeed, there is empirical evidence to suggest that hopelessness may function independently from depression, a distinction that may be particularly important when examining potential health effects of hopelessness and depression. For example, although hopelessness is often considered to be an essential feature of depression (24), research and clinical experience have repeatedly demonstrated the heterogeneity of depression and have found that hopelessness may be sufficient but that it is not necessary to cause depression (25–27). Studies have also shown that suicidal intent consistently is more strongly correlated with hopelessness than with depression and that the association between suicidal intent and hopelessness remains after controlling for the effects of depression (see Greene (27) for a review). Furthermore, men and women report similar levels of hopelessness despite the fact that depression is much more prevalent among women (28).

Taken together, the evidence suggests that feelings of hopelessness are associated with adverse physical and mental health outcomes. Nonetheless, much remains to be learned about these associations, particularly in population-based samples. The present study was conducted to examine the relationship between hopelessness and mortality due to all causes as well as cause-specific mortality and incidence of acute myocardial infarction (MI) and cancer in a randomly selected population of more than 2400 middle-aged men from the Kuopio region of eastern Finland. Available data on a wide variety of socioeconomic, behavioral, and psychosocial factors, including an independent measure of depression, as well as health status and prevalent disease, enabled us to determine the relative contributions of these factors to the observed associations.

METHODS

Study Population

The KIHD study is a population-based study of previously unestablished but promising risk factors for carotid atherosclerosis, IHD, and other outcomes (29) among middle-aged men from the Kuopio region in Eastern Finland, an area of high coronary morbidity and mortality (30). The total sample of KIHD participants consisted of 2682 men recruited in two cohorts: The first cohort included 1166 54-year-old men (83.3% of those eligible) enrolled in the study between March, 1984 and August, 1986; the second cohort included 1516 42-, 48-, 54-, and 60-year-old men (82.6% of those eligible) enrolled in the study between August, 1986 and December, 1989. The present analyses are based on 2428 men who had complete data on the measure of hopelessness, biological, behavioral, and socioeconomic covariates, disease history variables, and mortality outcomes.

Hopelessness Scale

Hopelessness, defined as negative expectancies about oneself and the future, was measured by two items from a battery of psychosocial questionnaires. The items were "I feel that it is impossible to reach the goals I would like to strive for" and "The future seems to me to be hopeless, and I can't believe that things are changing for the better"; responses were on a 5-point Likert scale (0 = absolutely agree; 1 = somewhat agree; 2 = cannot say; 3 = somewhat disagree; or 4 = absolutely disagree). The two items were moderately correlated (r = .53). Items were reverse-scored and summed to create a hopelessness score. Scores ranged from 0 to 8 with a mean (SD) of 2.73 (2.0). Three groups were formed according to low, moderate, or high scores on the hopelessness scale based on meaning of the scores and response options as follows: Individuals with the lowest scores (0, 1, or 2), comprising 52.8% of the sample, were the reference category for all analyses. Low scores on the hopelessness scale were indicative of general *disagreement* with each of the two statements. Those with hopelessness scores in the mid-range of the scale (3, 4, or 5) formed a "moderately hopeless" group (36.1% of the sample); moderate scores reflected a mixed response to the items. Men with high scores on the hopelessness scale (6, 7, or 8) formed a "highly hopeless" group (11% of the sample); high scores were indicative of general *agreement* with both statements. Hopelessness scores for the three groups were 1.14 (0.8), 3.87 (0.7), and 6.57 (0.8), respectively. Scores on the hopelessness scale increased with age ($p < .0001$; means ranged from 2.02 for 42-year-olds to 2.93 for 54- and 60-year-olds).

Outcomes

Mortality. All-cause mortality was ascertained by linkage to the national death registry. All deaths that occurred between study entry (March, 1984 to December, 1989) and December 31, 1993 were included. Deaths that were coded with the Ninth International Classification of Disease codes 390–459 were included in the analyses of cardiovascular deaths. All other deaths were included in the analyses of noncardiovascular deaths. Average follow-up time was 6.0 years (range = 3.1–8.8 years). In the present sample, there were 174 deaths during the follow-up period, 87 of which resulted from cardiovascular causes and 87 of which were due to noncardiovascular causes. Of the 87 noncar-

diovascular deaths, 29 were categorized as "external" or due to violence, injury, or accident, and 58 were classified as "internal" or due to disease or illness, including 40 cancer deaths.

Cancer Incidence. Information on incident cancer cases, ascertained through the Finnish Cancer Registry (31), was available through December 31, 1993. During this time, 73 cases of cancer were identified among cohort members. Forty-four KIHD participants who had a history of cancer at baseline were excluded from analyses of cancer incidence.

Myocardial Infarctions. MI were ascertained through the FINMONICA register for this area (32). Information on incidence of MI was available through December 31, 1992, during which time there were 95 first MI. Analyses of the MI data excluded 608 men with a history of angina or a previously diagnosed MI.

Data Analyses

Cox proportional hazards models (33) were used to assess the relationships between levels of hopelessness and mortality and incidence of cancer and MI. First, we calculated simple age-adjusted models that included two dummy variables representing the groups rated moderate and high in hopelessness. The reference group for all analyses was the group with the lowest scores on the hopelessness scale. To examine the influence of various categories of risk factors, we then fit a series of age-adjusted models to the data that also adjusted for biological factors (resting systolic blood pressure, high density and low density lipoprotein cholesterol, body mass index), behavioral covariates (physical activity, smoking, frequency of drunkenness), or social class variables (income, years of education). Next, we examined a series of age-adjusted models that also adjusted for perceived health status (self-report of "extremely bad" to "extremely good" overall health) or positive disease history (i.e., previous diagnoses of cardiovascular diseases, stroke, respiratory diseases, cancer, or diabetes or prevalent hypertension or exercise-induced ischemia at the baseline testing). Then, a model that adjusted for age and level of depression, measured by the MMPI Depression Scale, was fit to the data. Also, given previously identified associations between a lack of social connections and increased mortality in this population (34), a model that adjusted for age, quality, and availability of social support and participation in organizations was fit to the data.[1] In all models, covariates were represented by separate dummy variables. Twenty subjects from the censored group (i.e., "noncases") for whom social support data were not available were excluded from the Cox models that adjusted for these measures. Finally, a model that simultaneously adjusted for all of the risk factors listed above was calculated.

To determine if the associations between levels of hopelessness and mortality differed according to disease status, we then repeated the analyses stratifying according to the presence or absence of a history of cardiovascular diseases, including hypertension, stroke, asymptomatic and symptomatic coronary disease, cardiomyopathy, and congestive heart failure, and the presence or absence of exercise-induced ischemia, diabetes, cancer, and respiratory diseases.

RESULTS

Full Sample

All-Cause Mortality. An age-adjusted Cox model revealed a positive dose-response relationship between hopelessness and all-cause mortality with moderately hopeless men at more than twice the risk and highly hopeless men at more than three times the risk of death due to any cause, relative to the reference group of low scorers on the hopelessness scale (Relative Hazards (RH) = 2.26 (95% confidence interval: 1.59, 3.21) and 3.41 (95% confidence interval: 2.24, 5.21), respectively) (Fig. 1). This pattern of associations remained significant in Cox models that adjusted for biological, behavioral, or social class risk factors, perceived health status, positive disease history or prevalent disease, depression, or measures

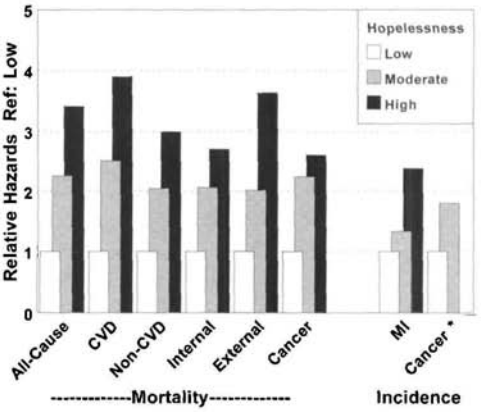

Fig. 1. Age-adjusted risk of all-cause and cause-specific mortality and incidence of myocardial infarction and cancer by level of hopelessness. Mortality analyses based on 2428 men; number of all-cause deaths = 174 (87 cardiovascular, 87 noncardiovascular, including 58 internal deaths (40 from cancer) and 29 external deaths). MI incidence analyses based on 1820 men with no history of MI or angina; number of MI = 95. Cancer incidence analyses based on 2384 subjects with no history of cancer; number of cases = 73. For cancer incidence analyses, moderately and highly hopeless groups are combined.

[1] Quality and availability of social support and organizational participation were measured by three separate scales consisting of 8, 3, and 6 items (Cronbach's α = .74, .76, and .83), respectively. Each scale was factor analytically derived from a pool of 69 items that assessed various aspects of social connections, including extent, quality, and satisfaction with social connections, marital status, religious practices and shyness. Each of these scales was associated with significantly increased risk of all-cause mortality in this population in an earlier study (see Ref. 34). Further details regarding these scales are available from the authors.

of social support. Furthermore, simultaneously adjusting for all of the covariates also revealed a significant dose-response relationship between hopelessness and all-cause mortality (Table 1).

Cause-Specific Mortality. Analyses that separated deaths into cardiovascular and noncardiovascular causes also revealed dose-response relationships between hopelessness and mortality (Fig. 1). Compared with the reference group of low scorers, men with moderate scores were at approximately two and one-half times the risk and men with high scores were at nearly four times the risk of cardiovascular mortality (RH = 2.52 (95% confidence interval: 1.52, 4.17) and 3.90 (95% confidence interval: 2.14, 7.11), respectively). Similarly, moderately hopeless men were at twice the risk, and highly hopeless men were at three times the risk of noncardiovascular mortality, relative to the reference group (RH = 2.05 (95% confidence interval: 1.26, 3.33) and 3.00 (95% confidence interval: 1.65, 5.44), respectively). These relationships remained significant in Cox models that included adjustments for the various categories of risk factors and covariates (Table 2). Indeed, this dose-response pattern of association was still evident for noncardiovascular mortality in the Cox model that simultaneously adjusted for all of the risk factors. For cardiovascular mortality, however, simultaneous risk factor adjustments resulted in point estimates of approximately 1.9 for both the moderately and highly hopeless groups (Table 2).

Additional age-adjusted Cox models that further examined the relationship between levels of hopelessness and noncardiovascular mortality revealed graded associations between hopelessness and both internal and external causes of noncardiovascular deaths (Fig. 1). Men with moderate or high scores were at significantly increased risk of mortality due to internal causes, relative to the group with low

TABLE 1. Hopelessness and All-Cause Mortality: KIHD[a]

Hopelessness Groups: Model Adjustments:	low		moderate		high	
	RH	95% CI	RH	95% CI	RH	95% CI
Age	referent		2.26	1.59, 3.21	3.41	2.24, 5.21
Age, SBP, BMI, lipids			2.27	1.60, 3.22	3.35	2.19, 5.11
Age, education, income			2.02	1.41, 2.90	2.80	1.80, 4.36
Age, behavioral factors[b]			2.05	1.44, 2.92	2.92	1.90, 4.47
Age, perceived health			2.03	1.43, 2.89	2.73	1.77, 4.22
Age, disease history			2.07	1.45, 2.95	2.74	1.77, 4.22
Age, MMPI depression			2.25	1.57, 3.20	3.37	2.19, 5.20
Age, social support			2.01	1.40, 2.89	2.91	1.87, 4.51
All risk factors			1.82	1.25, 2.65	2.09	1.30, 3.34

[a] N = 2428 (2408 in models with adjustments for social support). Number of deaths = 174. Low scores on the hopelessness scale ranged from 0 to 2, moderate scores ranged from 3 to 5, and high scores ranged from 6 to 8.

[b] Behavioral factors = smoking, physical activity, and frequency of drunkenness in a 12-month period.

RH, relative hazard ratio from the Cox proportional hazards models; SBP, resting systolic blood pressure; BMI, body mass index; lipids, low density and high density lipoprotein cholesterol.

TABLE 2. Hopelessness and Cause-Specific Mortality: KIHD[a]

Hopelessness Groups: Model Adjustments:	Cardiovascular Mortality						Noncardiovascular Mortality					
	Low		Moderate		High		Low		Moderate		High	
	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI	RH	95% CI
Age	referent		2.52	1.52, 4.17	3.90	2.14, 7.11	referent		2.05	1.26, 3.33	3.00	1.65, 5.44
Age, SBP, BMI, lipids			2.52	1.52, 4.18	3.66	2.00, 6.68			2.06	1.26, 3.35	3.05	1.68, 5.56
Age, education, income			2.25	1.33, 3.79	3.22	1.72, 6.05			1.83	1.11, 3.02	2.44	1.31, 4.56
Age, behavioral factors[b]			2.31	1.39, 3.85	3.37	1.84, 6.19			1.83	1.12, 2.98	2.53	1.38, 4.63
Age, perceived health			2.12	1.27, 3.55	2.77	1.49, 5.14			1.95	1.20, 3.18	2.71	1.47, 4.99
Age, disease history			2.06	1.23, 3.45	2.42	1.31, 4.49			2.05	1.26, 3.34	3.05	1.66, 5.60
Age, MMPI depression			2.39	1.43, 3.99	3.58	1.93, 6.63			2.12	1.30, 3.46	3.19	1.74, 5.88
Age, social support			2.21	1.31, 3.72	3.19	1.71, 5.95			1.85	1.12, 3.06	2.66	1.43, 4.95
All risk factors			1.93	1.12, 3.33	1.85	0.94, 3.64			1.79	1.06, 3.01	2.58	1.33, 5.01

[a] N = 2428 (2408 in models with adjustments for social support). Number of cardiovascular deaths = 87; number of noncardiovascular deaths = 87. Low scores on the hopelessness scale ranged from 0 to 2, moderate scores ranged from 3 to 5, and high scores ranged from 6 to 8.

[b] Behavioral factors = smoking, physical activity, and frequency of drunkenness in a 12-month period.

SBP, resting systolic blood pressure; BMI, body mass index; lipids, low density and high density lipoprotein cholesterol

hopelessness scores (RH = 2.06 (95% confidence interval: 1.14, 3.72) and 2.71 (95% confidence interval: 1.28, 5.75), respectively). In contrast, only men with high scores were at significantly increased risk of mortality due to external causes although a graded association was still evident (RH = 2.02 (95% confidence interval: 0.86, 4.76) and 3.64 (95% confidence interval: 1.35, 9.80) for moderate and high scorers, respectively). These elevations in risk remained significant in separate Cox models that adjusted for biological, behavioral, or social class risk factors, perceived health status, positive disease history or prevalent disease, depression, or social support, as well as in the model with simultaneous adjustments for all of the risk factors (RH for internal deaths = 1.93 (95% confidence interval: 1.01, 3.69) and 2.44 (95% confidence interval: 1.05, 5.67) for the moderate and high groups, respectively; and RH for external deaths = 1.68 (95% confidence interval: 0.68, 4.16) and 3.31 (95% confidence interval: 1.10, 9.91) for the moderate and high groups, respectively).

Cancer Mortality. A separate age-adjusted Cox model limited to the 40 internal deaths that were due to cancer revealed a dose-response relationship between levels of hopelessness and cancer mortality with both moderate and high scorers having more than a two-fold increase in risk (RH = 2.25 (95% confidence interval: 1.10, 4.58) and 2.61 (95% confidence interval: 1.03, 6.64), respectively) (Fig. 1).[2] These elevations in risk across levels of hopelessness remained apparent, and, in most cases, were significant or approached significance in subsequent Cox models that adjusted for the various covariates (RH ranged from 1.94 to 2.32 for the moderately hopeless group and from 2.11 to 2.72 for the highly hopeless group). Indeed, the observed increase in risk remained approximately two-fold for both moderately and highly hopeless groups in the model that adjusted for all of the risk factors simultaneously.

Cancer Incidence. Only eight incident cancer cases occurred among the men with high hopelessness scores; therefore, we examined the association between hopelessness and incident cancer by combining the moderately and highly hopeless groups and comparing them with those with low hopelessness scores. These Cox models also excluded 44 subjects who had a previous diagnosis of cancer. Hopelessness significantly predicted incident cancer cases ($N = 73$) in the age-adjusted model (RH = 1.80 (95% confidence interval: 1.11, 2.92)) (Fig. 1). These associations were relatively unchanged in subsequent Cox models with adjustments for biological or behavioral risk factors, socioeconomic status, depression, perceived health status, social support, or prevalent disease (Table 3).

Incidence of Acute Myocardial Infarctions. Age-adjusted Cox models showed that, among men with no known history of angina or MI, those reporting high levels of hopelessness were at significantly increased risk for a first MI, relative to men scoring low on the measure of hopelessness (RH = 2.39 (95% confidence interval: 1.35, 4.25) (Fig. 1). This association remained significant in Cox models that adjusted for biological, behavioral, or socioeconomic risk factors, perceived health status, depression, social support, or a positive disease history of cardiovascular disorders (other than MI or angina), stroke, diabetes, cancer, or respiratory diseases, prevalent hypertension, or exercise-induced ischemia. Indeed, this elevation in risk remained approximately two-fold in the Cox model that simultaneously adjusted for all of the risk factors noted above (Table 3). Men with moderate scores on the measure of hopelessness showed a 20 to 30% increased risk of MI, relative to men with low hopelessness scores, but these elevations were not significant.

Stratification By Disease Status

All-Cause Mortality. Among the 1647 "unhealthy" men with a positive disease history, a dose-response relationship between levels of hopelessness and all-cause mortality was observed with both moderately and highly hopeless men at significantly elevated risk of death due to any cause (RH = 2.37 (95% confidence interval: 1.61, 3.48) and 2.81 (95% confidence interval: 1.75, 4.50), respectively). Among the 781 "healthy" subjects without a disease history or prevalent disease, high scores on the measure of hopelessness were associated with greatly increased risk of mortality (RH = 6.07 (95% confidence interval: 2.35, 15.7)) whereas moderate scores were not (RH = 1.38 (95% confidence interval: 0.57, 3.35)) (Fig. 2). For both the unhealthy and healthy groups, the observed increases in risk remained significant in subsequent Cox models that separately adjusted for biological or behavioral risk factors, socioeco-

[2] We chose to include the 44 subjects who reported a previous diagnosis of cancer in the analyses of cancer mortality because only two cancer deaths occurred in men with a history of cancer and analyses excluding them produced essentially the same pattern of results as those reported in the text. Furthermore, men with a history of cancer did not differ in their reported levels of hopelessness from those without a history of cancer (mean hopelessness scores = 2.4 and 2.7, respectively).

TABLE 3. Hopelessness and Incidence of Cancer and Myocardial Infarction: KIHD[a]

Hopelessness Groups: Model Adjustments:	Cancer				Myocardial Infarction					
	Low		Moderate/High		Low		Moderate		High	
	RH	95% CI	RH	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age	referent		1.80	1.11, 3.92	referent		1.33	0.85, 2.08	2.39	1.35, 4.25
Age, SBP, BMI, lipids			1.86	1.15, 3.01			1.34	0.86, 2.09	2.15	1.21, 3.83
Age, education, income			1.62	0.98, 2.69			1.23	0.78, 1.94	2.05	1.13, 3.72
Age, behavioral factors[b]			1.60	0.98, 2.60			1.21	0.77, 1.90	2.27	1.27, 4.06
Age, perceived health			1.79	1.10, 2.91			1.27	0.81, 1.99	2.19	1.22, 3.93
Age, disease history			1.70	1.04, 2.78			1.32	0.85, 2.07	2.28	1.28, 4.07
Age, MMPI depression			1.69	1.03, 2.78			1.28	0.81, 2.01	2.31	1.29, 4.15
Age, social support			1.59	0.96, 2.64			1.34	0.84, 2.12	2.50	1.37, 4.57
All risk factors			1.42	0.83, 2.41			1.20	0.75, 1.94	2.05	1.08, 3.88

[a] Cancer incidence analyses: N = 2384 (2364 in models with adjustments for social support); number of cases = 73. MI incidence analyses: N = 1820 (1804 in models with adjustments for social support); number of MI = 95. Low scores on the hopelessness scale ranged from 0 to 2, moderate scores ranged from 3 to 5, and high scores ranged from 6 to 8.

[b] Behavioral Factors = smoking, physical activity, and frequency of drunkenness in a 12-month period.

SBP, resting systolic blood pressure; BMI, body mass index; lipids, low density and high density lipoprotein cholesterol.

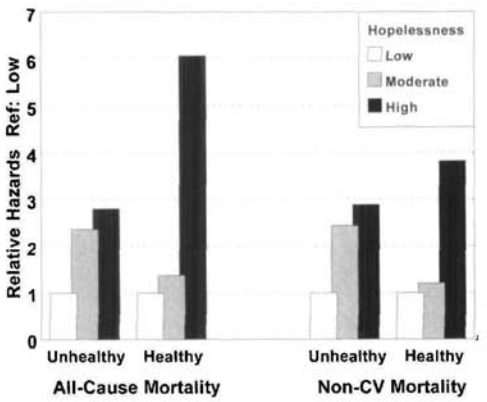

Fig. 2. Age-adjusted risk of all-cause and noncardiovascular mortality by level of hopelessness and stratified by disease status. Unhealthy subjects were defined as having a positive history of symptomatic or asymptomatic cardiovascular diseases, respiratory disease, diabetes, cancer, prevalent hypertension, and/or exercise-induced ischemia at baseline; healthy subjects had a negative disease history and no prevalent hypertension or ischemia. Unhealthy subjects: N = 1647; number of all-cause deaths: 147 (66 noncardiovascular deaths). Healthy subjects: N = 781; number of all-cause deaths: 27 (21 noncardiovascular deaths).

nomic status, perceived health, depression, or social support, as well as in the Cox models with simultaneous adjustments for all of the risk factors (RH ranged from 2.03 to 2.44 for the moderately hopeless group and from 2.18 to 2.89 for the highly hopeless group).

Cause-Specific Mortality. Too few cardiovascular deaths (N = 6) occurred among the healthy subjects to reliably estimate the risks associated with hopelessness in that group. However, among unhealthy subjects, a dose-response relationship was observed between levels of hopelessness and cardiovascular mortality (RH = 2.31 (95% confidence interval: 1.38, 3.88) and 2.76 (95% confidence interval: 1.46, 5.19), respectively), which remained significant after adjustments for the various categories of risk factors (data not shown).

The patterns of association that were observed for all-cause mortality were also apparent for noncardiovascular mortality. That is, a dose-response relationship was noted among the unhealthy group with both moderately and highly hopeless men at significantly elevated risk of noncardiovascular death (RH = 2.44 (95% confidence interval: 1.37, 4.37) and 2.89 (95% confidence interval: 1.42, 5.86), respectively), whereas for healthy men, risk was elevated among the most hopeless subjects only (RH = 1.21 (95% confidence interval: 0.46, 3.21) and 3.83 (95% confidence interval: 1.20, 12.2) for the moderate and high scorers, respectively) (Fig. 2). After adjusting for the various categories of risk factors, the increased risk of noncardiovascular mortality for unhealthy men remained significant, whereas the risk for the healthy men with high hopelessness scores remained elevated but became marginally significant (data not shown).

DISCUSSION

In this study, a simple 2-item measure of hopelessness was significantly associated with increased risk of all-cause mortality. Subsequent analyses of cause-specific mortality showed that hopelessness was

significantly related to death from both cardiovascular and noncardiovascular causes, including malignancies and all other internal or disease-related causes, and external causes, the majority of which were unintentional injuries. Hopelessness also significantly predicted first MI in the subset of participants with no known history of angina or MI. For the most part, adjustment for a broad array of biological, behavioral, social, psychological, and demographic risk factors or a positive disease history did not have a major effect on the elevated risk associated with high levels of hopelessness. Indeed, the observed relationships between hopelessness and mortality and incident MI were still evident in models that simultaneously adjusted for all risk factors. Of course, it is possible that certain variables that are part of the critical pathway between hopelessness and the various outcomes were excluded from our analyses or that some measures used had limited precision. However, the list of risk factors reflects a wide variety of potential pathways, and the measures used were collected using standardized protocols, and, in most cases are importantly associated with the outcomes. Thus, the pattern and robustness of the observed associations are particularly striking.

Although various researchers have measured hope (1, 4) and hopelessness (5) and have examined these constructs in relation to their physical and mental health effects, this is the first empirical study to show reliable associations between hopelessness and a broad range of mortality outcomes. Our findings are consistent with the NHEFS study that identified hopelessness as an independent predictor of IHD morbidity and mortality (11) and with several studies that have shown that vital exhaustion, of which hopelessness is one component, is importantly related to coronary heart disease outcomes (17–19). Our results also provide support for the idea that hopelessness can be distinguished from depression, particularly in relation to its health impact (27).

To our knowledge, no previous study has reported that hopelessness is related to incident cancer in a population-based sample, independent of behavioral, psychosocial, or sociodemographic risk factors. As more incident cancer cases become available, we will be able to conduct detailed analyses on the relationship between reported hopelessness and specific types of cancer. Our finding that hopelessness is independently associated with deaths due to cancer both replicates and extends previous research that has shown that hopelessness is associated with poorer survival among cancer patients (8–10). Approximately one-third of cancer deaths in this study were due to lung cancer, 25% were due to esophageal, stomach, or colorectal cancer, 12.5% were due to liver or kidney cancer, and the remaining 30% of cancer deaths were due to skin (5%), brain (5%), or other types of cancer. These small numbers did not allow us to separately examine whether or not hopelessness was associated with increased risk for specific types of cancer. The different kinds of cancer seen among our population and the pattern of results would suggest, however, that the effect of hopelessness is not limited to a particular cancer.

It is perhaps surprising that a simple and straightforward scale based on only two items can be so strongly and consistently related to a variety of mortality outcomes. The two items are moderately intercorrelated (r = .53), suggesting somewhat limited internal consistency. However, prior research has assessed hopelessness in various ways (1, 2, 4, 5, 11), and there is no "gold standard" by which to measure this construct. The items in our scale assessed feelings of hopelessness with regard to the future and the impossibility of reaching goals, concepts that are recognized as important in the definition of hopelessness (2, 5). These may be the most important aspects of hopelessness with respect to morbidity and mortality. Of interest, the individual items also were significantly related to mortality outcomes (age-adjusted RH for all-cause mortality was 2.11 (95% confidence interval: 1.51, 2.94) for the 14.7% of subjects who agreed with the item "The future seems hopeless . . . " and 1.83 (95% confidence interval: 1.35, 2.47) for the 28.7% of subjects who agreed with the item "It is impossible for me to reach my goals . . . "), indicating that each component contributed important variance to the observed associations. Nevertheless, the combined scale was most discriminating (Table 1). The one item from the General Health Questionnaire that significantly predicted IHD morbidity and mortality in the NHEFS (11) asked, "(During the past month), have you felt so sad, discouraged, hopeless or had so many problems that you wondered if anything was worthwhile?" and thus also assessed an individual's feelings of futility regarding the future. It appears then that this sense of giving up with regard to the future and one's personal goals has a particularly negative influence on health, which is consistent with both anecdotal reports in the clinical literature and public perceptions about the importance of hope (2).

It should be noted that hopelessness appears to be a relatively distinct psychological construct. Correlation analyses revealed small, albeit significant, associations between scores on the hopelessness scale and the MMPI Depression scale (r = .27) and the measures of social connections (r ranged from

−.18 to −.26) that were used as covariates in our models. Furthermore, hopelessness shared limited variance with self-ratings of poor health (r = .20). Thus, despite public perception or conventional "wisdom" that hopelessness is interchangeable with feelings of depression or isolation or a reflection of illness, our data indicate otherwise.

The pattern of results observed in this study is reminiscent of those that have led others to the notion of generalized resistance (35) and, more recently, the concept of allostatic load, which refers to the cumulative effect of stress-induced wear and tear on organ systems (36). These notions suggest that individuals in interaction with their environment develop a set of behavioral, social, psychological, and physiological adaptations or adjustments that have a cumulative, generic effect on health. That high levels of hopelessness were consistently associated with increased morbidity and mortality, independent of classic risk factors, in our data suggests that hopelessness may be a maladaptive psychological response that has a ubiquitous, negative impact on health. The pathophysiological mechanisms that mediate this effect are not known. Research has shown, however, that emotional states are associated with distinct cardiovascular, immunological, and neuroendocrine patterns of activation (37–39), and there is growing evidence for both direct anatomical and functional links between the central nervous system and the immune system (40). It may be that hopelessness operates through a variety of psychoneuroimmunological pathways.

The strength of our observed associations underscores the need to try to understand the individual, social, and environmental conditions that lead to the development of hopelessness. Our study was not designed to address this issue. However, we identified some interesting cross-sectional associations that may provide some clues. We found that increasing levels of hopelessness were significantly associated with increasing levels of depressive symptoms and decreasing levels of social support. Also, those who reported higher levels of hopelessness were less likely to report being financially secure, had lower incomes and less education, and were more likely to be current smokers and binge drinkers. Among smokers, there was a dose-response relationship between hopelessness and pack-years of cigarettes; similarly, among those who drank alcohol, average consumption of alcoholic beverages increased with increasing levels of hopelessness. Taken together, these findings indicate that poorer socioeconomic conditions, more unhealthy behaviors, and increasing levels of psychological distress accompany increasing levels of hopelessness. It is interesting to note, however, that adjustments for these various risk factors in the survival analyses generally did not diminish the observed dose-response relationships between hopelessness and mortality. This relative lack of confounding between hopelessness and behavioral, socioeconomic, and psychological factors studied here implies that the negative health impact of hopelessness is mediated through other, as yet unmeasured characteristics or unidentified pathways. The fact that the associations between hopelessness and mortality remained essentially intact in Cox models that simultaneously adjusted for the various categories of risk factors supports this idea. Additional prospective studies are required to disentangle cause-effect relationships between hopelessness and other psychosocial, behavioral, and sociodemographic characteristics that may contribute to negative health outcomes.

Among those subjects with a positive history of disease, a dose-response relationship between hopelessness and death due to any cause was identified with moderate and high scorers on the measure of hopelessness at approximately two to three times the risk of low scorers. However, among those without a history of disease, overall mortality was approximately five times greater for high scorers but was not elevated among moderate scorers. This pattern, also evident for noncardiovascular mortality, suggests that, in the absence of illness, hopelessness has pronounced deleterious effects at high levels only. In contrast, when underlying illness is present, hopelessness exerts its negative effect at lower levels. It may be that knowledge of one's disease contributes to feelings of hopelessness, which may be moderate or more pronounced depending on other life circumstances and experiences, and that the interactions among these factors lead to increasing risk of mortality with increasing levels of hopelessness. Among otherwise healthy individuals, however, feelings of hopelessness may be more related to psychological factors than to physical health factors and thus may not contribute to mortality until they reach high levels. Perhaps the pathophysiological mechanisms that underlie the associations between hopelessness and mortality also differ according to disease history. It remains a task of future studies to test these or alternative hypotheses about hopelessness, health status, and mortality.

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