

# Stress Reduction Prolongs Life in Women With Coronary Disease

## The Stockholm Women's Intervention Trial for Coronary Heart Disease (SWITCHD)

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**Background**—Psychosocial stress may increase risk and worsen prognosis of coronary heart disease in women. Interventions that counteract women's psychosocial stress have not previously been presented. This study implemented a stress reduction program for women and investigated its ability to improve survival in women coronary patients.

**Methods and Results**—Two hundred thirty-seven consecutive women patients, aged 75 years or younger, hospitalized for acute myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention were randomized to a group-based psychosocial intervention program or usual care. Initiated 4 months after hospitalization, intervention groups of 4 to 8 women met for a total of 20 sessions that were spread over a year. We provided education about risk factors, relaxation training techniques, methods for self-monitoring and cognitive restructuring, with an emphasis on coping with stress exposure from family and work, and self-care and compliance with clinical advice. From randomization until end of follow-up (mean duration, 7.1 years), 25 women (20%) in the usual care and 8 women (7%) in the stress reduction died, yielding an almost 3-fold protective effect of the intervention (odds ratio, 0.33; 95% CI, 0.15 to 0.74;  $P=0.007$ ). Introducing baseline measures of clinical prognostic factors, including use of aspirin,  $\beta$ -blockers, angiotensin-converting enzyme inhibitors, calcium-channel blockers, and statins into multivariate models confirmed the unadjusted results ( $P=0.009$ ).

**Conclusions**—Although mechanisms remain unclear, a group-based psychosocial intervention program for women with coronary heart disease may prolong lives independent of other prognostic factors. (*Circ Cardiovasc Qual Outcomes*. 2009;2:25-32.)

**Key Words:** coronary heart disease ■ women ■ psychosocial factors ■ intervention ■ mortality

Psychosocial factors have been widely found to increase risk and worsen prognosis in coronary disease.<sup>1,2</sup> These effects remain after statistical control for standard risk factors, suggesting that the risk associated with psychosocial burden is independent and real. Although women's major coronary disease occurs later in life, those women who have clinical events at a younger age have a worse prognosis than men.<sup>3</sup> Psychosocial factors have been hypothesized as relevant risk markers in this context, and risk profiles are known to differ between women and men.<sup>4,5</sup> For example, marriage has been shown to largely reduce cardiovascular risk in men, whereas stress from marriage increases risk in women.<sup>6</sup> In the Stockholm Female Coronary Risk study, marital stress was found to increase risk more strongly than job stress in female patients, even though they were all employed outside the home.<sup>7</sup> Despite these clinically significant findings, effective intervention methods to counteract women's psychosocial

stress have not been presented, and recent randomized behavioral intervention trials have failed to show cardiovascular benefits in women.<sup>8</sup>

Whereas most studies did not include women in sufficient numbers to examine gender differences, the Montreal Heart Study and the Enhancing Recovery in Coronary Heart Disease study were unique in that they recruited about as many female patients as male patients in their study groups. Interestingly, they found trends toward cardiovascular benefits in men, although there were no such effects in women.<sup>9,10</sup> Hence, there is a lack of knowledge about what constitutes an appropriate stress reduction intervention for women with coronary heart disease (CHD).

Because of the needs expressed by female coronary patients, we used a psychosocial intervention program based on cognitive behavior therapy principles,<sup>11</sup> in which we emphasized methods for reducing stress and coping with stress

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whether the stress originates from marriage or work. We used group meetings as the main therapeutic modality and ran same-sex groups with women only.<sup>12</sup> In a randomized clinical trial of women with CHD, we evaluated the program and followed patients for a period of up to 9 years.

## SUMMARY

- Psychosocial stress may accelerate atherosclerosis progression and worsen prognosis in women with coronary disease, but stress reduction programs that benefit women had not been identified before this trial.
- Psychosocial interventions that decrease mortality or improve rates of recurrence in women with coronary disease were not known.
- Based on findings from the Stockholm Female Coronary Risk study, we developed a cognitive stress intervention program for women who had experienced a severe coronary event.
- We randomized 237 women (mean age, 62 years) who were hospitalized in Stockholm for acute myocardial infarction or revascularization to either a group-based cognitive behavioral intervention or to usual care.
- Women who had experienced an acute coronary event received either 20 group-based sessions (4 to 8 women per group) for 1 year, or they received usual care only.
- Educational group sessions were aimed at improving knowledge of the heart, healthier lifestyle, training skills, and improving mastery of marital stress, coping with serious illness, counteracting anxiety and depression, improving social relations and social support, and practicing relaxation techniques.
- Over a mean of 7 years after entering the study, women in usual care had a mortality rate of 20%, whereas those in the psychosocial intervention had a mortality rate of 7%. No women were lost to follow-up.
- After multivariate control for clinical prognostic factors, the Stockholm Women's Intervention Trial for Coronary Heart Disease, using a group-based psychosocial intervention program for women with coronary disease, was shown to improve survival.

## Methods

### Study Organization

This study consisted of 237 women (mean age, 61.5±9.1 years; range, 35 to 75 years) who were consecutively hospitalized at the Karolinska University Clinics, Stockholm, Sweden, for acute myocardial infarction (AMI), coronary artery bypass grafting, or percutaneous coronary intervention. Among the patients recruited, about half had AMI, 20% had AMI but also underwent percutaneous coronary intervention or coronary artery bypass grafting, and 30% were hospitalized for percutaneous coronary intervention or for coronary artery bypass grafting only.

Women over 75 years of age, women who did not live in the hospital catchment area, women who did not speak Swedish, and

women who had serious comorbidity that prevented them from taking part in the program were not included.

A total of 387 patients met the inclusion criteria between August 1996 and January 2000. Of these, 150 patients declined to participate (n=140) or failed to show up for the baseline session and randomization (n=10). These patients were significantly older than the randomized patients (65 versus 62 years;  $P<0.001$ ). Of those who declined to participate, most reported that they were not able to commit to a 1-year intervention. Other reasons included inconvenience of transportation and unwillingness to participate in a group-meeting intervention program. The mean time between study enrollment and baseline assessment was 9 weeks (62 days), and the mean time between baseline measurement (and random assignment) and intervention was 7 weeks (49 days), yielding a mean of 16 weeks from enrollment to intervention.

### Randomization, Allocation, and Blinding

After eligibility determination and baseline assessment, the study coordinator obtained the treatment condition allocation from a hospital nurse who conducted such allocations for multiple studies and was not acquainted with the present study goals, procedures, or potential patients. The nurse allocated each patient to treatment condition based on unrestricted randomization, using a predetermined list of random numbers.

### Recruitment

Women were considered for enrollment and prescreened while they were still in the clinic, hospitalized for an acute event. Before the baseline and randomization session, those women who agreed to be contacted received a phone call from a hospital nurse who explained the purpose, procedures, and requirements of the study and invited the women to the baseline session. The 237 women who attended the baseline session provided their written consent and were randomized after the session. The project was approved by the Karolinska regional ethics committee.

### Assessments

At baseline, a detailed medical history, anthropometric measures, and blood samples were obtained. Prescribed medications were recorded and verified through scrutiny of hospital charts. Lifestyle factors including smoking history, educational level, and employment status were assessed. Weight was measured in kilograms and height in meters by the research nurse, and body mass index was expressed as weight (kg)/height (m<sup>2</sup>). A serum lipid profile was determined from fasting venous blood samples that were drawn by the research nurse. Total serum cholesterol and serum high-density lipoprotein levels were analyzed using standardized laboratory enzymatic methods.<sup>13</sup>

The Everyday Life Stress scale<sup>14</sup> was administered. This questionnaire includes 20 statements and refers to stress behaviors in everyday life situations expressed in terms of time urgency/impatience or easily aroused irritation/hostility (eg, "Other people's mistakes irritate me."). The scale correlates positively with the videotaped structured interview<sup>15</sup> used in the Recurrent Coronary Prevention Project.<sup>16</sup>

### Intervention

Two nurses with clinical experience from coronary care and independent consultation work with cardiac patients were recruited for this intervention. They received intensive training from an expert clinical psychologist. The contents of the program were focused on women's psychosocial risk-factor profile<sup>17</sup> and attempted to control behavioral risk factors, attenuate negative emotions, improve coping skills, reduce stress, and improve social support.<sup>17,18</sup>

The intervention methodology followed basic principles of cognitive behavioral intervention programs: communication of cardiovascular health knowledge, methods for self monitoring, recognizing cognitive distortions, cognitive restructuring, skills training, and role playing.<sup>11,19</sup>

The intervention was provided in 20 sessions, each 2 to 2.5 hours long. Groups consisting of 4 to 8 female patients met weekly for 10 weeks and thereafter monthly. They met during the day or in the evening to make participation possible for female patients who were working

and could not get time off. Groups met in the same location throughout the program, and the composition of the group was largely preserved. Sessions began with 5 to 10 minutes of relaxation, a technique to decrease arousal. Each session was focused on a given topic, with prepared educational material. Topics ranged from the cardiovascular system and its pathophysiology to clinical and behavioral risk factors. Opportunities for smoking cessation, for physical exercise, and for weight change were offered. The therapist made sure that every patient talked at each session. Some of these female patients reported never having talked freely in groups before. Within each session patients considered self-monitoring skills, recognition of cognitive distortions, and cognitive restructuring in their interactions.

Metaphors were frequently used to illustrate and facilitate understanding of adverse behavioral contexts. These were intended to help the patient to become aware of alternative interpretations in her own life context, and facilitate reinterpretations of life situations that were less threatening and emotionally loaded. Further topics were concerned with the negative emotional consequences of heart disease, hostility, depression, exhaustion, and stressful events at work and in the family, and were discussed along with strategies to cope with such emotions. Social relations, social roles, and social supports were highlighted, and traditional male and female roles in the work and family spheres were discussed. Finally, existential questions about life and death were raised along with strengths and weaknesses in each patient's personal life. By the end of the program, patient groups had become cohesive and mutually supportive of their participants, and many of them continued to meet socially long after the course. In all, 20 groups were run, each for a period of 1 year, and a total of 400 sessions were prepared, conducted, and monitored.

### Follow-Up

At 5 to 9 years of follow-up, we assessed all-cause mortality, using the hospital- and community-based registers of deaths and clinical events. These registers have been repeatedly shown to yield precise and reliable data.<sup>20,21</sup>

### Statistical Procedure

Baseline group comparisons of demographics, clinical measures, participation/nonparticipation, and follow-up time were conducted using a 2-sided *t* test or  $\chi^2$ /Fisher exact test. Empirical survival curves were produced using the Kaplan-Meier method to estimate proportions of surviving individuals by intervention status as well as by other subgroup status, and log-rank tests to evaluate statistical significance.

The hazard ratios and 95% CIs for all-cause mortality associated with intervention status were estimated using the Cox proportional hazard model. We assessed the potential statistical interactions between intervention status and statin use with the likelihood ratio test by including the individual variables and their cross-product term in the same model. In additional analysis, we examined more closely the possible interactions between intervention groups and statin use to address whether the effect of statins may vary by psychosocial intervention. To further determine whether modifying effects were present, we examined mortality risk and intervention status within different strata according to statin use/nonuse. Finally, the hazard ratios for all-cause mortality associated with intervention status and its combinations were estimated.

All multivariate models reported included the following covariates: age, education, diagnosis at index event, and relevant medications. In the primary analyses, we began with univariate analyses, which were followed by multivariate adjusted analyses that introduced covariates one at a time. At the end, all covariates that were significantly related to mortality were kept in the model. In all models, age was entered as a continuous variable. Education ( $\geq 8$  years [mandatory] versus  $< 8$  years), diagnosis at index event (AMI alone versus other diagnoses), and medications prescribed (yes versus no) were entered as dichotomous variables. An intention to treat principle was applied to all statistical analyses. As hard end points from studies of women have not been reported, we based our assumptions of necessary sample size on a study of men, using a similar intervention method, with a follow-up time of 4.5 years.<sup>16</sup>

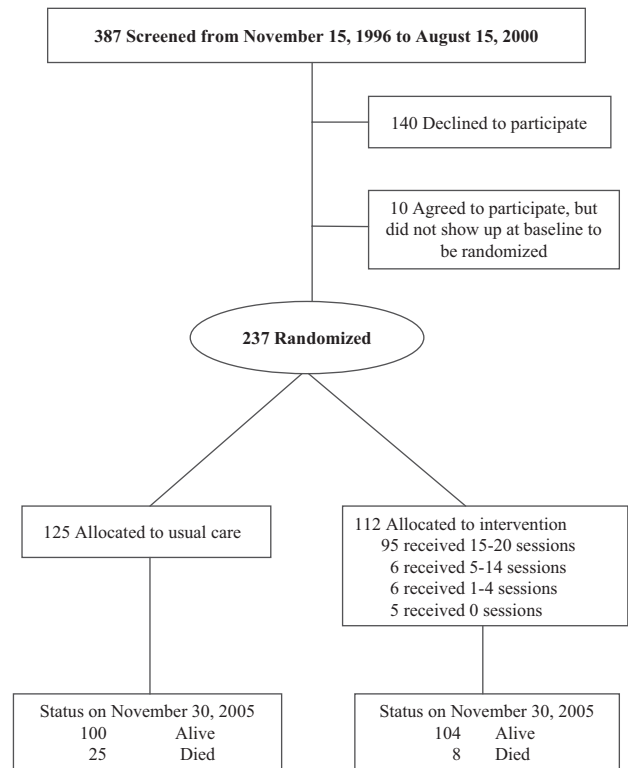


Figure 1. Flow diagram of subject progress.

That study reported a mortality rate in the control group of 11% and in the intervention group it was 5.2%, yielding a hazard ratio of 0.47. To have 80% study power to detect a significant effect of the intervention ( $P=0.05$ ; 2-sided), a total of 220 patients had to be included, 110 in each group. To obtain complete groups, we included 112 intervention female patients. Based on the previous study, we expected a 2-fold difference in mortality. Given the fact that we studied women and not men and that patient mortality rates have decreased since that study, we decided to follow our patients for twice as long, up to 9 years.

### Statement of Responsibility

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

There were 237 women who provided informed consent and were randomized to the intervention condition ( $n=112$ ) and the usual care condition ( $n=125$ ) and were available for a mean duration of 7.1 years (SD, 1.91) with a range of 5 to 9 years of follow-up of all-cause mortality. No female patient was lost to follow-up. Figure 1 provides a flow-chart diagram showing the disposition of all patients screened and randomized into the Stockholm Women's Intervention Trial for CHD (SWITCHD).

From the beginning of randomization on November 30, 1996, to the end of follow-up on November 30, 2005, 25 women in the usual care group (25 of 125 [20%]) and 8 women in the intervention group (8 of 112 [7%]) died, yielding a 3-fold protective effect (odds ratio, 0.33; 95% CI, 0.15 to 0.74;  $P=0.007$ ). Thus, all-cause mortality was reduced by 67% in the intervention as compared with the usual care condition.

**Table 1. Baseline Characteristics of Women Receiving the Intervention or Usual Care**

| Baseline Characteristics                     | Intervention (n=112) | Usual Care (n=125) | P    |
|--|----------------------|--------------------|------|
| Age (mean±SD), years                         | 61.4±9.1             | 61.6±9.1           | 0.84 |
| Living alone, %                              | 51.3                 | 48.7               | 0.78 |
| Mandatory education, %                       | 63.1                 | 61.5               | 0.83 |
| Family history of CHD, %                     | 57                   | 64                 | 0.61 |
| Diagnosis at index events                    |                      |                    | 0.08 |
| Acute myocardial infarct, %                  | 53.6                 | 48.0               |      |
| Revascularization, %                         | 37.5                 | 32.8               |      |
| Angina pectoris, %                           | 8.0                  | 19.2               |      |
| Heart failure, %                             | 0.9                  | 0                  |      |
| Ejection fraction <40%, %                    | 11.9                 | 17.9               | 0.26 |
| Body mass index (mean±SD), kg/m <sup>2</sup> | 25.8±4.2             | 26.5±5.3           | 0.31 |
| Lipids (mean±SD), mmol/L                     |                      |                    |      |
| Serum cholesterol                            | 5.1±1.2              | 5.0±1.1            | 0.90 |
| S-HDL  | 1.1±0.4              | 1.0±0.4            | 0.20 |
| Smoking, %                                   |                      |                    | 0.97 |
| Never  | 35                   | 34                 |      |
| Previous                                     | 55                   | 55                 |      |
| Current                                      | 10                   | 11                 |      |
| Medication use, %                            |                      |                    |      |
| Aspirin                                      | 90.0                 | 87.9               | 0.68 |
| β-blockers                                   | 82.7                 | 77.4               | 0.33 |
| Calcium-channel blockers                     | 17.3                 | 19.4               | 0.74 |
| ACE inhibitors                               | 21.8                 | 23.4               | 0.88 |
| Hormone replacement therapy                  | 10.9                 | 11.4               | 1.00 |
| Statins*                                     | 59.1                 | 43.5               | 0.02 |
| Warfarin                                     | 4.6                  | 4.8                | 1.00 |
| Antidiabetic treatment (oral or insulin), %  | 9.8                  | 12.8               | 0.30 |
| No. daily medication use, mean±SD            | 2.81±1.02            | 2.66±1.11          | 0.24 |
| Daily Stress Questionnaire, mean±SD          | 41.3±8.6             | 40.5±9.5           | 0.62 |

CHD indicates coronary heart disease; S-HDL, serum high-density lipoprotein; ACE, angiotensin-converting enzyme.

\*Statins: coenzyme A reductase inhibitors.

Table 1 shows baseline age, demographic information, diagnosis at index event, physical and biochemical characteristics, and prescribed medications. The groups were largely similar in these respects. The mean age was 61.5 years, 6 of 10 female patients had only mandatory education, half were living alone, and about 21% were working at the time of the index event. Most women were not overweight, and relatively few (10%) smoked. Lipid profiles were very similar in the 2 groups. Baseline daily stress levels were assessed using a standardized questionnaire. The groups did not differ in baseline stress behavior, as shown in Table 1.

**Table 2. Hazard Ratios and 95% CIs for Mortality in Relation to Intervention Status, Taking Prognostic Factors Into Account From the Same Multivariate Cox Propositional Hazard Model**

|                                | No. Subjects | No. Deaths | HR (95% CI)         | P     |
|--------------------------------|--------------|------------|---------------------|-------|
| Intervention vs control        | 112 vs 125   | 8 vs 0.25  | 0.31 (0.13 to 0.73) | 0.008 |
| Age (1-yr increment)           |              |            | 1.08 (1.03 to 1.13) | 0.002 |
| AMI diagnosis vs others        |              |            | 2.52 (1.06 to 5.99) | 0.04  |
| Ejection fraction <40% vs >39% |              |            | 2.72 (1.04 to 7.14) | 0.04  |
| Aspirin use vs no use          |              |            | 0.45 (0.19 to 1.07) | 0.07  |
| ACE inhibitors use vs no use   |              |            | 2.27 (0.88 to 5.83) | 0.09  |
| Statins* use vs no use         |              |            | 0.36 (0.16 to 0.81) | 0.01  |

HR indicates hazard ratio; AMI, acute myocardial infarct; ACE inhibitors, angiotensin-converting enzyme inhibitors.

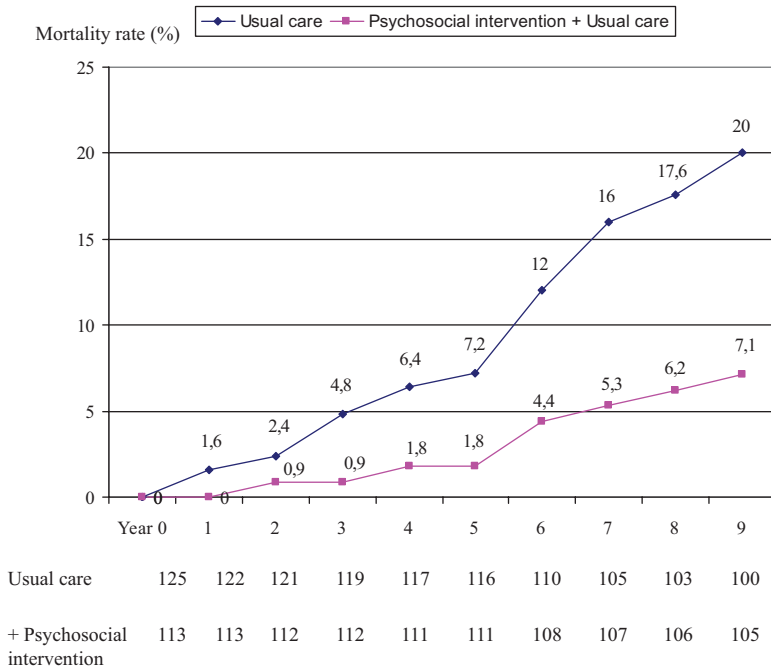
\*Statins: coenzyme A reductase inhibitors.

Most patients had been hospitalized for AMI with or without revascularization. The distribution of diagnoses did not differ significantly between stress reduction and usual care groups. However, there was a trend ( $P=0.08$ ) toward a higher prevalence of AMI in the stress intervention group and of more frequent angina pectoris in the usual care group.

Most patients and controls had been placed on aspirin (90% and 88%, respectively) and β-blockers (83% and 77%, respectively), the most common regimen for secondary prevention at the time. Calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors, estrogens, and warfarin were uncommon and similar in the 2 groups. Lipid-lowering agents were more common in the intervention (59%) as compared with the control group (44%), yielding a difference of 15%, which was statistically significant ( $\chi^2=5.6$ ,  $P=0.02$ ). All of the lipid-lowering agents were coenzyme A reductase inhibitors (statins), and no patient was on fibrates.

Antidiabetic treatment including oral antidiabetics and insulin was present at baseline in 27 patients. They were about equally distributed between groups (Table 1). During follow-up, 4 patients with antidiabetic treatment died (2 in each group). As antidiabetic treatment did not emerge as a predictor of mortality, it was not included in the final multivariate model presented in Table 2. Almost all of the patients were taking other medications as well. The number of drugs specified varied from 2 different drugs taken every day by 17 patients to more than 10 drugs taken daily by 19 patients. The mean number of medications taken by intervention ( $n=2.81\pm 1.02$ ) and usual care patients ( $n=2.66\pm 1.11$ ) did not differ significantly ( $P=0.24$ ).

Table 2 shows that multivariate modeling with age, socio-demographics, diagnosis, and ejection fraction at index event



**Figure 2.** All-cause mortality by therapeutic mode in women with CVD.

and medications at baseline largely confirmed the unadjusted results, the intervention program reaching a hazard ratio of 0.31 (95% CI, 0.13 to 0.73).

The independent protective effect of statin use was statistically significant ( $P=0.01$ ), whereas that of aspirin was borderline significant ( $P=0.07$ ). Of the other variables, older age and a more severe coronary diagnosis (AMI as compared with revascularization alone) had significant independent effects on mortality ( $P=0.002$  and  $P=0.01$ , respectively). Of all survival predictors, the intervention program carried the strongest independent effect, with a relative risk reduction of 69% ( $P=0.008$ ) (Table 2).

By scrutiny of outpatient and hospital charts, we obtained an estimate of specialized versus general care provided during follow-up (cardiologist or family practitioner). There was considerable variability in each group. Patients were seen by cardiologists and other specialists with varying frequency and intensity. In none of the groups was one single physician—cardiologist or other physician—responsible for the care of a patient throughout the entire follow-up period. All patients saw several doctors (often 10 or more) during the period. The intervention and usual care conditions did not differ in this respect ( $P>0.05$ ).

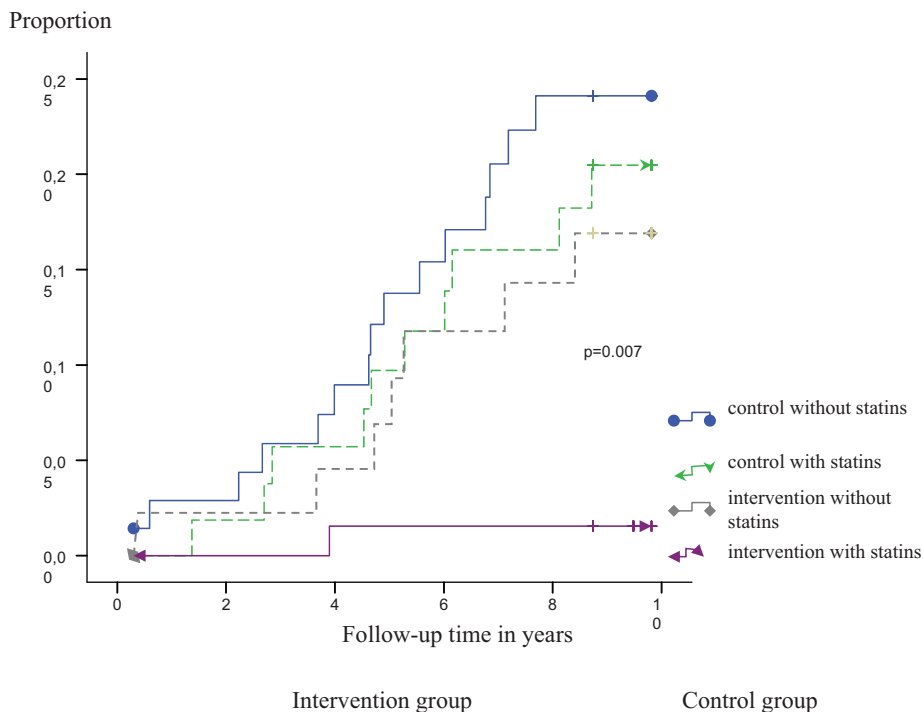
Figure 2 shows the censored cumulative all-cause mortality rates in the intervention and control groups over the 9-year follow-up period. Mortality differences were small during the first few years, but then increased thereafter with the steepest change appearing after the first 5 years. In the intervention group there were no deaths during the first 2 years.

To further explore psychosocial interaction with statins, cross-tabulation of statin use and group assignment (intervention versus usual care) in relation to mortality was performed as secondary analyses. They yielded the following results (Figure 3): Of the 65 women who received both cognitive intervention and statins, only 1 woman died, yielding a 9-year mortality of 1.5%.

Of the 45 women who received the program but not statins, 7 women died during the follow-up, yielding a 9-year mortality of 15.5%. Of the 54 women who did not receive the program but who were on statins at baseline, 10 women died (18.5%). Finally, among the 70 women who did not receive the program or statins, 15 women died (21.4%).

### Discussion

We found that a group-based psychosocial intervention program designed to reduce stress after an acute cardiac event resulted in a significant decrease in all-cause mortality when compared with usual care. During a mean follow-up of 7.1 years, women coronary patients who received the group-based program had almost 3 times the survival rate of female patients receiving usual care. The differences in mortality observed in SWITCHD could not be attributed to baseline differences in such clinical prognostic variables as age, education, severity of diagnosis, signs of heart failure, medication use, adiposity, family history of CHD, and smoking history or lipid profile. In general, as a consequence of successful randomization, the risk profiles and pharmacological treatment conditions seemed to be evenly distributed, with significant differences occurring only for lipid-lowering drugs. As assessed at baseline, statins were somewhat more common in the intervention group ( $P<0.05$ ), which hypothetically may have led to improved survival. However, after multivariable control, statin use did not “explain” the protective effect of the intervention, and the difference in statin usage did not influence the outcome of the trial. As expected, older age, a more severe diagnosis, and lower ejection fraction increased the mortality risk, whereas the intervention was the strongest protective factor, independently of statin use. Neither was the protective effect explained by more frequent or more qualified outpatient medical care in the post-hospitalization phase. Scrutiny of patient appointments and whether visits were made to a



**Figure 3.** Kaplan-Meier estimate of all-cause mortality by cognitive behavioral and statin therapy.

specialist versus a general practitioner did not reveal any significant differences between groups.

**The Psychosocial Intervention Program**

Psychosocial interventions have been shown to relieve emotional distress, to attenuate depressive feelings, and to strengthen social supports. Effects on hard end points, however, have rarely been demonstrated. Two clinical psychosocial intervention trials have detected significant effects on survival, but these were limited to male patients. In the Recurrent Coronary Prevention Project, almost 900 AMI patients (90% men) were randomized to coronary stress behavior modification with a significant beneficial effect on survival and recurrent nonfatal AMI.<sup>16</sup> In contrast, in Enhancing Recovery in Coronary Heart Disease, in which nearly half of the patients were women (44%), no positive net effect on survival was obtained.<sup>22</sup> In secondary analysis, however, a beneficial effect on survival was detected in men, whereas in women, a trend toward increased mortality was found.<sup>8</sup>

Several factors may help explain the present positive results. Because the intervention was initiated as a consequence of the observational female coronary risk study, the program had a specific focus on women’s daily stresses and on methods to relieve them. In an open and tolerant atmosphere, discussions of sensitive topics like marital and other family stresses were possible and indeed practiced. The discussions were kept confidential, the groups became cohe-

sive, and participants were highly and actively supportive of each other. Psychosocial exclusion criteria were not used, with the consequence that psychosocial risk factors were normally distributed and women were stressed, depressed, and isolated to a normal extent.

The study was conducted in groups of 4 to 8 women, and the groups remained the same throughout the program. All sessions were held as part of the outpatient activities in one and the same conference room, and if necessary, in the evening, so that patients who could not get time off from work could participate.

**Limitations**

Although SWITCHD found that stress reduction decreased mortality in women with severe CHD, it is not clear what elements of the intervention were responsible for this improvement. In designing the present intervention, we targeted such factors as reducing marital stress, increasing coping skills, and improving social support skills based on previous findings from the Stockholm Female Coronary Risk study.<sup>23</sup> We have also observed in repeated quantitative coronary angiography studies that increased levels of marital stress over time are associated with coronary disease progression, whereas decreased levels are associated with regression of coronary disease.<sup>24</sup> Alternative behavioral pathways, in addition to improved coping and social support skills, include enhanced stress reduction, improved health habits (eg, diet,

exercise, smoking, or alcohol), or better adherence to medications. That these factors could not be systematically assessed and monitored is a limitation of the study.

Another limitation of the present trial is that a large proportion of patients screened were unable to commit to a 1-year intervention. However, given the positive outcome of the present trial, physicians may become more willing to urge patients to participate in such an intervention, thereby enhancing participation. In this regard, it should be noted that participating in 20 visits over the course of a year may for most coronary patients be considered a small price to pay for decreased risk of mortality over a long period of time.

Still another limitation of SWITCHD is that because the potentiation by statins was an unexpected finding, we did not include procedures that might have allowed us to provide a biological explanation for the results. It is conceivable that the behavioral intervention may have interacted with statins to reduce inflammation or coagulation processes or delay atherosclerosis progression. Interestingly, in animal experiments (the Watanabe heritable hyperlipidemic rabbit), both statins<sup>25</sup> and affiliative behavior<sup>26</sup> have been found to attenuate the progression of atherosclerosis, possibly by decreasing inflammation. Psychosocial intervention may decrease sympathetic arousal and increase parasympathetic vagal tone<sup>27</sup> by an efferent neural signaling cholinergic antiinflammatory pathway that reflexively inhibits cytokine synthesis and protects against cytokine-mediated diseases.<sup>28,29</sup>

In conclusion, SWITCHD found that group-based psychosocial intervention may significantly reduce mortality in women with severe CHD. This is particularly important because previous trials using group-based intervention found such effects only in men.<sup>9,25</sup> The present study suggests that also women with severe CHD can benefit from psychosocial interventions, if they are aimed at reducing stresses specific for women and improving their social support skills. Women seem to benefit from long-range group-based interventions that promote social bonding and support and encourage reciprocal positive social interactions. "This group has become my life line," "I have learnt that if something bad occurs to me, I can handle it and I do not fall apart," and "One thing I have learnt from this program about stress: It just isn't worth dying for" were a few of the final comments from female participants.

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### Disclosures

None.

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