

Chronic Work Stress and Marital Dissolution Increase Risk of Posttrial Mortality in Men From the Multiple Risk Factor Intervention Trial

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Background: Acute life stressors can trigger premature death, but the role of more enduring, chronic stressors is less clear. We evaluated men's mortality risk associated with number of different work stressors and marital dissolution during the Multiple Risk Factor Intervention Trial (MRFIT).

Methods: Men without definite evidence of coronary heart disease (CHD) at study entry but with above-average risk for CHD mortality based on blood pressure, serum cholesterol levels, and/or cigarette smoking were recruited into MRFIT. Survivors at the end of the trial were followed up for mortality for an additional 9 years. All 12 336 survivors who completed the work-event checklist at the annual evaluations during the trial were included in the analyses of work stressors, whereas the 10 904 who were married at the start of the trial were included in the analyses of marital dissolution.

Results: Increasing number of different work stressors and divorce during the trial were associated with total and cardiovascular mortality during the 9-year follow-up period ($P < .01$ for linear trend), with a relative risk of 1.26 (95% confidence interval, 1.07-1.48) for those reporting 3 or more different work stressors compared with those reporting none, and relative risk of 1.37 (95% confidence interval, 1.09-1.72) for those who divorced compared with those who remained married for total mortality. Analyses were adjusted for age, intervention group, educational attainment, occurrence of a nonfatal cardiovascular event during the trial, smoking, diastolic blood pressure, alcohol consumption, and serum cholesterol level (the last 4 adjustments were trial averages).

Conclusion: Work and marital stressors increase risk for mortality in men.

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ACUTE LIFE stressors, including such diverse events as bereavement, earthquakes, terrorist activities, missile strikes, and episodes of extreme anger, can trigger myocardial infarction and death.¹⁻⁴ Less clear is the association of mortality with chronic, more enduring life stress and the accumulation of stressful life experiences across years.

Work-related stress is the most widely studied chronic life stressor relevant to cardiovascular disease (CVD).⁵⁻⁸ Individuals employed in jobs they or others describe as high in work strain, ie, jobs with high demands for performance and low decision-making latitude or with high demands and low rewards, are at elevated risk for all-cause and CVD mortality.^{6,9,10} However, individuals do not occupy jobs at random, and other characteristics, eg, low socioeconomic status, correlated with jobs that are demanding and low in control or reward, may account for the association between the work strain and elevated risk for

coronary mortality. Stated differently, job strain may be a pathway by which socioeconomic status has an impact on health. Indeed, statistical adjustments for cardiovascular risk factors and occupational prestige substantially reduce the effect size of job strain or reward on mortality.^{9,10}

Another important life stressor is an unhappy marriage, which can result in separation and divorce.¹¹ International studies show that divorced men have higher mortality rates than married men.¹² This pattern could result from certain biases, eg, married men who are quite ill could be "rejected" because they can no longer perform the breadwinner role, or divorced men in poor health could take longer to find a suitable new partner.¹³ On the other hand, divorce may have a negative effect on mental health, including increased negative affect, reduced sense of purpose and identity, and altered relationships with children and community, all of which may have physiological costs. The effects of marital dissolution could spill over to the quality

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SUBJECTS AND METHODS

DESIGN OF THE MRFIT

Screening for the MRFIT involved 361 662 men aged 35 to 57 years at 22 clinical centers in 18 US cities. On the basis of this initial screening, 12866 men were recruited into the trial without definite evidence of clinical coronary heart disease (CHD) but with above-average risk for death due to CHD because of high blood pressure, elevated serum cholesterol levels, and/or cigarette smoking.¹⁵⁻¹⁷ After recruitment, the MRFIT involved randomization of participants into special intervention (n=6428) or usual care groups (n=6438). The special intervention involved intervention visits designed to alter eating patterns to reduce the intake of saturated fats and cholesterol, to reduce weight, and to achieve smoking cessation. Details of the multifactor intervention program are described elsewhere.^{18,19}

MEASUREMENT OF WORK AND MARITAL STRESS

A checklist of life events was administered at study entry and during the first, second, third, fourth, and fifth annual examinations. This checklist did not include an option for indicating that an event had not occurred. As a result, a missing response on items in this questionnaire did not enable differentiation of missing data from intentional indications that an event had not occurred. However, the life-events checklist was administered along with a number of other questionnaires; therefore, we treated data as missing for participants with known missing data for 5 forced-choice questions that directly preceded or followed (depending on year) the life-events questionnaire. Missing data increased steadily from baseline (n=64 [0.5%]) to year 5 (n=1550 [12.0%]) because of participant death, missing questionnaire data, or study attrition.

The work-stress measure contained 7 life events (**Table 1**). These 7 items were associated with "feelings

of being overwhelmed by difficult life situations" using a χ^2 analysis of the entire sample, suggesting these items are experienced as stressors by most people. An eighth work item, retirement, was not associated with such feelings, and therefore was excluded. Repeated reports of an event (eg, being demoted) could reflect either multiple events or the participants' conceptualization of the event (eg, the demotion per se vs continued employment in a demoted position). In consequence, regardless of the number of times a participant reported the occurrence of a single event, the number of different stress domains with an occurrence reported at some time during the trial (at study entry and during the first through fifth annual examinations) was used. In the analysis of posttrial deaths, 4 groups (0, 1, 2, and ≥ 3 domains) were considered.

A question regarding marital status was administered at the start of the trial to identify those currently married. The life-events questionnaire included the following 3 relevant events: "separation from your wife because of marital problems," "starting to live with your wife again after having been separated," and "getting divorced." The response proportions of participants are shown in Table 1. For participants married at the start and alive at the end of the trial, the following 3 distinct categories were used: married during the trial (those not reporting separation or divorce), separated during the trial (those reporting a separation and/or reunion after separation during the trial but not reporting divorce), or divorced during the trial. Most trial survivors (n=10904 [88.4%]) were classified into 1 of these 3 categories (n=9817 for married, n=513 for separated, and n=574 for divorced).

RISK FACTOR ASSESSMENT

The following risk factors were considered: age at study entry, MRFIT group assignment (special intervention vs usual care), education measured on a scale from 1 (eighth grade or less) to 9 (graduate or professional degree), and measurements of diastolic blood pressure (DBP) (defined as the

of men's work life, leading to additional risk associated with the accumulation of work stressors.

The objective of the present study was to evaluate the effects of chronic work stress and marital dissolution on 9-year all-cause and CVD mortality in a large cohort of men enrolled in the Multiple Risk Factor Intervention Trial (MRFIT).¹⁴ Rather than categorize work stress indirectly by occupation or by self-reported subjective characteristics of the occupation, we assessed the accumulation of different types of work stressors across 6 years. To reduce the likelihood of interpretative ambiguities, we assessed the effects of marital dissolution only among those married at entrance into the MRFIT. Very detailed information regarding major cardiovascular risk factors was available to serve as statistical controls for health status.

RESULTS

CHARACTERISTICS OF PARTICIPANTS AS A FUNCTION OF WORK AND MARITAL STRESS

Differences in characteristics of survivors of the MRFIT as a function of reported stress during the trial are shown

in **Table 2** (work stress) and **Table 3** (marital status). Those experiencing high work stress during the trial were significantly younger at study entry, more likely to report cigarette smoking, more educated, and more likely to experience a nonfatal cardiovascular event during the trial ($P < .05$ for linear trends or χ^2 , depending on the variable) relative to those reporting no work stressors. Those reporting separation or divorce from a spouse during the trial were significantly younger at study entry, more likely to report cigarette smoking, and more educated and had lower serum cholesterol levels ($P < .01$ for linear trends or χ^2 , depending on the variable) relative to married participants.

WORK STRESS DURING THE TRIAL PREDICTING POSTTRIAL MORTALITY

Increasing numbers of different work stressors during the trial were associated with a significantly increased (based on linear trend analysis) risk for death due to all causes (RR, 1.15; $P < .01$) and CVD (RR, 1.26; $P < .003$). There was no association with non-CVD death, although neoplastic disease was inversely associated (RR, 0.83; $P = .09$)

average of 2 random-zero manometer readings), serum cholesterol concentration, and cigarette smoking (yes vs no) during annual examinations. Diastolic blood pressure (DBP), serum cholesterol level, and smoking were averaged across the available examination results for analytic purposes. Further details regarding these assessments are published elsewhere.^{20,21}

MORBIDITY AND MORTALITY ASCERTAINMENT

A nonfatal cardiovascular event during the trial was defined as angina or intermittent claudication by Rose questionnaire criteria,²² congestive heart failure, peripheral arterial occlusive disease, stroke, left-ventricular hypertrophy on electrocardiographic findings, impaired renal function, accelerated hypertension, coronary artery bypass surgery, serial electrocardiographic evidence of myocardial infarction, or definite clinical myocardial infarction.²³ Men were also asked in year 6 whether they were unemployed and the reason for their unemployment, which included disability and its cause. Causes included heart disease and circulatory disease.

Before the end of the trial in February 1982, deaths were ascertained using next-of-kin interviews, routine follow-up of missed clinic visits, responses to postcards sent to the usual care participants, and searches of publicly accessible files of deceased persons. Cause of death was assigned by a 3-member panel of cardiologists not associated with the MRFIT and unaware of the participants' group assignment. Details regarding ascertainment of mortality during the trial have been previously reported.¹⁴ Since February 1982, vital status has been ascertained by matching identifying information reported by participants at the time of enrollment with the National Death Index. The latest search of the National Death Index was for all deaths through December 1990 and is considered to be essentially 100% complete.²⁴ To determine cause of death, death certificates were collected and coded independently by 2 nosologists using the *International Classification of Diseases, Ninth*

Revision (ICD-9).¹⁴ Disagreements between the nosologists were adjudicated by a third nosologist. The ICD-9 codes corresponding to the cause-specific mortality categories considered in this study are reported elsewhere.¹⁴

STATISTICAL ANALYSES

Differences in participants' characteristics were tested as a function of the number of work stressors during the trial (grouped into 0, 1, 2, and ≥ 3 different stressors) and marital status using 2 analyses for dichotomous data and analyses of variance with linear trend analysis for continuous data.

Mortality after the trial was analyzed using Cox proportional hazard regression equations and 95% confidence intervals (CIs) for the relative risks (RRs) associated with the number of work stress domains represented during the trial or the occurrence of separation or divorce during the trial. To control for possible confounding variables, additional analyses included age, MRFIT group assignment, DBP, serum cholesterol level, cigarette smoking, and alcohol consumption (with the last 4 variables averaged across the available trial examinations) as covariates. Nonfatal cardiovascular event during the trial was also included as an additional control variable in further analyses of all-cause and CVD mortality. Contrasts were used to determine RRs corresponding to the comparison of no reported life stress with increasing numbers of different life stressors (ie, 1, 2, and ≥ 3) and the comparison of married with ever separated or ever divorced status. A polynomial contrast was specified to determine whether a significant linear trend was associated with the change in RRs across stress groups. A significant linear trend would suggest that an increasing number of stressors or increasing stress from marriage to divorce was associated with increasing risk for mortality. A test for the interaction of work stress and marital dissolution with the main effects in the model was conducted among those who were married at the beginning of the trial to evaluate whether the effects of work and marital stress were additive or interactive.

and digestive disorders were positively associated (RR, 2.22; $P = .004$).

With the addition of covariates, these results remained essentially unchanged (**Table 4**). However, the reduced risk for death due to neoplastic disease was no longer marginally significant (new $P = .31$). For work stress, significant linear trends demonstrated that an increasing number of different work stressors were associated with a significantly greater risk for death due to all causes ($P = .004$), CVD ($P = .006$), and digestive disorders ($P = .001$). Within the CVD category, cause of death was further categorized into a CHD category, including acute myocardial infarction (ICD-9 code 410) and other ischemic (coronary) heart disease (ICD-9 codes 411-414 and 429.2). An increasing number of work stressors were not associated with an increasing risk for acute myocardial infarctions ($P = .16$ for linear trend) but were significant for other ischemic (coronary) heart disease ($P = .02$ for linear trend). These trends reflect an increasing risk associated with greater numbers of different work stressors. For non-CVD mortality, an increasing number of work stressors was associated with an increasing risk for death due to digestive disorders ($P = .001$ for lin-

ear trend). This category of non-CVD death does not include deaths due to neoplastic disease associated with the digestive organs and peritoneum (ICD-9 codes 150-159); most of these deaths ($n = 32$) were due to liver disease (ICD-9 code 571). However, the linear trend associated with an increasing number of work stressors was unchanged when average alcohol consumption during the trial was added as a covariate ($P = .001$).

The above analyses considered the effect of a progressively greater number of different work stressors on mortality. We also considered the impact of specific work stressors (present vs not present during the trial) on posttrial mortality. After the inclusion of covariates (eg, DBP and occurrence of a nonfatal CVD event), the following work stressors were significantly associated with all-cause mortality: failure of a business (RR, 1.46 [95% CI, 1.09-1.94]; $P = .01$), being fired or laid off work (RR, 1.29 [95% CI, 1.05-1.60]; $P = .02$), and not being able to work because of a disability (RR, 1.59 [95% CI, 1.35-1.88]; $P < .001$). The following work stressors were significantly associated with CVD mortality: being fired or laid off work (RR, 1.21 [95% CI, 1.03-1.41]; $P = .02$) and not being able to work because of a disability (RR, 1.40

[95% CI, 1.24-1.59]; $P < .001$). The following work stressors were significantly associated with deaths due to digestive system disease: demotion (RR, 2.58 [95% CI, 1.21-5.48]; $P = .01$), inability to work because of a disability (RR, 2.47 [95% CI, 1.36-4.47]; $P = .003$), and personal troubles with coworkers (RR, 2.47 [95% CI, 1.43-4.27]; $P = .001$).

The strength of the association between mortality and work disability (particularly with CVD mortality) raises the possibility that the aforementioned effects of work stress on mortality are (1) spurious and reflect the effect of illness on work disability and subsequent risk for mortality, or (2) real and reflect the strong associations between work disability and work stress. There are several reasons to believe that the effects of work stress are real. First, when analyses of total mortality included unemployment due to any disability at the end of the trial

and the other covariates, including morbidity (ie, occurrence of a nonfatal CVD event), the linear trend for work stress remained statistically significant (RR, 1.15; $P = .01$). Unemployment due to any disability was also independently significant in this model (RR, 1.68; $P = .03$). Similarly, when analyses of CVD mortality included unemployment due to heart or circulatory disease at the end of the trial and the other covariates, including nonfatal CVD event, the linear trend for work stress remained statistically significant (RR, 1.22; $P = .01$), with unemployment due to heart or circulatory disease also an independent predictor (RR, 2.73; $P = .001$). Second, as noted above, other work-stress domains, in addition to work disability, were independent predictors of total and CVD mortality. Finally, work stress (not including work disability) during the first half of the trial was significantly greater for those subsequently reporting a work disability relative to those not reporting a work disability during the second half of the trial (means, 0.89 and 0.75, respectively; $F_{1,12785} = 19.38$; $P < .001$). This finding suggests that work stress precipitated a work disability, not that a work disability (caused by illness) precipitated work stress.

Table 1. Events in Each Stress Domain and Percentage of Men Who Reported That Event Occurred

Stress Domain, Items/Response Option	Frequency, %
Work stress*	
"A change to a new type of work"	51.0
"A demotion"	6.7
"A business failure"	4.6
"Personal troubles with your boss, fellow workers, or people working under your supervision"	28.9
"Not being able to work because of disability"	15.9
"Being fired or laid off of work"	10.5
"Problems getting a new job"	9.1
Marital stress	
Status at start of trial	
Never married	4.2
Separated	1.8
Divorced	4.4
Widowed	0.9
Married	88.7
Events during the trial among married at the beginning of the trial	
"Separation from your wife because of marital problems" or "Starting to live with your wife after having been separated"	4.7
"Getting divorced"	5.3

*Events occurred at baseline and during the 6 years of the trial.

MARITAL STRESS DURING THE TRIAL PREDICTING POSTTRIAL MORTALITY

Increasing marital stress was associated with marginally significantly greater risk for death (based on linear trend analysis) due to all causes (RR, 1.14; $P = .10$) and CHD (RR, 1.26; $P = .06$) (data not shown). It was not associated with CVD and non-CVD deaths. Increasing marital stress was associated with a significantly increased risk for death due to CHD other than myocardial infarction (RR, 1.52; $P = .007$), digestive disorders (RR, 3.22; $P < .001$), and accidents (RR, 2.33; $P = .002$).

With the addition of covariates, these results were even stronger (**Table 5**). For marital stress, significant linear trends demonstrated that an increasing degree of marital stress was associated with a significantly greater risk for death due to all causes ($P = .006$), CVD ($P = .04$), CHD ($P = .004$), CHD other than myocardial infarction ($P < .001$), digestive disorders ($P < .001$), and accidents ($P = .003$).

Table 2. Characteristics of All MRFIT Survivors as a Function of the Number of Different Work Stressors During the Trial*

Characteristic	No. of Work Stressors During the Trial				P Value for Linear Trend or χ^2
	0 (n = 3715)	1 (n = 4402)	2 (n = 2482)	≥ 3 (n = 1737)	
Mean age at entry into study, y	47.16	46.21	45.90	45.30	<.001
% In special intervention	50.34	50.57	49.64	47.96	.29
Smoking, %†	44.24	44.55	48.33	53.91	<.001
Diastolic blood pressure, mm Hg†	86.8	86.5	86.2	85.8	<.001
Serum cholesterol level, mg/dL‡	239.9	240.5	241.0	238.3	.17
Education§	5.21	5.41	5.51	5.60	<.001
Nonfatal CV event during trial, %	16.88	20.63	25.22	28.38	<.001

*MRFIT indicates Multiple Risk Factor Intervention Trial; CV, cardiovascular.

†Trial means.

‡To convert to millimoles per liter, multiply by 0.0259.

§Measured using a 9-point scale ranging from 1 (eighth grade or less) to 9 (graduate or professional degree).

Table 3. Characteristics of MRFIT Survivors Married at the Beginning of the Trial as a Function of Marital Status During the Trial*

Characteristic	Married (n = 9817)	Separated (n = 513)	Divorced (n = 574)	P Value for Linear Trend or χ^2
Mean age at entry into study, y	46.57	44.94	44.03	<.001
% In special intervention	49.96	54.97	47.56	<.05
Smoking, %†	44.60	58.62	58.06	<.001
Diastolic blood pressure, mm Hg†	86.4	86.6	86.2	.56
Serum cholesterol level, mg/dL†‡	241.0	236.4	236.5	<.005
Education§	5.36	5.60	5.59	<.01
Nonfatal CV event during trial, %	21.38	24.56	21.95	.23

*Marital status was determined using a marital status question administered at the start and life-events questions administered throughout the trial. Only those reporting being married at the start of the trial (n = 10 904) were included in these analyses. Groupings were created as follows: married indicates all married participants having no report of separation or divorce during the trial; separated, all participants reporting being separated or reunited after being separated but with no report of divorce; and divorced, all participants reporting divorce during the trial. Abbreviations are given in the first footnote to Table 2.

†Trial means.

‡To convert to millimoles per liter, multiply by 0.0259.

§Measurement is explained in the fourth footnote to Table 2.

Table 4. Cause of Death and Relative Risk During the 9-Year Posttrial Period Associated With Work Stress*

Cause of Death (No. of Deaths)	No. of Different Work Stressors During Trial, RR (95% CI)				P Value for Linear Trend
	0 (n = 3688)	1 (n = 4381)	2 (n = 2478)	≥3 (n = 1730)	
All causes (1505)	1.00	1.12 (0.98-1.27)†	1.19 (1.03-1.38)‡	1.26 (1.07-1.48)§	.004
All cardiovascular (771)	1.00	1.07 (0.89-1.29)	1.19 (0.97-1.46)†	1.34 (1.07-1.67)‡	.006
CHD (539)	1.00	1.10 (0.88-1.36)	1.41 (1.11-1.78)§	1.35 (1.03-1.76)‡	.007
Acute MI (270)	1.00	1.26 (0.92-1.73)	1.50 (1.07-2.12)‡	1.27 (0.85-1.89)	.16
Other CHD (289)	1.00	0.96 (0.70-1.30)	1.32 (0.96-1.83)†	1.42 (0.99-2.02)†	.02
All noncardiovascular (732)	1.00	1.16 (0.97-1.40)†	1.20 (0.97-1.48)†	1.16 (0.91-1.47)	.22
Neoplastic disease (488)	1.00	1.05 (0.85-1.31)	1.11 (0.86-1.42)	0.83 (0.61-1.14)	.31
Respiratory disease (43)	1.00	2.25 (0.93-5.44)†	3.12 (1.23-7.87)‡	2.15 (0.72-6.48)	.13
Digestive system disease (53)	1.00	1.38 (0.64-2.98)	1.55 (0.65-3.68)	3.71 (1.69-8.13)§	.001
Accidents (57)	1.00	0.86 (0.44-1.70)	0.82 (0.36-1.85)	1.84 (0.89-3.77)†	.13

*In all Cox proportional hazard models, the following characteristics were included as covariates: age, study group (special intervention vs usual care), educational attainment, occurrence of nonfatal cardiovascular event during the trial, smoking, diastolic blood pressure, alcohol consumption, and serum cholesterol level (the latter 4 variables were trial averages). Relative risks (RRs) correspond to comparison between no stress and increasing numbers of different work stressors (ie, 0, 1, 2, or ≥3). Numbers vary slightly from those in Table 2 because of missing covariate values in each analysis. CI indicates confidence interval; CHD, coronary heart disease; and MI, myocardial infarction.

† $P < .10$.

‡ $P < .05$.

§ $P < .01$.

ACCUMULATION OF WORK AND MARITAL STRESS DURING THE TRIAL PREDICTING POSTTRIAL MORTALITY

Marital status and work stress were strongly associated ($\chi^2 = 233.34$; $P < .001$). The proportion of participants reporting a separation or divorce steadily increased as the number of work stress domains increased (0, 6.5%; 1, 8.2%; 2, 11.9%; and ≥3, 19.7% reporting separation or divorce). Despite this association, marital status (RR, 1.23; $P = .01$) and work stress (RR, 1.16; $P = .02$) had independent effects on all-cause mortality in Cox models with both variables simultaneously entered. Therefore, work stress does not appear to function merely as a proxy for marital stress, or vice versa.

After entering the main effects for work and marital stress, the interaction term was entered. The interaction between the linear components of marital stress and work stress was significant ($P = .04$). To further analyze this interaction, work stress was considered within each

marital stress group. Work stress was not significantly associated with an increased risk for death (based on linear trend) due to all causes for married (RR, 1.11 [95% CI, 0.97-1.27]; $P = .14$) or separated (RR, 0.81 [95% CI, 0.50-1.31]; $P = .39$) men. However, for divorced men, an increasing number of work stressors during the trial was associated with a significantly increased risk for death due to all causes (RR, 1.69 [95% CI, 1.06-2.70]; $P = .03$ (**Figure**)). Results of the interaction tests for CVD mortality were nonsignificant, presumably because of small numbers.

COMMENT

The present study provides unique and strong evidence that the accumulation of different work stressors and separation or divorce during the 7 years of the MRFIT trial are predictors of subsequent all-cause and CVD mortality during the 9-year follow-up among men. These findings are statistically significant in analyses adjusting for

Table 5. Cause of Death and Relative Risk During the 9-Year Posttrial Period Associated With Marital Status*

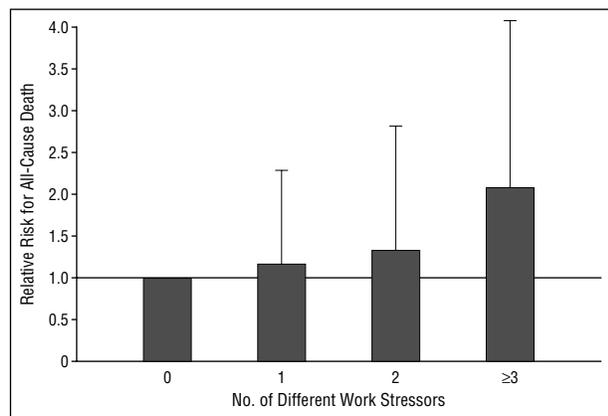
Cause of Death (No. of Deaths)	Marital Event During Trial Among Married Men at the Beginning of the Trial, RR (95% CI)			P Value for Linear Trend
	Married (n = 9816)	Separated (n = 513)	Divorced (n = 574)	
All cause (1332)	1.00	1.24 (0.98-1.57)†	1.37 (1.09-1.72)‡	.006
All cardiovascular (663)	1.00	1.43 (1.05-1.96)§	1.40 (1.01-1.92)§	.04
CHD (498)	1.00	1.02 (0.67-1.57)	1.66 (1.17-2.36)‡	.004
Acute MI (244)	1.00	1.31 (0.76-2.26)	1.15 (0.64-2.06)	.64
Other CHD (254)	1.00	0.74 (0.36-1.50)	2.17 (1.40-3.36)‡	<.001
All noncardiovascular (648)	1.00	1.04 (0.72-1.49)	1.37 (0.99-1.89)†	.06
Neoplastic disease (438)	1.00	0.77 (0.47-1.28)	0.94 (0.59-1.50)	.80
Respiratory disease (40)
Digestive system disease (42)	1.00	1.63 (0.49-5.39)	5.22 (2.44-11.17)‡	<.001
Accidents (50)	1.00	0.43 (0.06-3.13)	3.20 (1.48-6.89)‡	.003

*In all Cox proportional hazard models, the following characteristics were included as covariates: age, study group (special intervention vs usual care), educational attainment, occurrence of nonfatal cardiovascular disease during the trial, smoking, diastolic blood pressure, alcohol consumption, and serum cholesterol level (the latter 4 variables were trial averages). Relative risks (RRs) correspond to comparison between married vs separated or divorced. Numbers vary slightly depending on the number of participants with missing covariate values in each analysis. Other abbreviations are defined in the first footnote to Table 4. Ellipses indicate insufficient number of events for calculation of RR.

†P<.10.

‡P<.01.

§P<.05.



Relative risk with 95% confidence intervals of all-cause mortality during the posttrial follow-up as a function of work stress during the trial for divorced men only.

age, study group, educational attainment, occurrence of nonfatal CVD during the trial, smoking status, DBP, alcohol consumption, and serum cholesterol level. Subsidiary analyses also showed that statistical controls for unemployment due to disability did not affect the results for work stress. Thus, the effects of work stressors and separation or divorce were unlikely to be due solely to poor health status leading to more work stress or marital dissolution or due to work stress being a marker for low socioeconomic status (at least as indexed by educational attainment).

Furthermore, the accumulation of different work stressors among those men married at the beginning of the trial had the most adverse impact on all-cause mortality among those who were subsequently divorced during the trial. Thus, a synergistic adverse effect may occur when different domains of stressors co-occur in individuals' lives. Conversely, the accumulation of different work stressors did not affect the mor-

tality experience of those who remained married throughout the trial, suggesting that remaining married in midlife has protective effects in the face of adverse experiences at work.

This study had several limitations. First, the findings are restricted to men. Indeed, in contrast to the present findings, a recent study of female patients with coronary disease showed that work stress was not related to subsequent morbidity, although marital stress was.²⁵ Second, the work-stress checklist was imperfect, as it did not include an explicit indicator of no event or a rating of duration or intensity of the stressor. Furthermore, the cause or severity of work disability on the checklist was not known, although it was known whether work disability was severe enough to lead to unemployment at the end of the trial. Finally, although all analyses included covariate measures of health status that were carefully collected in a standardized fashion, with particular attention to CVD risk, unmeasured illnesses during the trial could affect both stress and mortality.

How does work stress or marital dissolution increase the risk for mortality? Work stress and marital dissolution may result in increasing levels of standard risk factors after the cessation of the trial. We are not able to evaluate this possibility, because MRFIT participants were not seen in the clinics after the conclusion of the trial. Work stress and marital dissolution can affect health behaviors, eg, by increasing smoking and alcohol consumption, altering dietary pattern, and disturbing restful sleep.^{26,27} However, for the most part, we were able to control statistically for these health behaviors, so other factors probably played an important role. Stress has an impact on a number of systems relevant to CVD mortality that were not assessed in MRFIT. In particular, stress may increase levels of circulating catecholamines, ambulatory blood pressure, and cortisol^{28,29}; may reduce heart rate variability and impair vagal tone^{30,31}; and may en-

hance platelet reactivity and release of platelet products.³² Stress also increases susceptibility to infectious disease^{33,34} and contributes to rapid progression in human immunodeficiency virus infection.^{35,36} Work stress and marital dissolution may result in poor decision making, causing risky behaviors.³⁷ Our data provide indirect support for this notion, because those men who reported more types of work stressors and divorce during the trial also tended to be at risk for accidental death.

Chronic stress at work or in primary relationships is subject to intervention at a clinical level and through work-based programs. As suggested by Rozanski et al,⁵ integrating psychosocial interventions at a clinical level is feasible by having physicians counsel their patients regarding psychosocial risks, by evaluating and implementing preventive interventions in clinical settings on a patient-specific basis, and by modifying the pathophysiological pathways connecting stress and early death. Work-based programs can provide counseling and training for resolving conflicts with bosses and coworkers. Avoiding marital strife, especially when stressed by work difficulties, can be assisted by adequate counseling and support mechanisms.

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