Proposal for an Exploratory Study:

Investigating the Role of Social Support
for Recurrent Myocardial Infarction
in High Risk Males

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Abstract

Coronary heart disease (CHD) is responsible for considerable morbidity and mortality. Research over the past decades has clarified traditional risk factors such as high cholesterol, elevated blood pressure, obesity, or smoking. Recent research has begun exploring controversial relationships between CHD and potential risk factors such as lack of social support, social isolation, depression, Type A behavior, and hostile temperaments. Due to lack of power or methodological flaws these studies have been unable to establish consistent findings or clarify a theoretical basis for observed correlations. This paper surveys traditional risk factor interventions, provides a brief summary of the literature on the social risk factors, and proposes an exploratory study to investigate a conceptual model of CHD progression and potential risk factors. The proposed study builds from the strengths of the ENRICHD trial and addresses its weakness while providing a comprehensive data set for exploring risk factor interactions. Understanding these interactions within a conceptual model would serve as the basis for further effectiveness trials that would translate to clinical practice.
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Coronary Heart Disease (CHD) is the single largest cause of death for American males and females. Given current rates, about every 26 seconds someone will suffer a coronary event, and about every minute someone will die from one. Of those that experience a coronary attack, about 42% will die within a year.\textsuperscript{1,3,4}

This paper is an analysis of current studies that investigate the relationship of social support and CHD in men, and a proposal for a pilot study to clarify the ambiguities of this relationship. This first section will survey the risk factors, burden, and preventive strategies for CHD in this population. The following sections will analyze the current literature on social interventions for this condition in the males, and outline the justifications and format of the pilot study.

Generally accepted risk factors for CHD include hypertension, hypercholesterolemia, smoking, diabetes, physical inactivity, obesity, and age. The majority of papers analyzing the above risk factors has been cross-sectional and has demonstrated a relationship between the presence of the risk factors and CHD. The studies have not been able to determine how well these risk factors correlate with the degree of CHD, nor the rate of progression. A recent paper by Phillips et al. analyzed the major predictors of CHD in men. Their study concluded that age, high-density lipoprotein (HDL-C) and free testosterone were the strongest predictors of degree of CHD in men.\textsuperscript{2} Further research may clarify this relationship.
Due to large studies such as the landmark Framingham study, we have been able to obtain large cross-sections of the American population and follow health behaviors or risk factors as related to coronary disease. Continuing study has clarified more risk factors such as high levels of homocysteine and a possible link with microbial infection. The American Heart Association issues an annual update of known risk factors and stratifies them according to race. The table below outlines the prevalence of these risk factors for American males:

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Total Population</th>
<th>Total Males</th>
<th>White Males</th>
<th>Black Males</th>
<th>Mexican American Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>13.0 M (6.9%)</td>
<td>7.1 M (6.4%)</td>
<td>8.9%</td>
<td>7.4%</td>
<td>5.6%</td>
</tr>
<tr>
<td>Hypertension (1+3 CHD)</td>
<td>1.2 M</td>
<td>715.0 K</td>
<td>650.0 K</td>
<td>66.0 K</td>
<td></td>
</tr>
<tr>
<td>Diabetes (Type 2)</td>
<td>502.2 K</td>
<td>254.0 K</td>
<td>224.5 K</td>
<td>24.6 K</td>
<td></td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>65.0 M</td>
<td>32.3%</td>
<td>30.6%</td>
<td>41.8%</td>
<td>27.8%</td>
</tr>
<tr>
<td>Hypertension (Prevalence 2002)</td>
<td>48.7 K</td>
<td>23.5 K</td>
<td>14.7 K</td>
<td>5.3 K</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis (Prevalence 2001)</td>
<td>48.1 M (22.9%)</td>
<td>23.6 M (2.0%)</td>
<td>25.1%</td>
<td>27.6%</td>
<td></td>
</tr>
<tr>
<td>Blood Cholesterol 2001</td>
<td>109.9 M (50.7%)</td>
<td>59.4 M (50.4%)</td>
<td>51.0%</td>
<td>37.3%</td>
<td>54.3%</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>31.7 M (18.3%)</td>
<td>17.6 M (17.2%)</td>
<td>17.8%</td>
<td>16.6%</td>
<td>17.6%</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>50.0 M (41.5%)</td>
<td>48.6 M (48.5%)</td>
<td>49.6%</td>
<td>46.6%</td>
<td>43.6%</td>
</tr>
<tr>
<td>GFR (mL/min)</td>
<td>64.7 M (26.4%)</td>
<td>38.0 M (31.0%)</td>
<td>40.6%</td>
<td>24.3%</td>
<td>40.1%</td>
</tr>
<tr>
<td>Proportion Lost to Disease</td>
<td>39.6%</td>
<td>39.8%</td>
<td>34.6%</td>
<td>46.1%</td>
<td></td>
</tr>
<tr>
<td>Mortality (Death Rate)</td>
<td>73.2 K</td>
<td>34.3 K</td>
<td>28.1 K</td>
<td>5.2 K</td>
<td></td>
</tr>
</tbody>
</table>

In 2001 the prevalence of CHD was comparable between races, yet nearly ten times as many whites died of CHD. Whites had higher total cholesterol and lower amounts of HDL-C. Almost 10% more blacks have high blood pressure. Larger
proportions of Hispanics were overweight and nearly 28% of men in all races were obese. Other studies in obesity may disagree with these measures. More blacks and Hispanics have diabetes, and again whites have greater mortality resulting from the disease.\textsuperscript{3,4}

Although researchers have not been able to correlate the risk factors with severity of disease, they have been able to determine the relative risk of developing CHD based upon the presence or absence of the factors. According to the World Health Organization (WHO), the risk of CHD decreases by 50 percent one year after quitting smoking and the relative risk approaches that of a lifetime nonsmoker after fifteen years. Nearly 35,000 nonsmokers die from CHD each year as a result of exposure to environmental tobacco smoke.\textsuperscript{5} Patients may achieve a 30 percent reduction in the incidence of CHD with a 10 percent reduction in total cholesterol.\textsuperscript{6} Those men with low HDL-C and high total cholesterol have the highest risk of heart attack, and those men with levels above 37 mg/dL are at high risk even with normal total cholesterol.\textsuperscript{3,4} Physical inactivity carries a 1.5 to 2.4 relative risk for CHD, an increase that is comparable to that observed for high blood pressure, high blood cholesterol, or cigarette smoking.\textsuperscript{7}

There is an inverse relationship between socioeconomic status (SES) and CHD. Although mortality for CHD has declined since the 1960’s this decline has not affected all segments of society equally. Low-income persons living in the most disadvantaged neighborhoods had hazard ratios of 3.1 (whites) and 2.5 (blacks) compared with high-income persons in the most advantaged neighborhoods.\textsuperscript{8} There has generally been an inverse relationship between SES indicators and hypertension, smoking, total cholesterol, body mass index, excess alcohol use, and sometimes diabetes. The most striking relationships are with smoking and hypertension. The relationship between SES and
cardiovascular disease has been widening, and accounting for the many confounding variables in studying these effects is challenging. Further research will need to understand this interdependent system.

There are many component causes that contribute to developing CHD, and there are multiple interventions to address this progression. Screening modalities including ECG, cholesterol measurements, glucose levels and blood pressure are methods to identify high-risk patients and even monitor the disease course as a proxy. Medications that improve lipid profiles, lower blood pressure, and inhibit platelet aggregation provide effective chemoprevention. Lifestyle habits such as physical inactivity and smoking behaviors may be amenable to change through intensive individual interventions, public education, and public policies that support healthy practices.

**Interventions with Traditional Risk Factors**

It seems logical that to effectively prevent CHD, a multifaceted intervention that addresses multiple risk factors would be the most effective. Many countries have attempted such primary prevention programs using a multiple risk factor intervention in the belief that such an approach would be effective and would lower costs. These plans have utilized combinations of counseling, education, and pharmacotherapy in both the primary care setting and in the workplace. The degree of risk factor control appeared to correlate with the reduction in disease incidence. Quasi-experimental studies such as the North Karelia Project and seemed to provide evidence in support of this multiple risk factor intervention.
More recent studies have brought these observations and assumptions under question. New evidence has stimulated a review of the methodology for multiple risk factor interventions within the primary care setting and within the community. Performing a meta-analysis has been difficult due to the vast heterogeneity of the interventions, insufficient detail in reporting, and sometimes poor study design. In 1995 the Cochrane Collaboration performed a systematic review of multiple risk factor interventions for primary prevention of CHD. They have periodically updated this review and the most recent update was on May 28th, 2003.

The Cochrane review demonstrated that multiple risk factor interventions were costly and ineffective for primary prevention of CHD in low-risk patients. The review focused on multiple risk factor interventions consisting of counseling, education, and pharmacotherapy in one-to-one or family-oriented settings. The study did reveal a positive effect for patients with hypertension, elevated cholesterol, or significant levels of other risk factors. Baseline levels of risk factors were strong predictors of the net falls experienced, thus suggesting that a multiple risk factor intervention might be more effective in targeted high-risk populations.

CHD is a major contributor to morbidity and mortality in the US. It represents a significant financial burden to individuals, the workplace, and to the health care system. Research has demonstrated that multiple risk factor interventions are ineffective in the primary prevention of CHD in low risk individuals. Interventions focusing on policy, community planning, targeted group settings, high-risk individuals, or national education may be more effective. The following section will survey the research investigating the dynamics of social support in this paradigm.
Summary of Literature for Social Support and CHD

For this summary, the author searched Medline utilizing the search terms: Coronary Heart Disease, Coronary Artery Disease, CHD, CAD, Social Support, Emotional Support, Instrumental Support, and Perceived Social Support. The search was limited to human studies reported in the English language between January of 1975 and March of 2005. This search yielded 41 pertinent articles, and further limiting the search to males restricted the pool to 19 articles. A full systematic review is beyond the scope of this paper. Findings from the pertinent articles are detailed below.

Researchers have investigated the relationship between low social support and cardiac outcomes due to CHD. Ruberman et al. noted that men with low perceived social support and high life stress were more than 4 times as likely to die after a myocardial infarction (MI). Gorkin et al. demonstrated that the level of perceived social support was a significant multivariate predictor of mortality in high stress men. Orth-Gomer et al. noticed that socially isolated men with CHD had 3 times the rate of total mortality in comparison to non-isolated men. Married men are significantly less likely to die post MI during hospitalization or follow up. Living alone is an independent risk factor for mortality post MI. Other researchers have uncovered that a lack of social support in itself is associated with increased morbidity and mortality in patients with CHD.

Accounting for other risk factors, lack of social support has been shown to predict cardiovascular morbidity and mortality. Of social support types, emotional support has the strongest influence on CHD.
In combination with other risk factors low social support has demonstrated a synergistic effect that researchers have yet to understand. Depression is an independent risk factor for morbidity and mortality post MI. Low social support is directly correlated with depressive symptoms one month after hospitalization when controlling for baseline depression, gender, disease severity, and age. The potential for hostile behavior predicts recurrent CHD events. Cynical hostility as depicted by an attitude of resentment, distrust, cynicism, and suspicion predicts CHD progression. Low social support and high hostility together increase risk of cardiac morbidity and mortality. Hostility may be an indirect predictor of CHD by means of its effect on social support, and low social support may have indirect effects through its influence on depression. Researchers are working to determine the direct and moderating effects of social support on cardiac outcomes. The below subsections attempt to group the heterogeneous literature by topic in order to clarify current research findings and directions for future study.

**Social Isolation**

Brummet et al. utilized the longitudinal data from the Moderators of Social Support (MOSS) Study to investigate the relationship of social isolation and cardiac mortality. Previous research had noted that psychological distress was a risk factor for cardiac mortality in patients with CHD, and that this distress was more severe in patients who feel that they lack social support. They used the Mannheim Social Support Interview to determine network social support. They then monitored the following variables to determine correlations and independent effects: number of confidants, number of individuals in the household, perceptions of social support, participation in
religious activities, depression, functional status, health perceptions, mental health, activities of daily living, perceived stress, hostility, income, disease severity, smoking, and exercise status. Accounting for all other variables, social isolation as determined by low network social support predicted increased cardiac mortality as demonstrated by the risk ratio of 2.11 with a 95% CI 1.39-3.19 (p< 0.0009) over the 24 months of the study. Isolated patients lacked confidants, were more likely to be unmarried, had little emotional support, and had lower perceptions of both social support and quality of relationships. Isolated patients had lower income and smoked more, both of which are risk factors for CHD; however, accounting for these variables did not significantly affect the risk ratio. Isolated patients had similar religious attendance, disease severity, depressive symptoms, and perceived stress in comparison to the socially connected. The isolated patients did demonstrate more hostility, yet accounting for this variable did not substantially affect the risk ratio (2.47 for cardiac mortality over 2 years).

The researchers concluded that network support affects cardiac mortality and that the relationship is nonlinear: those with very few social connections had a disproportionate increase in risk. In rebuttal to contrary arguments, the authors demonstrated that the isolated patients were neither sicker, nor did they delay medical care. They noted that patients that would benefit from more social connection are the very patients that are difficult to enroll in psychosocial interventions and have a high attrition rate. Interventions hoping to address social isolation will need to address this enrollment challenge.
Social Support and Hostility

Brummet et al. investigated the relationship between trait hostility and perceptions of social support in predicting depressive symptoms at 1 month after hospitalization for diagnostic angiography. They hypothesized several mechanisms to explain these potential effects. Chronic increases in sympathetic nervous system (SNS) function can lead to myocardial electrical instability, platelet activation, and myocardial workload. In addition, depression and low social support have been associated with detrimental health behaviors.

Through a study of 506 CHD patients they demonstrated an independent negative association of social support and depressive symptoms within the study parameters. They noted that hostility was a small, indirect predictor of postdischarge depressive symptoms by way of its negative effect on social support. This negative relation did not differ across gender, predicted risk classification, or age. They did not find evidence of hostility as an independent, direct predictor of depressive symptoms at 1 month. They commented that although hostility predicts initial coronary events, it does not seem to predict secondary events.

Angerer et al. devised their study from the literature that observed a synergistic relationship between hostility and low social support in affecting cardiac outcomes. Their study of 223 patients with CHD, documented by standardized angiography, showed a higher risk of progression for those that scored high on the State-Trait-Anger-Expression Inventory (STAXI) for outwardly expressed anger and who reported low social support. A multivariate analysis adjusting for confounding variables and
examining interaction with psychological variables showed that only patients with both high levels of outwardly expressed anger and low social support were at increased risk for progression (RR 3.19 over two years). They found that the quality of the social support, in particular the quality of emotional support, predicted the largest effect on CHD progression. The quantity of social support was a stronger predictor of mortality, but may reflect the availability of medical assistance. Cynical hostility was associated with the presence of CHD, yet it was not associated with progression. The authors note prior research in which all-cause mortality for highly cynical men has been moderated through coronary risk factors, and that intense treatment of these risk factors in their study may have leveled any differences with less cynically hostile men.

Hostility, isolation and male sex may be dangerous combination. Researchers are attempting to understand the pathogenesis of this relationship, and to determine differences in subgroup populations. Interventions with populations of hostile men will be challenging by the nature of the population. Continued research in this field will assist the translation into clinical application.

Social Relationships and Cardiac Reactivity

Bloor et al. commented that although many studies have demonstrated that low social support increases cardiac mortality, little is known about the underlying mechanisms. Based on prior research, they proposed cardiac reactivity as a potential physiologic mechanism. Exaggerated cardiovascular responses over time may increase CHD. Social support during acute stress reduces cardiovascular responses. In addition, recalling relationships through memory influences cardiac function. Their study of forty-
three men and sixty-six women analyzed cardiac reactivity during prompted relationship recall. They hypothesized that aversive, indifferent, or ambivalent relationships would have higher cardiac reactivity during recall than supportive ones. They also predicted a gender difference in response.

Their results did not support a difference in cardiac reactivity during recall of the four types of relationships; however, they did reveal gender differences in response. Contrary to the finding that men are generally more reactive to achievement-oriented laboratory task, women demonstrated a higher sympathetic activation upon recall. Women were also more responsive to the negative qualities of relationships. Overall, the women were more reactive to relationship-oriented topics. The authors were unsure why cardiac reactivity increased in similar ways for the recall of different types of relationships. They postulated that recall of especially positive relationships might have generated excitement or that recall bias might have influenced physiologic response. The physiologic link between sympathetic nervous system stimulation and CHD is scientifically sound. More research is necessary to determine if social support has a consistent role of influencing cardiac reactivity in this cascade.

Social Support as Related to CHD and Quality of Life

Bosworth et al. examined the relationship between perceived social support and domain-specific health-related quality of life (HRQOL) in a sample of 4278 cardiac catheterization patients. Accounting for age, gender, race, education, and CHD severity, regression models indicated that a lack of social support was significantly associated with lower levels of HRQOL across eight measured domains. The eight domains included:
physical function, physical role function, bodily pain, general health, emotional role function, social function, mental health, and vitality.

Variations in the subgroups offer insight and stimulate questions for future clinical applications. Social support played a more beneficial role for whites than for minorities, and in general minorities had higher levels of HRQOL. Minority patients with low social support had markedly higher levels of general health, social functioning, and mental health than whites with similar social support. When both the minorities and whites reported high levels of social support, these differences diminished. This finding raises the questions of whether low social support is more detrimental to whites, whether there are different perceptions of social support in minority communities, or even whether there are different baselines of social support between the communities. Females reported lower HRQOL across all domains, yet the authors proposed that this might be due to women’s willingness to report symptoms. This study illustrates potential effects of social support on the HRQOL for patients living with CHD. With the increasing longevity of our population, more citizens will be living with CHD, and the resultant decreases in HRQOL due to the disease will be of increasing importance. It will be necessary to further investigate these questions in the relationship between CHD, social support, and HRQOL. Decreases in HRQOL may feed back to affect moderating variables of CHD progression such as depression, hostility, health behaviors, and social support.
Low Perceived Social Support, Depression, and CHD

Investigators of the Enhancing Recovery in Coronary Heart Disease (ENRICHD) developed a large multi-center, randomized trial that aimed to determine whether treatment of depression and low perceived social support increases reinfarction-free survival after acute myocardial infarction. The study was an effectiveness trial that enrolled 2,481 participants of diverse race, sex, and socioeconomic backgrounds. The participants were randomized to individualized treatment for depression and/or low social support, or to standard medical care.

Depression and low perceived social support (LPSS) after myocardial infarction are predictors for increased morbidity and mortality. No clinical trial had tested the effects of increasing social support and reducing depression on clinical endpoints following acute MI. Multiple studies have investigated the independent effects of each predictive variable. Researchers have demonstrated that depression is an important predictor of morbidity and mortality in CHD patients independent of previous cardiac history, CHD severity, or residual left ventricular function. Post-MI patients report a prevalence of major depression between 15 and 20%, and an additional 27% report symptoms of minor depression. Studies to improve social support that utilized group-based cognitive behavioral therapy and psycho-education, or individual nurse delivered home-based interventions have demonstrated lower mortality, fewer recurrent MI’s, and increased quality of social interaction. Some studies have been unable to replicate these results and demonstrated that those that responded early continued to improve while those that did not initially respond continued to worsen. Supporters of social support interventions note that the studies reporting no effect were often limited by
power or design and analysis flaws. The ENRICHD trial was designed to have the power and execution to answer this debate.

The investigators attempted to modify the intervention methods to meet the needs of different populations and individuals. This process of catering the intervention to the recipient reflected an appreciation of the complex web of mediating variables in social support and an effort to determine the optimal therapy for population subgroups. The investigators utilized a series of tools to discern a participant’s level of depression, perceived stress, perceived social support, instrumental and emotional needs, and beliefs relating to social ties and network availability. In addition, they identified the degree of participant’s social integration, current satisfaction with specific sources of support, and preference for different types of support. As one can see, their efforts to profile each participant’s needs were remarkable. From this data they decided upon individual psychotherapy, group therapy, and pharmacotherapy consisting of an SSRI or nortriptyline.

The researchers chose a Cognitive Behavioral Therapy (CBT) model based upon prior research demonstrating effectiveness in treating depression across diverse population, and for its ability to address perceptions of social support. Individual psychotherapy ranged from six sessions to a maximum of six months, depending on the patient’s progress. Group therapy was contingent upon availability and ran for up to twelve weeks. Treatment for depression continued until the patient had a therapeutic response to counseling or medication. A modified form of the Perceived Social Support Scale (PSSS) measured progress in the domain of social support. Treatment for low perceived social support (LPSS) continued until the participant engaged in at least one
satisfying and supportive social relationship, was able to do ‘self therapy,’ and achieved a criterion score on the modified PSSS for at least two consecutive sessions.

Researchers utilized creative means to bolster adherence in this complex intervention and population. At conclusion, they had a high retention rate of 93.02% with those completing the study participating for a mean of 28.3 months and those lost to follow-up averaging 19 months. The creative methods to assure this adherence rate and the ability to adapt the intervention to the diverse population represent strengths of this study.

The investigators executed the study design well, and the results of this large trial have had a significant impact in the field of social support study. The treatment of LPSS and depression included the individually catered cognitive behavioral therapy and selective serotonin receptor inhibitors (SSRI’s) when applicable. The study noted a marginal and statistically significant decrease in depression and LPSS, however was unable to demonstrate any significant difference in event free survival over the 29 month course of the study (p<0.001.)

In contrast, an early study known as the Recurrent Coronary Prevention Project (RCPP), which used group-based cognitive behavioral therapy to reduce Type A behavior, decreased depression and improved the quality of social interaction. This 5-year clinical trial randomized patients to one of three arms, including aggressive education with traditional pharmacotherapy, cognitive behavioral therapy, standard private practice, and then included a dropout comparison group voluntarily discontinuing therapy. The cognitive behavioral intervention decreased Type A behavior patterns as well as CHD morbidity and mortality.37
Comparing the two studies, the RCPP enrolled primarily white men (92%), while the ENRICHD trial enrolled a large percentage of women (44%) and minorities (34%). Exploratory post hoc analysis of the ENRICHD data revealed that in the white males were younger, healthier, better educated, and less likely to live alone. The RCPP population was primarily younger than 65, non-diabetic, only 30% had hypertension, 89% were married, 52% completed college, and had lived longer than 6 months after the MI. Overall the populations in the two studies were markedly different; however, the white populations had many similarities that make comparisons within this subgroup worthwhile.

One important difference across all groups is the timing of the study, including both the point of initiation and the duration. The ENRICHD study hypothesized that since the first six months post MI were the most dangerous for recurrent MI, they would begin the intervention immediately following the MI. Treatment lasted for six months. The RCPP began after six months and treatment persisted for up to 4.5 years. These differences raise the questions of whether an intervention would be successful when employed in a population likely to live past six months and whether a longer intervention is necessary to realize clinical results. Further differences between the studies leave room for exploration, and warrant research into the conflicting results.

Some researchers feared that negative results in the ENRICHD trial would doom further research in the field. Closer analysis of the ENRICHD data when taken in the context of prior studies generates more questions for future investigation. The post hoc subgroup analysis demonstrated that white men received a marginal positive effect, white women and minority men received no effect, and minority women received a marginal
negative effect. Although the ENRICHD trial had statistically significant decreases in depression and LPSS, these differences were marginal and may not have been clinically significant on the order to affect CHD as demonstrated in other trials. Editorials questioned whether larger treatment effects and measurements of potentially synergistic or antagonistic variables such as hostility, negative affect, arousal, self-efficacy, and coping skills would offer more insight. Others recommended following sub-clinical markers of disease that might mediate the relationship between the psychosocial outcomes and medical endpoints. In light of this analysis, further research will be challenged to improve upon the ENRICHD trials comprehensive design.\textsuperscript{40 41 42 43}

**Critique of Literature**

In the reviewed literature, social support measures included emotional, network, instrumental, and perceived support. The quality of emotional support is a predictor of CHD progression.\textsuperscript{20 21} Social isolation is an independent predictor of CHD mortality across all groups.\textsuperscript{15 12} Those with low network social support are likely to have isolation, lack a confidant, have little emotional support, and have a lower perception of both social support and quality of support.\textsuperscript{25} High levels of expressed anger coupled with low social support increase risk of CHD progression (RR 3.19 over 2 years).\textsuperscript{24} Research in social support as related to cardiac reactivity have been inconclusive other than illustrating gender differences of women being more reactive to relationship-oriented topics.\textsuperscript{32} For patients after cardiac catheterization, lack of social support was associated with decreased HRQOL across all domains.\textsuperscript{33}
Studies have attempted to increase the perception of social support, skills for developing and maintaining social support, and resolve internal conflicts inhibiting social support. Small power and post hoc analysis limit the ability to analyze the differences between how these interventions function in different subgroups. The ENRICHD trial presents a comprehensive effort to cater the intervention to the needs of individuals; however, its results leave researchers asking if there is no effect, if the intervention is inadequate, or if they are measuring the wrong indices. The RCPP presents positive results in a homogenous population that limits external validity.\textsuperscript{37}

The preliminary results of the ENRICHD trial may have indicated no effect of the interventions on reinfarction-free survival rates, but should we accept this conclusion as the death knoll for further research in this area? The ENRICHD trial was well-powered, had a diverse population, had high adherence rates, and had thorough execution of the interventions as designed. When we look closer, however, we can see potential methodological flaws in the intervention design and begin to understand the risks of advancing to a large effectiveness trial without the tried theoretical foundation of efficacy trials.

The ideal flow of research may be of consistent efficacy trials translating to effectiveness trials with wide external validity. However in recent years, researchers have become aware of a lack of this translation to useful clinical information, and have begun to design effectiveness trials that might steer clinical practice. Positive results from a study with external validity can influence evidence-based guidelines; however, negative results may offer little clinical value when the moderating variables of a condition are poorly understood and one cannot speak to how the proposed intervention functions in
disease progression. Without a model that has been tested in consistent efficacy trials, one cannot say ‘what’ is not working, but rather that ‘something’ is not working. This situation has potential harms in that large effectiveness trials are expensive in terms of fiscal, medical, and personal resources of the participants, providers, and society. There is also the potential for medical harm with employing poorly understood interventions on a large scale. With this understanding, let us look at the ENRICHD trial from a different perspective.

The researchers aimed to devise a cost-effective, generalizable intervention that was adaptable to the specific needs of individuals of diverse backgrounds. They based much of this intervention on research demonstrating that low perceived social support and depression were risk factors for recurrent acute myocardial infarction (AMI). They intervened in the sixth month period immediately following the initial myocardial infarction when patients are at highest risk for recurrent AMI.

When analyzing this study one has to ask:

- What are the moderating variables of social support or depression influencing recurrent AMI?
- Which of these variables are amenable to an intervention?
- Which of these variables would be the most effective in changing health outcomes?
- Would this list change for different populations?
- At what point in the disease progression are different variables effective?
- What is the required duration of intervention to sufficiently influence the key variables?
- How will you measure these variables and outcomes?
In the ENRICHD trial they assumed:

- perception of low social support was the key variable
- individual CBT and group therapy could shift perception of social support
- they could adapt the intervention to different populations
- recurrent AMI at less than six months would respond to intervention in similar ways as those after the high-risk period
- this shift could be accomplished in a short period
- the PSSS would adequately track changes and determine therapy length

Although the researchers executed the study protocol with relative consistency throughout the large trial, the study protocol with its designed variability was by nature inconsistent. This variability could be a strength or a weakness. As a strength it is adaptability that broadens external validity. As a weakness, we only know that many different types of interventions were used to influence LPSS and that this was measured by the PSSS. We lack the details and final measures to determine the effects of moderating variables. This approach places tremendous importance on the PSSS and on perceived social support as the key variable. It gives us little information about other social support variables influencing health outcomes. Although the initial surveys to determine the needs of the individuals included analysis of social networking, social skills, etc., they have not reported final outcome measures for these variables. Most importantly, the researchers concluded treatment based upon the PSSS. If perceived social support is not actually the key variable for all populations, then this would lead to early termination of therapy and potentially to falsely negative results that one might generalize to all social support interventions in this area of research.

Further investigation reveals that the group therapy intervention, which might be most effective in promoting social skills and social support, was not available to many participants due to timing or geographic constraints. A review of the literature reveals
that group social support interventions typical demonstrate an initial worsening of symptoms and only yield their benefit after months of meeting. The group intervention employed in this study only lasted 12 weeks at the maximum. It is likely that the individuals in the group therapy received an adequate intervention, and that many participants that could benefit from the group session did not receive this therapy at all.

From this analysis one can see that negative findings in large effectiveness trials that lack the tested theoretical foundation of efficacy trials can be harmful if misinterpreted. Accepting their findings without investigating the theoretical underpinnings can potentially limit further research in a field. Such studies can potentially cause medical harm to patients and can consume valuable resources. Balancing the responsibility towards effectiveness trials with the responsibility for a sound theoretical basis, researchers must analyze effectiveness study methods and results to guide further research. The ENRICHD trial offers valuable insight into how to perform a large-scale behavioral intervention adapted to patient needs and how to maintain high adherence rates. It would be an error to accept its conclusions without further investigation.

Perceived social support may not be the key variable, and interventions that influence variables such as social skills may be more effective. Focusing on perceived social support does not consider the complex dynamic of human interactions in which perceptions and actions are constantly changing and providing feedback. It assumes a pseudo-unilaterality in which the individual is either separate from the surrounding environment or that effects move in one direction. This false perception may be an artifact of our research that has not monitored social support as an interdependent system.
Further research will need to utilize a conceptual model that can track this interdependent system and find the most effect point for intervention. The following conceptual model is such an attempt.

**Conceptual Model**

Prior research has demonstrated a consistent relationship between measures of low social support and poor coronary outcomes. Other factors such as depression, trait hostility, outward expression of anger, cynical hostility, and depression have performed as independent predictors of cardiac morbidity and mortality in some trials. Studies have attempted to clarify the relationship of these factors with elements of social support, and their physiologic mechanism of action in CHD progression. Mixed results in these efforts have raised questions about how these factors interact differently in various subgroups. These conflicting results may serve to draw out the mechanism of action when the characteristics of the groups are considered.

The following conceptual model provides an outline for further research. The model presents the different types of social support acting through physiologic responses to affect CHD. The mechanism of interaction may occur through perceptual changes or through the fulfillment of basic human needs for connection, reassurance, validation, and support. Gender and race moderate this effect through unknown mechanisms that may be the result of unique cultural perceptions, functions of support within those groups, or physiologic differences in stress response. Social support also acts through the mediating variable of health behaviors that affect physiologic responses directly. Hostility is an independent actor through physiologic response on CHD. It also has an indirect effect
through decreasing social support as outlined above. Depression is an independent predictor acting through physiologic responses, and it also has an interaction with social support in which social support may decrease depression or depression may cause withdrawal from social support.

Genetics or heredity exerts a direct influence on the tendency toward depression or exaggerated physiologic response. This effect may be closely linked with culture, race, and gender. When considering the effects of culture, race and gender, the interaction may be complex and may influence reporting. For instance cultural norms of hostility expression may affect the frequency of the behavior, its perception, and its scoring on self-report forms. These unique characteristics of subgroups may prove important in creating interventions that fit the dynamics of each population.

The model below presents a simplified interaction of predictive variables with CHD progression. The text boxes below the flow diagram detail elements within each variable. These elements represent potential outcome measurements for a study and such data may help to clarify the complex interactions of social support and CHD in males. Appreciating this complexity we must understand that these interactions occur within the context of culture which may influence the magnitude and direction of effect through the moderator of perception.
Conceptual Model for Interaction of Predictive Variables with Coronary Artery Disease

From the literature it is apparent more than perception of social support is important in the relationship of social support and CHD. Appreciating the complexity and interdependence, one must consider how to affect social skills, perception of support, emotional support, and network support. Would it be possible to affect them all or would it be more feasible to focus on one? Without an understanding of how the variables
interact, it may not be possible to isolate the most effective variable until an exploratory study has tested the model. One must also consider what outcomes to measure, the duration of the study, and what would be the most appropriate setting for intervention and measurement. Finally, given that those most in need of the intervention will likely be the most resistant to participate, how can one overcome this challenge of enrollment?

The proposed study incorporates a relatively new practice model that has developed for the treatment of chronic disease. The development began at Kaiser Permanente when John Scott developed the Cooperative Health Care Clinic (CHCC) in 1990. This model, which has subsequently become known as the group visit, combines individual medical care, guided discussion, and a support group. This model could present an ideal setting for a facilitator to teach social skills in a group environment while also using Cognitive Behavioral Therapy methods to shift perceptions of low social support. If well facilitated over a sufficient duration, the group visit can become a source of emotional support.

Typically the group visits involve a period of obtaining clinical data such as measuring vitals or registering new complaints. These periods would be an opportunity to collect data throughout the course of the study, including lab values of physiologic responses such blood pressure, cortisol levels to monitor stress, or lipid levels to monitor cholesterol. The ability to collect such data throughout the course of the study would be valuable in clarifying the interaction of mediating variables, physiologic responses, and coronary outcomes.

Success in group visits has been dependent on a competent facilitator and the ability to frame the meeting as a medical clinic visit. Successfully framing the visit as
such may address the enrollment challenges mentioned earlier. The reluctant participants may be more likely to attend something labeled as a clinic visit that offers more time with the provider, than an intervention thought of as optional, additional, or as unneeded. Borrowing from the positive aspects of the ENRICHD trial, investigators could utilize their enrollment techniques such as telephone follow-ups to decrease attrition and improve participation.

Various methods may counter the weaknesses of the ENRICHD trial. The proposed study would need to at least measure the levels of emotional, network, and perceived support at enrollment and at conclusion in order to understand how these variables interact and influence CHD progression. If researchers were to monitor this data throughout the course of the study, they could correlate the fluctuations with the clinical data and markers of physiologic responses. This comprehensive data set would allow a thorough analysis of the interaction in the conceptual model. Multiple linear regression modeling could clarify interactions and independent variables. Researchers would need to find a balance where such comprehensive data collection does not inhibit the functionality of the intervention.

In the group visit model a competent facilitator could teach social skills, provide a safe environment to practice these skills, and address obstacles to effective communication and emotional support. Proponents of group visits claim that the visits have proven effective for improving patient education and compliance.\textsuperscript{47} Masley et al. have outlined a group visit plan for such high-risk groups, and have successfully implemented a dietary change intervention in a group visit model of individuals with CHD.\textsuperscript{48,49}
Again, the facilitator would need to normalize these sessions and frame them in a non-threatening, appealing context that participants can view as an integral part of their medical care. The participants would need to know that they would still have independent time with their provider, and that these sessions are an essential complement to their care that actually affords them more services from their health care team. To encourage participation and investment in the intervention, the facilitator may take suggestions from the group for designing the content of their future education components. It may be possible to have participants take turns as co-facilitators or planners of the sessions. The skillful clinical facilitator could utilize these opportunities as teachable moments to help with social skills such as communication and self-confidence. Another aspect to aid participation that could augment emotional and network support is a buddy system in which each group member is paired with another and is responsible for calling weekly to check on progress or challenges. Such pairings are likely to generate some level of discomfort and conflict, and it would be up to the facilitator to utilize these instances as opportunities to learn new skills or shift perceptions.

As mentioned earlier, support group interventions may initially demonstrate worse outcomes and need a sufficient duration to have a positive effect. The support group is a critical aspect of the group visit, and because of this structure, the study would need to run longer than the brief period allotted in the ENRICHD trial. Typically group visits enroll 8-20 participants and ideally the study would continue the intervention for at least one year. The proposed study would enroll 8-12 participants per group and each group would meet twice monthly for the first two months, and then once monthly for the remaining ten.
In summary, the intervention would be based in a group visit format enrolling 8-12 participants per group and meeting for a total of 14 visits over the duration of a year. The visits will be an integral part of their medical care and will provide time for individual medical care or questions. The group visit format would provide an environment to teach healthy behaviors, social skills, provide emotional and network support, and shift negative perceptions of social support. Participants will aid in devising the content of the educational component of the future group visits and will be encouraged to co-facilitate a future session. The visit will have a component of open discussion that functions as a support group to answer group questions about CHD or express emotions around challenges and successes. Each participant will be paired with a buddy in their group whom they will contact once weekly to check on progress and challenges.

This interaction will also provide an opportunity to practice social skills and to cultivate emotional support. The intervention will present predictable challenges to the participants, and it will be the role of a skillful facilitator to utilize these moments as learning opportunities to acquire new skills, shift negative perceptions, and open to empathetic support.

The study will measure perceived support through the Perceived Social Support Scale (PSSS), network support through the Mannheim Social Support Interview, hostility through the State Trait Anger Expression Inventory (STAXI), emotional support through the Inventory of Socially Supportive Behaviors (ISSB), and health related QOL through the Medical Outcomes Study 36-item Short Form (MOS SF-36). The investigators will repeat these measures at three-month intervals for a total of four measurements, including
the conclusion of the intervention. During each group visit investigators will monitor blood pressure, serum cholesterol, and serum cortisol level. Participants will complete a brief inventory investigating health behaviors including diet, exercise, and medication compliance at each session. This comprehensive data set will provide information throughout the course of the study that will allow for comparison of interactions in the conceptual model. The following table details the reliability and validity of these tools.

**Summary Table of Measure Characteristics:**

<table>
<thead>
<tr>
<th>Tool</th>
<th>Measure</th>
<th>Validity</th>
<th>Reliability</th>
<th>Source</th>
</tr>
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</table>

Scale: poor-adequate-good
Potential weaknesses of this intervention arise from its comprehensive nature, reliance on the skillful facilitation of a provider, challenges with participation, and potential challenges with external validity in the current medical environment. An initial pilot of the study including twelve groups may be helpful for testing feasibility before expanding to a larger trial. This low enrollment of 96-144 participants may not provide the necessary power for all of the subgroup analyses; however, it would provide guidance for adjusting the intervention to a larger scale. To expand to the larger trial the researchers would mirror the power calculations of the ENRICHED trial. They would have a target sample size of 3000 participants to yielded an 88% power to detect a 30% person difference in complying patients or an observed treatment effect of 24% in all patients. Randomization would use a block algorithm, varying block sizes by 2, 4, and 6. The comprehensive data set from this expanded trial would provide many opportunities for hypothesis testing and for analyzing intervention effects in predefined sub-groups of race, gender, support type, and depression.

Without a successful facilitator, participation may wane and the participants may not acquire new skills, support, or perceptions. Care must be taken in choosing, training, and monitoring facilitators throughout the course of the study. In early group visits up to 30-50% of patients did not want to participate. The investigators will need to address this enrollment challenge through active framing and creative methods in order to reach those patients which may need the intervention the most but may be reluctant to participate. Finally, providers have faced difficulty with reimbursement for group visits and have had most success in large HMO environments. Unless the medical environment
changes or providers find a way to successfully bill for group visits, feasibility may be limited to these HMO environments.

From the literature summary, one can see possible influences of social support on the progression of CHD. Currently researchers do not understand this relationship or how to intervene to improve health outcomes. The literature has explored numerous variables in this complex relationship and these studies have been unable to clarify the interactions of the moderating variables. The ENRICHD trial attempted a cost-effective intervention to improve cardiac outcomes, however this effectiveness trial had methodological flaws that left researchers unsure of how to interpret its negative outcomes. The proposed study and conceptual model attempt to address the weaknesses of the ENRICHD trial while incorporating its strengths. The study will provide a foundation for devising a larger trial in which analysis of the comprehensive data set may reveal the interactions of variables in the progression of CHD. Understanding this interaction will provide the theoretical basis for designing future interventions that may translate to effective programs for reducing recurrent myocardial infarction in high-risk groups.

References:


