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The Role of Comprehensive Lifestyle Changes in the Prevention and Treatment of Coronary Heart Disease

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Abstract

Chronic non-communicable diseases including coronary heart disease and type 2 diabetes have become a worldwide epidemic. As of 2002, type 2 diabetes is considered a risk equivalent to coronary heart disease (CHD) in most persons with type 2 diabetes. Both diseases share the same underlying risk factors. In the INTERHEART Study, 9 risk factors have been identified that are relevant in the etiology and prognosis of CHD, accounting for 90% of CHD risk in men and 94% in women. These risk factors are medical as well as psychological in nature and are potentially modifiable by lifestyle changes. The aim of this dissertation was to investigate the role of comprehensive lifestyle changes in the prevention and treatment of CHD. Findings of this dissertation were based on 1 completed randomized phase III trial (i.e., *Lifestyle Heart Trial*; LHT; n=48) and 2 health-insurance sponsored multi-site demonstration projects (phase IV; the completed *Multicenter Lifestyle Demonstration Project*, MLDP, n=440; the ongoing *Multisite Cardiac Lifestyle Intervention Program*, MCLIP, n>2000). The comprehensive lifestyle intervention that was evaluated in these stage III and IV trials consisted of a low-fat, plant-based diet, exercise, stress management, and group support sessions. Follow-ups ranged from 3 months to 5 years.

The following questions were addressed in this dissertation: 1.) Can comprehensive lifestyle changes improve psychological well-being in patients with CHD for up to 5 years and are these changes associated with changes in cardiac variables and well-being in the LHT? 2.) Can patients with CHD and type 2 diabetes in the MLDP make comprehensive lifestyle changes experiencing similar improvements in coronary risk factors and quality of life when compared to CHD patients without type 2 diabetes over 1 year? 3.) Can CHD patients at risk for heart failure with a left ventricular ejection fraction (LVEF) ≤ 40% (stage B according to the guidelines of the American College of Cardiology/American Heart Association) in the MLDP make comprehensive lifestyle changes to achieve a similar improvement in medical risk factors and quality of life as those with a LVEF >40% over 1 year? 4.) Is attendance to the intervention's social support groups in the MLDP associated with CHD patients' adherence to the other 3 program components and with improvements in coronary risk factors and quality of life over 1 year? 5.) Can depressed patients at high risk for CHD (i.e., ≥3 coronary risk factors and/or type 2 diabetes) in the

MCLIP make comprehensive lifestyle changes over 3 months and benefit in terms of reductions in depression and improvements in coronary risk factors over 3 months?

Results from the LHT (phase III) demonstrated reductions in psychological distress and hostility in the experimental group (compared to controls) after 1 year. By 5 years, improvements in hostility tended to be maintained relative to the control group, but reductions in psychological distress were only reported by experimental patients with very high 5 year program adherence. Improvements in diet were related to weight reduction and to decreases in percent diameter stenosis, and improvements in stress management to decreases in percent diameter stenosis at both follow-ups.

Results from the MLDP (phase IV) showed that, regardless of disease severity (i.e., CHD ± type 2 diabetes, CHD + LVEF ≤ 40% or >40%), patients were able to make comprehensive lifestyle changes, experiencing similar improvements in coronary risk factors and quality of life. In regard to patients' social support group attendance in the MLDP, improvements in systolic blood pressure, health behaviors, and quality of life were related to social support group attendance, favoring those who attended more sessions. The associations between support group attendance to systolic blood pressure and to four quality of life (QOL) subscales ('bodily pain', 'social functioning', 'mental health', and the 'mental health' summary score) remained significant when controlling for changes in health behaviors, but dropped to a non-significant level for the QOL subscales 'physical functioning', 'general health', and 'role-emotional'.

Results from the MCLIP (phase IV) showed that initially depressed patients at risk for CHD were able to make comprehensive lifestyle changes. In addition, 73% of patients who were clinically depressed at baseline fell below the cut-off for depression on the Center for Epidemiological Scale–Depression scale (CES-D) by the 3-months follow-up.Depressed patients who became non-depressed also reduced dietary fat intake, perceived stress, and hostility and increased exercise and SF-36 Mental Component Scores more than patients who remained non-depressed and than those who remained or became depressed.

In sum, this dissertation demonstrates the importance of targeting multiple health behaviors in the prevention and treatment of CHD. Medical as well as psychological risk factors can be improved by comprehensive lifestyle changes delaying the onset or the progression of CHD. Results from the LHT

(phase III) suggest that lifestyle changes improve psychological well-being (e.g., depression, hostility) for at least 1 year and that an improved lifestyle is associated with benefits regarding cardiac variables over 5 years. Patients in the LHT may have psychologically adapted or habituated to their new lifestyle after 1 year. Associations between improved lifestyle and improvements in cardiac profiles, however, were still evident at 5 years. Results from the MLDP (phase IV) suggest that lifestyle changes are feasible for patients with differing disease severity. Coronary heart disease patients with diabetes and CHD patients at risk for heart failure were able to make and maintain lifestyle changes with similar improvements in clinical profiles when compared to patients who were less severely diseased. In regard to patients' social support group attendance in the MLDP, results suggest that attendance is independently related to reductions in systolic blood pressure while improvements in quality of life are in part due to improved health behaviors that were facilitated by increased social support group attendance. Results from the MCLIP (phase IV) suggest that comprehensive lifestyle changes are feasible for initially depressed patients at risk for CHD. Seventy-three percent of patients who were clinically depressed at baseline became non-depressed by the 3-months follow-up. In these patients reductions in depression may have also contributed to improvements in health behaviors and psychological well-being.

Evaluation der Rolle von umfassenden Lebensstilveränderungen in der Prävention und Behandlung von koronaren Herzerkrankungen

Zusammenfassung

Die Epidemie von chronischen nicht ansteckenden Erkrankungen wie koronaren Herzerkrankungen (KHK) und Typ-2-Diabetes hat sich weltweit ausgebreitet. In der INTERHEART Studie wurden 9 Risikofaktoren identifiziert, die eine Rolle in der Ätiologie und Prognose von KHK spielen und die 90% des KHK Risikos bei Männern und 94% des Risikos bei Frauen ausmachen. Diese Risikofaktoren sind sowohl medizinischer als auch psychologischer Natur und sind potenziell modifizierbar durch Lebensstilveränderungen. Das Ziel dieser Dissertation war die Rolle von umfassenden Lebensstil-veränderungen in der Prävention und Behandlung von KHK zu erforschen. Befunde dieser Dissertation basieren auf einer abgeschlossenen randomisierten kontrollierten Studie (Phase III, *Lifestyle Heart Trial*, LHT, n=48) und zwei von Krankenversicherungen finanzierten Mehrzentrenstudien (Phase IV; dem abgeschlossenen *Multicenter Lifestyle Demonstration Project*, MLDP, n=440 und dem fortlaufenden *Multisite Cardiac Lifestyle Intervention Program*, MCLIP, n=2700). Die umfassende Lebensstilveränderungsintervention, die in diesen Phase III und IV Studien evaluiert wurde, besteht aus einer niedrig fetthaltigen, pflanzenbasierten Diät, Sport, Stress Management und Gruppenunerstützung. Nacherhebungen reichten von 3 Monaten bis zu 5 Jahren.

Den folgenden Fragen wurde im Rahmen dieser Dissertation nachgegangen: 1.) Führen umfassende Lebensstilveränderungen zu Verbesserungen im psychischem Wohlbefinden bei KHK-Patient/innen über den Zeitraum von 5 Jahren und sind diese Lebensstilveränderungen mit Veränderungen in koronaren Variablen und psychischem Wohlbefinden im Rahmen des LHT verbunden? (*Kapitel 2*) 2.) Können KHK Patient/innen mit Typ-2-Diabetes über den Zeitraum von einem Jahr umfassende Lebensstilveränderungen durchführen und können bei ihnen im Vergleich zu KHK-Patient/innen ohne

Typ-2-Diabetes ähnliche Verbesserungen in koronaren Risikofaktoren und Lebensqualität im Rahmen des MLDP vermerkt werden? (*Kapitel 4*) 3.) Können KHK-Patient/innen, die ein erhöhtes Risiko für Herzversagen haben und eine linksventrikuläre Auswurffraktion von ≤40% (Stadium B nach den Richtlinien des American College of Cardiology und der American Heart Association, 2005) im Vergleich zu KHK-Patient/innen mit einer linksventrikulären Auswurffraktion von >40% über ein Jahr umfassende Lebensstilveränderungen durchführen und erleben sie im Vergleich zu KHK-Patient/innen mit einer linksventrikulären Auswurffraktion von >40% ähnliche Verbesserungen in koronaren Risikofaktoren und Lebensqualität im Rahmen des MLDP? (*Kapitel 5*) 4.) Hängt die Teilnahme an der Gruppenunterstützung der Intervention im Rahmen des MLDP mit der Befolgung der anderen drei Komponenten der Intervention zusammen und mit Verbesserungen in koronaren Risikofaktoren und Lebensqualität? (*Kapitel 6*) 5.) Hängt die Durchführung umfassender Lebensstilveränderungen mit einer Verminderung von depressiver Symptomatik und Verbesserungen in koronaren Risikofaktoren bei Frauen und Männern mit hohem KHK-Risiko im MCLIP zusammen? (*Kapitel 7*)

Kapitel 1 stellt einen allgemeinen Überblick über die Rolle von umfassenden Lebensstil-veränderungen in der Prävention und Behandlung von KHK dar. In Kapitel 2 werden bezüglich der Frage, ob umfassende Lebensstilveränderungen zu Verbesserungen des psychologischen Wohlbefindens bei Herzpatienten über den Zeitraum von 5 Jahren führen und ob diese Lebensstilveränderungen mit Veränderungen in koronaren Variablen und psychischem Wohlbefinden zusammenhängen, Befunde des LHT (Phase III) dargestellt. Ergebnisse des LHT weisen auf eine Reduktion in psychologischem Distress und Feindseligkeit in der Versuchsgruppe (im Vegleich zur Kontrollgruppe) nach einem Jahr hin. Nach 5 Jahren wurde ein Trend zur Aufrechterhaltung der Reduktion von Feindseligkeit im Vegleich zur Kontrollgruppe vermerkt. Verminderungen des psychologischen Distress nach 5 Jahren wurden nur in Patient/innen der Versuchsgruppe vermerkt, die eine sehr hohe 5-Jahres Interventionscompliance zeigten. Verbesserungen in der Ernährung hingen mit Gewichtsabnahme und mit einer Reduzierung des prozentualen Durchmessers der Stenose zusammen. Verbesserungen im Stress Management waren ebenfalls mit einer Reduzierung des prozentualen Durchmessers der Stenose korreliert. Diese Befunde

wurden bei beiden Folgenuntersuchungen (d.h., nach einem und 5 Jahren) festgestellt und weisen darauf hin, dass Lebensstilveränderungen psychisches Wohlbefinden über den Zeitraum von einem Jahr verbessern können und dass diese Veränderungen ebenfalls auf lange Sicht mit verbesserten koronaren Variablen verbunden sind.

In Kapitel 3 wird einleitend zu Kapitel 4 spezifisch auf die Rolle von umfassenden Lebensstilveränderungen bei KHK Patient/innen mit und ohne Typ-2-Diabetes eingegangen. In Kapitel 4 werden dann Befunde zu der Fragestellung präsentiert, ob KHK Patient/innen mit Typ-2-Diabetes über den Zeitraum von einem Jahr umfassende Lebensstilveränderungen durchführen können und ob bei ihnen im Vergleich zum KHK Patient/innen ohne Typ-2-Diabetes ähnliche Verbesserungen in koronaren Risikofaktoren und Lebensqualität vermerkt werden können. Befunde des MLDP (Phase IV) zeigen, dass Patient/innen, unabhängig vom Krankheitsschweregrad (d.h. KHK± Typ-2-Diabetes), in der Lage waren umfassende Lebensstilveränderungen durchzuführen mit ähnlichen Verbesserungen in koronaren Risikofaktoren und Lebensqualität.

In Kapitel 5 können ähnliche Befunde des MLDP (Phase IV) für den Vergleich von KHK Patient/innen mit einer linksventrikulären Auswurffraktion von ≤40% zu Patient/innen mit einer linksventrikulären Auswurffraktion >40% aufgewiesen werden. Beiden Patientengruppen war es möglich umfassende Lebensstilveränderungen durchzuführen und ähnliche Verbesserungen in koronaren Risikofaktoren und Lebensqualität konnten vermerkt werden. In Anbetracht der schlechten Prognose von Patient/innen mit erhöhtem Risiko für Herzversagen weisen diese Befunde auf den Nutzen einer gezielten Lebensstilveränderungsintervention in dieser Patientengruppe hin, um ein Fortschreiten der Erkrankung zu vermeiden.

In Kapitel 6 wurde erforscht, ob die Teilnahme an der Gruppenunterstützung der Intervention im Rahmen des MLDP (Phase IV) mit der Befolgung der anderen drei Komponenten der Intervention zusammenhängt und mit Verbesserungen in koronaren Risikofaktoren und Lebensqualität. Es konnte gezeigt werden, dass Verbesserungen des systolischen Blutdrucks, der Gesundheitsverhaltensweisen und der Lebensqualität mit der Teilnahme an der Gruppenunterstützung zusammenhängen. Patient/innen, die

an mehr Gruppenunterstützungssessions teilnahmen, profitierten mehr. Die Assoziationen zwischen Teilnahme an der Gruppenunterstützung und systolischem Blutdruck und vier der Lebensqualitäts-subskalen ("bodily pain", "social functioning", "mental health", und der "mental health" Summenscore) blieben signifikant, nachdem für Veränderungen im den Gesundheitsverhaltensweisen kontrolliert wurde, aber verloren an Signifikanz für die Subskalen "physical functioning", "general health", und "role-emotional". Diese Ergebnisse unterstreichen die Relevanz von Gruppenunterstützung in der Veränderung von Gesundheitsverhaltensweisen bei KHK-Patient/innen.

Kapitel 7 widmet sich der Frage, ob umfassende Lebensstilveränderungen für Patient/innen mit depressiver Symptomatik und hohem KHK-Risiko durchführbar sind. Ausserdem wurde eruiert, ob umfassende Lebensstilveränderungen mit einer Verminderung von depressiver Symptomatik und Verbesserungen in koronaren Risikofaktoren bei Frauen und Männern mit hohem KHK-Risiko im MCLIP zusammenhängt. Befunde des MCLIP (Phase IV) zeigten, dass Patient/innen mit initialer depressiver Symptomatik in der Lage waren umfassende Lebensstilveränderungen durchzuführen. Ausserdem war die depressive Symptomatik bei 73% der Patient/innen nach 3 Monaten signifikant reduziert (<16 auf der Center for Epidemiological Scale–Depression Skala). Patient/innen mit reduzierter depressiver Symptomatik reduzierten überdies den Fettgehalt ihrer Ernährung und wahrgenommenen Stress und Feindseligkeit und verbesserten ihr Sportverhalten und SF-36 Mental Component Scores mehr als Patient/innen, die über den Zeitraum von 3 Monaten nicht-depressiv blieben oder solche, die depressiv blieben oder depressiv wurden. In Anbetracht der grossen Relevanz von Depression in der Ätiologie von KHK deuten diese Ergebnisse auf die grosse Bedeutung der Behandlung von Depression in der Prävention von KHK hin.

Die Ergebnisse dieser Dissertation weisen auf die Wichtigkeit der gezielten Veränderung multipler Gesundheitsverhaltensweisen in der Prävention und Behandlung von KHK hin. Sowohl medizinsche als auch psychologische Risikofaktoren können durch Lebensstilveränderungen verbessert werden und das Eintreten oder Fortschreiten von KHK verzögern. Ergebnisse des LHT (Phase III, siehe Kapitel 2) weisen darauf hin, dass Lebensstilveränderungen psychisches Wohlbefinden (z.B., Depression,

Feindseligkeit) über den Zeitraum von einem Jahr verbessern können und dass diese Veränderungen ebenfalls auf lange Sicht mit verbesserten koronaren Variablen verbunden sind. Patient/innen des LHT haben sich möglicherweise nach einem Jahr an ihren neuen Lebensstil psychologisch adaptiert oder habituiert. Die Zusammenhänge zwischen verbessertem Lebensstil und verbesserten koronaren Profilen waren allerdings auch nach fünf Jahren vemerkbar. Ergebnisse des MLDP (Phase IV) deuten darauf hin, dass Lebensstilveränderungen für Patient/innen mit unterschiedlichem Schweregrad praktikabel sind. KHK Patient/innen mit Typ-2-Diabetes und jene mit erhöhtem Risiko für Herzversagen waren in der Lage Lebensstilveränderungen durchzuführen und aufrechtzuerhalten und erlebten im Vergleich zu weniger schwer erkrankten Patient/innen (z.B. KHK Patient/innen ohne Typ-2-Diabetes) ähnliche Verbesserungen der klinischen Profile (siehe Kapitel 4 und 5). Des Weiteren scheint ein unabhängiger Zusammenhang zwischen der Teilnahme an der Gruppenunterstützung im Rahmen des MLDP und Reduktionen des systolischen Blutdrucks zu bestehen, wohingegen Verbesserungen der Lebensqualität teilweise durch verbesserte Gesundheitsverhaltensweisen bedingt sind, welche durch Gruppenunterstützung beeinflusst werden (siehe Kapitel 6). Abschliessend weisen die Befunde des MCLIP (Phase IV) auf einen Zusammenhang zwischen Lebensstilveränderungen und reduzierter depressiver Syptomatik und verbesserten Koronarfaktoren bei Patient/innen mit hohem KHK-Risiko hin (siehe Kapitel 7).

CHAPTER 1

Introduction

Chronic non-communicable diseases (CNCDs) including coronary heart disease (CHD) and type 2 diabetes have become a worldwide epidemic (Lopez et al., 2006; World Health Organization, 2005, American Heart Association, 2007). These diseases currently account for approximately 60% of all deaths worldwide (Daar et al., 2007). In the next 15 years, 388 million people worldwide are estimated to die of one or more of these CNCDs.

According to the World Health Organization (2005), 80% of premature deaths from heart disease, stroke, and diabetes can be prevented with behavioral and pharmaceutical interventions. The INTERHEART Study identified 9 risk factors as relevant in the etiology and prognosis of CHD, accounting for 90% of CHD risk in men and 94% in women (Yusuf et al., 2004). These risk factors are medical (history of hypertension or diabetes, abdominal obesity), behavioral (regular physical activity, daily consumption of fruits and vegetables, regular alcohol consumption, smoking), and psychosocial (e.g., stress at work, depression) in nature (Rosengren et al., 2004; Yusuf et al., 2004). All of these risk factors are potentially modifiable by lifestyle changes.

The Role of Lifestyle Changes in the Prevention of Diabetes, Heart Disease, and Heart Failure

The importance of lifestyle in the prevention of type 2 diabetes, CHD, and associated co-morbidities of hypertension, hyperlipidemia, and obesity has been well-documented (Costacou & Mayer-Davis, 2003; Toobert, Stryker, Glasgow, Barrera, & Angell, 2005; Tuomilehto et al, 2001). Numerous studies testing lifestyle interventions have demonstrated improvements in cardiovascular risk factors (Boulé, Haddad, Kenny, Wells, & Sigal, 2001; Boulé, Kenny, Haddad, Wells,

& Sigal, 2003; Clark, Hartling, Vandermeer, & McAlister, 2005; Elmer et al., 2006; Hu & Willett, 2002; Kronenberg et al., 2000; Look AHEAD Research Group, 2007; Orchard et al., 2005; Stampfer et al., 2000; Wister et al., 2007) and a reduction of progression from impaired glucose tolerance to type 2 diabetes (Lindström et al., 2006; Pan et al., 1997; The Diabetes Prevention Program Research Group, 2002). Participation in lifestyle interventions that are embedded in standard cardiac rehabilitation also seems to be beneficial in preventing the progression of CHD. Chapter 3 contains a detailed review of studies investigating the role of lifestyle in prevention strategies targeted at patients with both, CHD and type 2 diabetes.

The Role of Psychosocial Risk Factors in the Etiology and Prognosis of CHD

A growing body of evidence indicates that psychosocial factors confer CHD risk in addition to common cardiac risk factors (e.g., Berkman et al., 2003; Hemingway & Marmot, 1999; Kuper, Marmot, & Hemingway, 2002; Rozanski, Blumenthal, Davidson, Saab, & Kubzansky, 2005). Multiple interactions of these psychosocial risk factors with each other and with the environment have been suggested. Orth-Gomer, Weidner, Anderson & Chesney (in press) propose three pathways by which psychosocial risk factors can influence the etiology and prognosis of CHD. All 3 pathways involve interactive relationships with stressful social environments (e.g., work stress).

The first pathway represents an interactive relationship between stressful social environments and emotional response styles such as trait anger and depression (Kuper, Marmot, & Hemingway, 2002). Trait anger is characterized by "mistrust and cynicism and can lead to antagonistic or aggressive behavior" (Orth-Gomer, Weidner, Anderson, & Chesney, in press). Recent studies indicate that trait anger or symptoms of anger seem to be predictive of CHD morbidity and cardiac events (Eaker, Sullivan, Kelly-Hayes, D'Agostino, & Benjamin, 2004; Hill-Golden, 2006; Williams, Nieto, Sanford, Couper, & Tyroler, 2002; Williams, Nieto, Sanford, & Tyroler, 2001; Williams et al., 2000). The personality construct of trait anger originated from research on type A behavior. Friedman and colleagues (1986) were the first to acknowledge the relevance of Type A behavior in the etiology and prognosis of CHD (Ragland & Brand,

1988). Type A behavior is defined as a cluster of personality characteristics including a sense of time urgency, loud and explosive speech, impatience, hostility/anger, and competitiveness. Hostility, a component of type A behavior, predicted recurrent events among postmenopausal women with CAD (Chaput et al., 2002) and was a major risk factor for CVD mortality in the Multiple Risk Factor Intervention Trial (MRFIT) over a follow-up of 16 years (Matthews, Gump, Harris, Haney, & Barefoot, 2004).

Depression is another response style that is relevant in genesis and pathogenesis of CHD. Depression is a major risk factor for incident CHD (Hemingway & Marmot, 1999; Kuper, 2002), predicts cardiac events in patients with stable coronary artery disease (Frasure-Smith & Lesperance, 2008), and is highly prevalent in patients among patients with diabetes compared to those without diabetes following major cardiac events (Milani & Lavie, 1996). The presence of diabetes appears to double the risk of comorbid depression (Anderson, Freedland, Clouse, & Lustman, 2001), which is associated with poor glycemic control and increased risk for diabetes complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001; Lustman et al., 2000), including initial CHD events and progression (Clouse et al., 2003; Frasure-Smith et al., 2000). Depression is also implicated in the development of metabolic syndrome. In fact, a recent prospective cohort study found that depressive symptoms at baseline predicted an increased risk of developing metabolic syndrome in initially healthy women over 15 years (Räikkönen, Matthews, & Kuller, 2007). Depression is associated with a more sedentary lifestyle, smoking, obesity, lack of exercise, and poor glycemic control (Gonzalez et al., 2007; Goodman & Whitaker, 2002; Katon et al., 2004; Patton et al., 1998; Rajala et al., 1994; Steptoe et al., 1997). Hence, depression and these health behaviors may influence coronary risk synergistically.

The second pathway suggested by Orth-Gomer & colleagues (in press) involves the direct association of stressful social environments, such as those characterized by low socioeconomic status, and health behaviors (i.e., unhealthy dietary habits, physical inactivity, smoking) (Lantz et al., 2001). People living in low socioeconomic environments may be limited in their daily physical activity because of

higher crime rates in certain neighborhoods and may have limited access to grocery stores that sell healthy foods (Kristenson, Erikson, Sluiter, Starke, & Ursin, 2004).

The third pathway suggests that social stress can lead to maladaptive breathing habits (i.e., apneic breathing) that can alter the set point for blood gases and plasma volume (Anderson & Chesney, 2003). Sleep apnea is a major risk factor for chronic hypertension (Hagens et al., 2006) and represents a characteristic of chronic heart failure (Mortara et al., 1997) and is associated with incrased CHD mortality in patients with chronic heart failure (LaRovere et al., 2007). Orth-Gomer and colleagues (in press) consider all 3 pathways major routes influencing the etiology and prognosis of CHD.

Another psychological factor not included in this model is social support. Social support may act as a direct buffer against susceptibility to disease (Hemingway & Marmot, 1999; Kuper, 2002; Steptoe, 1999) or as an indirect buffer for a depressive response style. Support for the first hypothesis comes from the Stockholm Female Coronary Risk Study, that showed that a lack of social integration independently predicted recurrent cardiac events in women with CAD (Horsten, Mittleman, Wamala, Schenck-Gustafsson, & Orth-Gomer, 2000). These findings were confirmed by another study showing that patients with small social networks were at elevated risk for CHD mortality (Brummett et al., 2001), which was unrelated to disease severity, demographics, or psychological distress. Support for the second hypothesis comes from Horsten and colleagues (2000) suggesting a cluster of social isolation and depression as an explanation for a poor prognosis and a higher risk of recurrent cardiac events in patients with CHD. Lack of social support may lead to increased depressive symptomatology, particularly in patients with CAD (Brummett et al., 1998), and thereby affect survival (Barefoot et al., 1996; Frasure-Smith, Lesperance, & Talajic, 1995). However, as socially isolated patients generally do not report higher levels of psychological distress, they may not feel the need to engage more socially, which could potentially present a problem in the enrollment of these patients in interventions designed to reduce mortality (Brummett et al., 2001).

Psychologial Treatments in Prevention Interventions

Because of the importance of pychosocial risk factors in the prognosis of CHD, most standard cardiac rehabilitation interventions include psychological treatment or stress management techniques to address psychosocial risk factors such as depression and stress (Berkman et al., 2003; Frasure-Smith et al., 1997; Grace et al., 2005; Hofman-Bang et al., 1999; Jones & West, 1996; Kuper, Marmot, & Hemingway, 2002; Lisspers et al., 1999; Rees, Bennett, West, Davey & Ebrahim, 2004) and to help patients increase effective coping with these psychosocial risk factors (Rees, Bennett, West, Davey, Ebrahim, 2004). However, effects of psychological interventions on psychosocial risk factors such as depression and anxiety are often small (Frasure-Smith et al., 1997; Grace et al., 2005; Hofman-Bang et al., 1999; Kuper, Marmot, & Hemingway, 2002; Lisspers et al., 1999; Rees, Bennett, West, Davey & Ebrahim, 2004) and can sometimes not be isolated from behavioral (i.e., exercise, diet, smoking cessation) or pharmaceutical interventions in cardiac rehabilitation. A recent meta-analysis by Linden, Phillips, & Leclerc (2007) attempted to dissect the effects of psychological treatment of cardiac patients from those of behavioral interventions. Linden and colleagues (2007) found that psychological treatments, primarily focusing on the reduction of depression and distress, reduced mortality and recurrence of cardiovascular events. Interestingly, these effects were limited to psychological treatment initiated two months after the cardiac event indicating that psychological treatment benefited patients most who lacked psychological resources to recover from the cardiac event without professional help.

Findings on the benefits of psychological interventions and associations of reduced psychosocial risk factors with standard coronary risk factors in patients at high risk for CHD are rare. Only a few studies have assessed changes in depressive symptoms and associations of reduced depressive symptoms with standard coronary risk factors in patients with type 2 diabetes. Georgiades and colleagues (2007) found that cognitive-behavioral therapy significantly reduced symptoms of depression in patients with diabetes, over a 1-year period. However, these reductions were not associated with changes in HbA1c or fasting glucose levels. Toobert and colleagues (2007) found no significant changes in depression over 2 years in postmenopausal women with diabetes who participated in a comprehensive lifestyle intervention

(diet, exercise, stress management, smoking cessation) compared to a usual care group. Thus, psychological treatment after two months may be particularly beneficical in patients undergoing cardiac rehabilitation. The role of psychological treatment in patients at risk for CHD, however, is still largely unknown.

Ouline of the Dissertation

The current dissertation evaluated a comprehensive lifestyle change program (described below) that included two behavioral intervention components (i.e., low-fat diet, moderate exercise) and two intervention components targeted at reducing psychological stress and supporting patients in adhering to the other program components. Outcomes included in this dissertation were medical as well as psychological and included changes in health behaviors, coronary risk factors, quality of life, and psychological risk factors (depression, hostility, anger, perceived social support). Patient groups analyzed in this dissertation included patients with CHD, patients with CHD and type 2 diabetes, and patients with ≥3 cardiovascular risk factors and/or type 2 diabetes. Follow-ups ranged from 3 months to 5 years.

The empirical chapters of this dissertation (i.e., Chapters 2 and 4-7) are based on data coming from a.) the Lifestyle Heart Trial (LHT), a stage III trial, conducted at the San Francisco Bay Area from 1988-1993 following 48 patients with CHD over 1 and 5 years b.) the insurance-sponsored Multicenter Lifestyle Demonstration Project (MLDP), a stage IV observational study, conducted at 8 different hospital sites in the U.S. from 1993-1997, that included 440 CHD patients (91 of which had type 2 diabetes; 236 of which had a documented left ventricular ejection fraction) with 3-months and 1-year follow-ups, and c.) the insurance-sponsored observational stage IV Multisite Cardiac Lifestyle Intervention Program (MCLIP), conducted at 22 hospital sites in the U.S. (1998-ongoing), that includes >2000 patients thus far who were followed over 3 months (including CHD patients and patients with ≥3 cardiovascular risk factors and/or type 2 diabetes; data presented in Chapter 7 are solely based on 997 patients with ≥3 cardiovascular risk factors and/or type 2 diabetes and with complete Center of the Epidmiological Scale Depression Scale (CES-D) data that were collected from September 1998 to

December 2007). Patient recruitment, inclusion and exclusion criteria of these three studies have been described in detail previously (Billings, 2000; Daubenmier et al., 2007; Koertge et al., 2003; Ornish et al., 1990; Ornish et al., 1998).

Design of the Comprehensive Lifestyle Change Program evaluated in this Dissertation

To acquaint patients and their spouses/partners with the comprehensive lifestyle change program, the treatment intervention began with a twelve-hour intensive orientation seminar at the hospital site (offered either over two or three days). The orientation program included daily lectures that provided the scientific rationale for the components of the program (i.e., diet, exercise, stress management, group support) as well as demonstration sessions. Following the orientation, patients attended program sessions three times per week for 12 weeks. Two of these three weekly sessions focused on the four program components in one-hour blocks. The third weekly session consisted of a one-hour aerobic exercise session (for example on a treadmill) and one-hour lectures designed to meet the education objectives. Overall, 36 sessions were offered during the first 3 months of the program. Over the following 40 weeks, patients continued to meet in intervention groups once a week for a 4-hour session, focusing on the program components. In addition, they were instructed to follow the diet and exercise program and practice stress management on their own (Billings, 2000).

Adherence to the Individual Components of the Lifestyle Change Program

Detailed information of the components of the lifestyle change program has been reported previously (Billings, 2000; Ornish et al., 1998).

Diet: Two meals per week were provided as part of the evening meetings at the hospital site. In addition, periodic potluck dinners were held, for which patients and their spouses prepared food at home to bring to the group meetings for an evening meal. The diet was a low-fat, whole-foods, vegetarian diet including fruits, vegetables, grains, legumes, and soybean products without caloric restriction. It excluded caffeine and animal products except egg whites and one cup of non-fat milk or yoghurt per day. This

averaged 10 mg of cholesterol intake per day. The diet guidelines overall emphasized the consumption of complex carbohydrates and discouraged the use of simple sugars. Alcohol, which was not served and neither discouraged nor encouraged, was restricted to one drink (one cocktail or glass of wine or beer) per day in those without prior alcohol abuse. Sodium intake was restricted only for hypertensive patients. The meals contained approximately 10% of daily calories from fat, 15% from protein, and 75% from predominantly complex carbohydrates. It was nutritionally adequate and met the recommended daily allowances for all nutrients except vitamin B12, which was supplemented. The adherence goal for diet was to restrict the percentage of calories from fat to 10%.

Moderate Exercise: The exercise prescription followed the guidelines of the American College of Sports Medicine (Franklin, 1991). Each patient was prescribed an exercise level according to a baseline treadmill exercise stress test; these levels were updated during each of the following times when subsequent treadmill tests were performed. Patients were asked to exercise a minimum of 30 minutes per session exercising with their prescribed target heart rates and/or perceived exertion levels. The adherence goal for exercise was three hours per week. Target heart rates were calculated at 50-80% of maximal heart rate achieved during the treadmill test using the Karvonen formula (Karvonen, Kentala, & Mustata, 1957). If ischemia occurred during the baseline stress test, the heart rate at which 1 mm of ST segment depression first occurred was designated the maximum heart rate. In addition, patients were trained to identify exertion levels by means of the Borg Perceived Exertion Scale (Borg, 1982) and asked to maintain exertion levels of 11-14 (fairly light to somewhat hard) on the 6-20 point scale. Most patients' exercise consisted of brisk walking on their own. On site, they were supervised on treadmills, exercise bicycles, stair climbers, rowing machines, and hand ergometers.

Stress Management: Patients were instructed to practice one hour of stress management per day (Ornish et al., 1990; Ornish et al., 1998). Specifically a 1-hour practice included 30 minutes of stretching based on the asanas (English: poses) in hatha yoga, 15 minutes of progressive relaxation, 5 minutes of breathing, 8 minutes of meditation and 2 minutes of visualization of patients' arteries dilating with

increased blood flow to the heart in that order (Billings, 2000; Billings, Scherwitz, Sullivan, & Ornish, 1996; Ornish et al., 1990).

Group Support: the two weekly groups were designed to provide support to help patients adhere to the lifestyle change program. Group support sessions were led by a clinical psychologist who facilitated group interactions. Group members were encouraged to express their feelings and to avoid problem-solving and giving advice or finding solutions, but instead to listen to each other with empathy and compassion (Billings, 2000; Billings, Scherwitz, Sullivan, Sparler, & Ornish, 1996; Schulz et al., in press).

In regard to *smoking cessation*, participants had to quit smoking before entering the study.

Previous Phase III and IV Research on the Comprehensive Lifestyle Change Program

The first randomized controlled trial asking patients to make comprehensive lifestyle changes and following them for 5 years was the Lifestyle Heart Trial conducted in the San Francisco Bay Area (Gould et al., 1995; Ornish et al., 1998; Ornish et al., 1990). In this trial, patients were asked to make intensive dietary and lifestyle changes. Compared to a randomized control group, intervention participants reduced their coronary risk factors, showed a 91% reduction in frequency of angina, showed a 2.5 time reduction in cardiac events (Ornish et al., 1998) as well as significant improvement in myocardial perfusion as revealed by cardiac PET imaging (Gould et al., 1995) and plaque regression as revealed by quantitative coronary angiography (Ornish et al., 1990). This trial was a phase III trial designed to evaluate the effectiveness of the intervention in comparison to a control group. The sample size of this clinical trial was rather small (n=48) and patients were predominantly male and white. Nevertheless, results of this trial prompted several health plans to provide insurance coverage for the Ornish Program.

Consequently, two multi-site demonstration projects were conducted representing the phase IV research (i.e., “long-term surveillance of an intervention… (which) do not involve control groups…”; (Friedman, Furberg, & DeMets, 1998, p. 5) of the Ornish trials (Weidner & Ornish, 2006). Both employ the same intervention as the LHT with clinical assessments at baseline, 3 and 12 months. The first

demonstration project, the Multicenter Lifestyle Demonstration Project (MLDP; 1993-97), was conducted at 8 geographically diverse sites in the USA (440 patients (21% female) with CHD and a control group matched by disease severity provided by Mutual of Omaha Insurance Company). Analyses of MLDP data from a subgroup of CHD patients eligible for a revascularization procedure indicated that experimental group patients were able to avoid revascularization for at least 3 years by making comprehensive lifestyle changes without increasing cardiac morbidity and mortality relative to matched control patients who were also eligible for a procedure and received the procedure at study entry (Ornish, 1998). Comparisons of changes in risk factors and quality of life in men to those of women indicated similar benefits and were comparable to those observed in the intervention group of the LHT (Koertge et al., 2003).

The second demonstration project, the Multisite Cardiac Lifestyle Intervention Program (MCLIP; 1998-ongoing) consists of 22 sites and is currently covered by several health plans, of which Highmark, Inc., West Virginia Public Employees Insurance Agency, and Mountain State Blue Cross Blue Shield include the program as a defined benefit. Current enrollment in the MCLIP exceeds 2,000 patients (i.e., patients with at least 3 coronary risk factors and/or type 2 diabetes, patients with CHD). The relative importance of each program component for cardiac outcomes and quality of life has been evaluated by Daubenmier and colleagues (2007). Results indicated that improvements in dietary fat intake, exercise, and stress management are individually, additively, and interactively related to coronary risk and psychosocial factors in patients with CHD in the MLCIP. Other Phase IV research findings indicate that patients, regardless of socioeconomic status and symptom severity, can follow the program recommendations, showing significant reductions in cardiac risk profiles and improvements in quality of life (Frattaroli, Weidner, Merritt-Worden, Frenda, & Ornish, 2008; Govil, Weidner, Merritt-Worden, & Ornish, 2007). Results of the MCLIP prompted Medicare/Medicaid to include the intervention as a defined benefit. As of 2007, the U.S. Centers for Medicare and Medicaid Services have included this program as a defined cardiac rehabilitation benefit for Medicare beneficiaries with coronary heart disease (CMS, 2007).

Aim of the Dissertation and Outline of the Chapters

The aim of this dissertation was to investigate the role of comprehensive lifestyle changes in the prevention and treatment of CHD. Specifically, adherence to a comprehensive lifestyle change intervention and related coronary and psychological outcomes were investigated in several patient populations (pre- to post CHD) involving two stages of research (stages III and IV, Friedman, Furberg, & DeMets, 1998). The following five questions were addressed in this dissertation: 1.) Can comprehensive lifestyle changes improve psychological well-being in patients with CHD for up to 5 years and are these changes associated with changes in cardiac variables and well-being in the LHT? 2.) Can patients with CHD and type 2 diabetes make comprehensive lifestyle changes experiencing similar improvements in coronary risk factors and quality of life when compared to CHD patients without type 2 diabetes over 1 year in the MLDP? 3.) Can CHD patients at risk for heart failure with a left ventricular ejection fraction (LVEF) ≤ 40% (stage B according to the guidelines of the American College of Cardiology/American Heart Association, 2005) make comprehensive lifestyle changes to achieve a similar improvement in medical risk factors and quality of life as those with a LVEF >40% over 1 year in the MLDP? 4.) Is attendance to the interventions social support groups in the MLDP associated with CHD patients' adherence to the other 3 program components and with improvements in coronary risk factors and quality of life over 1 year? 5.) Can depressed patients with metabolic syndrome (i.e.., ≥3 coronary risk factors and/or type 2 diabetes) in the MCLIP make comprehensive lifestyle changes over 3 months and benefit in terms of reductions in depression and improvements in coronary risk factors?

This dissertation consists of five empirical chapters (i.e., Chapters 2 and 4-7) and one review article (Chapter 3): Chapter 2 focuses on the psychological outcomes in the Lifestyle Heart Trial. Chapter 3 is an introduction to the empirical chapter 4 and gives an overview of the literature on secondary prevention strategies of CHD in patients with type 2 diabetes. Chapters 4 and 5 empirically examine the feasibility and benefits of a comprehensive lifestyle intervention in patients with CHD and type 2 diabetes and in CHD patients at risk for heart failure with a LVEF ≤ 40% in the MLDP. Chapter 6 investigates

whether the intervention's social support group sessions are associated with changes in coronary and psychological outcomes in CHD patients in the MLDP. Chapter 7 examines whether comprehensive lifestyle changes are associated with reductions in depression and with improved coronary risk factors in men and women at high risk for CHD in the MCLIP.

The main focus of Chapter 2 is to compare psychological outcomes (psychological distress, anger, hostility, perceived social support by group (intervention group, n=28; control group, n=20) and time (baseline, 1, 5 years) and examine the relationships of lifestyle changes to cardiac variables in the Lifestyle Heart Trial. Chapter 3 reviews the feasibility of lifestyle interventions in the secondary prevention of CHD in patients with diabetes. Chapter 4 examines whether CHD patients with and without diabetes could make changes in lifestyle with similar improvements in clinical profiles. Major outcomes include changes in health behaviors, coronary risk factors, and quality of life. Chapter 4 analyzes whether CHD patients at risk for heart failure with a LVEF $\leq$ 40% can make changes in lifestyle with similar improvements in clinical profiles as patients with a LVEF > 40%. Chapter 6 analyzes changes in coronary risk factors, health behaviors, and quality of life by tertiles of social support group attendance of CHD patients in the MLDP. Chapter 7 examines whether depressed patients at high risk for CHD (i.e.., $\geq$3 coronary risk factors and/or type 2 diabetes) in the MCLIP were able to make comprehensive lifestyle changes over 3 months and benefit in terms of reductions in depression and improvements in coronary risk factors. Specifically, clinical and psychological outcomes were compared in 3 groups of MCLIP participants with $\geq$3 cardiovascular risk factors and/or diabetes: (1) depressed patients who became non-depressed (CES-D $\leq$16); (2) patients who remained or became depressed (CES-D >16); (3) non-depressed patients who remained non-depressed.

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CHAPTER 2

Long-Term Effects of Lifestyle Changes on Well-Being and Cardiac Variables among CHD Patients

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Abstract

Objective: To focus on psychological well-being in the Lifestyle Heart Trial (LHT), an intensive lifestyle intervention including diet, exercise, stress management, and group support that previously demonstrated maintenance of comprehensive lifestyle changes and reversal of coronary artery stenosis at 1 and 5 years. **Design & Main Outcome Measures:** The LHT was a randomized controlled trial using an invitational design. We compared psychological distress, anger, hostility, and perceived social support by group (intervention group, n=28; control group, n=20) and time (baseline, 1, 5 years) and examined the relationships of lifestyle changes to cardiac variables. **Results:** Reductions in psychological distress and hostility in the experimental group (compared to controls) were observed after 1 year ($p<.05$). By 5 years, improvements in hostility tended to be maintained relative to the control group, but reductions in psychological distress were only reported by experimental patients with very high 5 year program adherence. Improvements in diet were related to weight reduction and to decreases in percent diameter stenosis, and improvements in stress management to decreases in percent diameter stenosis at both follow-ups (all $p<.05$). **Conclusion:** These findings illustrate the importance of targeting multiple health behaviors in secondary prevention of CHD.

KEYWORDS: lifestyle changes, psychological well-being, cardiac variables

Introduction

Coronary heart disease (CHD) remains the leading cause of death in most industrialized countries (American Heart Association, 2007 Update). Intensive efforts have been made to identify risk factors of CHD. In the INTERHEART Study, 9 potentially modifiable risk factors have been identified that play a major role in the etiology and prognosis of CHD, accounting for 90% of CHD risk in men and 94% in women (Yusuf et al., 2004). Among these are psychosocial factors such as depression and stress. Similarly, several reviews have examined the evidence for causal relationships of psychosocial factors to CHD (Rozanski, Blumenthal, Davidson, Saab, & Kubzansky, 2005; Schneiderman, Antoni, Saab, & Ironson, 2001). Psychosocial factors such as hostility, depression, and anxiety which are often summarized as "psychological distress" are regarded as risk factors for CHD morbidity and mortality (Chaput et al., 2002; Matthews, Gump, Harris, Haney, & Barefoot, 2004; Kuper, Marmot, & Hemingway, 2002; Hemingway & Marmot, 1999; Rasul, Stansfeld, Hart, & Davey Smith, 2005). Social support, on the other hand, appears to act as a buffer for stress (Hemingway & Marmot, 1999) and sense of coherence plays a role in the adoption and maintenance of health behaviors relevant to secondary prevention of CHD (Kuuppelomäki & Utriainen, 2003; Lindmark, Stegmayr, Nilsson, Lindahl, & Johansson, 2005).

It remains unclear whether secondary prevention programs for CHD that target psychosocial risk factors are effective in improving psychological well-being. For example, patients with ischemic heart disease significantly reduced psychological distress after participation in cardiac rehabilitation including regular stress management and exercise compared to patients receiving usual care over a 4-month follow-up (Blumenthal et al., 2005). Exercise-based cardiac rehabilitation has also been shown to be beneficial in reducing hostility in patients with high levels of hostility over a similar length of follow-up (Lavie & Milani, 1999, 2005) as well as depression for up to 1 year (Lett, Davidson, & Blumenthal, 2005). However, a few studies testing psychological or stress management interventions in cardiac rehabilitation have only found minimal reductions in anxiety and depression (Frasure-Smith et al., 1997; Grace, Abbey, Pinto, Shnek, Irvine, & Stewart, 2005; Hofman-Bang et al., 1999; Kuper, Marmot, & Hemingway, 2002; Lisspers et al., 1999; Rees, Bennett, West, Davey & Ebrahim, 2004). Indeed, two large randomized

clinical trials did not show any differences in psychological status between rehabilitation group patients participating in psychological interventions and control group patients (Berkman et al., 2003; Jones & West, 1996).

It should be noted that follow-up in the majority of these studies was limited to 3-12 months. Only two studies reported findings beyond 1 year. One study included a 9-year follow-up after a 3-months behavioral intervention (exercise, psychosocial group intervention, and individual psychological therapy) which did not indicate that changes in lifestyle led to further reductions in negative affect beyond 3 months (Denollet & Brutsaert, 2001). However, improvements in affect during the first 3 months of follow-up seemed to have a beneficial effect on prognosis in CHD patients over 9 years. Another study included a 4.5-year follow-up and investigated whether an intervention that included intensive cardiac and type A counseling for 4-6 months and monthly meetings for the remainder of the study would alter type A behavior and CHD prognosis in post myocardial infarction patients (Friedman et al., 1986). The authors found that the intervention not only reduced type A behavior but also cardiac morbidity and mortality over 4.5 years in post myocardial infarction patients when compared to a control group that only received cardiac counseling or to a no treatment comparison group. In sum, there is limited knowledge about long-term effects (i.e., >1 year) of maintained lifestyle changes on psychological well-being.

The goals of the present analyses were to evaluate: (a) the long-term effects of comprehensive lifestyle changes (i.e., diet, exercise, stress management, group support) on psychological well-being; and to identify (b) associations of individual lifestyle changes with changes in specific cardiac variables in patients with CHD over 5 years who participated in the Lifestyle Heart Trial (LHT). The main focus of the LHT was to evaluate whether comprehensive lifestyle changes could halt or reverse the progression of heart disease. Previous reports demonstrated significant reductions in coronary plaque burden and improvements in health behaviors and coronary risk factors at 1 and 5-year follow-ups in the lifestyle intervention group relative to a control group receiving usual care (Gould et al., 1995; Ornish et al., 1990; Ornish et al., 1998). However, recent interest in psychosocial variables in cardiac research has increased (e.g., Rozanski, Blumenthal, Davidson, Saab, & Kubzansky, 2005; Berkman et al., 2003) and findings of

our two recent demonstration projects, the Multicenter Lifestyle Demonstration Project and the Multisite Cardiac Lifestyle Intervention Program, both observational studies, indicate that patients who make comprehensive lifestyle changes experience improvements in psychosocial risk factors (Daubenmier et al., 2007; Pischke et al., 2006; Koertge et al., 2003). This prompted us to analyze the psychosocial variables that had been assessed in the LHT. Thus, we compared psychosocial outcomes over the course of 5 years in 38 CHD patients who were either randomly assigned to an experimental group, participating in a 1-year lifestyle intervention, or to a control group receiving usual care during the same time period.

Method

The study was approved by the Human Research Committees of both Pacific Medical Center (PMC) and University of California, San Francisco (UCSF) and fully informed written consent was obtained from each patient. The design, recruitment, and study population, including eligibility criteria, have been described previously (Gould et al., 1992; Gould et al., 1995; Ornish et al., 1990; Scherwitz & Ornish, 1994). Briefly, the LHT was a randomized controlled trial using an invitational design (Zelen, 1979). Men and women with coronary atherosclerosis documented by quantitative coronary arteriography (40-74 years of age) were recruited from the San Francisco Bay Area (Ornish et al., 1998). At baseline, there were 28 patients in the experimental group and 20 patients in the control group. Analyses of coronary risk factors, clinical events, and coronary artery percent diameter stenosis at the 5-year follow-up are based on 35 patients who had 5-year follow-up quantitative coronary arteriography (Ornish et al., 1998) and 38 patients with complete psychosocial and health behavior questionnaires.

Psychosocial Measures

All psychosocial questionnaires were administered at baseline, 1, and 5 years.

Goldberg's 30-item General Health Questionnaire (GHQ), a screening tool for psychological distress originally developed to screen for psychiatric disorders (O'Rourke, MacHale, Signorini, & Dennis, 1998), assesses anxiety and depression, social dysfunction, and insomnia (e.g., “Have you recently been feeling mentally alert and wide awake?”; Goldberg, 1972). Psychometric properties have

been reported elsewhere (Stansfeld, Fuhrer, Shipley, & Marmot, 2002; Stansfeld & Marmot, 1992). Strong associations of the GHQ with clinical psychiatric disorder and depression suggest that it is a good proxy for depression and the quality of social interactions (Goldberg, Rickels, Downing, & Hesbacher, 1976; Stansfeld & Marmot, 1992). The insomnia subscale of the GHQ contains items similar to the vital exhaustion scale by Appels and colleagues (2006).

An adapted version of the *Social Support Questionnaire* (Berkman & Syme, 1979; Seeman & Syme, 1987) was administered to assess *instrumental social support* (e.g. help with household tasks, a ride, or a loan of money) and *adequacy of social support.*

The *Sense of Coherence (SOC) questionnaire* is a 13-item scale assessing patients' perceptions of the degree to which their lives are comprehensible, manageable, and meaningful (Antonovsky, 1987). SOC is associated with subjective state of health (Suominen, Helenius, Blomberg, Uutela, & Koskenvuo, 2001) and plays a major role in the adoption and maintenance of health behaviors relevant to secondary prevention of CHD (Kuupelomaeki & Utriainen, 2003; Lindmark, Stegmayr, Nilsson, Lindahl, & Johansson, 2005). Information on validity and reliability of this measure has been reported previously (Antonovsky, 1993).

Spielberger's state and trait anger scales (Spielberger, Jacobs, Russell, & Crane, 1983) were used to assess proneness to anger. This measure consists of two subscales measuring anger-reaction and anger-temperament. An angry temperament has been associated with an increased risk for cardiac events (Williams, Nieto, Sanford, & Tyroler, 2001). Psychometric information has been reported elsewhere (Moreno, Fuhriman, & Selby, 1999).

Type A behavior was assessed using a clinical *Hostility and Time Urgency Interview* (Friedman & Powell, 1984). Each interview was videotaped and scored for 35 separate observable characteristics that were subsequently categorized as either *time urgency* or *hostility* by a trained interviewer whose ratings had been shown to be reliable in the Western Collaborative Group Study (Ragland & Brand, 1988).

Intervention: the Lifestyle Change Program

To acquaint patients with the lifestyle program, the treatment intervention began with a week-long residential retreat at a local resort hotel. Patients' spouses or partners were invited to attend. During the retreat, patients and partners attended daily lectures on the rationale for the lifestyle intervention, nutrition lectures, cooking classes, and grocery store tours. Patients received three hours of stress management training, one hour of aerobic exercise, and one hour of group support meetings per day led by a clinical psychologist. Following the retreat, patients attended program sessions in groups two times per week for 1 year. Sessions focused on the four program components in 1-hour blocks. In addition, they were instructed to follow the diet, exercise, and practice stress management on their own [for further detail see (Billings, 2000; Ornish et al., 1990; Ornish et al., 1998)]. Thus, one-hundred and four sessions (4 hrs each) were offered during the 1-year intervention. After 1 year of intensive lifestyle intervention, patients were given the option to continue the Ornish Program lifestyle on their own in a self-directed community (Billings, 2000), which was not part of the research protocol. Patients paid for their own transportation and for potluck food they brought to the group meetings. Yoga instruction, group support, and the meeting space were paid for by the Preventive Medicine Research Institute. Five years after study entry, all patients were invited for systematic re-assessment (Ornish et al., 1998).

Adherence to the Individual Components of the Lifestyle Change Program

Detailed information of the components of the lifestyle change program has been reported previously and is therefore only described here briefly (Billings, 2000; Ornish et al., 1998). *Diet:* percent of calories from fat; goal: 10%; adherence to the dietary guidelines was calculated using a formula that was validated by previous research (based on 3-day food diary; for more detail see Daubenmier et al., 2006; Ornish et al., 1998); *Moderate Exercise:* hours per week; goal: 3 hrs/week (e.g., brisk walking; according to the guidelines of the American College of Sports Medicine, 1986); *Stress Management:* hours per week; goal: 1 hr/day (Ornish et al., 1990; Ornish et al., 1998); specifically a 1-hour practice included 30 minutes of stretching based on the asanas (English: poses) in hatha yoga, 15 minutes of progressive relaxation, 5 minutes of breathing, 8 minutes of meditation and 2 minutes of visualization of

patients' arteries dilating with increased blood flow to the heart in that order (Billings, 2000; Billings, Scherwitz, Sullivan, & Ornish, 1996; Ornish et al., 1990); *Smoking Cessation:* Smokers (N=4) in the experimental group agreed to quit smoking when entering the study; *Group Support:* the two weekly groups were designed to provide support to help patients adhere to the lifestyle change program. Group members were encouraged to express their feelings and to avoid problem-solving and giving advice or finding solutions, but instead to listen to each other with empathy and compassion (Schulz et al., in press; Billings, 2000; Billings, Scherwitz, Sullivan, Sparler, & Ornish, 1996).

Overall Adherence to the Lifestyle Change Program

A lifestyle index, based on a formula validated in previous research (Daubenmier et al., 2006; Ornish et al., 1998), measured overall adherence to intervention guidelines and was calculated as the mean percentage of adherence to each lifestyle behavior. Zero equaled no compliance and 1 equaled 100% compliance. A score was created for each of the four elements, as well as a cumulative score for the entire program adherence divided by the 4 elements:

$$\frac{t + (u/35 + v/420)/2 + (x/3 + y/180)/2 + z}{4}$$

where t is the smoking compliance, u is the stress management (times/wk), v is also stress management (minutes/wk), x is exercise (times/wk), y is also exercise (minutes/wk), and z is the dietary compliance score [also see (Daubenmier et al., 2006; Ornish et al., 1998)]. Some of the patients did more than the recommended level and thus had a score greater than 100%.

Statistical Analysis

Comparisons of group differences at baseline (experimental vs. control group; five year graduate vs. drop-out) were performed with two-sample t-tests for continuous variables and with χ^2- tests for categorical variables. ANOVAs for repeated measures with one within factor at 3 levels (time: baseline, 1, 5 years) and one between factor (experimental vs. control group) were computed to test for the effects of time, group, and their interactions on psychosocial outcomes and on health behaviors. Significant interactions

were followed up by multiple comparisons testing for group differences ($p<.05$; Bonferroni adjusted). For exploratory purposes, we also followed marginally significant interactions with multiple comparisons in this rather small sample. In addition, we computed two sets of multivariate analysis of variance (MANOVA) including group as the independent variable and change scores (baseline - 1 year, baseline – 5 years, respectively) for the 7 psychological outcomes (i.e., psychological distress, social support, sense of coherence, trait anger, state anger, hostility, time urgency) as dependent variables. To test for differences in changes in psychological outcomes over 5 years by adherence, patients in the experimental group were divided into two adherence groups based on a median split and ANOVAs for repeated measures were performed. Bivariate Pearson's correlations were used to analyze associations between changes in health behaviors and changes in psychosocial outcomes and cardiac variables over 1 and 5 years in the entire sample. SPSS (Version 14.0, 2005, SPSS, Inc., Chicago, IL) was used to perform the statistical analysis.

Results

Baseline Characteristics

Medical and demographic characteristics in this predominantly male sample (96% male in the experimental group; 80% male in the control group) have been reported previously (Ornish et al., 1998). Patients in the two groups did not significantly differ in age, income, and marital status (Table 1). Patients in the experimental group were more likely to be employed outside the home ($p< .05$) and tended to be more educated ($p<.10$) than controls. No significant group differences in health behaviors and psychosocial outcomes were found at baseline.

Participant Characteristics at Follow-Ups

Psychosocial outcomes and adherence to health behaviors of patients with complete data at 1 and 5 years can be seen in Table 2. At 1 year, patients in the experimental group reduced psychological distress more than control group patients ($p<.05$). Specifically, reductions in insomnia ($p<.05$) and a trend for improvements in social dysfunction ($p<.08$) were observed in experimental compared to control group

patients. Reductions in hostility were marginally greater in the experimental compared to the control group. Regardless of group, sense of coherence, state anger, time urgency, and social support remained constant over 1 year.

At 5 years, reductions in psychological distress reverted to baseline. However, improvements in hostility tended to be maintained in the experimental relative to the control group. Reductions in time urgency were observed in all patients regardless of group from baseline to 5 years ($p<.01$). Sense of coherence remained constant in the experimental group over the 5-year follow-up and was increased in the control group from 1 to 5-year follow-up ($p<.01$). State anger and social support remained constant over the 5-year follow-up in both groups.

Results of the 2 sets of MANOVA confirmed findings from the individual ANOVAs. That is, significant group differences for 1 year changes in psychological distress and hostility indicated that the experimental patients reduced psychological distress [$F(1,33) = 4.64$, $p<.05$] and hostility [$F(1,33) = 4.97$, $p<.05$] more than controls. No significant changes in psychological outcomes were noted from baseline to 5 years.

Changes in health behaviors and medical outcomes over 1 and 5 years have been reported previously (Ornish et al., 1998). Briefly, patients in the experimental group significantly reduced dietary fat intake and improved exercise and stress management relative to controls at 1 and 5 years (all $p<.001$). Experimental group patients met program requirements in regard to diet and exercise at 5 years. They fell 1 hour short of the recommended stress management at 5 years.

Beneficial effects of comprehensive lifestyle changes on coronary risk factors (i.e., weight, total cholesterol, low-density lipoprotein), clinical events, and coronary artery percent diameter stenosis for at least 4 years after participation in the Lifestyle Heart Trial have been reported elsewhere (Ornish et al., 1998). We correlated changes in health behaviors with changes in the improved cardiac variables only (i.e., weight, blood pressure, total cholesterol, low-density lipoprotein, percent diameter stenosis) over 1 and 5 years.

Associations of health behavior changes to changes in cardiac variables over 1 and 5 years for all patients can be seen in Table 3. The most robust relationships (i.e., significant at $p<.05$ at both follow-ups) were observed for improvements in diet to weight reduction and to decreases in percent diameter stenosis, and for improvements in stress management to decreases in percent diameter stenosis (all $p<.05$). The association between improvements in stress management and reductions in percent diameter stenosis remained significant after controlling for improvements in diet ($p<.01$), whereas the association between improvements in diet and reductions in percent diameter stenosis rendered non-significant after controlling for improvements in stress management (not shown).

Associations between changes in health behaviors and changes in psychological well-being over 1 year (not shown) were noted as follows: reductions in dietary fat were associated with reductions in psychological distress ($r = .39$, $p<.05$) and improvements in stress management were related to reductions in trait anger ($r = .36$, $p<.05$). No statistically significant associations between changes in health behaviors and changes in psychological well-being over 5 years were found. However, it is noteworthy that the magnitude of the association of improvements in stress management to reduced trait anger over 5 years was similar ($r=.22$) to the one observed at 1 year, but no longer statistically significant at the conventional level.

In order to investigate whether high program adherence was required to affect psychological well-being as shown previously for cardiac outcomes by Ornish and colleagues (1998), we compared psychosocial outcomes by 5-year program adherence for the experimental group using a median split (lower adherence: 0-118%, N=10 vs. higher adherence: 119%-174%, N=9) (not shown). At both follow-ups, experimental group patients with high adherence reported significantly greater reductions ($p<.05$) in psychological distress (baseline: 25.9 ± 11.1; 1-year follow-up: 14.3 ± 7.8; 5-year follow-up: 17.4 ± 8.6) compared to the low adherence group (baseline: 28.7 ± 9.7; 1-year follow-up: 23.0 ± 11.9; 5-year follow-up: 34.9 ± 12.1). Trait anger, type A behavior, and hostility were reduced from baseline to 5-year follow-up regardless of adherence group ($p<.01$). Overall, patients in the higher adherence group showed lower

levels of psychological distress ($p<.05$), sense of coherence ($p<.05$), and tended to report greater perceived social support ($p<.10$) than those with lower adherence at all time points.

Complete 5-year follow-up data for psychosocial questionnaires were not available for 19% of patients (25% in the experimental group; 10% in the control group). Baseline comparisons of patients with complete data to those lacking follow-up information did not indicate significant group differences in age, marital and employment status, as well as psychosocial status, coronary risk factors, and health behaviors.

Discussion

Patients in the experimental group showed greater improvements in psychological well-being than those in the control group at 1 year. Specifically, reductions in overall psychological distress, insomnia, and hostility were more pronounced in the experimental group when compared to the control group. These results are similar to studies reporting relatively short-term (i.e., ≤ 1 year) improvements in psychological well-being (i.e., reductions in psychological distress, hostility, anxiety, and depression) in patients with CHD after participation in cardiac rehabilitation that included psychological or stress management interventions (Daubenmier et al., 2007; Pischke et al., 2006; Blumenthal et al., 2005; Lavie & Milani, 2005, 1999; Koertge et al., 2003). Although some have questioned the importance of such relatively small short-term improvements in psychological outcomes (e.g., Berkman et al., 2003; Jones & West, 1996), these improvements may be related to cardiac outcomes over the long-term.

In fact, findings from a study by Denollet & Brutsaert (2001), including 9-year clinical event data, indicated that improvements in negative affect induced by a 3-months intensive lifestyle intervention reduced CHD mortality 9 years later. Similarly, altering type A behavior by an intervention including intensive cardiac and type A counseling for 4-6 months and monthly for 4.5 years seemed to reduce cardiac morbidity and mortality over 4.5 years in post myocardial infarction patients when compared to a control group that only received cardiac counseling or to a no treatment comparison group (Friedman et al., 1986). It has also been suggested that behavioral treatment programs for insomnia are associated with

better maintenance of sleep improvements at long-term follow-up (Jacobs, Pace-Schott, Stickgold, & Otto, 2004; Morin, Colecchi, Stone, Sood, & Brink, 1999). Similar to our finding of greater reductions in insomnia in patients in the experimental group relative to the controls at 1 year, Appels et al. (2006) reported reductions in vital exhaustion (i.e., tiredness, exhaustion, irritation) after 18 months in revascularized patients who had participated in a 4-months behavioral intervention including group meetings targeting coping with stressors, the practice of relaxation exercises, and physical exercise.

In our study, most improvements in psychological well-being in the experimental group, evident at 1 year, were not evident by 5 years, except for a trend in reduced hostility in the experimental group. These findings suggest that patients may have psychologically adapted or habituated to their new lifestyle (63% of patients exceeded 100%). It is well-known from research in the field of positive psychology that as people "rise in their accomplishments and possessions, their expectations also rise. Soon they habituate to the new level, and it no longer makes them happy" (p.36) (Diener, 2000). It is conceivable that experimental group patients in our study may have adapted to their new lifestyle, no longer deriving happiness from their new lifestyle changes. As a result, their perception of general well-being may have reverted to baseline levels.

The relative absence of an overall intervention effect on psychological well-being in the experimental group beyond 1 year may have also been due to differences in adherence to comprehensive lifestyle changes within this group. This assumption could, in part, be confirmed by results comparing patients in the high program adherence group to the low adherence group. Patients with very high adherence experienced significantly greater reductions in psychological distress over 5 years than those with lower adherence. Patients with higher adherence also reported a stronger sense of coherence and perceived more social support throughout follow-up than those with lower adherence. Thus, patients with very high adherence possibly still strived for higher goals [cf. (Diener, 2000)], and maintained improvements in general well-being over the long-term.

In regard to the relationship of health behavior change to psychological well-being over 1 year, we found that improvements in diet were associated with reductions in psychological distress. This

finding is consistent with a study by Weidner and colleagues (1992) suggesting that individuals who changed their diet from a high-fat to a low-fat, high complex-carbohydrate diet also reduced depression and hostility. Improvements in psychological well-being may have improved eating behavior and contributed to an increased sense of self-efficacy (Bandura, 1977). Similarly, in the Multisite Cardiac Lifestyle Intervention Program (MCLIP) reductions in dietary fat were related to reductions in perceived stress, especially among those who also increased exercise (Daubenmier et al., 2007). Additionally, increases in stress management in our study were associated with reductions in trait anger over one year. This latter finding is consistent with a recent study reporting reduced anger with regular yoga practice (Shapiro et al, 2007).

In regard to the relationship of health behavior change to cardiac variables, we found that changes in each of the health behaviors were associated with cardiac variables over 1 and 5 years, with the most robust relationships (i.e., significant at $p<.05$ at both follow-ups) observed for improvements in diet to weight reduction and to decreases in percent diameter stenosis, and for improvements in stress management to decreases in percent diameter stenosis (all $p<.05$). The significant relationship between increases in stress management and reductions in percent diameter stenosis could not be explained by dietary changes over the course of 5 years. This finding indicates that alleviating psychological distress by practicing stress management may benefit patients' cardiac profile independently from adherence to diet.

One limitation of our study was the lack of power due to the LHT's small sample size. However, it is noteworthy that, despite the lack of power, significant group differences were detected. In fact, the magnitude of effects was supported by some of the effect sizes exceeding .09, suggesting medium effects (Cohen, 1987). Similar associations between improvements in health behaviors and improved cardiac outcomes were observed in the ongoing MCLIP, a stage IV clinical trial evaluation, employing the same intervention as the LHT in a sample of 869 CHD patients over 3 months (Daubenmier et al., 2007). For example, reductions in dietary fat intake and increases in stress management predicted reductions in weight and improvements in lipid profiles, and increases in exercise were associated with improvements in total cholesterol (Daubenmier et al., 2007). Another limitation of the LHT is that psychological well-

being was only assessed at 1- and 5-year follow-up. We therefore do not know whether psychological well-being persisted for more than 1 but less than 4 years.

In sum, lifestyle changes improve psychological well-being for 1 year and are associated with improved cardiac variables over 5 years, illustrating the importance of targeting multiple behaviors in secondary prevention of CHD.

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Table 1. Baseline Characteristics [Lifestyle Heart Trial (LHT): N=48].

Measure	Experimental Group	Control Group	p-value
	Mean±SD (N)	**Mean±SD (N)**	
Age (yrs)	57 ± 8 (28)	59 ± 10 (20)	.493
Education (yrs)	16 ± 3 (28)	14 ± 3 (20)	.068
	N (%)	**N (%)**	
Married/living with someone	22 (79%)	15 (75%)	.497
Employed outside the home	22 (79%)	9 (45%)	.017
Psychosocial outcomes			
Psychological distress	27.5 ± 10.6 (26)	23.9 ± 9.0 (17)	.247
Depression & Anxiety	6.0 ± 3.5 (26)	4.7 ± 3.6 (17)	.236
Social dysfunction	4.1 ± 1.8 (26)	3.8 ± 1.0 (17)	.534
Insomnia	5.8 ± 2.5 (26)	4.9 ± 1.5 (17)	.197
Social support	19.7 ± 4.1 (27)	20.3 ± 5.2 (16)	.683
Instrumental support	4.2 ± 2.6 (27)	4.5 ± 2.9 (16)	.744
Adequacy of social support	15.4 ± 2.5 (27)	15.8 ± 3.6 (17)	.730
Sense of Coherence	43.9 ± 6.9 (27)	47.7 ± 6.4 (17)	.082
State anger	21.4 ± 9.4 (25)	20.0 ± 7.5 (16)	.618
Trait anger	29.9 ± 8.0 (27)	26.7 ± 6.8 (17)	.175
Type A behavior	35.3 ± 12.0 (27)	35.1 ± 11.7 (20)	.953
Time urgency	25.7 ± 8.7 (27)	26.2 ± 8.3 (20)	.873
Hostility	9.9 ± 5.3 (26)	8.9 ± 5.7 (20)	.550

Health behaviors			
Diet (% of calories from fat)	30.8 ± 8.1 (28)	29.3 ± 10.9 (20)	.594
Exercise (hrs/week)	2.4 ± 3.8 (27)	2.1 ± 3.2 (17)	.848
Stress management (hrs/week)	.74 ± 1.6 (27)	.21 ± .51 (17)	.189

Table 2. Psychosocial outcomes and health behaviors of all patients with complete data at baseline, 1 and 5 years in the LHT.

Measure	Group	Baseline	1 year	5 years	p-value Time	η_p^2	p-value Group	η_p^2	p-value Time x Group	η_p^2
		Mean±SD (N)	Mean±SD	Mean ± SD						
Psychological distress	**Experimental group**	27.3± 10.2 (18)[a]	18.7 ± 10.8[b]	26.2 ± 13.6[a]	.050	.089	.869	.001	.047	.091
	Control group	23.7 ± 9.3 (16)[a]	23.6 ± 12.2[a]	23.3 ± 11.0[a]						
Depression and Anxiety	**Experimental group**	6.1 ± 4.0 (18)[a]	3.5 ± 3.9[a]	5.9 ± 5.6[a]	.155	.058	.496	.015	.062	.086
	Control group	4.5 ± 3.7 (15)[a]	4.5 ± 4.6[a]	3.8 ± 4.1[a]						
Social dysfunction	**Experimental group**	4.2 ± 1.5 (18)[a]	2.4 ± 1.5[b]	3.4 ± 1.3[a]	.005	.151	.405	.022	.070	.080
	Control group	3.8 ± 1.0 (16)[a]	3.5 ± 1.7[a]	3.6 ± 1.5[a]						
Insomnia	**Experimental group**	5.7 ± 1.9 (18)[a]	3.7 ± 2.3[b]	4.9 ± 2.3[ab]	.216	.047	.672	.006	.016	.122
	Control group	4.8 ± 1.5 (16)[a]	5.3 ± 2.0[a]	4.9 ± 2.2[a]						
Social support	**Experimental group**	19.6 ± 4.0 (19)	21.5 ± 5.2	20.4 ± 4.3	.620	.015	.817	.002	.314	.036
	Control group	20.2 ± 5.3 (15)	19.8 ± 3.7	20.5 ± 6.3						
Instrumental support	**Experimental group**	3.7 ± 2.4 (19)	5.4 ± 3.4	5.0 ± 2.8	.328	.034	.699	.005	.251	.042
	Control group	4.4 ± 3.0 (15)	4.1 ± 2.2	4.7 ± 3.7						
Adequacy of social support	**Experimental group**	15.9 ± 2.5 (19)	16.1 ± 2.8	15.4 ± 2.2	.817	.006	.946	.000	.537	.019
	Control group	15.8 ± 3.7 (16)	15.6 ± 2.7	15.8 ± 3.7						
Sense of Coherence	**Experimental group**	43.8 ± 7.2 (19)[a]	45.7 ± 6.9[a]	44.8 ± 5.8[a]	.103	.067	.119	.072	.009	.134
	Control group	47.9 ± 6.5 (16)[ab]	45.6 ± 5.7[a]	49.9 ± 5.1[b]						
State anger	**Experimental group**	21.7 ± 10.3 (17)	20.9 ± 10.3	20.5 ± 6.4	.547	.020	.531	.013	.917	.003

	Control group	20.2 ± 7.7 (15)	20.0 ± 5.8	18.5 ± 5.4						
Trait anger	**Experimental group**	31.3 ± 7.9 (19)	26.8 ± 7.1	28.7 ± 8.0	.038	.094	.135	.066	.106	.066
	Control group	26.3 ± 6.9 (16)	25.9 ± 5.6	25.0 ± 5.8						
Type A behavior	**Experimental group**	35.7 ± 11.4 (19)	25.5 ± 8.8	23.6 ± 7.7	.001	.307	.131	.068	.191	.049
	Control group	35.9 ± 11.6 (16)	30.8 ± 9.4	30.0 ± 8.6						
Time urgency	**Experimental group**	25.4 ± 8.9 (19)	19.9 ± 6.0	17.0 ± 5.5	.001	.300	.111	.075	.396	.028
	Control group	27.1 ± 8.6 (16)	22.1 ± 7.5	22.1 ± 4.6						
Hostility	**Experimental group**	10.3 ± 5.0 (19)[a]	5.6 ± 4.7[b]	6.6 ± 4.3[b]	.029	.102	.457	.017	.081	.073
	Control group	8.8 ± 5.4 (16)[a]	8.6 ± 5.9[a]	7.9 ± 5.4[a]						
Diet (% of	**Experimental group**	29.8± 8.0 (20)[a]	6.2 ± 1.2[b]	8.4 ± 4.4[b]	.001	.602	.001	.545	.001	.531
Calories from	**Control group**	29.9 ± 10.8 (18)[a]	28.8 ± 8.4[a]	27.5 ± 11.5[a]						
Fat)										
Exercise (hrs/wk)	**Experimental group**	1.5 ± 2.1 (19)[a]	4.6 ± 2.0[b]	3.5 ± 2.5[c]	.001	.278	.402	.021	.001	.204
	Control group	2.3 ± 3.3 (16)[a]	2.6 ± 3.3[a]	2.9 ± 2.7[a]						
Stress Management	**Experimental group**	.68 ± 1.8 (19)[a]	10.0 ± 4.5[b]	5.9 ± 5.5[c]	.001	.464	.001	.482	.001	.422
(hrs/wk)	**Control group**	.22 ± .52 (16)[a]	.56 ± 1.2[a]	1.3 ± 2.9[a]						

Mean scores sharing a common superscript in a row of this table were not significantly different at the .05 level (Bonferroni adjusted).

η_p^2 – The partial Eta squared is the proportion of the effect + error variance that is attributable to the effect.

Table 3. Associations between changes in health behaviors (baseline – 1 year, baseline – 5 years) and changes in coronary risk factors (baseline -1 year, N ranging from 37-46; baseline – 5 years, N ranging from 32-36) in all participants of the LHT.

	Δ % calories from fat		**Δ Exercise (hrs/wk)**		**Δ Stress management (hrs/wk)**	
	Δ 1y	**/ Δ 5y**	**Δ 1y**	**/ Δ 5y**	**Δ 1y**	**/ Δ 5y**
Δ Weight (kg)	.69**	.35*	.58**	.17	.43**	.10
Δ Systolic blood pressure	-.03	.02	.06	.04	.10	.14
Δ Diastolic blood pressure	.03	.10	.18	.06	.07	.01
Δ Total cholesterol	.13	.07	.22	.32†	.38*	.21
Δ Low-density lipoprotein	.25	-.03	.14	.22	.37*	.20
Δ % Diameter stenosis	.32*	.40*	.26	.10	.38*	.53**

Change scores of the 3 health behaviors were created so that higher values reflect greater improvements in each health behavior (i.e., for exercise and stress management, baseline values were subtracted from 1- and 5-year values; for dietary fat intake, 1- and 5-year values were subtracted from baseline values). Change scores for coronary risk factors were created so that higher values reflect greater improvements in each coronary risk factor (i.e., for weight, systolic and diastolic blood pressure, total cholesterol, low-density lipoprotein, % diameter stenosis, baseline values were subtracted from 1- and 5-year values).

** $p < .01$
* $p < .05$
† $p < .10$

CHAPTER 3

Perspectives in Practice

The Role of Lifestyle in Secondary Prevention of Coronary Heart Disease in Patients with Type 2 Diabetes

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Abstract

It is unclear whether standard cardiac rehabilitation programs (i.e. moderate changes in diet and exercise) are of benefit to coronary heart disease (CHD) patients with diabetes. These patients not only tend to have more comorbidities, but are also less likely to be referred to such programs than CHD patients without diabetes. This report reviews the role and practicalities of lifestyle interventions in the secondary prevention of CHD in patients with diabetes, with a special focus on results from our 2 multisite comprehensive lifestyle change interventions. These interventions emphasize a very low-fat, high complex carbohydrate diet, moderate exercise, stress management and group support. We conclude that participation in a multicomponent secondary prevention program employing the above interventions may be of benefit not only to CHD patients in general, but in particular to those with CHD and diabetes.

KEYWORDS: cardiac rehabilitation, coronary heart disease, diet, exercise, lifestyle

Introduction

Diabetes is a major cause of mortality and morbidity worldwide (McKinlay & Marceau, 2000). It has been estimated that the prevalence of diabetes, in parallel with the prevalence of obesity, will reach epidemic proportions this decade, increasing by 46% worldwide from 2000 to 2010 (from 150 million to 220 million people; with 90% having type 2 diabetes) (Zimmet, Alberti, & Shaw, 2001). The impact will be most pronounced in developing countries and in disadvantaged minority populations (Zimmet, Alberti, & Shaw, 2001). The global adoption of a sedentary, stressful lifestyle, the consumption of high-fat foods, refined carbohydrates and the decreased consumption of a whole-foods, plant-based diet appear to be major contributors to this escalating problem and associated complications (Zimmet, Alberti, & Shaw, 2001, Hu, van Dam, & Liu, 2001; Haskell, 2003; Surwit & Schneider, 1993; Garg et al., 1994).

The major health problem associated with diabetes is cardiovascular disease (CVD), especially coronary heart disease (CHD) (Zimmet, Alberti, & Shaw, 2001). In fact, patients with type 2 diabetes have as high a risk for myocardial infarction (MI) as MI patients have for a recurrent event (Haffner, Lehto, Rönnemaa, Pyörälä, & Laakso, 1998), leading the United States (US) National Cholesterol Education Program Panel to classify diabetes as a risk equivalent to CHD in most persons with type 2 diabetes [Third Report of the National Cholesterol Education Program (NCEP) Expert Panel, 2002]. This problem appears to be especially pronounced among women with diabetes. For example, the relative risk of death from CHD is 2.58 in women with diabetes and 1.85 in men with diabetes (Lee, Cheung, Cape, & Zinman, 2000). Similarly, sex-specific models from the Framingham Heart Study based on persons who have had a prior CHD event confirm diabetes as a significant predictor of subsequent CHD events in women (D'Agostino et al., 2000). The mechanisms for the increased incidence and severity of atherosclerosis in type 2 diabetes have been described elsewhere [Marso & Ellis, 2003; Third Report of the National Cholesterol Education Program (NCEP) Expert Panel, 2002].

While death rates from CHD years in developed countries have been decreasing over the past 15 due to numerous advances in the field of cardiovascular medicine, these improvements have not been realized among CHD patients with diabetes [Third Report of the National Cholesterol Education Program

(NCEP) Expert Panel]. This suggests that efforts at secondary prevention of CHD may be less effective for those with CHD and diabetes than those with CHD alone. This article addresses the role of lifestyle in secondary prevention in patients with CHD and diabetes, presents results from our comprehensive lifestyle change program, and provides a discussion of practical issues.

Secondary Prevention Approaches: The Role of Lifestyle

The importance of lifestyle in both primary and secondary prevention of type 2 diabetes, CHD and associated comorbidities of hypertension, hyperlipidemia and obesity has been well documented (Costacou & Mayer-Davis, 2003; Gaede et al., 2003; Knowler et al., 2002; Toobert, Glasgow, Nettekoven, & Brown, 1998; Tuomilehto et al., 2001). For example, comprehensive lifestyle changes (low-fat diet, exercise, stress management) can improve cardiac risk factors and stop or even reverse the progression of heart disease (Koertge et al., 2003; Ornish, 2002; Ornish et al., 1998; Ornish, 1998). Also, lifestyle changes (e.g. exercise, stress management, social support) have been shown to be beneficial in patients with type 2 diabetes (Toobert et al., 2003) and in those with impaired glucose tolerance (IGT) (Lindström et al., 2003).

Moderate diet and exercise recommendations are the conventional lifestyle interventions for type 2 diabetes patients and CHD patients in traditional cardiac rehabilitation. Research supports a diet rich in whole grains, fibre, fruits and vegetables for the prevention and treatment of both diabetes and CHD [Third Report of the National Cholesterol Education Program (NCEP) Expert Panel, 2002; Hu & Willett, 2002; Anderson Randles, Kendall, & Jenkins, 2004]. Higher intakes of whole grains and fibre are associated with decreased risk of diabetes (Fung et al., 2002; Liu et al., 2000), as well as improved glycemic control and insulin sensitivity in patients with diabetes (Chandalia et al., 2000; Järvi et al., 1999). Preliminary research also suggests that decreases in saturated fat, trans fatty acids and cholesterol, and increases in omega-3 fatty acids are associated with decreased incidence of diabetes, improved glycemic control and insulin sensitivity (Costacou & Mayer-Davis, 2003 ; Hu, van Dam, & Liu, 2001), and improvements in CHD risk factors [Hu & Willett, 2002; Third Report of the National Cholesterol

Education Program (NCEP) Expert Panel, 2002]. In the UK Prospective Diabetes Study, each 1% reduction in glycosylated hemoglobin (A1C), induced either by dietary changes and/or by medication (sulphonylurea, insulin), was associated with a 37% decrease in risk for microvascular complications and a 21% decrease in risk for events (e.g. non-fatal heart failure, death related to diabetes, cataract extraction) (Stratton et al., 2000). Consequently, the American Dietetic Association and Dietitians of Canada recommend a low-fat, fibre-rich, diet as a healthful option for patients with diabetes (Position of the American Dietetic Association and Dietitians of Canada, 2003). The Canadian Diabetes Association recommends a low-fat, high-fibre, low-glycemic-index diet (Canadian Diabetes Association Clinical Practice Guideline Expert Committee, 2003)

With respect to exercise, moderate physical activity (both endurance and resistance training) is beneficial for CHD patients with diabetes, although it is underutilized (Standards of medical care for patients with diabetes mellitus, 2003). Also, Hu and colleagues demonstrated that increased physical activity (regular walking) was associated with a substantially reduced risk for CV events in women with type 2 diabetes (Hu et al., 2001). Regular, moderate-intensity exercise improved insulin sensitivity in patients with type 2 diabetes and IGT (Sato, Nagasaki, Nakai, & Fushimi, 2003). Although patients with diabetes, especially those with CHD, require more careful assessment prior to exercise, they may achieve additional benefits including improvements in blood pressure (BP) control, cardiac fitness, collateral circulation and reduced blood coaguability (Sato, Nagasaki, Nakai, & Fushimi, 2003). Comprehensive research reviews, exercise guidelines, and exercise benefits for type 2 diabetes and CHD have been presented in detail by the American Diabetes Association (Standards of medical care for patients with diabetes mellitus, 2003) and the American College of Sports Medicine (Albright et al., 2000).

In addition to diet and exercise, stress management and group support may be of benefit to patients with type 2 diabetes and/or CHD. Improved glucose metabolism was reported among patients with type 2 diabetes participating in a group-based stress management training program (Surwit et al., 2002). Stress management was also associated with improvements over a 6-month follow-up period in several CHD risk factors including improved glycemic control and quality of life in postmenopausal

women with diabetes (Toobert et al., 2003). Furthermore, stress management was associated with a reduction in CHD events over a 5-year follow-up in male CHD patients (Blumenthal et al., 2002).

Research on the effects of social support is rather limited. The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial compared recurrent events and psychosocial outcomes of CHD patients receiving social support in the framework of cognitive behaviour therapy (either in groups or individually) to those receiving usual care (Writing committee for the ENRICHD Investigators, 2003). Although the intervention appeared to improve depression and social isolation, it did not increase event-free survival (Writing committee for the ENRICHD Investigators, 2003). However, providing social support to patients (weekly group meetings) in conjunction with dietary change and moderate exercise seemed helpful in the secondary treatment of CHD in male and female patients enrolled in a cardiac rehabilitation program (O'Farrel, Murray, Huston, LeGrand, & Adamo, 2000).

While evidence for a beneficial effect of lifestyle in patients with diabetes and those with CHD has been accumulating, only a few studies examine lifestyle interventions among patients with established CHD and type 2 diabetes (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004; Milani & Lavie, 1996; Pischke et al., 2006; Sumner et al., 2003; Suresh, Harrison, Houghton, & Naqvi, 2001; Vergès et al., 2004), although such interventions may be especially important in this group (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004). CHD patients with diabetes seem to have greater difficulties adhering to and benefiting from standard cardiac rehabilitation compared to those without diabetes, mostly due to a greater adverse risk profile at program entry and an exacerbation of medical problems during the intervention (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004; Suresh, Harrison, Houghton, & Naqvi, 2001; Vergès et al., 2004). For example, Suresh colleagues reported higher prevalence of obesity, history of hypertension, and left ventricular failure in CHD patients with diabetes compared to those without diabetes at program entry (Suresh, Harrison, Houghton, & Naqvi, 2001). Furthermore, CHD patients with diabetes in this study were also less well medicated (e.g. ASA, beta-blockers, lipid-lowering drugs) and were less likely to attend exercise classes than those without diabetes (Suresh, Harrison, Houghton, & Naqvi, 2001). Banzer and colleagues reported similar differences in risk factor profiles

between CHD patients with and without diabetes (body mass index [BMI], waist circumference, hypertension, triglycerides, peripheral vascular disease, fitness levels) (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004). In fact, 62% of the CHD patients with diabetes withdrew from the intervention due to an exacerbation of a medical problem (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004). Thus, it may not be surprising that CHD patients with diabetes showed less improvement in traditional CV risk factors (Milani & Lavie, 1996) and exercise capacity (Vergès et al., 2004) than those without diabetes.

Psychological factors may also be important in secondary prevention of CHD in patients with type 2 diabetes. The presence of diabetes appears to double the risk of comorbid depression (Anderson, Freedland, Clouse, & Lustman, 2001), which is associated with poor glycemic control and increased risk for diabetes complications (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001; Lustman et al., 2000), including initial CHD events and progression (Clouse et al., 2003; Frasure-Smith et al., 2000). A higher incidence of depression among patients with diabetes compared to those without diabetes following major cardiac events has also been reported (Milani & Lavie, 1996). Hence, tackling depression, a major risk factor for CHD, especially in patients with diabetes, should be a major focus of cardiac intervention (Clouse et al., 2003). Support for the notion that levels of depression can improve in CHD patients with diabetes comes from finding that, despite a less favourable improvement in traditional CV risk factors, patients enrolled in an exercise-based cardiac rehabilitation study experienced improvements in depression, anxiety and quality of life (Milani & Lavie, 1996). It therefore appears that CHD patients with diabetes need to be targeted in standard cardiac rehabilitation with more aggressive approaches such as intensive multicomponent interventions to improve traditional coronary risk factors and psychosocial outcomes (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004).

Results from the Multicentre Lifestyle Demonstration Project (MLDP) and the Multisite Cardiac Lifestyle Intervention Program (MCLIP)

The MLDP was a study of 440 patients with CHD that examined whether patients in geographically diverse regions (8 hospital sites across the USA) could make comprehensive lifestyle changes resulting in similar benefits as those reported in the original Lifestyle Heart Trial, a study of 48 CHD patients randomized to an intensive lifestyle change program or a control group (Koertge et al., 2003; Ornish et al., 1998; Ornish, 1998). The MCLIP is an expansion of the MLDP with ongoing enrollment at 22 US sites (as of December, 2004, 1245 CHD patients had completed the 3-month follow-up). In both studies, ~30% of the CHD patients also were diagnosed with diabetes.

The lifestyle change program in both studies consisted of a multicomponent intervention. Patients met in groups 3 times per week for the initial 3 months of the program, and were instructed to improve diet (plant based, very low fat), to increase exercise (3 h/week at moderate intensity according to guidelines of the American College of Sports Medicine), to practice stress management (1 h per day yoga-based practice), and to participate in group support sessions. Patients continued meeting in 4-h intervention sessions once a week for the following 9 months. In each of these sessions, all 4 intervention components were targeted (Ornish, 2002). Standard coronary risk factors and quality of life were assessed at baseline, 3 months and 1 year. Patients in the MLDP who were eligible to receive a revascularization procedure at study entry, but opted instead for the lifestyle-change program, were matched in age, sex and disease severity to controls who also were eligible for a procedure and received the procedure. Patients from both of these groups were followed for 3 years in order to track adverse events. Results from this subgroup of patients indicated that 77% of intervention-group patients were able to avoid revascularization for at least 3 years by making comprehensive lifestyle changes without an increase in cardiac events (Ornish, 1998).

With regard to risk factors and quality of life in the MLDP, both women and men showed similar improvements in standard coronary risk factors (e.g. plasma lipids, body weight) and in quality of life (Koertge et al., 2003). Analyses of MLDP data by diabetic status revealed that patients with diabetes

(especially women) had a more adverse sociodemographic (e.g. less spouse support) and medical risk factor profile (e.g. BMI, systolic BP), and reported poorer quality of life than patients without diabetes. Yet, patients with diabetes were able to adhere to the recommended changes in diet and lifestyle. After 3 months of the intervention, patients with diabetes, regardless of gender, showed significant improvements in body weight (mean decrease of 5.0 kg), body fat, LDL-C, exercise capacity, and quality of life. These changes were maintained over a 1-year period. No significant changes in triglycerides and HDL-C were noted. By the end of 12 months, improvements in glucose-lowering medications (i.e. discontinuation of or a change from insulin to oral antihyperglycemic agents) were noted for 19.8% of the patients with diabetes (Pischke et al., 2006).

Preliminary analyses of the 3-month follow-up data from the MCLIP support these findings. Specifically, significant improvements in medical and psychosocial risk factors in patients with diabetes of both sexes (e.g. weight, systolic BP, total cholesterol, LDL-C, exercise capacity, depression, hostility, stress, quality of life) were noted. Furthermore, both sexes had improved glycemic control (mean decrease in A1C from 7.6 to 6.7%, $p<0.001$) and 22% of the sample had a reduction in diabetes medications (Sumner et al., 2003). Thus, analyses of data from both the MLDP and the MCLIP suggest that, in spite of their worse risk factor profile at program entry, patients with diabetes were able to make comprehensive changes in diet and lifestyle, showing similar improvements in CHD risk factors and quality of life when compared to their non-diabetic counterparts (Pischke et al., 2006; Sumner et al., 2003).

Practical Issues

Only a small proportion of CHD patients with type 2 diabetes attend cardiac rehabilitation programs. Suresh and colleagues suggest this problem is due to referral practices favouring those with a better prognosis (Suresh, Harrison, Houghton, & Naqvi, 2001). This bias is not unique to CHD patients with diabetes, but also applies to those with CHD in general. For example, Ades estimates only 10 to 20% of appropriate candidates in the US currently participate in formal rehabilitation programs (Ades, 2001).

Women and elderly persons are especially less likely to be referred to these programs (Ades, 2001). Thus, it appears that those with a poorer prognosis (i.e. those most in need) are less likely to be selected for cardiac rehabilitation. In addition, Toobert and colleagues (2002) suggest that improved recruitment procedures may yield more representative samples of patients (Toobert, Strycker, Glasgow, & Bagdade, 2002).

Once patients are referred, adherence to targeted lifestyle behaviours tends to be especially low among patients with CHD and type 2 diabetes (Glasgow, Toobert, & Hampson, 1991; O'Loughlin, Paradis, Gray-Donald, & Renaud, 1999). One reason for low adherence to lifestyle interventions in general may be that changing one's health behaviours is often seen as a personal responsibility (Jack, 2005). This "blame the victim" mentality promotes the idea that patients should comply with health-behaviour change on their own (Jack, 2005). Patients with both CHD and diabetes may be particularly affected by this mentality.

On the other hand, it has been pointed out that providing highly trained medical staff, tailored medical and educational interventions, and patient-provider follow-up will enhance the effectiveness of lifestyle change programs in patients with diabetes (Jack, 2005). However, in countries lacking universal health insurance (e.g., US) intensive lifestyle modification programs face many challenges including the pressure to generate funds to conduct lifestyle interventions; the development of administrative and physician support to run the programs; the need to reach a wider socioeconomic range of patients (Jack, 2005); and the need for widespread insurance/government reimbursement (McKinlay & Marceau, 2000; Zimmet, Alberti, & Shaw, 2001). Thus, translating lifestyle interventions from research-based settings into healthcare settings may require "major shifts in public policy to create an environment for the whole community or nation in which individual behavioral initiatives can succeed" (Zimmet, Alberti, & Shaw, 2001).

Cost Effectiveness of Lifestyle Interventions

According to the American Diabetes Association, the direct medical and indirect expenditures attributable to diabetes were an estimated US $131 billion in 2002 in the US. Direct medical expenditures (US $91.8 billion) comprised US $23.2 billion for diabetes care, US $24.6 billion for chronic complications of diabetes (primarily CHD), and US $44.1 billion for medical conditions associated with diabetes (Hogan, Dall, & Nikolov, 2003). In 2000, the cost of managing complications from type 2 diabetes was estimated at Can $18,635 for the first year of treatment after an acute MI and Can $1193 for the annual treatment post-MI (O'Brien, Patrick, & Caro, 2003).

Information on cost effectiveness of lifestyle modification programs in CHD patients with type 2 diabetes is limited. However, some indication for cost savings (in addition to medical benefits) comes from the Diabetes Prevention Program (DPP), a study of patients with IGT. In the DPP, patients in the intensive lifestyle change (ILC) group received individual counselling in diet, exercise and behaviour-modification skills (goals: 7% weight loss, 150 minutes/week of moderate exercise), the second intervention group received standard lifestyle advice plus metformin, and the control group received standard lifestyle advice and a placebo. The intensive lifestyle intervention and the metformin intervention reduced the risk of developing type 2 diabetes by 58% and 31%, respectively, when compared to the control group (Knowler et al., 2002).

Modelling the long-term health economic implications of the DPP in Australia, France, Germany, Switzerland and the United Kingdom, Palmer and colleagues report that incorporation of the DPP interventions (ILC, metformin) into clinical practice was projected to lead to an increase in diabetes-free years of life, improved life expectancy, and cost savings in Australia, Germany, France, Switzerland (only minor cost increases in the United Kingdom) when compared to the control group (Palmer et al., 2004).

In terms of lifestyle interventions with CHD patients, Blumenthal and colleagues reported that a 4-month stress management intervention in male CHD patients resulted in a significant reduction of medical costs over a 5-year period compared to a usual-care control group (Blumenthal et al., 2002). Similarly, Ornish and colleagues demonstrated cost effectiveness of a 1-year comprehensive lifestyle

modification program (MLDP) in CHD patients and their matched controls in a 3-year follow-up (Ornish, 1998). The cost savings for the intervention group amounted to US $29,529 per person in 1998 (Ornish, 1998). Considering that revascularization procedure costs have increased substantially over the years (US $83,919 for coronary artery bypass graft [CABG] and US $39,255 for percutaneous transluminal coronary angioplasty [PTCA] in 2003 [Agency for Healthcare Research and Quality, 2005]), while costs for the lifestyle intervention have remained relatively stable (US $7,000 in 1998 [Ornish, 1998] vs. US $7,500 in 2003 [Perelson et al., 2005]), the savings are even greater today. Also, current analyses of data from a subset of patients with established CHD and/or elevated CV risk factors in MCLIP showed significant reduction in claims' utilization for a 3-year period compared to a matched control group (Perelson et al., 2005).

Medicare is currently conducting a National Multi-site Demonstration Project to test the feasibility and cost effectiveness of providing payment for comprehensive CV modification program services (including the lifestyle intervention that was employed in the MLDP and MCLIP) for CHD patients with and without diabetes (Medicare Preventive Services, 2005).

Conclusions

Secondary prevention programs emphasizing comprehensive lifestyle changes may benefit not only CHD patients in general, but especially those with CHD *and* diabetes. In addition, preliminary evidence suggests that comprehensive lifestyle changes may be feasible and even cost effective. Thus, integrating comprehensive lifestyle changes into standard CV risk modification programs and making them more accessible to a wider public may be the necessary first steps towards improving care for patients with CHD and diabetes.

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CHAPTER 4

Comparison of Coronary Risk Factors and Quality of Life in Coronary Artery Disease Patients With--vs--Without Diabetes Mellitus

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Abstract

It is unclear whether patients with coronary artery disease (CAD) and diabetes mellitus (DM) can make comprehensive lifestyle changes showing similar changes in coronary risk factors and quality of life when compared to CAD patients without DM. We examined medical characteristics, lifestyle, and quality of life by diabetic status and gender in the Multicenter Lifestyle Demonstration Project (MLDP), a study of 440 non-smoking patients with CAD [347 men, 15.9% (N=55) diabetic; 93 women, 38.7% (N=36) diabetic]. Patients met in groups to improve lifestyle (plant-based, low fat diet; exercise; stress management) for 1 year. Follow-ups were conducted at 3 and 12 months. At baseline, body mass and systolic blood pressure were significantly elevated among patients with DM. Men with DM had a worse medical history (e.g., hypertension, hyperlipidemia, and family history of CAD) than those without DM. Patients with DM, especially women, reported poorer quality of life than patients without DM. Both groups of patients were able to adhere to the recommended lifestyle, evidencing significant improvements in weight (M= -5 kg), body fat, low-density lipoprotein cholesterol (LDL-C), exercise capacity and quality of life. No significant changes in triglycerides and high-density lipoprotein cholesterol (HDL-C) were noted. By the end of 12 months, improvements in glucose lowering medications [i.e., discontinuation or a change from insulin to oral hypoglycemic agents (OHA)] were noted for 19.8% (N=18) of patients with DM. In conclusion, CAD patients with DM are able to follow a comprehensive lifestyle change program, evidencing similar improvements in coronary risk factors and quality of life as those without DM.

KEYWORDS: lifestyle intervention, diabetes, coronary risk factors, quality of life

Introduction

The aim of this investigation was to examine whether CAD patients with DM are able to make more intensive changes in diet and lifestyle and show similar improvements in clinical risk factors and quality of life when compared to CAD patients without DM. To address this question, we compared data from male and female CAD patients with DM (predominantly type 2) to those without DM. All patients participated in the Multicenter Lifestyle Demonstration Project (MLDP; Koertge et al., 2003; Ornish, 1998), a multi-component lifestyle intervention emphasizing exercise, diet, and stress management [to be found especially beneficial for patients with DM (Surwit & Schneider, 1993; Pischke, Weidner, Marlin, Ornish, in press)].

Methods

Design, recruitment, and procedure of the MLDP

The main aim of the MLDP was to examine whether patients can avoid revascularization by making comprehensive lifestyle changes without increasing cardiac events. Patients were classified into either "Group 1" or "Group 2". Group 1 patients had angiographically documented CAD severe enough to warrant revascularization (by insurance coverage policy standards) at study entry, but opted for lifestyle changes instead (deemed medically safe). Control group patients, matched to Group 1 patients on procedure eligibility, age, sex, left ventricular ejection fraction, and a cardiac score (Ornish, 1998), were provided by Mutual of Omaha. Comparisons between the Group 1 intervention group and the control group indicated that 77% of intervention group patients were able to avoid revascularization for at least 3 years by making comprehensive lifestyle changes without increasing cardiac events (Ornish, 1998). Group 2 patients consisted of those who had previous CABG or PTCA, were in stable condition, and received the intervention. The focus of this study was on the intervention groups, as only events were monitored in the control group. The sample size of the intervention groups allowed for stratification by diabetic status. For more detail on the MLDP see Koertge et al. (2003) and Ornish (1998).

A program staff member contacted potential participants after referral to the program either by their physicians or by self-referral as a result of local media publicity. Eligible patients (determined by interview) were sent a description of data collection activities, a release of medical records form, and a medical history questionnaire (including medication). A baseline physical assessment (anthropometrics) was completed during the interview. A second interview was scheduled with the hospital team after the intake interview and records review; this included the administration of psychosocial and behavioral questionnaires, instructions for completion of a 3-day diet diary, a blood draw for baseline lipid profile, and a treadmill exercise stress test. Medical and behavioral variables and quality of life were reassessed at 3 and 12 months.

Subjects

The protocol was approved by the Committee on the Protection of Rights of Human Subjects and written informed consent was obtained from the participants. The sample was comprised of 440 study participants with CAD [347 men, 15.9% (N=55) with DM; 93 women, 38.7% (N=36) with DM] who participated in the intervention arm of the MLDP. The group with DM included 9 patients with type 1 DM, 3 men (0.9% of the male sample) and 6 women (6.5% of the female sample). Eligibility criteria for study participation have been reported previously (Koertge et al., 2003; Ornish, 1998). Briefly, patients were non-smoking, had diagnosed CAD with either a history of coronary artery bypass surgery or percutaneous transluminal coronary angioplasty (Koertge et al., 2003).

Measures

History of hypertension, hyperlipidemia, myocardial infarction, chest pain, cerebrovascular accident, DM, revascularization procedures, and familial CAD were assessed. Patients were classified as having type 1 or type 2 DM according to the guidelines of the American Diabetes Association (1998). Medical variables including height, weight, % body fat (skin fold measurement), blood pressure (Perloff et al., 1993), angina pectoris (Rose, Blackburn, Gillum, & Prineas, 1982), plasma lipids and lipoproteins, and exercise capacity [i.e., functional capacity assessed by symptom-limited maximal graded exercise testing using the Bruce protocols (Franklin, Whaley, & Howley, 1991)] were assessed at baseline, 3

months and 12 months. Metabolic equivalents (METs), a measure of energy expenditure, were automatically calculated by the testing device during the exercise testing (1 MET equals approximately 3.5 mg of oxygen consumed per minute per kilogram of body weight) (Franklin, Whaley, & Howley, 1991). Diet assessment was based on a 3-day food diary (Rimm et al., 1992). Currently prescribed medications were documented at baseline and at each follow-up. Types of medication included antihypertensives [e.g., ACE (angiotensin converting enzyme) inhibitors], vasodilators (e.g., nitrates), serum glucose lowering agents [regular insulin, OHAs: glipizide, glyburide, tolbutamide, glucophage, micronase, metformin], antilipemics, and antiarrhythmics. Quality of life was assessed by the MOS SF-36 (Medical Outcomes Study 36-item short-form health survey) at baseline, 3-, and 12-months (Ware & Sherbourne, 1992). To summarize the physical and mental components of the SF-36, two aggregate scores were computed (Ware & Kosinski, 2001). Higher scores on the SF-36 reflect better quality of life. Validity and reliability information of the MOS SF-36 and its summary scores have been reported previously (Jenkinson, Wright, & Coulter, 1994; Ware et al., 1998).

Intervention: The Lifestyle Change Program

The program began with a twelve-hour orientation seminar at the hospital, offered over 2 to 3 days, and consisted of scientific lectures and demonstrations (e.g., cooking). Patients then attended sessions in groups 3 times per week for 12 weeks. Two of the 3 weekly sessions focused on the program components in 1-hour blocks. The third weekly session consisted of a 1-hour aerobic exercise session (e.g., on treadmills) and 1-hour lectures designed to facilitate long-term adherence to the program. Patients continued meeting in groups weekly for the following 40 weeks. In addition, they were instructed to exercise and practice stress management on their own (also see Billings, 2000; Koertge et al., 2003; Ornish, 1990).

Adherence to the Lifestyle Change Program

Diet: percent of calories from fat (based on 3-day food diary; goal: 10%). *Exercise:* hours per week (according to the guidelines of the American College of Sports Medicine, Franklin, Whaley, &

Howley, 1991; goal: 3 hrs/week). *Stress management:* hours per week (goal: 1 hr/day). *Attendance of intervention groups:* number of sessions attended divided by the number of sessions offered.

Statistical Analysis

Comparisons of group differences (presence/absence of diabetes; first year graduate vs. drop-out) in baseline demographic, clinical, risk factor, and psychosocial variables were performed with two-sample t-tests (for continuous variables) and with Chi-square tests (for categorical variables) for men and women separately. ANOVAs for repeated measures with two between factors (sex, diabetic status) and 1 within factor at 3 levels (time: baseline, 3 months, 1 year) were computed to test for the effects of sex, diabetes, time and their interactions on coronary risk factors, lifestyle behaviors, and quality of life. To control for unequal Ns in the analyses, ANOVAs for repeated measures with unweighted sums of squares were computed (Diehl & Staufenbiel, 2002; SPSS Base 10.0 User's Guide, 1999; Tabachnick & Fidell, 2001). Bonferroni adjustments were made for comparisons between baseline, 3-months, and 12-months (Diehl & Staufenbiel, 2002). However, as the 10 medical outcomes are highly correlated (e.g., cholesterol and LDL-C; SBP and DBP), adjustments for multiple measures were applied as follows: we computed a p-value half-way between the nominal p-value of the variable under consideration and the p adjusted for all 10 outcomes [(nominal p +Kp)/2)]. Resulting non-significant findings are indicated in Table 4. All analyses were preformed with and without data from the 9 patients with Type 1 DM; no significant differences emerged, results are therefore reported on the entire sample. SPSS 10.1 was used to perform the statistical analysis.

Results

Baseline Characteristics

Baseline characteristics are presented in Tables 1 and 2. Patients with DM did not differ from patients without DM in age, education, marital status, and spousal support. Patients with DM were less

likely to be employed outside the home than patients without DM. Men (but not women) with DM were more likely to have had a history of hypertension hyperlipidemia, and angina pectoris during the previous 30 days than men without DM. Among men, body mass index, body weight, systolic blood pressure, and resting heart rates were significantly higher among those with DM than those without. Women with DM weighed more than women without DM. Patients with DM of both sexes had lower METs than patients without DM. Patients with DM did not differ from patients without DM in diastolic blood pressure and plasma lipids. Patients with DM of both sexes reported an overall lower quality of life than patients without DM. There were no significant group differences in health behaviors, except that patients with DM exercised significantly less than their counterparts without DM. Patients with DM of both sexes were significantly more often prescribed nitrates than patients without DM. Furthermore, men with DM were more often prescribed ACE-inhibitors, calcium channel-blockers, than those without DM. The same pattern of prescription was observed for ACE-inhibitors among women, but not for calcium channel-blockers (for serum glucose lowering agents at baseline and follow-up in patients with DM see Table 3).

Participant Characteristics at Follow-Ups

Measures of anthropometric and medical variables, adherence to the program, and quality of life of patients with complete data at all time points can be seen in Table 4. Regardless of sex or DM, all patients lost a significant amount of weight and body fat, significantly lowered heart rates, LDL-C, and improved their METs. Most of the changes were already evident at three months and were maintained over 1 year.

On average, improvement of patients with DM was the same as in patients without DM, although patients with DM weighed more, had a greater percentage of body fat, higher resting heart rates, and lower METs than patients without DM across follow-up time points. Women had significantly lower HDL-C levels than men regardless of DM. By the end of the 1-year follow-up, all patients significantly improved their diet, exercise, and stress management. All patients met program recommendations with regard to diet. All patients, except women with DM (2.8±1.4 hours of exercise/week), exercised the

prescribed amount of 3 hours per week. However, patients with DM only practiced stress management 4 hours/week (without DM: 5 hours/week). Women with DM reported practicing less stress management than women without DM at all 3 time points. Attendance of group support sessions decreased significantly over time. Patients with DM attended an average of 91% and patients without DM attended an average of 92% of the group support meetings offered during the first 3 months of the intervention. At 1 year, an average of 76% of the group meetings were attended by patients with DM and 78% by those without DM. Patients with DM and women as a group reported lower quality of life at all 3 time points. However, all patients regardless of sex and diabetic status improved their quality of life over time (see Table 4).

Participants lost to follow-up

For a comparison of those who completed the 12-month follow-up to those who did not (21% of the men and 27% of the women), see our previous report (Koertge et al., 2003). Briefly, women who completed the follow-up were younger and more likely to be employed at baseline; men completing the study reported a worse medical history at baseline, but indicated more partner support. In the sample with DM (N=91), comparing those who completed the program (N=69; 76%) to those who did not (N=22; 24%), completers were significantly younger ($p < .01$) and had more years of education ($p < .05$). No other differences emerged. Drop-out rates in the MLDP ranged from 21% to 27% depending on sex and diabetic status, and compare favorably to those in other follow-up studies with cardiac patients (Carney et al., 2004; Ades, 2001).

Discussion

The results of the present study indicate that, despite their worse medical and psychosocial risk factor profile at program entry (also evident in other studies; Banzer, Maguire, Kennedy, O'Malley, & Ballady, 2004; Milani & Lavie; 1996; Suresh, Harrison, Houghton, & Naqvi, 2001), CAD patients with DM are able to make comprehensive lifestyle changes. At 3 months, improvement in risk factors, lifestyle, and

quality of life of patients with DM paralleled that of CAD patients without DM and was maintained for the entire follow-up. Even women with DM, the most medically and psychosocially disadvantaged group in our sample, were able to follow the intervention and showed significant improvements in CAD risk factors (e.g., weight, body fat, LDL-C, METs, but no change in HDL-C and triglycerides) and quality of life. These findings underscore the need for more aggressive approaches such as intensive multi-component interventions when targeting CAD patients with DM (Banzer, Maguire, Kennedy, O'Malley, & Ballady, 2004). Medicare is currently conducting a National Demonstration Project testing the feasibility and cost-effectiveness of such an intervention for CAD patients with and without DM (Centers for Medicare & Medicaid Services, 2000).

Quality of life also improved in both groups of patients at 3 months and was maintained at 1 year. Considering that the SF-36 correlates negatively with measures of depression (e.g., Callahan, Bertakis, Azari, Helms, Robbins, & Miller, 1997; McKee, Cunningham, Jankowski, & Zayas, 2001; Nemeroff & O'Connor, 2000), increased quality of life may also indicate improvements in depression, a risk factor for CAD (Nemeroff & O'Connor, 2000), especially among women with DM (Clouse et al., 2003). One limitation of the present study was the fact that only the intervention group of the MLDP, but not the matched control group, had systematic assessment of coronary risk factors and quality of life (Ornish, 1998). Thus, inferences about the effectiveness of the intervention cannot be made. Furthermore, as in any multi-component intervention, we do not know the relative importance of each component. While the role of exercise and diet in CAD prevention is fairly well established (Ades, 2001), there also is evidence that stress management may reduce clinical events in patients with CAD (Blumenthal et al., 2002), reduce hemoglobin A1c in patients with DM (Surwit et al., 2002), and may affect DM control by facilitating adherence to diet or exercise regimens often prescribed for diabetes management (Surwit & Schneider, 1993).

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Table 1. Demographic and Medical Characteristics at Baseline

Variable	Diabetic men (N = 55)	Non-diabetic men (N = 286)	p Value	Diabetic women (N = 36)	Non-diabetic women (N = 57)	p Value
Age (yrs)	59 ± 10	58 ± 11	.54	58 ± 11	60 ± 10	.19
Education (yrs)	16 ± 3	16 ± 3	.68	15 ± 3	15 ± 3	.44
Married or cohabitating	47 (85%)	253 (88%)	.98	23 (64%)	35 (61%)	.10
Employed outside the home	33 (60%)	202 (70%)	<.05	11 (31%)	31 (54%)	.06
Spousal participation	30 (55%)	138 (48%)	.07	8 (22%)	15 (26%)	.87
Family history of CAD*	40 (73%)	156 (54%)	.08	23 (66%)	35 (61%)	.38
Previous cigarette smoker	40 (73%)	199 (69%)	.70	19 (53%)	33 (58%)	.63
Systemic Hypertension	41 (75%)	121 (42%)	<.01	23 (64%)	29 (51%)	.38
Hyperlipidemia†	36 (66%)	170 (59%)	<.01	24 (67%)	42 (74%)	.70

Previous myocardial infarction	24 (44%)	157 (54%)	.36	17 (47%)	37 (65%)	.09
Previous coronary angioplasty	20 (36%)	137 (47%)	.10	21 (58%)	26 (46%)	.23
Previous coronary bypass	31 (56%)	139 (48%)	.52	14 (39%)	17 (30%)	.37
Angina pectoris (during past 30 d)	34 (63%)	110 (38%)	<.01	17 (47%)	32 (56%)	.40
Medication						
Nitrates	22 (40%)	76 (26%)	<.05	18 (50%)	15 (26%)	<.05
Beta-blockers	23 (42%)	145 (50%)	.19	20 (56%)	25 (44%)	.27
Angiotensin-converting enzyme inhibitors	21 (38%)	49 (17%)	<.01	10 (28%)	11 (19%)	.34
Calcium antagonists	35 (64%)	124 (43%)	<.05	23 (64%)	37 (65%)	.92
Diuretics	8 (15%)	22 (8%)	.22	11 (31%)	12 (21%)	.30
Antihypertensives	5 (9%)	13 (5%)	.35	1 (3%)	1 (2%)	.74
Lipid lowering therapy	30 (55%)	149 (51%)	.31	16 (44%)	36 (63%)	.08

* Family history of CAD was considered positive if a male (<60 years of age) or female (<70 years of age) first-degree relative had CAD, mycocardial infarction, or a cerebrovascular accident.

† Hyperlipidemia was defined as LDL cholesterol > 100 mg/dL, or HDL cholesterol ≤35 mg/dL, or triglycerides ≥200 mg/dL (National Cholesterol Education Program guidelines Adult Treatment Panel II for individuals with established CHD).

Table 2. Medical Risk Factors, adherence to Lifestyle Intervention, and Quality of Life at Baseline

Variable	Diabetic men (N = 55)	Non-diabetic men (N = 286)	p Value	Diabetic women (N = 36)	Non-diabetic women (N = 57)	p Value
Systolic Blood Pressure (mm Hg)	139 ± 21	130 ± 19	<.01	135 ± 19	135 ± 19	.98
Diastolic Blood Pressure (mm Hg)	81 ± 10	79 ± 10	.33	77 ± 10	79 ± 10	.34
Heart Rate at rest (beats/min)	73 ± 14	68 ± 12	<.05	78 ± 12	73 ± 14	.09
Body Mass Index (kg/m²)	30.5 ± 5.8	27.3 ± 5.2	<.01	30.7 ± 5.5	28.8 ± 7.1	.19
Body Weight (kgs)	92.8 ± 18.0	86.1 ± 15.6	<.01	81.6 ± 16.8	73.5 ± 16.8	<.05
Body Fat (%)	24.5 ± 7	22.8 ± 5.9	.07	34.7 ± 6.3	34.2 ± 5.6	.72
Total Serum Cholesterol (mg/dL)	197 ± 52	195 ± 54	.84	214 ± 41	226 ± 48	.24
Low-density lipoprotein cholesterol (mg/dL)	114 ± 38	119 ± 46	.50	133 ± 36	138 ± 44	.63
High-density lipoproetein cholesterol (mg/dL)	35 ± 11	35 ± 10	.94	43 ± 12	45 ± 12	.50
Triglycerides (mg/dL)	244 ± 142	216 ± 156	.23	228 ± 140	217 ± 93	.66
Exercise Capacity (METs; ml O_2/min/kg)	8.7 ± 2.9	10.2 ± 2.9	<.01	6.7 ± 1.9	8.1 ± 2.4	<.01
Diet (% of Calories from Fat)	14.4 ± 8.3	12.9 ± 8.4	.26	17.8 ± 7.8	16.4 ± 9.4	.50
Exercise (hrs/wk)	1.7 ± 1.7	2.4 ± 2.2	<.05	1 ± 1.1	1.7 ± 1.5	<.05

Stress Management (hrs/wk)	0.5 ± 1.3	0.5 ± 1.3	.69	0.37 ± 0.78	0.83 ± 1.5	.10
MOS SF-36: Physical Health†	43.1 ± 9.0	48.3 ± 8.9	<.01	39.4 ± 8.5	44.0 ± 9.5	<.05
MOS SF-36: Mental Health†	46.5 ± 11.4	48.1 ± 10.1	.32	43.0 ± 10.3	47.7 ± 9.7	<.05

† Scores were standardized to have a mean of 50 and a SD of 10 based on a 1998 representative sample of the general US population.

Table 3. Changes in glucose lowering regimen from baseline to 1 year among patients with DM (N = 91)

Changes*		**Baseline***	**1 Yr**
No change: 62 (68.1%)			
	16 (17.6%)	No Medication - Insulin levels controlled by diet	No Medication - Insulin levels controlled by diet
	25 (27.5%)	Insulin	Insulin
	21 (23.1%)	Oral antiglycemic	Oral antiglycemic
Improvement: 18 (20%)			
	1	Insulin	Discontinued insulin without adopting another medical regimen
	6	Insulin	Oral antiglycemic
	11	Oral antiglycemic	Discontinued oral antiglycemic without adopting another regimen
Worsening: 6 (6.6%)			
	1	Oral antiglycemic	Insulin
	1	No medication	Insulin
	4	No Medication	Oral antiglycemic

* Five patients with diabetes (5.4%) dropped out by the 1-year follow-up, 2 of them were on an insulin regimen, 2 on an oral antiglycemic agent, and 1 was not medicated at baseline.

Table 4. Medical Risk Factors, adherence to Lifestyle Intervention, and Quality of Life of Patients with Complete Data at Baseline, 3 and 12 months by Diabetic Status and Gender [ANOVAs for repeated measures with two between factors (sex, diabetic status) and one within factor at three levels (time: baseline, 3 months, 1 year)].

Measure	Diabetic Status	Baseline Mean ± SD (N)	3 months Mean ± SD	12 months Mean ± SD	p-value Time	p-value Diabetic status (DM)	p-value Gender
Body Weight	**Diabetic men**	95.3 ± 18.9 (43)[a]	90.9 ± 16.7[b]	89.9 ± 15.6[b]	<.001	<.01	<.001
(kgs)	**Non-diabetic men**	85.7 ± 15.8 (220)[a]	81.3 ± 13.3[b]	81.0 ± 13.1[b]			
	Diabetic women	80.3 ± 17.4 (21)[a]	76.4 ± 16.3[b]	75.2 ± 15.5[b]			
	Non-diabetic women	75.5 ± 17.7 (43)[a]	70.6 ± 16.2[b]	69.7 ± 16.3[b]			
Body Fat (%)	**Diabetic men**	24.6 ± 6.8 (40)[a]	21.9 ± 6.4[b]	20.7 ± 6.3[b]	<.001	.158	<.001
	Non-diabetic men	22.3 ± 5.8 (195)[a]	19.4 ± 5.0[b]	18.8 ± 5.2[b]			
	Diabetic women	35.4 ± 6.1 (17)[a]	31.1 ± 7.5[b]	30.4 ± 7.1[b]			
	Non-diabetic women	34.9 ± 5.5 (37)[a]	31.8 ± 5.6[b]	30.5 ± 5.8[b]			
Systolic Blood	**Diabetic men**	137 ± 19 (40)[a]	132 ± 19[a]	134 ± 21[a]	.795	.131	.735
Pressure	**Non-diabetic men**	131 ± 18 (165)[a]	126 ± 18[a]	128 ± 18[a]			
(mm Hg)	**Diabetic women**	132 ± 15 (18)[a]	129 ± 16[a]	132 ± 20[a]			
	Non-diabetic women	136 ± 20 (33)[a]	129 ± 19[a]	134 ± 16[a]			

Diastolic Blood	**Diabetic men**	80 ± 10 (40)[a]	74 ± 9[b]	75 ± 11[b]	<.03*	<.02*	.900
Pressure	**Non-diabetic men**	79 ± 10 (164)[a]	74 ± 11[b]	76 ± 10[b]			
(mm Hg)	**Diabetic women**	77 ± 11 (18)[a]	72 ± 14[b]	72 ± 10[b]			
	Non-diabetic women	81 ± 8 (33)[a]	77 ± 10[b]	78 ± 11[b]			
Heart rate at rest	**Diabetic men**	73 ± 14 (38)[a]	69 ± 13[b]	72 ± 13[a]	<.001	<.05*	<.01
(beats/min)	**Non-diabetic men**	68 ± 13 (178)[a]	64 ± 11[b]	67 ± 12[a]			
	Diabetic women	77 ± 11 (19)[a]	73 ± 14[b]	77 ± 12[a]			
	Non-diabetic women	76 ± 14 (33)[a]	71 ± 14[b]	73 ± 12[a]			
Total Serum Cholesterol	**Diabetic men**	199 ± 55 (41)[a]	177 ± 69[b]	171 ± 37[b]	.052	.704	<.01
(mg/dl)	**Non-diabetic men**	195 ± 57 (207)[a]	177 ± 55[b]	180 ± 37[b]			
	Diabetic women	210 ± 33 (20)[a]	204 ± 43[b]	192 ± 41[b]			
	Non-diabetic women	222 ± 42 (40)[a]	204 ± 39[b]	204 ± 44[b]			
Low-density lipoprotein Cholesterol	**Diabetic men**	116 ± 37 (35)[a]	97 ± 32[b]	95 ± 27[b]	<.01	.401	<.05*
(mg/dl)	**Non-diabetic men**	121 ± 48 (193)[a]	101 ± 41[b]	105 ± 34[b]			
	Diabetic women	125 ± 31 (19)[a]	115 ± 35[b]	101 ± 23[b]			
	Non-diabetic women	135 ± 40 (39)[a]	115 ± 39[b]	116 ± 36[b]			
High-density lipoprotein Cholesterol	**Diabetic men**	35 ± 12 (38)[a]	31 ± 9[b]	34 ± 9[b]	.122	.162	<.001
(mg/dl)	**Non-diabetic men**	35 ± 10 (198)[a]	31 ± 8[b]	34 ± 9[b]			
	Diabetic women						

	Non-diabetic women	41 ± 10 (20)[a]	38 ± 10[b]	41 ± 12[b]			
		47 ± 13 (40)[a]	43 ± 16[b]	47 ± 15[b]			
Triglycerides	**Diabetic men**	321 ± 488 (41)[a]	277 ± 251[a]	280 ± 359[a]	.804	.177	.409
(mg/dl) *	**Non-diabetic men**	213 ± 158 (204)[a]	230 ± 166[a]	222 ± 129[a]			
	Diabetic women	240 ± 155 (20)[a]	262 ± 151[a]	248 ± 176[a]			
	Non-diabetic women	202 ± 83 (40)[a]	244 ± 173[a]	208 ± 97[a]			
Exercise Capacity	**Diabetic men**	8.8 ± 2.8 (37)[a]	10.8 ± 2.7[b]	10.8 ± 2.4[b]	<.001	<.01	<.001
(METs;	**Non-diabetic men**	10.4 ± 2.9 (180)[a]	11.9 ± 2.6[b]	12.5 ± 2.8[b]			
ml O_2/min/kg)	**Diabetic women**	6.9 ± 2.1 (20)[a]	8.4 ± 2.6[b]	8.5 ± 2.8[b]			
	Non-diabetic women	8.3 ± 2.8 (33)[a]	9.0 ± 2.9[b]	10.0 ± 3.0[b]			
Diet (% of Calories	**Diabetic men**	14.2 ± 7.8 (38)[a]	6.5 ± 2.1[b]	6.4 ± 2.8[b]	<.001	<.04	<.001
from Fat)	**Non-diabetic men**	12.6 ± 7.8 (172)[a]	6.2 ± 2.3[b]	6.2 ± 2.6[b]			
	Diabetic women	19 ± 7.7 (20)[a]	7.1 ± 2.1[b]	8.9 ± 5.3[b]			
	Non-diabetic women	15.9 ± 8.7 (33)[a]	6.8 ± 2.5[b]	7.1 ± 3.3[b]			
Exercise (h/wk)	**Diabetic men**	1.8 ± 1.7 (44)[a]	4.0 ± 3.3[b]	3.8 ± 2.5[b]	<.001	.500	<.001
	Non-diabetic men	2.4 ± 2.0 (217)[a]	4.1 ± 2.1[b]	3.6 ± 2.1[b]			
	Diabetic women	1.1 ± 1.1 (28)[a]	3.0 ± 1.3[b]	2.8 ± 1.4[b]			
	Non-diabetic women	1.6 ± 1.5 (46)[a]	3.3 ± 1.5[b]	3.0 ± 1.7[b]			
Stress Management	**Diabetic men**	0.5 ± 1.3 (45)[a]	5.5 ± 2.4[b]	4.6 ± 2.6[b]	<.001	<.02	.317

(h/wk)	**Non-diabetic men**	0.5 ± 1.3 (218)[a]	5.6 ± 2.5[b]	4.8 ± 2.9[b]			
	Diabetic women	0.3 ± 0.7 (28)[a]	4.9 ± 2.7[b]	3.5 ± 2.8[b]			
	Non-diabetic women	0.6 ± 1.1 (46)[a]	5.7 ± 2.2[b]	5.1 ± 2.5[b]			
Intervention Group	**Diabetic men**		.93 ± .08 (51)[a]	.80 ± .19[b]	<.001	.570	<.03
(% attendance)	**Non-diabetic men**		.93 ± .10 (272)[a]	.78 ± .20[b]			
	Diabetic women		.89 ± .13 (33)[a]	.71 ± .21[b]			
	Non-diabetic women		.92 ± .10 (54)[a]	.76 ± .23[b]			
MOS SF-36:	**Diabetic men**	43.6 ± 8.6 (42)[a]	48.2 ± 8.2[b]	48.5 ± 7.7[b]	<.001	<.01	<.02
Physical Health[†]	**Non-diabetic men**	48.6 ± 9.1 (211)[a]	51.8 ± 7.5[b]	52.9 ± 7.3[b]			
	Diabetic women	41.7 ± 8.1 (23)[a]	47.5 ± 7.3[b]	46.8 ± 6.3[b]			
	Non-diabetic women	43.3 ± 9.6 (43)[a]	47.7 ± 8.8[b]	50.6 ± 7.9[b]			
MOS SF-36:	**Diabetic men**	46.5 ± 12.1 (42)[a]	50.3 ± 9.2[b]	51.8 ± 10.1[b]	<.001	<.01	.053
Mental Health[†]	**Non-diabetic men**	48.4 ± 10.3 (211)[a]	52.9 ± 8.8[b]	52.1 ± 9.7[b]			
	Diabetic women	40.0 ± 10.1 (23)[a]	47.4 ± 10.5[b]	46.2 ± 12.5[b]			
	Non-diabetic women	47.5 ± 9.7 (43)[a]	54.4 ± 8.9[b]	52.0 ± 9.2[b]			

[a,b] Means in the same row that do not share superscripts indicate significant changes over time (P<.05)

[*]Winsorizing statistical outliers (i.e., replacing values ± 3 SD's of the mean with "most extreme acceptable values" in the distribution of this variable) did not yield significantly different results.

[†] Scores were standardized to have a mean of 50 and a SD of 10 based on a 1998 representative sample of the general US population.

[‡] Adjustments for multiple medical outcomes rendered this finding non-significant.

After adjusting for multiple medical outcomes, only one significant 2-way interaction remains involving time and DM on resting heart rate. Two additional significant 2-way interactions could be found: one 2-way interaction involving gender and DM on mental health and one 2-way interaction involving the effects of gender and time on dietary fat. These effects indicate lowest heart rates among patients without DM at 1year and lowest mental health scores among women with DM. The highest fat intake was observed among women at baseline.

CHAPTER 5

Lifestyle Changes and Clinical Profile in Coronary Heart Disease Patients with an Ejection Fraction of ≤40% or >40% in the Multicenter Lifestyle Demonstration Project

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Abstract

Background: Lifestyle changes are recommended for coronary heart disease (CHD) patients at risk of heart failure (HF) [ACC/AHA stage B; left ventricular ejection fraction (LVEF) <40%]. However, it is not clear whether changes in lifestyle are feasible or beneficial in these patients. **Aim:** To investigate the feasibility of intensive lifestyle changes for CHD patients at risk for HF. **Methods:** We compared 50 patients (18% female) with angiographically documented LVEF ≤40% (mean = 33.4±7.2; range: 15-40%) and 185 patients (18% female) with LVEF >40% (mean = 58.2±9.6; range: 42-87%), who were participants in the Multicenter Lifestyle Demonstration Project (MLDP). All were non-smoking CHD patients. The MLDP was a community-based, insurance-sponsored intervention (low-fat, plant-based diet; exercise; stress management) implemented at 8 sites in the US. Coronary risk factors, lifestyle and quality of life (SF-36) were assessed at baseline, 3 and 12 months. **Results:** Regardless of LVEF, patients showed significant improvements (all $p < .05$) in lifestyle behaviours, body weight, body fat, blood pressure, resting heart rate, total and LDL-cholesterol, exercise capacity, and quality of life by 3 months; most improvements were maintained over 12 months. **Conclusion:** CHD patients at risk for heart failure with a LVEF <40%, can make changes in lifestyle to achieve similar medical and psychosocial benefit to patients with a LVEF >40%.

KEYWORDS: heart failure (ACC/AHA stage B), left ventricular ejection fraction, diet, lifestyle, coronary risk factors, quality of life

Introduction

Prevalence of heart failure (HF) remains high and prognosis poor (The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology, 2005). The importance of early intervention in patients at risk for HF has been emphasized (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure, 2005). One group of patients at high risk for HF and associated mortality are those classified as stage B according to the guidelines of the American College of Cardiology/American Heart Association (ACC/AHA) [i.e., patients with structural heart disease and left ventricular ejection fraction (LVEF) ≤40% but without current signs or symptoms of HF] (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure, 2001; Scrutinio et al., 1994; Solomon et al., 2005). While medical treatments vary according to each stage of the disease (Stage A: high risk for HF but no structural heart disease or symptoms of HF; Stage C: structural heart disease with prior or current symptoms of HF; Stage D: refractory HF requiring specialized interventions) (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure, 2001; Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure, 2005; Yancy, 2005), lifestyle changes (e.g., smoking cessation, regular exercise, reduced alcohol intake) are recommended regardless of stage (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure, 2005; Yancy, 2005).

In two randomised controlled trials, intensive lifestyle changes (low-fat diet, exercise, stress management) have been shown to reduce cardiac risk factors in patients with coronary heart disease (CHD) and slow the progression of the disease (Ornish, 1990; Ornish et al., 1983), which is the major underlying cause of HF (Dei Cas, Metra, Nodari, Dei Cas, & Gheorghiade, 2003). However, it is not clear whether patients at risk for HF (i.e., stage B patients with LVEF ≤40%) can adhere to an intensive lifestyle change program and benefit from making such changes.

There is some indication from small studies that single-component interventions targeting exercise are related to improvements in symptoms, LVEF, exercise capacity, and quality of life in patients

with chronic HF (Dracup et al., 1994; Lloyd-Williams, Mair, & Leitner, 2002; Smart, Haluska, Jeffriess, Marwick, 2005). Promoting multiple lifestyle behaviours in stage A and B patients may be of even greater importance for stabilizing clinical status and reducing the rate of disease progression (Dei Cas, Metra, Nodari, Dei Cas, & Gheorghiade, 2003; Fox et al., 2001; Yancy, 2005). However, it is not clear whether these CHD patients can follow comprehensive lifestyle changes, particularly patients with reduced LVEF, given their disease severity.

The aim of this study was to investigate whether CHD patients at risk for HF (ACC/AHA stage B) can make comprehensive changes in diet, exercise, and stress management to achieve a similar improvement in medical risk factors and quality of life as those with LVEF>40%. Data from a subsample (n=440) of the Multicenter Lifestyle Demonstration Project [MLDP] comparing outcomes of patients with a LVEF ≤40% to those with a LVEF >40%, were analysed. Findings based on the entire sample of the MLDP have been reported elsewhere (Koertge et al., 2003; Ornish, 1998; Pischke et al., 2006).

Methods

Recruitment and procedure

Recruitment and methodology have been described previously (Koertge et al., 2003; Ornish, 1998; Pischke et al., 2006). Briefly, MLDP was a multi-site, insurance-sponsored, secondary prevention study of patients with angiographically documented CAD severe enough to warrant revascularization (according to the coverage policy standards of the Mutual of Omaha Insurance Company) but who instead opted for lifestyle changes instead. (This was deemed medically safe.). The study also included patients who had previous coronary artery bypass graft (CABG) or percutaneous transluminal bypass graft (PTCA) and were in a stable condition. Medical history was assessed at baseline; all other variables were assessed at baseline, 3 months and one year.

Participants

Participants in the present study were a subgroup (N=236) of patients from the intervention arm of the MLDP [N=440; 347 men; 93 women; sex differences have been reported elsewhere (Koertge et al.,

2003)]; who had angiographically determined LVEF at study entry and were in a medically stable condition. The MLDP was an ambulatory, community-based, Phase IV clinical trial evaluation, conducted between 1993 and 1997. Eligibility criteria for study participation have been reported previously (Koertge et al., 2003; Ornish, 1998). Briefly, patients were excluded from the study if they had one or more of the following conditions: (1) left main CAD with >50% occlusion or left main equivalent CAD; (2) CABG within the past 6 weeks; (3) angioplasty within the previous 6 months; (4) myocardial infarction within the last month; (5) chronic congestive heart failure with New York Heart Association class symptoms III or greater and unresponsive to mediations; (6) malignant uncontrolled ventricular arrhythmias; (7) hypotensive blood pressure response to exercise testing; and (8) diagnosed homozygous hypercholesterolaemia. This investigation conforms with the principles outlined in the Declaration of Helsinki (Br Med J 1964;ii:177). The research protocol was approved by the Committee on the Protection of Rights of Human Subjects and written informed consent was obtained from all participants. Patients were placed into one of two groups: those with a LVEF ≤40% (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure, 2001) who were at risk for HF [ACC/AHA, 2005 (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure, 2005), Stages B (N=49) or C (N=1)[1]] or those with a LVEF >40%. All patients were non-smokers at study entry.

Measures

Determination of LVEF

In the group with a LVEF ≤40%, ejection fraction had been determined by left ventricular contrast angiography with direct left ventriculography in 46 patients (92%) and by quantitative two-dimensional echocardiography in 4 patients (8%). In the group with LVEF >40%, 177 patients (96%) had

[1] Stage C patient (1) was not excluded from the sample secondary to a history of HF, controlled with medication, and physician approval to participate in the program.

undergone left ventricular contrast angiography with direct left ventriculography and 8 patients (4%) had undergone quantitative two-dimensional echocardiography.

Medical Variables

Recorded medical variables included; history of hypertension, hyperlipidaemia, myocardial infarction, chest pain, cerebrovascular accident, diabetes, revascularization procedures, familial CHD, height, weight, % body fat (skin fold measurement), blood pressure, angina, plasma lipids and lipoproteins, and exercise capacity. Exercise capacity was assessed by a symptom-limited treadmill test according to the Bruce protocol (Bruce, 1971), and the guidelines of the American College of Sports Medicine (Franklin, Whaley, & Howley, 1991). In brief, patients following the conventional Bruce treadmill protocol started the test at 1.7 mph, 10% grade (for 3 min) and continued in 3-minute intervals (i.e., at 2.5 mph, 12% grade; at 3.4 mph, 14% grade; at 4.2 mph, 16% grade; 5.0 mph, 18% grade; and 5.5 mph, 20% grade). The test was discontinued in the event of limiting symptoms (angina, dyspnoea, or fatigue), abnormalities of rhythm or blood pressure, or marked and progressive ST-segment deviation. Target heart rates were not used as a predetermined end point. Metabolic equivalents (METs), a measure of energy expenditure, were automatically calculated by the testing device during the exercise testing (1 MET equals approximately 3.5 mg of oxygen consumed per minute per kilogram of body weight). Diet assessment was based on a 3-day food diary. Types of medication documented included anti-hypertensives (e.g. ACE-inhibitors, beta-blockers), calcium channel blockers, nitrates and cardiac glycosides (e.g. digoxin).

Quality of Life

Quality of life was measured by the Medical Outcomes Study 36-item Short Form Health Survey (MOS SF-36) and summarized as physical and mental health aggregate scores (Ware & Kosinski, 2001). Validity and reliability information for the MOS SF-36 have been reported previously (Jenkinson, Wright, & Coulter, 1994).

Intervention: The Lifestyle Change Program

The program began with a twelve-hour weekend orientation. Patients then attended program sessions in groups three times per week for 12 weeks. Two of these weekly sessions focused on the four program components (diet, exercise, stress management, group support) in 1-hour blocks. The third weekly session consisted of a 1-hour aerobic exercise session (for example on a treadmill) and 1-hour of lectures. Overall, 36 sessions were offered during the first 3 months of the program. Over the following 40 weeks, patients continued to meet in intervention groups once a week for a 4-hour session, focusing on the program components. In addition, they were instructed to follow the diet and exercise program and practice stress management on their own (Ornish, 1998).

Adherence to the Lifestyle Change Program

Diet: percent of calories from fat (based on 3-day food diary; goal: 10%). *Exercise:* hours per week [according to the guidelines of the American College of Sports Medicine, (Bruce, 1971; Franklin, Whaley, & Howley, 1991); goal: 3 hrs/week]. *Stress management:* hours per week of yoga/meditation (goal: 1 hr/day). *Attendance at intervention groups:* number of sessions attended divided by the number of sessions offered.

Statistical Analysis

Comparisons of group differences at baseline (LVEF $\leq$ 40% or >40%; first year graduate vs. drop-out) were performed with two-sample t-tests for continuous variables and with Chi-square tests for categorical variables. ANOVAs for repeated measures with one within factor at three levels (time: baseline, 3 months, 1 year) and one between-subjects factor (LVEF: $\leq$40%, >40%) were computed to test for the effects of time and LVEF and their interaction on coronary risk factors, lifestyle behaviours, and quality of life. All analyses were re-run with sex as a between-subjects factor. Significant sex differences are indicated in the results. Bonferroni adjustments were made for multiple comparisons. SPSS 12.0 was used to perform the statistical analysis.

Results

Baseline Characteristics

Baseline characteristics of all patients are presented by LVEF in Table 1. Patients with a LVEF <40% had fewer years of education than those with a LVEF >40%. However, in the US 14 or more years of education are equivalent to a college degree indicating that both samples were college educated. As expected, patients with LVEF ≤40% were more likely to have a worse medical history (i.e., previous myocardial infarction, cardiac procedures; $p<.01$) than those with a LVEF >40% but showed similar clinical profiles as those with a LVEF >40%. However, patients with a LVEF <40% had higher heart rates but had lower systolic blood pressure and were less likely to report symptoms of angina than those with a LVEF >40% (all $p<.05$). As expected, patients with a LVEF <40% were more aggressively medicated at baseline to improve ventricular function which may have been beneficial in reducing symptoms of angina. Patients with a LVEF <40% were more likely to use angiotensin-converting enzyme inhibitors, diuretics, and digoxin than those with a LVEF >40% (all $p<.05$). However, they were less likely to be on nitrates and calcium antagonists than patients with a LVEF >40% (all $p<.05$).

Participant Characteristics at Follow-Up

Table 2 shows all outcomes by LVEF and time points. Regardless of LVEF, patients showed reductions in weight, body fat, systolic and diastolic blood pressure, resting heart rate, total cholesterol, LDL-C, and improved their METs at 3 months (all $p<.05$). Improvements in body weight, diastolic blood pressure, total cholesterol, LDL-C, and METs were maintained over 1 year. Body fat was reduced at 3 months and further reduced at 1 year in all patients. Systolic blood pressure and resting heart rate improved at 3 months but reverted to baseline levels at 1 year. Triglyceride levels remained constant and HDL-C reverted to baseline levels at 1 year. Overall, patients with a LVEF ≤40% improved similarly compared to those with a LVEF >40%, although patients with a LVEF ≤40% had higher heart rates and lower levels of systolic blood pressure at all time points. Patients with a LVEF ≤40% lowered their total cholesterol similarly compared to their counterparts over 3 months but reverted to baseline levels at 1 year, whereas patients with a LVEF >40% maintained the reductions ($p<.05$). The expected main effects

for sex were noted, indicating that women had lower body weight and METs and higher percentages of body fat, higher heart rate, and HDL-cholesterol than men at all 3 time points (all p<.01). No significant main effects or interactions were observed for the other outcomes Medications remained relatively stable during the study period. Use of ACE-inhibitors in patients with LVEF ≤40% vs. >40% remained the same in 68% vs. 81% of patients, 14% vs. 4% stopped medication from baseline to 1 year, 8% vs. 2% were not medicated at baseline but at 1 year and 10% vs. 13% did not have complete data at 1 year. Use of beta-blockers in patients with LVEF ≤40% vs. >40% remained constant in 72% vs. 72% of patients over time, 16% vs. 9% stopped medication , 2% vs. 6% were not medicated at baseline, but at 1 year, and 10% vs. 13% did not have complete data at 1 year.

Regarding angina (data not shown) in patients with a LVEF ≤40% versus those with a LVEF >40%; 58% vs. 52%, respectively, stayed the same, 24% vs. 31% improved symptoms, 8% vs. 4%, worsened over the course of 1 year, and 10% vs. 13% had missing data at 1 year.

By the end of the 1-year, and already evident at 3-months, both groups significantly improved diet, exercise, and stress management. All patients met program requirements regarding diet and exercised the prescribed amount of three hours per week at 3 months and 1 year regardless of LVEF, although patients with a LVEF ≤40% improved exercise more from baseline to 1 year than patients with a LVEF >40% (p<.01). Patients with LVEF ≤40% and those with LVEF >40% fell short of the recommended stress management by only 1.1 and 1.4 hours, respectively, per week at 3 months and by 1.6 and 2.4 hours, respectively, at 1 year. Patients in both groups attended an average of 92% of the group support meetings offered during the first 3 months of the intervention and 77% during the remaining follow-up.

All patients showed improvements in both the physical and mental health summary scores at 3 months which were maintained at 1 year (p<.001).

Participants lost to follow-up

A comparison of baseline characteristics in patients with complete data and those without complete data at 1 year (20%), found that patients with a LVEF ≤40% and complete data were more likely to be married or cohabitating ($p < .01$), their spouses were more likely to participate in the program ($p < .01$), and they were more likely to be medicated with nitrates at baseline ($p < .05$), than those without complete data. No other differences emerged. Comparing baseline characteristics of those patients with complete data to those without complete data at 1 year (24%) in patients with a LVEF >40%, found that patients with complete data were more likely to have their spouses participate in the program ($p < .01$), reported higher scores on the physical health summary score of the MOS SF-36 ($p < .05$), and had higher METs ($p < .01$) than those without complete data.

Discussion

Our results indicate that comprehensive lifestyle changes are feasible for CHD patients with a LVEF ≤40%, despite their worse medical history at baseline. These patients were able to make similar changes in lifestyle as those with a LVEF >40% over the course of 3 months, and were able to maintain most of these changes over 1 year. The patients also showed similar improvements in body weight and body fat, blood pressure, heart rate, lipid profile, exercise capacity, and quality of life.

The magnitude of lifestyle changes in this subsample of CHD patients with a LVEF <40% (stage B), was similar to (and sometimes exceeded) that observed in patients with a LVEF >40% and also to that reported in the experimental group of an earlier randomised controlled clinical trial [Lifestyle Heart Trial (LHT); (Ornish, 1990)]. For example, by the end of 1 year, stage B patients reported similar levels of dietary fat intake (6.4% of total calories from fat) when compared to patients with LVEF>40 (6.3%), and the LHT experimental group (6.8%). Exercise levels among stage B patients (4.4 hrs/week) were similar to those observed in patients with LVEF >40% (3.5 hrs/week) and equalled those observed in the LHT experimental group (4.4 hrs/week). Stage B patients practiced stress management for a similar amount of

time (5.3 hrs/week) as patients with LVEF >40% (4.6 hrs/week), but for fewer hours than the LHT experimental group patients (9.6 hrs per week).

Stage B patients also showed significant risk factor reduction, which was comparable to that observed in patients with a LVEF >40% and the LHT experimental group over the same time period (Ornish, 1990). For example, LDL-C levels, blood pressure, body weight, and body fat were significantly lowered, and triglyceride levels and HDL-C remained constant over 1 year in all three groups. METs improved similarly in stage B patients when compared to patients with a LVEF >40% over the course of 1 year (data not available for LHT). For total cholesterol levels, similar reductions were noted after 3 months in both groups. However, patients with a LVEF <40% reverted to baseline levels after 1 year whereas patients with a LVEF >40% maintained their improvements. Similar improvements in CHD risk factors were noted in another more recent (ongoing) phase IV trial (Daubenmier et al., 2007).

Our subsample of stage B patients not only improved lifestyle behaviours and clinical profile, but also showed similar improvements in quality of life (MOS SF-36 summary scores), as patients with LVEF >40% from baseline to 1 year, reaching the minimally clinically important difference of 3-5 points (Hays & Morales, 2001). Considering that the MOS SF-36 correlates negatively with measures of depression (Callahan et al., 1997), increased quality of life may also indicate improvements in depression, a major risk factor for the incidence of HF, especially in elderly women (Williams et al., 2002), and highly prevalent in post-MI patients with a reduced LVEF (Van Melle et al., 2005).

Comparing patients who completed the 1-year follow-up, to those who did not, few significant differences emerged. One major difference was that patients with a LVEF <40% who completed the 1 year follow-up, were more likely to be married or cohabitating and have their spouses participate in the program. A similar pattern was observed in patients with LVEF >40%. This finding underscores the importance of partner support for comprehensive lifestyle interventions. Patients with LVEF >40% with complete data, also reported greater physical health (SF-36) and higher exercise capacity than those without complete data, indicating that greater psychological well-being and physical fitness at baseline may have affected program participation.

Our findings contribute to the current knowledge of stage B patients with LVEF <40%. To date, there is limited evidence that these patients benefit from traditional (i.e., exercise-focused) cardiac rehabilitation, with regard to clinical risk factors and general well-being (Dubach et al., 1997; Giannuzzi et al., 1997; Oberman et al., 1995). Some reports have suggested that patients participating in these exercise-based interventions are able to remain clinically stable and pursue a more physically active lifestyle (Ehsani, Miller, Miller, Ballard, & Schechtman, 1997). Our results indicate that targeting multiple lifestyle behaviours to modify major risk factors appears to be of use in this population.

There are several limitations to our study. The MLDP was a Phase IV clinical trial evaluation based on insurance data from Mutual of Omaha, covering lifestyle intervention at 8 different hospital sites in the U.S. Phase IV research typically consists of long-term surveillance of an intervention shown to be effective in previous Phase III trials. According to Friedman et al. (Friedman, Furberg, & DeMets, 1998), no control groups are necessary for Phase IV trials. Glasgow et al. (Glasgow, Lichtenstein, & Marcus, 2003) also acknowledge decreased experimental rigor during this phase of research. Thus, our Phase IV research presents a unique opportunity to examine whether comprehensive lifestyle intervention works under real-world conditions (Glasgow, Lichtenstein, & Marcus, 2003), providing us with important information about its feasibility for patients at risk for HF. A second limitation is the fact that our sample consisted of predominantly white participants. This is a major shortcoming, considering that the prevalence of HF is higher and survival is worse in African-Americans than in the general population (Thomas et al., 2005; Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure, 2005). Furthermore, there were very few women with LVEF <40%, which precluded meaningful analysis by sex. Thirdly, LVEF was not assessed at follow-up. However, data from an earlier clinical trial in patients with LVEF ≥40% indicated that the same lifestyle changes significantly improved LVEF compared to a control group receiving usual care (Ornish et al., 1983).

In summary, patients with reduced LVEF were able to adhere to comprehensive lifestyle changes, evidencing similar improvements in clinical profile and quality of life compared to those with a LVEF >40%. Considering that the prevalence of HF is increasing and its prognosis is poor, comprehensive

lifestyle interventions aimed at the modification of major risk factors in CHD should target patients at risk for HF to improve clinical outcomes and prevent further progression and clinical deterioration into the more severe and costly stages of the disease.

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Table 1. Demographic characteristics, medical history, medication, medical risk factors, lifestyle behaviors, and quality of life by left ventricular ejection fraction (LVEF) at baseline.

Measure	**LVEF≤40** **N=50**	**LVEF>40** **N=185**	**p-value**
Age (yrs; Mean, SD)	56.9 ± 10.1	59.0 ± 9.8	.187
Gender (% male)	82%	82%	.966
Education (yrs; Mean, SD)	14.5 ± 2.8	16.0 ± 3.1	<.01
Married or cohabitating (%)	88%	82%	.425
Employed outside the home (%)	59.2%	65.9%	.258
Spousal participation (%)	51%	46.7%	.494
Left ventricular ejection fraction (Mean, SD)	33.4 ± 7.2	58.2 ± 9.6	<.001
Family history of CAD[*](%)	64%	55.9%	.475
History of Diabetes (%)	20%	21.5%	.847
Previous cigarette smoker (%)	72%	59.7%	.110
Systemic Hypertension (%)	56%	46.8%	.247
Hyperlipidemia[†] (%)	58%	60.2%	.951
Previous myocardial infarction (%)	80%	49.5%	<.001
Previous coronary angioplasty (%)	60%	37.1%	<.01
Previous coronary bypass (%)	50%	30.1%	<.01
Angina pectoris (during past 30 d) (%)	42%	59.1%	<.05
Beta-blockers (%)	66%	54.8%	.157
Angiotensin-converting enzyme inhibitors (%)	58%	14%	<.001
Anti-platelet or anti-coagulants (%)	84%	82%	.773
Nitrates (%)	28%	43.8%	<.05
Diuretics (%)	28%	5.4%	<.001
Calcium antagonists (%)	38%	60.8%	<.01
Digoxin (%)	21.7%	6.1%	<.01

Antiarrhythmics (%)	2.0%	3.8%	.541
Lipid lowering therapy (%)	58%	52.7%	.504
BMI (kg/m²; Mean, SD)	29.2 ± 5.0	28.1 ± 5.8	.240
Body Weight (kgs; Mean, SD)	89.0 ± 17.6	84.6 ± 17.9	.124
Body fat (%; Mean, SD)	15.6 ± 8.3	13.7 ± 8.9	.286
Systolic Blood Pressure (mm Hg; Mean, SD)	126.0 ± 16.5	133.5 ± 19.3	<.05
Diastolic Blood Pressure (mm Hg; Mean, SD)	78.5 ± 9.8	79.1 ± 9.7	.675
Heart Rate at rest (beats/min; Mean, SD)	74.0 ± 13.6	68.4 ± 12.9	<.01
Total Serum Cholesterol (mg/dL; Mean, SD)	204.4 ± 37.5	202.2 ± 60.2	.812
LDL Cholesterol (mg/dL; Mean, SD)	125.0 ± 34.3	123.6 ± 49.1	.862
HDL Cholesterol (mg/dL; Mean, SD)	35.3 ± 10.4	36.7 ± 11.5	.472
Triglycerides (mg/dL; Mean, SD)[*]	248.6 ± 185.6	221.4 ± 154.3	.305
Exercise Capacity (METs; 3.5 ml.kg-1.min-1; Mean SD)	9.1 ± 3.2	9.1 ± 2.9	.968
Diet (% of Calories from Fat; Mean, SD)	15.6 ± 8.3	13.7 ± 8.9	.189
Exercise (hrs/wk; Mean, SD)	1.9 ± 1.9	2.1 ± 2.1	.488
Stress Management (hrs/wk; Mean, SD)	.23 ± .67	.62 ± 1.5	.089
Physical Health[‡] (Mean, SD)	44.8 ± 10.0	45.7 ± 9.6	.556
Mental Health[‡] (Mean, SD)	47.6 ± 11.3	47.8 ± 10.6	.903

[*] Family history of CAD was considered positive if a male (<60 years of age) or female (<70 years of age) first-degree relative had CAD, mycocardial infarction, or a cerebrovascular accident.

[†]Hyperlipidemia was defined as LDL cholesterol > 100 mg/dL, or HDL cholesterol ≤35 mg/dL, or triglycerides ≥200 mg/dL (National Cholesterol Education Program guidelines Adult Treatment Panel II for individuals with established CHD).

[‡] Scores were standardized to have a mean of 50 and a SD of 10 based on a 1998 representative sample of the general US population; higher scores indicate better quality o life.

Table 2. Medical risk factors, lifestyle behaviors, and quality of life of patients with complete data and left ventricular ejection fraction ≤ or > 40% at baseline, 3 months, and 1 year (LVEF≤40: N=39; LVEF>40: N=142).

Measure	**Left ventricular ejection fraction (LVEF)**	**Baseline**	**3 months**	**12 months**	**p-value Time**	**p-value Group**	**p-value Time x Group**
		Mean±SD	**Mean±SD**	**Mean ± SD**			
Diet (% of Calories from Fat)	LVEF≤ 40	15.1 ± 7.5[a]	6.4 ± 2.2[b]	6.3 ± 2.5[b]	<.001	.389	.449
	LVEF>40	13.5 ± 8.2[a]	6.3 ± 2.5[b]	6.5 ± 2.7[b]			
Exercise (hrs/wk)	LVEF≤ 40	1.9 ± 1.9[a]	4.4 ± 3.0[b]	4.4 ± 3.4[b]	<.001	.113	<.05
	LVEF>40	2.0 ± 1.8[a]	3.7 ± 1.8[b]	3.5 ± 2.0[b]			
Stress Management (hrs/wk)	LVEF≤ 40	.24 ± .68[a]	5.9 ± 2.3[b]	5.3 ± 2.8[c]	<.001	.430	.145
	LVEF>40	.55 ± 1.42[a]	5.6 ± 2.5[b]	4.6 ± 3.1[c]			
Group Support (% attendance)	LVEF≤ 40		.92 ± 1.3[a]	.77 ± .21[b]	<.001	.907	.910
	LVEF>40		.92 ± 1.1[a]	.77 ± 2.1[b]			
Body Weight (kgs)	LVEF≤ 40	90.5± 17.1[a]	84.9 ± 16.0[b]	84.1 ± 15.8[b]	<.001	.065	.149
	LVEF>40	84.2 ± 17.5[a]	80.1 ± 15.1[b]	79.4 ± 14.8[b]			
Body fat (%)	LVEF≤ 40	27.1 ± 6.4[a]	23.3 ± 6.1[b]	22.6 ± 6.5[c]	<.001	.109	.212
	LVEF>40	24.3 ± 8.1[a]	21.6 ± 7.6[b]	20.6 ± 7.3[c]			
Systolic Blood Pressure (mm Hg)	LVEF≤ 40	125.5 ± 15.3[a]	121.9 ± 17.1[b]	122.8 ± 20.3[a]	<.05	<.01	.572

	LVEF>40	134.3 ± 18.4[a]	127.4 ± 18.5[b]	131.8 ±18.5[a]			
Diastolic Blood Pressure (mm Hg)	LVEF≤ 40	78.5 ± 9.3[a]	72.1 ± 9.1[b]	74.5 ± 10.9[b]	<.001	.360	.880
	LVEF>40	79.2 ± 9.9[a]	73.8 ± 10.7[b]	76.0 ± 10.0[b]			
Heart Rate at rest (beats/min)	LVEF≤ 40	75.9 ± 12.9[a]	68.0 ± 13.6[b]	73.9 ± 16.3[a]	<.001	<.01	.404
	LVEF>40	68.7 ± 12.9[a]	64.0 ± 12.9[b]	67.6 ± 11.7[a]			
Total Serum Cholesterol (mg/dL)	LVEF≤ 40	204.6 ± 37.4[a]	176.4 ± 35.8[b]	189.5 ± 45.7[a]	<.001	.804	<.05
	LVEF>40	201.9 ± 65.4[a]	191.2 ± 72.1[b]	184.9 ± 42.3[b]			
Low-density lipoprotein cholesterol	LVEF≤ 40	126.7 ± 32.6[a]	98.2 ± 27.6[b]	109.1 ± 38.4[b]	<.001	.851	.190
(mg/dL)	LVEF>40	124.8 ± 52.6[a]	106.5 ± 47.5[b]	107.0 ± 36.2[b]			
High-density lipoprotein cholesterol	LVEF≤ 40	34.9 ± 10.4[a]	31.5 ± 12.5[b]	36.2 ± 14.1[a]	<.001	.864	.089
(mg/dL)	LVEF>40	36.9 ± 11.8[a]	31.9 ± 8.8[b]	34.8 ± 10.5[a]			
Triglycerides (mg/dL)	LVEF≤ 40	258.8 ± 208.7[a]	253.2 ± 137.5[a]	246.3 ± 155.8[a]	.268	.592	.187
	LVEF>40	215.3 ± 151.1[a]	266.8 ± 210.9[a]	232.5 ± 144.1[a]			
Exercise Capacity (METs; 3.5	LVEF≤ 40	8.9 ± 3.4[a]	10.5 ± 3.0[b]	10.6 ± 2.7[b]	<.001	.413	.359
ml.kg-1.min-1)	LVEF>40	9.2 ± 2.8[a]	10.7 ± 2.8[b]	11.4 ± 3.2[b]			
Physical Health* (MOS SF-36)	LVEF≤ 40	44.8 ± 10.3[a]	48.0 ± 9.3[b]	49.4 ± 8.9[b]	<.001	.272	.985
	LVEF>40	46.2 ± 9.7[a]	49.7 ± 8.5[b]	51.0 ± 7.8[b]			
Mental Health * (MOS SF-36)	LVEF≤ 40	48.2 ± 10.9[a]	51.3 ± 10.6[b]	52.9 ± 11.4[b]	<.001	.873	.481
	LVEF>40	47.6 ± 10.5[a]	52.2 ± 9.2[b]	51.7 ± 10.1[b]			

Mean scores sharing a common superscript in a row of this table were not significantly different at the .05 level.

* Scores were standardized to have a mean of 50 and a SD of 10 based on a 1998 representative sample of the general US population; higher scores indicate better quality of life.

CHAPTER 6

Social Support Group Attendance is related to Blood Pressure, Health Behaviors, and Quality of Life in the Multicenter Lifestyle Demonstration Project

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Abstract

Changes in coronary risk factors, health behaviors, and health-related quality of life (HRQOL) were examined by tertiles of social support group attendance in 440 patients (21% female) with coronary artery disease (CAD). All patients participated in the Multicenter Lifestyle Demonstration Project (MLDP; 8 hospital sites in the U.S.A.), an insurance-covered multi-component cardiac prevention program including dietary changes, stress management, exercise, and group support for 1 year. Significant improvements in coronary risk factors, health behaviors, and HRQOL were noted at 1 year. Several of these improvements (i.e., systolic blood pressure, health behaviors, HRQOL) were related to social support group attendance, favoring those who attended more sessions. The associations between support group attendance to systolic blood pressure and to four HRQOL subscales (bodily pain, social functioning, mental health, and the mental health summary score) remained significant when controlling for changes in health behaviors, but dropped to a non-significant level for the HRQOL subscales 'physical functioning', 'general health', and 'role-emotional'. These results suggest an independent relationship of social support group attendance to systolic blood pressure while improvements in quality of life may be in part due to improved health behaviors facilitated by increased social support group attendance.

KEYWORDS: Social support group attendance, coronary artery disease, coronary risk factors, health behaviors, quality of life

Introduction

Social support has been ascribed a key role in the etiology and prognosis of coronary heart disease (CHD) (e.g., Hemingway & Marmot, 1999; Strike & Steptoe, 2004). The availability of social support has also been associated with better recovery from myocardial infarction (MI) and surgery (e.g., Fontana et al., 1989; Kulik & Mahler, 1989; for a review, Schwarzer & Rieckmann, 2002), lower depression, a major coronary risk factor (e.g., Frasure-Smith & Lespérance, 2005; Rowan et al., 2005), and enhanced quality of life. For example, Bosworth and colleagues (Bosworth et al., 2001) found perceived social support among CHD patients to be related to higher levels of health-related quality of life (HRQOL) in all domains of the SF-36 quality of life questionnaire, even after taking disease severity and demographic variables into account.

As evidence for the role of social support in both etiology and prognosis of CHD is accumulating, researchers and clinicians alike recognize the need for inclusion of social support groups as part of comprehensive cardiac prevention programs. The physiological and behavioral pathways through which social support may affect coronary artery disease (CAD) progression or recovery from cardiac events have not been fully explored. However, research shows that support from social networks can instill, monitor, and enhance health behaviors, such as engaging in exercise (Fleury, 1993; Lippke, 2004; Oldridge, 2003), and thereby promote health and well-being (e.g., Boutin-Foster, 2005). Therefore, inclusion of support groups together with health education and stress management in traditional exercise-based cardiac rehabilitation programs may help to maximize the benefits of cardiac rehabilitation (e.g., Dusseldorp et al., 1999; Linden, 2000; Linden et al., 1996). Indeed, behavioral interventions including support groups have shown to improve outcomes, such as blood pressure, body weight, lipid profiles, and quality of life (e.g., Aldana et al., 2003; Dusseldorp et al., 1999; Haskell et al.,1994; Koertge et al., 2003), as well as psychosocial risk factors such as depression (e.g., for a review, Shen et al., 2005).

Despite of the effectiveness of multi-component cardiac rehabilitation in the reduction of coronary risk, little is known about the role of support group attendance in relation to medical outcomes, health behavior change, and quality of life. In their extensive review of cardiac interventions that included

support groups, Hogan et al. (2002) concluded that there were no effects of support group attendance on coronary risk factors (e.g., obesity, smoking habits), but some support for a positive effect of group support attendance on health behavior change (stress management) (Rahe et al., 1979).

The purpose of the present analyses is to examine the relationship between level of support group attendance and changes in coronary risk factors and health behaviors, as well as HRQOL. Specifically, we examined health behaviors, coronary risk factors, and quality of life in patients of the Multicenter Lifestyle Demonstration Project (MLDP) to address the following questions: (1) Is social support group attendance associated with changes in medical coronary risk factors; (2) is social support group attendance associated with patients' adherence to the program guidelines in terms of diet, exercise and stress management, and (3) is social support group attendance associated with changes in HRQOL.

Method

Recruitment, procedure, and study design

Recruitment, methodology, and eligibility criteria have been described previously (Ornish, 1998; Koertge et al., 2003, Pischke et al., 2006). Briefly, the MLDP was an ambulatory, community-based, Phase IV clinical trial evaluation, conducted between 1993 and 1997, including patients who were classified into either "Group 1" or "Group 2". Group 1 consisted of men and women who had been diagnosed with CAD angiographically or by a positron emission tomography (PET) scan, or by using stress thallium or echo tests that showed myocardial ischemia sufficient to provide a clinical indication by Mutual of Omaha Insurance Company's (Omaha, Nebraska) coverage policy standards for coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). Instead these patients opted for lifestyle changes. (This was deemed medically safe.) Group 2 patients consisted of those who had previous CABG or PTCA and were in a stable condition. Patients were excluded from the study if they had one or more of the following conditions: (1) left main CAD with >50% occlusion or left main equivalent CAD; (2) CABG within the past 6 weeks; (3) angioplasty within the previous 6 months;

(4) myocardial infarction within the last month; (5) chronic congestive heart failure with New York Heart Association class symptoms III or greater and unresponsive to medications; (6) malignant uncontrolled ventricular arrhythmias; (7) hypotensive blood pressure response to exercise testing; and (8) diagnosed homozygous hypercholesterolaemia. The MLDP also included a control group that consisted of group 1 patients who were identified from the Mutual of Omaha database and matched to the intervention group participants' characteristics, such as age, gender, and left ventricular ejection fraction. All control group patients were within 1 month of having undergone revascularization. The main purpose of this comparison group was to determine whether comprehensive lifestyle changes would decrease primary outcomes. Results from this comparison have been reported elsewhere (Ornish et al., 1998).

Hospital site selection was based on location in geographically diverse areas with sufficient population density (>500,000 within a 60-minute drive of the site); a sizeable cardiology program; the demonstration of interest and support from key physicians; and the ability to convince large health insurance providers of the value of including the program in their benefit plan. Accordingly, the MLDP was conducted at 8 different cities in the US including Omaha, Nebraska; New York, New York; Des Moines, Iowa; Ft. Lauderdale, Florida; Columbia, South Carolina; Concord, California; Boston, Massachusetts; and La Jolla, California. Medical history was assessed at baseline; all other variables were assessed at baseline, 3 months, and 1 year.

Participants

Participants in the present study were CHD patients from the intervention arm of the MLDP [N=440; 347 men; 93 women; sex differences have been reported elsewhere (Koertge et al., 2003)]. This investigation conforms with the principles outlined in the Declaration of Helsinki (Br Med J 1964;ii:177). The research protocol was approved by the Committee on the Protection of Rights of Human Subjects and written informed consent was obtained from all participants. For this investigation patients were placed into one of three groups based on a tertile split on % group support sessions attended during the 12 months study period: those with low social support group attendance (≤78%; N=169), medium social support group attendance (>78% to ≤90%; N=143), and high social support group attendance (>90%;

N=128). We then compared medical outcomes, program adherence, and quality of life at baseline and 12-month follow-up by tertiles of social support group attendance.

Intervention: The Lifestyle Change Program

The program began with a twelve-hour weekend orientation. Patients then attended program sessions in groups three times per week for 12 weeks. Two of the three weekly sessions focused on the four program components (diet, exercise, stress management, group support) in 1-hour blocks. The third weekly session consisted of a 1 hour aerobic exercise session (e.g., on treadmills) and 1-hour lectures. Overall, 36 sessions were offered during the first 3 months of the program. For the following 40 weeks patients continued meeting in intervention groups once weekly for a 4-hour session, focusing on all four program components. In addition, they were instructed to follow the diet, exercise and practice stress management on their own (for further detail see Billings, 2000; Billings, Scherwitz, Sullivan, Sparler & Ornish, 1996).

The Four Components of the Lifestyle Change Program

Support Group: The support group model that was employed in the MLDP originated from the First Lifestyle Heart Trial and the Lifestyle Heart Trial (LHT), two earlier randomized clinical trials with CAD patients undergoing intensive lifestyle changes (Ornish et al., 1990; Ornish et al., 1983). The support group was conceptualized as a forum to promote adherence to the other program components (Billings et al., 1996). The group meetings were structured as follows: Program participants met twice-weekly for a 1-hour group support session directed by a clinical psychologist or licensed mental health professional who held the roles of educator, role model, and moderator of the group process. The groups were initiated to help participants to adhere to the program by sharing their emotions, practical problems with the lifestyle change, and other current issues in their lives. The appreciative, open forum allowed participants to freely express their feelings in a supportive, safe environment. Male and female participants and their spouses/partners were encouraged to participate in group sessions. They gathered in groups of 8-14 people after a potluck dinner and formed a circle sitting in chairs. In this format, participants spent an hour talking and listening to one another. Group support sessions typically started

with a brief meditation that included closing the eyes and focusing on breathing. Following this meditation, participants were instructed by the group leader to "recall an event or experience in the last week that was upsetting, uplifting, or otherwise stimulated a feeling or set of emotions" (p.245; Billings, Scherwitz, Sullivan, Sparler & Ornish, 1996). Then each participant was instructed to choose one word that best characterized his/her present feeling and to share it with the group. Group members were encouraged to further inquire about expressed feelings avoiding problem-solving and giving advice or finding solutions, but instead to listen to the other group members with empathy and compassion. For more details see Billings, Scherwitz, Sullivan, Sparler, & Ornish (1996).

Diet: The Ornish diet is a plant-based, very low-fat (10% calories from fat), whole foods diet, which excludes caffeine and limits animal products to egg whites and one cup of non-fat dairy per day. Alcohol consumption was not encouraged, but allowed up to one drink per day. Sodium intake was restricted only for hypertensive patients.

Aerobic Exercise: Patients were instructed to implement a regular moderate exercise regimen into their lifestyle. According to the guidelines of the American College of Sports Medicine (Franklin et al., 1991), participants were requested to exercise at least 3 hours per week (minimum of 30 minutes per session; e.g., brisk walking). Furthermore, they were instructed to exercise at their individual target heart rate (65-85% maximal heart rate).

Stress Management: Patients were instructed to practice one hour of stress management per day (Ornish et al., 1990; Ornish et al., 1998). This 1 hour practice included 30 minutes of stretching based on the asanas (English: poses) in hatha yoga, 15 minutes of progressive relaxation, 5 minutes of breathing, 8 minutes of meditation and 2 minutes of visualization, in that order (Billings, 2000; Billings, Scherwitz, Sullivan, Sparler & Ornish, 1996; Ornish et al., 1990). Patients were asked to practice these techniques for at least one hour each day. Patients could choose the time of the day and the length and type of each stress management technique practiced. To support their efforts, patients received audiotapes for home practice.

Measures

Demographic Variables: Participants' age, gender, marital status, and spousal participation in the program were assessed at baseline. Also, information on family history of CAD, previous myocardial infarction and medical procedures, education, employment, previous cigarette smoking, diabetes, hypertension and hyperlipidemia were collected.

Support group attendance was measured as percentage of group support sessions attended out of all sessions offered within one year. Tertiles of attendance were identified: participants in the first category attended up to 78% of all sessions ('low'), participants in the middle category attended up to 90% of sessions ('medium'), and in the third category, attendance rates exceeded 90% ('high').

Coronary Risk Factors: Weight was measured with clothing and without shoes. Blood pressure was measured using a calibrated sphygmomanometer (Perloff et al., 1993). Plasma lipids and lipoproteins [total cholesterol; low-density lipoprotein cholesterol (LDL-C); high-density lipoprotein cholesterol (HDL-C)] were based on fasting blood samples analyzed at Baylor College of Medicine in Houston, TX. Standard laboratory methods of the Baylor School of Medicine Atherosclerosis Laboratory used enzymatic and colorimetric measurement procedures of Boehringer Mannheim.

Health Behaviors: Dietary intake was assessed by 3-day food diaries. Nutrient content was determined using a standard software program (Professional Diet Analyzer version 4.1, The CBORD Group, Inc., Ithaca NY). Diet adherence was assessed by percentage of calories from fat with 10% fat as adherence goal. Adherence to exercise and stress management were measured in minutes/week. Adherence goals were at least 3 hours of moderate, aerobic exercise/week, and a minimum of 1 hour of stress management/day (7 times/week, 420 minutes).

Health-related quality of life (HRQOL) was assessed using the Medical Outcomes Study (MOS) 36- Item Short-Form Health Survey (SF-36) (Ware & Sherbourne, 1992). HRQOL refers to preferably self-reported physical, mental, and social aspects of health (e.g., Hayes & Morales, 2001; Sherbourne et al., 1992). The MOS SF-36 is a widely used and accepted measure of HRQOL across

various clinical populations (Schlenk et al., 1998) including heart disease patients (e.g., Hawkes et al., 2003).

Statistical Analysis

Analyses are based on tertiles of support group attendance. Change scores for HRQOL and coronary risk factors were computed as 1-year minus baseline values. Change scores for each health behavior were computed as 1-year minus baseline differences in diet adherence (% calories from fat) and minutes spent exercising and practicing stress management per week. Statistical procedures employed include two-sample t-tests (for continuous variables) and $\chi 2$- tests (for categorical variables). Analyses of covariance (ANCOVA) were conducted to assess the relationship between support group attendance and changes in health behaviors, coronary risk factors, and quality of life, controlling for baseline values. Bonferroni post-hoc comparisons were employed to follow up on significant between-group differences. Statistical analyses were performed using SPSS 12.0 (Chicago: SPSS Inc; 2003).

Results

Baseline characteristics by tertile of support group attendance are presented in Table 1. A total of 440 patients (21% women) were initially enrolled in the study. At baseline, the three groups were similar, with the exception of age and physical functioning. Patients in the lowest attendance group were, on average, 3 years older than those in the medium attendance group and reported less physical functioning than those in the highest attendance tertile.

On average, patients in the lowest attendance tertile attended 32 group support sessions [SD=13; interquartile range (IQR): 23-44; Median=33] during the 1-year program. The mean number of sessions for the medium tertile was 52 (SD=6; IQR: 51-55; Median=52), and the mean number of sessions for the high tertile group was 59 (SD=5; IQR: 58-61; Median=59).

Table 1. Baseline Characteristics by Tertiles of Support Group Attendance.

	Support Group Attendance			
	Low (≤78%) (n = 169)	**Medium (>78% to ≤ 90%) (n = 143)**	**High (>90%) (n = 128)**	**p**
Demographic Characteristics				
Age (years)	59.9[a] ± 10.7 (n = 168)	56.7[b] ± 10.5 (n = 142)	58.1[ab] ± 9.0 (n = 127)	<.05
Sex (% male)	76.6%	80.4%	82.8%	n.s.
Education (years)	16.0 ± 3.1 (n = 166)	15.8 ± 2.8 (n = 140)	15.4 ± 3.0 (n = 126)	n.s.
Married/cohabitating	74.4% (n = 168)	89.5% (n = 143)	83.6% (n = 128)	n.s.
Employed	58.1% (n = 167)	67.1% (n = 143)	66.4% (n = 128)	n.s.
CAD Family History	54.5% (n = 167)	62.9% (n = 140)	61.1% (n = 126)	n.s.
History of Smoking	65.7%	65.7%	68.0%	n.s.
Diabetes Mellitus	24.9%	15.4%	21.1%	n.s.
Hypertension	44.4%	47.6%	56.3%	n.s.
Hyperlipidemia	62.1%	59.4%	64.1%	n.s.
Previous MI	50.3 %[a]	62.2 % [a]	48.4 % [a]	<.05
Previous PTCA	43.8%	47.6%	50.0%	n.s.
Previous CABG	45.6%	48.3%	43.8%	n.s.
Coronary risk factors, Health Behaviors, and HRQOL				
Body Weight (in kg)	84.3 ± 17.8 (n = 164)	85.5 ± 18.5 (n = 141)	85.1 ± 16.1 (n= 128)	n.s.
Systolic BP (mmHg)	133.1 ± 21.2 (n = 158)	130.6 ± 18.1 (n = 138)	133.3 ± 18.5 (n = 122)	n.s.
Diastolic BP (mmHg)	78.9 ± 10.1	78.4 ± 10.4	80.3 ± 9.9	n.s.

	(n = 158)	(n = 138)	(n = 122)	
HDL-C (mg/dl)	37.5 ± 10.7	36.4 ± 11.7	36.1 ± 11.4	n.s.
	(n = 152)	(n = 138)	(n = 125)	
LDL-C (mg/dl)	123.0 ± 38.7	119.0 ± 39.1	120.5 ± 39.3	n.s.
	(n = 146)	(n = 136)	(n = 124)	
Total Cholesterol (mg/dl)	205.1 ± 49.7	195.6 ± 38.7	195.7 ± 41.0	n.s.
	(n = 157)	(n = 139)	(n = 127)	
LDL/HDL Ratio (mg/dl)	3.5 ± 1.2	3.4 ± 1.3	3.6 ± 1.5	n.s.
	(n = 146)	(n = 136)	(n = 124)	
Triglycerides (mg/dL)[§]	226.5 ± 132.3	212.3 ± 111.5	210.4 ± 118.8	n.s.
	(n = 155)	(n = 139)	(n = 126)	
Diet (% calories from fat)	14.1 ± 9.1	14.0 ± 8.3	13.9 ± 8.5	n.s.
	(n = 127)	(n = 134)	(n = 124)	
Stress Management	32.3 ± 75.4	37.0 ± 92.2	31.2 ± 63.9	n.s.
(min/week)	(n = 166)	(n = 141)	(n = 122)	
Exercise (min/week)	107.1 ± 125.2	135.2 ± 117.4	137.4 ± 117.4	<.10
	(n= 165)	(n = 121)	(n = 121)	
Physical Functioning	70.3[a] ± 23.0	73.9[ab] ± 21.8	76.7[b] ± 19.0	<.05
	(n = 166)	(n = 142)	(n = 128)	
Role Physical	58.7 ± 40.4	64.1 ± 39.2	63.7 ± 38.3	n.s.
	(n = 166)	(n = 142)	(n = 128)	
Bodily Pain (reverse-	68.7 ± 25.1	69.0 ± 22.7	68.2 ± 22.8	n.s.
scored)	(n = 166)	(n = 142)	(n = 128)	
General Health	56.6 ± 21.2	57.5 ± 20.0	59.2 ± 21.9	n.s.
	(n = 166)	(n = 142)	(n = 128)	
Vitality	52.9 ± 20.1	53.7 ± 21.7	55.5 ± 23.4	n.s.
	(n = 166)	(n = 142)	(n = 128)	
Social Functioning	75.9 ± 24.1	78.1 ± 22.9	79.1 ± 23.7	n.s.

	(n = 166)	(n = 142)	(n = 128)	
Role Emotional	71.1 ± 38.2	72.8 ± 36.1	74.3 ± 36.9	n.s.
	(n = 166)	(n = 142)	(n = 127)	
Mental Health	69.9 ± 17.0	69.9 ± 17.2	69.6 ± 16.5	n.s.
	(n = 166)	(n = 142)	(n = 128)	
Physical Health Sum	45.4 ± 9.6	46.6 ± 9.5	47.1 ± 9.2	n.s.
Score	(n = 166)	(n = 142)	(n = 127)	
	47.2 ± 10.7	47.4 ± 10.7	47.6 ± 10.8	
Mental Health Sum Score	(n = 166)	(n = 142)	(n = 127)	n.s.

Note: Means in the same row that do not share superscripts differ at $p<.05$; Values are expressed as mean ± SD.

§ Statistical outliers were windsorized (i.e., values ± 3 SDs of the mean were replaced with "most extreme acceptable values" in the distribution of this variable).

Changes in Coronary Risk Factors, Health Behaviors, and HRQOL

Changes in coronary risk factors, health behaviors (diet, exercise, stress management) and HRQOL from baseline to 1-year by support group attendance are reported in Table 2. Overall improvements in these variables for women and men have been reported previously (Koertge et al., 2003). Analyses by group attendance tertiles show that systolic blood pressure, all 3 health behaviors, and quality of life were related to group attendance. The effect for systolic blood pressure was due to significantly greater changes in systolic blood pressure among patients in the medium attendance tertile (-4.4 mm Hg) compared to participants in the lowest attendance tertile (+1.4 mm Hg). The reduction in the highest attendance group was -3.3 mm Hg. Because the magnitude in reduction in systolic blood pressure in the highest attendance group was similar to that found in the medium attendance group, we tested the lowest attendance group against the two higher attendance groups and found a significant group difference ($p<.05$; not shown). This finding suggests that significant reductions in systolic blood pressure occurred in those patients who attended at least 78% of group sessions. The effect for triglycerides was

due to significantly greater reductions in triglycerides in the low attendance group compared to the medium attendance group.

In regard to health behaviors, participants in the low attendance category consumed significantly more calories from fat, exercised less and practiced less stress management compared to participants who were in the highest tertile of group attendance. Significant differences were also found for changes in stress management between patients in the low and medium and between the medium and high tertiles. Attendees in the highest group support tertile practiced significantly more stress management than program participants in the medium tertile and attendees in the medium group support tertile practiced significantly more stress management than those in the low tertile. Also, participants in the low and medium attendance tertiles exercised significantly fewer minutes than their counterparts in the highest attendance tertile.

Participants in the medium and high attendance tertile exceeded the target exercise duration of 3 hours (180 min) per week, whereas in the low attendance group patients did not meet these program guidelines (low: *M*=173.7 min, *SD*=106.7; medium: *M*=201.9 min, *SD*=106.3; high: *M*=247.6 min, *SD*=142.4) (not shown). On average, stress management techniques were practiced less than recommended (1 hour per day/420 minutes per week) regardless of support group attendance (low: *M*=201.3 min, *SD*=168.32; medium: *M*=280.2 min, *SD*=157.6; high: *M*=331.2 min, *SD*=179.1) (not shown). Furthermore, in accordance with the program guidelines, all participants, regardless of support group attendance, were able to limit the percentage of dietary fat intake to less than 10% (low: *M*=7.5 %, *SD*=4.4; medium: *M*=6.6 %, *SD*=3.0; high: *M*=6.3 %, *SD*=2.5) (not shown).

The overall improvements in HRQOL observed in the entire sample (Koertge et al., 2003) were also significantly related to level of support group attendance. Improvement in all HRQOL scales was significantly greater the more support group sessions were attended for 6 out of the 8 subscales of the SF-36 (i.e., physical functioning, bodily pain, general health, social functioning, role-emotional, mental health) and the mental health summary score. Trends toward greater quality of life were also observed for the subscale vitality and the physical health summary score ($p<.10$). Considering that improvements of

more than 5 points on SF-36 subscales are considered as clinically important (e.g., Hayes & Morales 2001), it should be noted that participants in the medium and high attendance tertile reported clinically important changes across all dimensions of the SF-36 whereas participants in the lowest attendance tertile showed improvements of this extent only in physical functioning, role-physical, general health, and vitality.

Because of significant differences in health behaviors between attendance groups (low vs. high tertile for diet and exercise; low vs. medium vs. high tertile for stress management), analyses for SBP, triglycerides, and quality of life subscales were rerun controlling for differences in these health behaviors. The relationship between more frequent support group attendance and better HRQOL remained significant ($p<.05$) when comparing low vs. high attendees regarding bodily pain, social functioning, mental health, and the mental health summary score. Group differences between low and medium attendees in bodily pain remained significant as well after controlling for all changes in health behaviors ($p<.05$). Similarly, the group differences in improvements in systolic blood pressure remained significant ($p<.05$) after controlling for changes in stress management (not shown), but rendered non-significant for triglycerides.

Table 2. Changes in Coronary Risk Factors, Health Behaviors, and HRQOL from Baseline to 1-Year (controlling for baseline) by Tertiles of Support Group Attendance.

Baseline to 1-Year Changes	**Support Group Attendance**			**p**
	Low (<78%) IQR: 23-44	**Medium (>78% - ≤90%) IQR: 51-55**	**High (>90%) IQR: 58-61**	
Δ Body Weight (in kg)	-4.1 ± 5.9 (n = 77)	-5.1 ± 4.8 (n = 129)	-5.2 ± 6.2 (n = 124)	n.s.
Δ Systolic BP (mmHg)	1.4[a] ± 18.9 (n = 62)	-4.4[b] ± 18.7 (n = 105)	-3.3[ab] ± 18.2 (n = 105)	<.05
Δ Diastolic BP (mmHg)	-2.1 ± 10.7 (n = 62)	-2.7 ± 12.3 (n = 105)	-4.1 ± 11.0 (n = 104)	n.s.
Δ Total Cholesterol (mg/dl)	-19.2 ± 47.3 (n = 74)	-14.6 ± 34.8 (n = 121)	-14.2 ± 35.2 (n = 120)	n.s.
Δ HDL-C (mg/dl)	.78 ± 9.3 (n = 72)	-1.6 ± 9.4 (n = 119)	-1.1 ± 9.1 (n = 116)	<.10
Δ LDL-C (mg/dl)	-14.9 ± 33.2 (n = 69)	-17.2 ± 34.1 (n = 115)	-15.6 ± 33.7 (n = 114)	n.s.
Δ LDL/HDL Ratio (mg/dl)	-.46 ± 1.2 (n = 69)	-.33 ± 1.2 (n = 115)	-.40 ± 1.1 (n = 114)	n.s.
Δ Triglycerides (mg/dL)[§]	-22.4 ± 117.1[a] (n = 74)	20.7 ± 110.2[b] (n = 120)	16.5 ± 104.9[ab] (n = 119)	<.05
Δ Diet (% calories from fat)	-5.2[a] ± 7.7 (n = 63)	-7.3 [ab] ± 8.4 (n = 114)	-7.4[b] ± 8.4 (n = 113)	<.05
Δ Stress Mg. (min/week)	171.1[a] ± 180.5	247.1[b] ± 181.8	305.2[c] ± 178.7	<.001

	(n = 109)	(n = 135)	(n = 120)	
Δ Exercise (min/week)	68.0[a] ± 126.3	66.6[a] ± 124.6	116.7[b] ± 159.9	<.001
	(n = 108)	(n = 135)	(n = 119)	
Δ Physical Functioning	9.4[a] ± 18.7	10.8[ab] ± 16.9	12.02[b] ± 17.5	<.05
	(n = 79)	(n = 134)	(n = 126)	
Δ Role Physical	13.9 ± 42.3	17.4 ± 38.3	19.4 ± 35.9	n.s.
	(n = 79)	(n = 134)	(n =126)	
Δ Bodily Pain (reverse-	2.9[a] ± 24.1	10.7[b] ± 22.8	10.8[b] ± 19.8	<.01
scored)	(n = 79)	(n = 134)	(n = 126)	
Δ General Health	8.2[a] ± 24.1	11.6[ab] ± 16.3	15.0[b] ± 18.0	<.01
	(n = 79)	(n = 134)	(n = 126)	
Δ Vitality	10.8 [a] ± 19.3	10.9 [a] ± 18.9	14.5 [a] ± 19.0	<.05
	(n = 79)	(n = 134)	(n = 126)	
Δ Social Functioning	4.3[a] ± 22.9	7.6[ab] ± 24.3	10.0[b] ± 25.9	<.05
	(n = 79)	(n = 134)	(n = 126)	
Δ Role Emotional	4.6[a] ± 39.1	9.2[ab] ± 38.2	15.7[b] ± 38.5	<.01
	(n = 79)	(n = 134)	(n = 125)	
Δ Mental Health	4.1[a] ± 19.6	7.2[ab] ± 14.6	10.9[b] ± 15.6	<.01
	(n = 79)	(n = 134)	(n = 126)	
Δ Physical Health Sum Score	3.8 ± 9.0	5.1 ± 8.0	5.2 ± 7.6	<.10
	(n = 79)	(n = 134)	(n = 125)	
Δ Mental Health Sum Score	2.1[a] ± 10.5	3.5[ab] ± 10.0	6.0[b] ± 10.9	<.01
	(n = 79)	(n = 134)	(n = 125)	

Note: Values are expressed as mean ± SD; Means in the same row that do not share superscripts differ at $p<.05$

[§] Statistical outliers were windsorized (i.e., values ± 3 SDs of the mean were replaced with "most extreme acceptable values" in the distribution of this variable).

Participants lost to follow-up

Complete follow-up data were not available for 21% of men and 27% of women. Regardless of group attendance, women in the follow-up were younger ($p<.01$) and more likely to be employed ($p<.05$) than those who did not complete follow-up. Men completing the follow-up were more likely to have had a history of PTCA ($p<.05$), a family history of CAD ($p<.01$), were more often previous smokers ($p<.05$), consumed less alcohol ($p<.05$), and were more likely to live with someone ($p<.05$) than those who did not (Koertge et al, 2003). As expected, most of the patients without complete follow-up data were in the low social support group attendance group (52% of patients in this group had complete follow-up information; 94% and 98% had complete follow-up information in the medium and high attendance groups, respectively). Baseline comparisons of patients with complete data in the low attendance group to those lacking follow-up information in that same group indicated that the former were more likely to be medicated with antiarrhythmics ($p <.05$) and were more likely to have had a history of cigarette smoking than those without complete data ($p<.05$). No other differences in demographic variables, health behaviors, coronary risk factors or quality of life were found.

Discussion

The present study examined whether the improvements in coronary risk factors, health behaviors, and quality of life noted in the entire sample of patients participating in the MLDP (Koertge et al, 2003) were related to attendance of social support groups offered over a 12 months period.

Support group attendance was indeed associated with several outcomes. Reductions in systolic blood pressure were found in those who attended >78% of group support sessions. This finding remained significant after controlling for changes in health behaviors, indicating that reductions in blood pressure may be independently related to social support group attendance. This finding is consistent with other studies that have reported similarly beneficial effects of social support on blood pressure in CAD patients participating in psychosocial interventions in conjunction with standard cardiac rehabilitation (Gump,

Polk, Kamarck, & Shiffman, 2001; Krantz & McCeney, 2002; Linden et al., 1996; Steptoe, Lundwall, & Cropley, 2000). The mechanisms by which social support group attendance may influence systolic blood pressure remain unclear. The social support received from the group may have helped patients acquire additional coping strategies that alleviated stress, with positive consequences for systolic blood pressure (cf. Uchino, 2006). The support groups in our intervention emphasized the sharing of personal-emotional experiences (Billings, 2000) which are related to reduced worrying, anxiety, and depression in patients enrolled in a similar comprehensive lifestyle change program (Kronenwetter et al., 2005). Spiegel and colleagues (2007), who employed similar support groups, reported reductions in stress, improved emotion regulation, and prolonged survival in estrogen-receptor negative patients with metastatic breast cancer. Thus, it is conceivable that stress reductions experienced in the groups may have contributed to the observed improvements in systolic blood pressure in this study.

In regard to health behaviors, frequent support group attendance was related to behavior change among patients in this study. 'High attendees' reduced dietary fat intake more and practiced more stress management and exercise compared to 'low attendees'. More frequent participation in group sessions may have enabled patients to witness and inquire about the struggle and successes of other group members with lifestyle changes, to learn strategies to better implement the new routine into their lives, to observe role models, and to share their own success with others (Billings et al., 1996; Boutin-Foster, 2005). In conjunction with feelings of connectedness and community, group attendance may have influenced participants' motivation to adhere to the program guidelines and to overcome barriers for the implementation of new health behaviors. In support of this notion, empirical studies on exercise behavior found that group cohesion and perceived social support were associated with greater exercise adherence (e.g., Fraser & Spink, 2002; Spink & Carron, 1992). Especially important for long-term adherence to exercise behavior are perceptions of social support at the early stages of an intervention (Courneya & McAuley, 1995). The open format and informal structure of the group in this intervention allowed for manifold interactions between the participants and may have provided this support. However, it is important to note that, despite greater improvements in health behaviors in the highest compared to the

lowest group attendance tertile, participants across all attendance tertiles met the intervention guidelines for dietary fat intake (10% calories from fat) and exercise (3 hrs/week) by the end of 1 year. Even the low attendance group practiced a mean of 3.5 hours per week of the recommended 7 hrs/week of stress management.

Analysis of changes in HRQOL over one year signified that patients who attended the most support group sessions improved significantly more than their counterparts who were less involved in the patient community. The importance of improvements in HRQOL has been underlined by studies demonstrating an inverse relationship between SF-36 subscales and depression (e.g., Callahan et al., 1997; Findler et al., 2001). Increases in quality of life measured by the MOS SF-36 in our study may therefore not only indicate better quality of life but also reductions in depression. The improvements in quality of life were, in part, mediated by improvements in health behaviors. However, when controlling for changes in health behaviors, associations between group attendance and HRQOL remained significant for 4 subscales of the HRQOL (i.e., bodily pain, social functioning, mental health, and the mental health summary score), but rendered non-significant for 3 of the HRQOL subscales (i.e., physical functioning, general health, and role-emotional). This suggests that improvements of some aspects of quality of life seem to be related to improved health behaviors, but others may be independently linked to support group attendance.

Interestingly, high frequency of support group attendance was not only related to statistically significant improvements in HRQOL, but also to clinically meaningful changes [i.e., improvements of 5 points and more on the SF-36 subscales are considered clinically meaningful (e.g., Hays & Morales, 2001; Ware et al., 1993)]. Patients in the medium and high support group attendance tertiles showed changes in HRQOL well exceeding 5 points for all of the SF-36 subscales. Improvements of clinical importance in HRQOL were even evident among patients in the low attendance tertile.

It is noteworthy that patients in this study generally showed relatively high rates of attendance of group support sessions. On average, patients in the lowest attendance tertile attended 32 group support sessions (SD=13; IQR: 23-44; Median=33) during the 12-months intervention. The mean number of

sessions for the medium tertile was 52 (SD=6; IQR: 51-55; Median=53), and the mean number of sessions for the high tertile group was 59 (SD=5; IQR: 58-61; Median=59). Thus, support group attendance in our study, even in the low attendance tertile, was high relative to other behavioral interventions including support groups. For example, in the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial, patients only attended a median of 11 sessions (IQR: 6-19 sessions) over 6 months (Berkman et al., 2003).

Some study limitations should be noted. Only 52% of 'low attendees' completed the 1-year follow-up compared to 94% in the medium and 98% in the high attendance group which may have biased our results. However, 'low attendees' with complete data did not differ in their baseline characteristics from those without complete data, except for more frequent use of anthiarrhythmic medication and a higher likelihood of previous cigarette smoking. Secondly, quantity or quality of support interactions during the support group sessions were not assessed in this study. Thirdly, this study assessed the relationship of support group attendance to outcomes rather than randomizing patients to different support group conditions. Therefore, causal relationships cannot be assessed. It is possible that outcomes were affected by unknown third factors not measured. Also, reciprocal/interactive relationships of HRQOL and support group attendance across the study period were not assessed in this study.

To conclude, results of the present study suggest that more frequent support group attendance as part of a comprehensive lifestyle change intervention was related to reductions in blood pressure, improvements in health behaviors and quality of life. While improvements in quality of life may, in part, be due to improved health behaviors associated with increased support group attendance, our results point to an independent relationship of social support group attendance to systolic blood pressure. These findings underscore the importance of including social support groups in cardiac rehabilitation, not only for the potential benefits of lowering blood pressure but also for improvements in health behaviors and quality of life.

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CHAPTER 7

Comprehensive Lifestyle Changes are related to Reductions in Depression and Improvements in Coronary Risk Factors in Women and Men at High Risk for Coronary Heart Disease

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Abstract

Background: Depression, a risk factor for coronary heart disease (CHD), may be an obstacle to health behavior change. **Purpose:** To investigate whether an intervention targeting multiple health behaviors improves depression and whether this improvement is related to changes in health behaviors, coronary risk factors, and quality of life in patients at high risk for CHD (i.e., ≥ 3 coronary risk factors and/or diabetes). **Methods:** All patients [310 men, 27% >16 on the Center for Epidemiological Scale–Depression scale (CES-D); 687 women, 38% CES-D score >16] enrolled in the Multisite Cardiac Lifestyle Intervention Program were asked to make changes in diet, to engage in moderate exercise, and to practice stress management over 3 months. Patients were grouped into: (1) depressed patients who became non-depressed (CES-D score ≤ 16, n=248; 73%); (2) patients who remained or became depressed (CES-D score >16, n=76); (3) non-depressed patients who remained non-depressed (n=597). **Results:** At baseline, depressed patients had a more adverse medical and behavioral status than non-depressed patients. Patients who became non-depressed at follow-up (group 1) reduced dietary fat intake, perceived stress, and hostility and increased exercise and SF-36 Mental Component Scores more than patients in the other 2 groups. **Conclusion:** Targeting multiple health behaviors appears to benefit initially depressed patients at high risk for CHD.

KEY WORDS: high risk for coronary heart disease, depression, coronary risk factors, quality of life, lifestyle changes

Introduction

Over the past two decades the number of patients at high risk for coronary heart disease (CHD) has dramatically increased (Eckel, Grundy, & Zimmet, 2005). This worldwide development is driven by the global epidemic of obesity and diabetes (Eckel, Grundy, & Zimmet, 2005). In the US, approximately 35 to 40% of the population meets the criteria for the metabolic syndrome (Ford, 2005), a constellation of metabolic risk factors including glucose abnormalities (i.e., elevated plasma glucose, impaired glucose tolerance), central obesity, dyslipidemia, and hypertension (Bianchi, Penno, Romero, Del Prato, & Miccoli, 2007; Grundy et al., 2005). No consensus has yet been reached regarding the inclusion of type 2 diabetes as an additional criterion for the metabolic syndrome. For example, the World Health Organization and the International Diabetes Federation include type 2 diabetes as a criterion for metabolic syndrome, whereas the National Cholesterol Education Program (NCEP)-ATP III Guidelines do not. Regardless of the exact definition of the syndrome, the risk for major cardiac events in patients with this syndrome is at least twice as high as for those without the syndrome (Eckel, Grundy, & Zimmet, 2005). For patients with type 2 diabetes, the added diagnosis of metabolic syndrome confers an approximate 5-fold greater risk for cardiac events (Eckel, Grundy, & Zimmet, 2005).

Lifestyle modification is currently the primary treatment recommendation to prevent progression of the metabolic syndrome to coronary heart disease (Grundy et al., 2005). In particular, bodyweight reduction, regular physical activity, and dietary changes are recommended to reduce the underlying behavioral risk factors of the syndrome (Bianchi, Penno, Romero, Del Prato, & Miccoli, 2007; Grundy et al., 2005; Yusuf et al., 2004). Lifestyle interventions addressing these behavioral risk factors have been tested in numerous studies and have demonstrated improvements in cardiovascular risk factors (Boulé, Haddad, Kenny, Wells, & Sigal, 2001; Boulé, Kenny, Haddad, Wells, & Sigal, 2003; Costacou & Mayer-Davis, 2003; Elmer et al., 2006; Hu & Willett, 2002; Kronenberg et al., 2000; Orchard et al., 2005; Stampfer, Hu, Manson, Rimm, & Willett, 2000; The Look AHEAD Research Group, 2007; Toobert, Stryker, Glasgow, Barrera, Angell, 2005; Tuomilehto et al., 2001; Wister et al., 2007) and a delay in the onset of type 2 diabetes (Lindström et al., 2006; Pan et al., 1997; The Diabetes Prevention Program

Research Group, 2002). In addition to behavioral risk factors, psychological factors have been linked to the etiology and prognosis of metabolic syndrome.

A recent prospective cohort study found that high levels of depressive symptoms at baseline predicted an increased risk of developing metabolic syndrome in initially healthy women over 15 years (Räikkönen et al., 2007). Similarly, depression was associated with approximately 60% increased odds for metabolic syndrome in 652 women with suspected coronary artery disease [i.e., women who received coronary angiography; Vaccarino et al., 2008]. These results were independent of demographic factors, behavioral risk factors, and functional status. In this study, women with both elevated depressive symptoms (i.e., elevated Beck Depression Inventory Scores) and a previous diagnosis of depression (Vaccarino et al., 2008) were compared to women with one of these two conditions. The number of metabolic syndrome risk factors increased gradually by severity of depression across these three depression groups. Women with both elevated depressive symptoms and a previous diagnosis of depression had a 2.6 times higher risk for cardiovascular disease over a median follow-up of 5.9 years. Thus, it would be advisable to target depression in lifestyle interventions that modify behavioral risk factors of the metabolic syndrome.

It is known that depression is an obstacle to lifestyle changes that are necessary to reduce cardiovascular risk factors and to prevent heart disease. Depressed patients may find it difficult to follow lifestyle changes (Vickers, Nies, Patten, Dierkhising, & Smith, 2006). Depression is associated with a more sedentary lifestyle, smoking, obesity, lack of exercise, and poor glycemic control (Gonzalez et al., 2007; Goodman & Whitaker, 2002; Katon et al., 2004; Patton, Carlin, Coffey, Wolfe, Hibbert, & Bowes, 1998; Rajala, Uusimäki , Keinänen-Kiukaanniemi, & Kivelä, 1994; Steptoe et al., 1997). Engaging in exercise or improving one's lifestyle, on the other hand, has been shown to have a strong antidepressant effect in patients with coronary heart disease and in healthy non-depressed patients (Farmer et al., 1988; Lett, Davidson, & Blumenthal, 2005).

To date, there are no studies that have investigated changes in depression in patients with metabolic syndrome participating in lifestyle interventions. Only two studies have assessed changes in

depression in patients with type 2 diabetes participating in lifestyle interventions providing conflicting results. Toobert and colleagues (2007) evaluated changes in depression in postmenopausal women with diabetes who participated in a comprehensive lifestyle intervention (diet, exercise, stress management, smoking cessation) compared to a usual care group but did not find significant changes in depression over 2 years. In contrast, Georgiades and colleagues (2007) found that cognitive-behavioral therapy significantly reduced depression in patients with diabetes (71% female) over 1 year. However, these reductions were not associated with changes in HbA1c or fasting glucose levels and differences due to gender were not tested.

The purpose of this study was to evaluate whether (1) depressed patients with metabolic syndrome (i.e.., ≥3 coronary risk factors and/or type 2 diabetes) can make comprehensive lifestyle changes over 3 months, (2) whether they can benefit in terms of reductions in depression and (3) whether these reductions in depression are associated with reductions in cardiovascular risk factors and improvements in health behaviors, glycemic control, and psychological outcomes.

Method

Participants

The present investigation included 997 patients with metabolic syndrome (i.e., ≥3 coronary risk factors and/or diabetes) (310 men, 687 women) who enrolled in the Multisite Cardiac Lifestyle Intervention Program (MCLIP) from September 1998 to December 2006. The MCLIP is an on-going comprehensive lifestyle change program for the prevention of CHD administered by insurance companies. The MLCIP included 2 groups of patients: one arm included patients with CHD, the second arm included patients at high risk for CHD. The protocol was approved by the Committee on the Protection of Rights of Human Subjects and written informed consent was obtained from all participants. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. Patient recruitment and inclusion and exclusion criteria for CHD patients have been described elsewhere (Daubenmier et al., 2007).

Briefly, patients were eligible for the program's high CHD risk arm if they had either a family history of premature CHD (i.e., 1st-degree relative with myocardial infarction or sudden cardiac death; male relative: < age 55, female relative: < age 65) or were a male aged >45 years or female aged >55 years. In addition, eligible patients must have presented with at least two other of the following documented cardiovascular risk factors: current cigarette smoking (within past 5 years), hypertension (blood pressure >140/90 mmHg or on antihypertensive medication), low HDL-C (<40 mg/dl or on medications for lipid therapy), elevated apolipoprotein (a) (>30 mg/dl or on medications for elevated lipids), total cholesterol >240 (or on medications for elevated lipids), LDL>160 (or on medications for elevated lipids), high sensitivity c-reactive protein greater than 3 mg/dl and less than 10 mg/dl, obesity (BMI >30), insulin resistant state as per American Heart Association/National Heart, Lung, and Blood Institute diagnosis guidelines [including any three of the following criteria: abdominal obesity (men: waist >40 in; women: waist >35 in), triglycerides >150 mg/dL, HDL (men: <40 mg/dL, women: <50 mg/dL), blood pressure ≥130/85 mmHg, either fasting glucose ≥ 110 mg/dL], type 2 diabetes. The diagnosis of type 2 diabetes was defined as a "coronary risk equivalent" (Third Report of the National Cholesterol Education Program (NCEP) Expert Panel, 2002) indicating that a diagnosis of type 2 diabetes only sufficed to be eligible for the program.

Exclusion criteria included 1) current tobacco user not concurrently enrolled in a smoking cessation program with 2-month history of smoking cessation, 2) primary residence more than a one-hour commute from the program site, unless approved, 3) history of substance abuse disorder without documentation of minimum one-year abstinence, 4) history of a significant psychiatric disorder without documentation of minimum one-year stability, 5) impaired cognitive function, such as dementia or delirium, 6) English language illiteracy unless program site could accommodate, 7) non-ambulatory, 8) uncooperative spouse or partner, defined as obstructive in attitude or behavior, 9) likely to be disruptive to group setting.

Two different methods were employed to examine the third question addressed in this study, that is whether reductions in depression are associated with reductions in cardiovascular risk factors and

improvements in health behaviors, glycemic control, and psychological outcomes over 3 months in patients at high risk for CHD. First, we compared cardiac and psychological outcomes of 3 groups of patients with metabolic syndrome based on their depression scores [Center for Epidemiological Scale–Depression scale (CES-D)]: (1) depressed patients who became non-depressed (CES-D ≤16 at 3 months, n=248; 73%); (2) patients who remained or became depressed (CES-D >16 at 3 months, n=129); (3) non-depressed patients who remained non-depressed (CES-D ≤ 16 at 3 months; n=602). Second, we analyzed associations of changes in depression as a continuous variable with changes in cardiovascular risk factors, health behaviors, and psychological outcomes.

Measures

At baseline, demographic information and medical history were documented.

Depression

At baseline and at 12 weeks, depression was assessed by the Center for Epidemiological Scale–Depression scale (CES-D) (Radloff, 1977). Participants were asked to indicate how often they experienced specific depressive symptoms during the past week. Total scores range from 0 to 60 with higher scores indicating endorsement of more symptoms. To determine depression, a CES-D cutoff score of 16 was used. A CES-D score ≥16 is widely used to diagnose minor depression (i.e., a clinically relevant level of depressive symptoms) in healthy and CVD populations (Anstey & Luszcz, 2002; Penninx et al., 1999; Shinar et al., 1986; Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977) and has high predictive validity for acute coronary syndrome events and for mortality in initially healthy patients (Anstey & Luszcz, 2002; Lesperance, Frasure-Smith, Juneau, & Theroux, 2000; Rowan, Haas, Campbell, MacLean, & Davidson, 2005; Rugulies, 2002). Similarly, a CES-D score ≥16 has been used frequently in patients with type 2 diabetes to assess depressive symptoms (Saydah, Brancati, Golden, Fradkin, & Harris, 2003; Vickers, Nies, Patten, Dierkhising, & Smith, 2006). Diabetic patients exceeding 15 points on the CES-D scale had a 54% increased mortality, after controlling for sociodemographic, lifestyle, and health-status variables (Zhang et al., 2005).

Medical Variables

Height, weight, and blood pressure were measured by trained health professionals. Fasting blood samples were collected and analyzed for total cholesterol, HDL-C, LDL-C, triglycerides, and glycated hemoglobin (for diabetic patients) (HbA1c). Exercise tolerance was assessed by maximal treadmill or bicycle ergometry testing. Medications (anti-depressants, beta-blockers, angiotensin-converting enzyme inhibitors, calcium antagonists, diuretics, lipid-lowering, oral antiglycemics, and insulin) were assessed at baseline and 3-months follow-up.

Other Psychosocial Variables

In addition, hostility was evaluated using the Cook-Medley Hostility scale, a 27-item measure containing 3 subscales: cynicism, hostile affect, and aggressive responding (Barefoot, Dodge, Peterson, Dahlstrom, & Williams, 1989). Total scores range from 0 to 27 with higher scores reflecting greater hostility. Psychological stress was assessed by the 10-item Perceived Stress Scale, which measures the degree to which situations during the past month are appraised as stressful (Cohen, Kamarck, & Mermelstein, 1983). Individual responses ranged from 0 (never) to 4 (very often) and total scores ranged from 0 to 40, with higher scores indicating greater perceived stress. Quality of life was measured by the Medical Outcomes Study 36-item Short Form Health Survey (MOS SF-36) (Ware, Snow, Kosinski, & Gandek, 1993) and summarized as physical and mental health aggregate scores (Ware & Kosinski, 2001).

Lifestyle Change Program

Patients attended an onsite program twice a week for 3 months for a total of 104 hours (for further detail see Daubenmier et al., 2007, Govil, Weidner, Merritt-Worden, & Ornish, in press). All patients were encouraged to eat a very low-fat, plant based diet (10% daily calories from fat, 15% from protein, and 75% from complex carbohydrates), engage in moderate aerobic exercise for a minimum of three hours per week and strength training activities at least twice per week, practice stress management for one hour per day, and attend group support sessions for two hours each week for 12 weeks. All patients were individually prescribed exercise levels (typically walking) according to their baseline treadmill test results. Target training heart rates were calculated with Karvonen formula, unless otherwise indicated, at

intensities of 45-80% of the maximal heart rate achieved on the exercise test (for further detail see Frattaroli, Weidner, Merritt-Worden, Frenda, & Ornish, in press). Patients were asked to exercise for a minimum of 3 hours per week and to spend a minimum of 30 minutes per session exercising within their target heart rates. This study was approved by each site's institutional review board and all subjects gave informed consent.

Adherence to the Lifestyle Change Program

Diet: percent of calories from fat (based on 3-day food diary; goal: 10%). *Exercise:* hours per week [according to the guidelines of the American College of Sports Medicine (Whaley, Brubaker, & Otto, 2006); goal: 3 hrs/week). *Stress management:* hours per week of yoga/meditation (goal: 1 hr/day). *Attendance of intervention groups:* number of sessions attended divided by the number of sessions offered.

All risk factor, adherence, quality of life, and psychological status measurements were made at baseline and 12 weeks (see Daubenmier et al., 2007, for more details). In addition, a lifestyle index, based on a formula validated in previous research (Daubenmier et al., 2007; Ornish et al., 1998; Pischke, Scherwitz, Weidner, & Ornish, in press), measured overall adherence to intervention guidelines and was calculated as the mean percentage of adherence to each lifestyle behavior. Zero equaled no compliance and 1 equaled 100% compliance.

Statistical Analyses

For baseline comparisons, patients were categorized into one of two groups according to their levels of depression: no depression (CES-D score <16) vs. depression (CES-D score ≥16). Baseline group differences were tested using chi-squared ($\chi 2$) analyses and multi-way frequency analyses (for categorical variables) and independent samples t-tests and ANOVAs (for continuous variables). Changes in depression grouping (i.e. percentage of patients moving from one depression group to another over the follow-up) were assessed using the McNemar test. Group effects, time effects, and group-by-time

interactions for coronary risk factors, quality of life, psychosocial outcomes, and adherence to lifestyle changes were tested with repeated measures ANOVAs and Bonferroni adjustments. In addition, separate analysis was performed for the 11 patients who became depressed at 3 months. Bivariate Pearson's correlations were used to analyze associations between 3-months changes in depression and 3-months changes in coronary risk factors, psychosocial outcomes, quality of life, and adherence [using the lifestyle index, (Pischke, Weidner, Scherwitz, & Ornish, in press)] as continuous variables in patients who became non-depressed. Statistical analyses were performed using SPSS 14.0 (SPSS Inc., Chicago).

Results

Baseline characteristics

Baseline characteristics are listed in Table 1. Nine-hundred and ninety-seven patients with ≥ 3 coronary risk factors and/or diabetes and complete CES-D baseline data were included in our analyses. Three-hundred and forty-one patients (82 men, 259 women) had a CES-D score ≥16 and 656 patients (228 men, 428 women) had a CES-D score <16. The sample was 94% Caucasian.

Depressed patients were more likely to be Caucasian, to be medicated with antidepressants and gastrointestinal medication, to have higher body mass, to have higher diastolic blood pressure, and higher levels of hostility, and perceived stress, and to consume more dietary fat, while non-depressed patients were older, had higher SF-36 Physical and Mental Component scores and practiced more stress management.

Regardless of depression group, men were more likely to be married, to be employed, to have a college degree, to have a history of smoking, systemic hypertension (among diabetic patients, men were less likely to be hypertensive), be medicated with calcium antagonists and lipid lowering drugs than women. Men also exercised more, weighed more, had higher METs, diastolic blood pressure, total cholesterol/HDL ratios, hostility, and SF-36 Physical Component scores, while women were significantly more likely to be diabetic, to be medicated with diuretics and antidepressants, and to have higher body

mass, higher body fat, total cholesterol levels, HDL cholesterol, LDL cholesterol, and higher perceived stress levels.

Significant sex by depression group interactions for levels of education, HbA1c-levels, and SF-36 Physical Component scores indicated that depressed men had higher levels of education than non-depressed men, while depressed women had lower HbA1c-levels and SF-36 Physical Component scores than non-depressed women.

Changes in Depression

Baseline and 3-months depression data were available for 921 of the 997 patients (92%). As can be seen in Table 2, of the 341 patients (76% female) reporting depression (CES-D ≥16) at baseline, 73% became non-depressed (83% of the men and 69% of the women), 19% remained depressed (12% of the men and 21% of the women), and 8% (5% of the men and 9% of the women) had missing 12-week data. Of the 656 patients (61% female) not reporting depression (CES-D <16) at baseline, 91% remained non-depressed (92% of the men and 91% of the women), 2% became depressed (.4% of the men and 2% of the women), and 7% had missing 12-week data (8% men and 7% of the women). Overall, there was significantly more improvement than worsening in depression ($p<.001$). There was no significant relationship between sex and change in depression, with all subgroups showing significant improvements over time.

Lifestyle Behaviors, Coronary Risk Factors, and Psychosocial Outcomes

Table 3 shows all outcomes by depression status and time points. Significant time effects were noted for all variables regardless of depression status: Patients who became non-depressed, who remained non-depressed, and those who remained or became depressed improved on all lifestyle behaviors, coronary risk factors, and psychosocial outcomes from baseline to 3 months [except HDL cholesterol, which was significantly reduced, as expected in the context of a low-fat diet (Brinton, Eisenberg, & Breslo, 1995); except for triglyceride levels ($p<.05$), all $p<.01$].

These time effects were modified by group for exercise and dietary fat intake, perceived stress, hostility, and SF-36 Mental Component scores (all $p<.05$). Patients who became non-depressed reduced dietary fat intake, perceived stress, and hostility more and increased exercise and SF-36 Mental Component scores more than patients in the other two groups.

Time effects were modified by sex for exercise capacity, SF-36 Physical Component Scores, weight, total cholesterol, LDL-cholesterol, triglyceride levels, total cholesterol/HDL ratios, and HbA1C levels (all $p<.05$), suggesting that men improved their exercise capacity and SF-36 Physical Component Scores more and reduced their weight, total cholesterol, LDL-cholesterol, triglyceride levels, total cholesterol/HDL ratios, and HbA1C levels more than women.

Time effects were modified by sex and group for stress management, triglyceride levels, and depression (all $p<.05$). Follow-up analyses indicated that in patients who remained or became depressed, men increased stress management and reduced depression more than women. In patients who became non-depressed and in those who remained non-depressed, men reduced triglyceride levels more than women.

Group-by-sex interactions were noted for exercise, group support attendance, HbA1c levels, hostility, and depression (all $p<.05$). In the group of patients who became non-depressed, men exercised more and had higher HbA1c-levels than women across time points. Follow-up analyses for the significant group-by-sex interactions for group support attendance ($p<.001$) and depression ($p<.05$) rendered sex differences in the individual depression groups non-significant. Follow-up analyses revealed that men had higher hostility scores than women across time points in all three depression groups.

In addition, the following main effects were noted for depression group: Patients who became non-depressed consumed more dietary fat ($p<.01$) and weighed more ($p<.001$) than patients who remained non-depressed. Patients who remained non-depressed had the highest SF-36 Mental Component Scores ($p<.001$) and the lowest levels of perceived stress ($p<.001$) and depression ($p<.001$), followed by those who became non-depressed, followed by those who remained or became depressed. Also, patients who remained non-depressed had higher SF-36 Physical Component Scores ($p<.01$) and lower levels of

hostility ($p<.001$) than patients in the other 2 groups. Patients who remained non-depressed and those who became non-depressed attended more group sessions than those who remained or became depressed ($p<.001$).

The following main effects were noted for sex: Men exercised more ($p<.01$), and attended more group support sessions ($p<.001$), weighed more ($p<.01$), had higher diastolic blood pressure ($p<.05$), higher exercise capacity ($p<.001$), and higher hostility levels ($p<.001$), while women had higher body fat ($p<.001$), higher total cholesterol ($p<.001$), higher LDL cholesterol ($p<.01$), and higher HDL cholesterol ($p<.001$).

All patients met program requirements regarding exercise (3 hrs/week) and practiced stress management more than 6 hours per week at 3 months. Except for women who remained or became depressed, all patients reduced their dietary fat intakes to <10%.

In sum, depressed patients who became non-depressed at follow-up also reduced dietary fat intake, perceived stress, and hostility and increased SF-36 Mental Component scores and exercise more than patients in the other 2 groups.

Analysis of the data from the 11 patients who became depressed indicated that these patients experienced similar risk factor reductions as the rest of the sample (not shown), except for diastolic blood pressure which was not significantly reduced (baseline: 81.6 ± 10.6, 3 months: 76.0 ± 8.6), and triglyceride levels and total cholesterol/HDL ratios which increased over the follow-up (baseline: 133.3 ± 58.7, 3 months: 150.9 ± 68.4; baseline: 4.4. ± 1.4, 3 months: 4.5 ± 1.8, respectively).

In order to examine whether changes in depression as a continuous variable are associated with changes in cardiovascular risk factors, health behaviors, and psychological outcomes in patients who became non-depressed, correlations were performed. Associations were noted as follows: In both, men and women who became non-depressed over the course of 3 months, reductions in depression were associated with decreases in weight ($r=.33$, $p<.01$, $r=.17$, $p<.05$, respectively). These associations became marginally significant when controlling for baseline depression and age ($r=.22$, $p<.10$, $r=.14$, $p<.10$, respectively). Reductions in depression were also associated with reductions in systolic blood pressure in

women (r=.13, p<.10) and with reduced triglyceride levels in men, but only after controlling for baseline depression and age (r=.32, p<.01).

Regarding psychosocial outcomes, reductions in depression were associated with reductions in hostility (r=.50, p<.01, r=.17, p<.05, respectively) and perceived stress (r=.54, p<.01, r=.51, p<.001, respectively), and with improvements in SF-36 Mental Component scores (r=.70, r=.41, both p<.001) in both sexes, and with improved SF-36 Physical Component scores (r=.16, p<.05) in women. Associations between reductions in depression and improvements in hostility rendered marginally significant when controlling for baseline depression and age. Similarly, associations with mental health became non-significant after controlling for baseline depression and age. The relationships between reductions in depression and physical health and triglyceride levels in men were significant after controlling for baseline depression and age (r=.28, p<.05; r=-.32, p<.01). In regard to changes in lifestyle, reductions in depression were associated with increases in stress management in men with and without controlling for baseline depression and age (r=.26, p<.05, r=.31, p<.05, respectively) and were marginally related to improvements in the lifestyle index in men (r=.24, p<.10) without controlling for baseline depression and age.

In sum, in both, men and women who became non-depressed over the course of 3 months, reductions in depression were associated with weight reductions. In women reductions in depression were also related to reductions in systolic blood pressure; in men, an association of reductions in depression with increases in stress management and in the lifestyle index was noted.

Changes in Medications

Changes in medications are presented in Table 4. Follow-up medication data were not collected at seven hospital sites. All other 17 hospital sites (n=783) had, on average, 76.5% complete data. We therefore only report changes in medications over 3 months for these 17 sites. Medication use, including anti-depressant medication, remained unchanged for over 90% of patients who became or remained non-depressed. This was also true for patients who remained depressed, except for oral antiglycemic use in

diabetic patients of that group. Eighty-four percent of diabetic patients in this group remained on medication or were not medicated, 8% started medication, and 8% stopped medication throughout follow-up.

Participants Lost During Follow-up

22 men (7%) and 54 women (8%) did not complete the 12-week follow-up. Patients completing the follow-up (n = 921) were more likely to have a college degree ($p<.001$), to be medicated with anticoagulants ($p<.05$), insulin ($p<.05$), and hormone replacement medication ($p<.05$) than those not completing the follow-up. They also had higher body mass ($p<.05$), higher CES-D scores ($p<.05$), and higher levels of hostility ($p<.01$), and exercised less ($p<.05$), and were older ($p<.05$) than those not completing the follow-up. No other statistically significant differences were noted.

Discussion

Consistent with other studies (Farmer et al., 1988; Katon et al., 2004), our findings indicated that depressed patients practiced less health behaviors (i.e., diet and stress management) and had worse coronary risk factor profiles and psychological status than non-depressed patients at baseline. Hence, our first question addressed in this study was whether depressed patients at high risk for CHD can make comprehensive lifestyle changes over 3 months. All patients, regardless of depression group, met program requirements regarding exercise (3 hrs/week) and practiced stress management more than 6 hours per week at 3 months. All patients reduced their dietary fat intake to <10% (except for women who remained or became depressed who reduced dietary fat intake to 11%). Some of these improvements in health behaviors were more pronounced in patients who became non-depressed during follow-up. These patients reduced dietary fat intake and increased exercise more than patients who remained or became depressed and than those who remained non-depressed over 3 months. No time-by-group-sex interactions were noted for health behavior change. Thus, reductions in depression may have been associated with similar improvements in health behaviors in men and women.

The second question addressed in this study was whether comprehensive lifestyle changes are beneficial in terms of reductions in depression in patients at high risk for CHD over 3 months. Seventy-three percent of patients who were clinically depressed at baseline became non-depressed by the 3-months follow-up. It is unlikely that reductions in depression were due to changes in anti-depressant use throughout follow-up as anti-depressant use remained constant in 98% of patients who became non-depressed during follow-up.

In addition, no sex differences in changes in depression could be noted in our study. Consistent with the gender distribution of lifetime prevalence of depression, which is approximately twice as high in women as in men (Breslau, Schulz, & Peterson, 1995), the group that became non-depressed in our study included 73% women. Only a few other studies have investigated the effects of lifestyle or psychological interventions on depression in women yielding mixed results. For example, Toobert and colleagues (2007) examined the effects of comprehensive lifestyle changes in postmenopausal diabetic women and did not find significant changes in depression compared to a usual care group over 2 years. In contrast, Georgiades and colleagues (2007) found that cognitive-behavioral therapy significantly reduced depression in a predominantly female (71%) sample of patients with diabetes over 1 year. However, no gender differences were tested in this study. Another study reporting changes in depressive symptoms in healthy non-depressed women indicated that recreational higher levels of physical activity at baseline were associated with less depressive symptoms eight years later (Farmer et al., 1988).

Our results indicate that addressing depression in behavioral interventions may be beneficial for both, women and men at high risk for CHD (including patients with diabetes). The American Diabetes Association (2006) recommends screening for psychosocial problems such as depression in patients with type 2 diabetes and an incorporation of psychological treatment into routine care to address these psychosocial problems. However, according to the ADA, psychological treatment is only indicated when adherence to the medical regimen is poor. One could also argue that addressing depression in patients participating in lifestyle interventions may potentially facilitate the modification of behavioral and coronary risk factors of the metabolic syndrome.

To address this question, we compared cardiac and psychological outcomes of depressed patients who became non-depressed (Group 1) to patients who remained or became depressed (Group 2) and to those who remained non-depressed (Group 3) over 3 months. Our results show that, all patients, regardless of depression group, significantly improved coronary risk factor profiles, glycemic control (in patients with diabetes), and psychological outcomes over 3 months. Improvements in cardiovascular risk factors in our entire sample were similar to those noted in other lifestyle interventions (Costacou & Mayer-Davis, 2003; Elmer et al., 2006; Hu & Willett, 2002; Kronenberg et al., 2000; Orchard et al., 2005; Stampfer, Hu, Manson, Rimm, & Willett, 2000; The Look AHEAD Research Group, 2007; Toobert, Stryker, Glasgow, Barrera, Angell, 2005). However, it is noteworthy that, despite their worse clinical profiles at baseline (e.g., bodymass, diastolic blood pressure), depressed patients who became non-depressed improved clinical profiles to a similar degree as non-depressed patients. In contrast, patients who became or remained depressed did not reduce diastolic blood pressure, triglyceride levels, and total cholesterol/HDL ratios.

We had also hypothesized that patients who became non-depressed would experience greater improvements in cardiovascular risk factors compared to patients in the other two groups. However, no significant time-by-depression group interactions were found for cardiovascular risk factors. Only two marginally significant time-by-group interactions emerged for weight and diastolic blood pressure. The trend for weight suggested that patients who became non-depressed reduced weight more (-16.0 ± 9.7 lbs) than patients who remained non-depressed (-13.6 ± 5.5 lbs) and patients who remained or became depressed (-11.6 ± 7.1 lbs). Regarding diastolic blood pressure, reductions were similar in patients who became non-depressed (-7.2 mmHg) and in those who remained or became depressed (-7.7 mmHg), but lower in who remained non-depressed (-6.2 mmHg). In addition, one significant time-by-group-by-sex interaction for triglyceride levels suggested that men who became non-depressed reduced triglyceride levels more than women in this group. In sum, our results suggest that reductions in depression were generally not closely linked to changes in cardiovascular risk factors. Similarly, Georgiades and

colleagues (2007) did not find direct associations between reductions in depression and improvements in glycemic control in patients with type 2 diabetes.

In regard to psychosocial outcomes, depressed patients in our study who became non-depressed also improved psychological well-being more than patients in the other two groups. Specifically, these patients reduced hostility and perceived stress and improved quality of life (i.e., SF-36 Mental Component Score: vitality, social functioning, role-emotional functioning and mental health) more than patients in the other two groups. Depressive symptoms have been previously linked to all domains of quality of life in primary care patients (Brenes, 2007). It is therefore plausible that reductions in depression may have been accompanied by improvements in hostility, perceived stress, and mental health. However, we can only speculate which program component affected psychological well-being in patients who became non-depressed. Findings of another study, using the same intervention as the MCLIP, indicated that the intervention's social support group attendance was associated with improvements in mental health (even after controlling for diet, exercise, and stress management; Schulz et al., in press). Some have even suggested that psychological treatment similar to the social support group intervention in the MCLIP may have a stronger effect on patients' well-being than pharmacotherapy (Pampallona, Bollini, Tibaldi, Kupelnick, & Munizza, 2002).

For exploratory purposes, we also analyzed associations of changes in depression as a continuous variable with changes in cardiovascular risk factors, health behaviors, and psychological outcomes in the group of patients that became non-depressed (Group 1). Contrary to findings of another study (Hainer et al., 2008), in both, men and women who became non-depressed over the course of 3 months, reductions in depression were associated with weight reductions. In women reduced depression scores were also related to reductions in systolic blood pressure; in men, an association of reduced depression scores with increases in stress management and in the lifestyle index was noted.

Patients completing the follow-up were more likely to have a college degree and were more medicated than those not completing the follow-up. However, they were older, exercised less, had higher bodymass, and worse psychological status than those not completing the follow-up suggesting that

patients with worse medical and psychological status at baseline may have been more motivated to make lifestyle changes.

Several limitations of our study should be noted. First, a self-report measure for depression was employed in our study. The use of a clinical diagnostic interview for depression would have improved the validity of the assessment of depression in our study. However, the employment of self-report questionnaires such as the CES-D is common when it is not feasible to conduct psychiatric diagnostic interviews (Davidson, Rieckmann, & Rapp, 2005). Secondly, this study did not include a control group. The MCLIP was a phase IV clinical trial evaluation based on insurance data of 22 sites in the U.S. Phase IV research typically consists of long-term surveillance of an intervention shown to be effective in previous stage III trials. Therefore, no assumptions about cause-effect relationships between changes in lifestyle and changes in psychological outcomes and coronary risk factors can be made. Thirdly, our sample was predominantly white limiting generalizability of our findings to an ethnically more diverse population. One advantage of this study was that women comprised 69% of our total sample. This participation rate is unusually high and may, in part, be explained by the inclusion of support groups and stress management in the program which may be more appealing to women than standard exercise-based cardiac rehabilitation (Moore & Kramer, 1996).

In sum, targeting multiple health behaviors appears to benefit initially depressed patients at high risk for CHD. Initially depressed patients were able to adhere to comprehensive lifestyle changes. In addition, 73% of patients who were clinically depressed at baseline fell below the cut-off for depression on the CES-D by the 3-months follow-up. In these patients reductions in depression may have also contributed to improvements in health behaviors and psychological well-being. Thus, depressed patients at risk for CHD should be targeted in lifestyle interventions to reduce the prevalence of depression in these patients and to facilitate health behavior change.

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Table 1. Patient Characteristics by Depression (CES-D ≤ 16 vs. >16) and Sex at Baseline.

	No Depression (CES-D≤16) at Baseline		**Depression (CES-D>16) at Baseline**		**Sex p**	**Group p**	**Sex- x-Group P**
	Men N=228	Women N=428	Men N=82	Women N=259			
Demographics							
Age, Mean (SD)	56 (10)	56 (9)	54 (10)	53 (9)	.99	<.001	.28
Ethnicity, N (% Caucasian)	213 (93%)	388 (91%)	79 (96%)	247 (95%)	.23	<.05[b]	.45
Education, N (% college degree)	139 (61%)	203 (47%)	59 (72%)	107 (41%)	<.001	.40	<.05
Married or Cohabitating, N (%)	185 (81%)	289 (68%)	64 (78%)	170 (66%)	<.001	.20	.86
Employed outside the Home, N (%)	159 (70%)	247 (58%)	60 (73%)	160 (62%)	<.01	.46	.71
Medical History, N (%)							
Previous cigarette smoker	94 (41%)	134 (31%)	33 (40%)	70 (27%)	<.01	.15	.69
Systemic hypertension1	112 (49%)	183 (43%)	49 (60%)	126 (49%)	<.05	.06	.54
Systemic hypertension in patients with DM1	61 (27%)	132 (31%)	29 (35%)	86 (33%)	<.01	.45	.47
Hyperlipidemia[2]	206 (90%)	368 (86%)	77 (94%)	231 (89%)	.06	.19	.80
Diabetes mellitus	70 (31%)	175 (41%)	30 (37%)	107 (41%)	<.05	.40	.45
Type 2 DM	69 (30%)	158 (37%)	29 (35%)	100 (39%)	<.05	.87	.40
Medication, N (%)							
Beta blockers	54 (24%)	95 (22%)	23 (28%)	48 (19%)	.19	.48	.26
Angiotensin-converting enzyme inhibitors	67 (29%)	131 (31%)	30 (37%)	83 (32%)	.86	.33	.55
Calcium antagonists	32 (14%)	32 (7%)	13 (16%)	30 (12%)	<.01	.09	.39
Diuretics	25 (11%)	92 (21%)	15 (18%)	51 (20%)	<.01	.34	.10
Anticoagulants	118 (52%)	206 (48%)	43 (52%)	134 (52%)	.46	.40	.53
Lipid lowering	107 (47%)	157 (37%)	30 (37%)	98 (38%)	<.05	.28	.09
Oral antiglycemics	37 (16%)	97 (23%)	17 (21%)	48 (19%)	.64	.37	.53
Insulin	5 (2%)	24 (6%)	3 (4%)	16 (6%)	.09	.36	.90
Antidepressant	19 (8%)	58 (14%)	13 (16%)	59 (23%)	<.01	<.001	.97
Arthritis medication	12 (5%)	32 (7%)	5 (6%)	27 (10%)	.09	.09	.70
Gastrointestinal medication	21 (9%)	39 (9%)	6 (7%)	42 (16%)	.15	<.01	.07
Hormone replacement	---	67 (16%)	---	40 (15%)	---	---	---

	No Depression (CES-D≤16) at Baseline		Depression (CES-D>16) at Baseline		Sex p	Group p	Sex- x-Group p
	Men N=228	Women N=428	Men N=82	Women N=259			
Coronary risk factors, Mean (SD)							
Body Mass Index (kg/m^2)	33.8 (7.3)	34.8 (8.3)	34.5 (7.2)	37.2 (8.4)	<.01	<.05	.16
Body Weight (lbs)	235.1 (54.5)	203.2 (51.1)	243.2 (54.8)	217.8 (51.7)	<.001	<.01	.42
Body Fat (%)	30.2 (9.0)	39.6 (8.0)	31.1 (7.8)	40.8 (8.0)	<.001	.11	.84
Functional Capacity (METs)	9.9 (2.9)	8.1 (2.5)	9.8 (3.1)	7.8 (2.5)	<.001	.32	.83
Systolic Blood Pressure (mmHg)	135.6 (15.9)	134.1 (17.1)	135.0 (17.2)	135.5 (16.7)	.71	.74	.45
Diastolic Blood Pressure (mmHg)	81.8 (9.8)	80.2 (9.8)	84.8 (10.7)	82.2 (9.7)	<.01	<.01	.49
Total Cholesterol (mg/dl)	193.8 (45.2)	209.1 (44.6)	197.6 (37.3)	211.0 (45.6)	<.001	.40	.77
HDL Cholesterol (mg/dl)	41.5 (10.4)	50.5 (12.6)	39.7 (9.0)	50.5 (13.5)	<.001	.30	.32
LDL Cholesterol (mg/dl)	116.8 (36.8)	122.6 (37.5)	116.8 (31.8)	122.5 (37.9)	<.05	.99	.99
Triglycerides (mg/dl)	195.5 (157.0)	188.9 (134.5)	204.0 (81.9)	195.6 (135.6)	.47	.46	.93
Total Cholesterol/HDL-C Ratio	4.9 (1.5)	4.4 (1.3)	5.1 (1.2)	4.4 (1.4)	<.001	.13	.38
HbA1c (%)	7.5 (1.7)	7.8 (1.7)	8.2 (2.2)	7.3 (1.4)	.20	.49	<.01
Fasting glucose	150.4 (59.2)	161.8 (61.5)	166.0 (67.5)	150.9 (58.5)	.83	.78	.12
Depression (CES-D)	7.0 (4.4)	7.3 (4.6)	23.5 (7.3)	24.4 (7.3)	.16	<.001	.48
Hostility (Cook-Medley)	7.7 (4.5)	6.3 (4.1)	12.2 (5.1)	9.3 (7.1)	<.001	<.001	.07
Perceived Stress Scale	11.8 (6.3)	13.1 (6.4)	21.3 (7.3)	22.9 (7.0)	<.01[a]	<.001[b]	.76
Quality of Life, Mean (SD)							
Physical Component Score (MOS SF-36)[†]	46.2 (9.2)	44.3 (10.4)	45.5 (10.8)	40.4 (10.6)	<.001	<.01	<.05
Mental Component Score (MOS SF-36)[†]	49.8 (10.4)	50.3 (9.9)	35.2 (11.6)	37.0 (11.7)	.15	<.001	.42
Lifestyle Behaviors							
Dietary Fat Intake (% of total calories)	30.6 (10.8)	30.4 (10.3)	34.0 (9.7)	32.2 (10.2)	.23	<.01	.33
Exercise (hrs per week)	1.2 (1.9)	1.1 (1.6)	1.2 (1.7)	.7 (1.1)	<.01	.14	.21
Stress Management (hrs per week)	.5 (1.3)	.5 (1.4)	.3 (1.0)	.2 (.9)	.52	<.05	.76

Note. Some sites failed to collect complete baseline information on education, employment status, history of cigarette smoking, and medication; therefore, data are shown for 64%- 96% of men with no depression at baseline (n = 147 to n=218), 66%-94% of women with no depression at baseline (n=284 to n=402), 63%-98% of men with depression at baseline (n=52 to n=80), and 63%-94% of women with depression at baseline (n=164 to n=243), depending on the variable.
Note. One woman who was non-depressed at baseline had had a silent myocardial infarction.

Note. Diabetes type. Among non-depressed patients at baseline 1 man (1.5%) and 16 women (9.4%) had type 1 diabetes and among depressed patients at baseline 1 man (3.3%) and 8 (7.5%) had type 1 diabetes.
[1] Systemic hypertension was defined as <140/90 mmHg, or <130/80 mmHg for patients with diabetes.
[2] Hyperlipidemia was defined as LDL cholesterol ≥ 100 mg/dl, or HDL cholesterol ≤ 40 mg/dl, or triglycerides ≥ 150 mg/dl.
[†] Scores were standardized to have a mean of 50 and a SD of 10 based on a 1998 representative sample of the general US population.

Table 2. Number of Patients by Depression (CES-D < 16 vs. >16) at baseline and 12 weeks.

			Depression at 12 weeks	
		Total	**No Depression (CES-D≤16) at 12 weeks**	**Depression (CES-D>16) at 12 weeks**
Depression at Baseline	**No Depression (CES-D≤16) at Baseline**	**210 men, 398 women**	209 men, 388 women	1 man, 10 women
	Depression (CES-D>16) at Baseline	**78 men, 235 women**	68 men, 180 women	10 men, 55 women
	Total	**288 men, 633 women**	**277 men, 568 women**	**11 men, 65 women**

Note. McNemar test, p<.001, with significant reductions in depression over 12 weeks. 12-week data for depression were missing for 22 men and 54 women (18 men and 30 women with CES-D<16 at baseline, 4 men and 24 women with CES-D>16 at baseline).

Table 3. Means (SD) of risk factors, psychosocial outcomes, quality of life, and lifestyle behaviors at baseline and 12 weeks (among patients with complete CES-D data).

	Became Non-Depressed		**Remained Non-Depressed**		**Remained or Became Depressed**	
	Men N=68	Women N=180	Men N=209	Women N=388	Men N=11	Women N=65
CHD Risk Factors						
Weight (lbs) [a, b, c, d]						
Baseline	244.1 (53.2)	218.9 (52.2)	234.8 (55.0)	201.4 (50.6)	226.6 (57.6)	216.2 (55.0)
12 weeks	224.8 (47.4)	204.2 (47.4)	217.4 (48.6)	189.9 (48.3)	212.8 (56.8)	205.0 (51.8)
Change	-8%	-7%	-7%	-6%	-6%	-5%
Body fat [a, b]						
Baseline	31.1 (7.2)	40.9 (7.7)	30.2 (8.8)	39.4 (7.9)	26.5 (6.9)	40.3 (8.5)
12 weeks	26.6 (7.8)	37.4 (6.9)	26.2 (7.8)	35.9 (7.7)	23.2 (7.3)	36.3 (8.9)
Change	-15%	-9%	-13%	-9%	-13%	-9%
Exercise Capacity (METs) [a, b, d]						
Baseline	9.8 (3.2)	7.9 (2.4)	10.0 (3.0)	8.1 (2.5)	9.5 (3.3)	7.7 (2.5)
12 weeks	12.2 (3.1)	9.6 (2.5)	12.5 (3.1)	10.0 (2.6)	12.1 (4.3)	9.3 (2.4)
Change	25%	22%	25%	24%	27%	21%
Systolic BP (mmHg) [b]						
Baseline	134.4 (16.0)	135.2 (16.2)	135.9 (16.1)	134.3 (17.1)	139.1 (22.1)	135.8 (18.9)
12 weeks	119.7 (15.0)	123.5 (13.5)	123.2 (13.1)	122.7 (14.3)	129.3 (21.9)	124.0 (14.3)
Change	-11%	-9%	-9%	-9%	-7%	-9%
Diastolic BP (mmHg) [a, b]						
Baseline	85.0 (10.6)	81.6 (9.0)	82.0 (9.9)	80.2 (9.7)	83.5 (11.9)	83.6 (11.0)
12 weeks	75.3 (9.2)	75.5 (8.2)	75.2 (8.5)	74.3 (8.3)	77.1 (7.1)	75.7 (8.4)
Change	-11%	-7%	-8%	-7%	-8%	-9%
Total Cholesterol (mg/dl) [a, b, d]						
Baseline	199.4 (35.8)	209.5 (46.2)	193.2 (45.1)	209.2 (44.3)	201.8 (41.3)	212.4 (41.8)
12 weeks	158.8 (32.9)	182.3 (42.9)	156.4 (34.9)	182.6 (40.3)	154.8 (24.2)	191.6 (41.1)
Change	-20%	-13%	-19%	-13%	-23%	-10%
HDL Cholesterol (mg/dl) [a, b]						
Baseline	39.6 (9.0)	50.4 (14.1)	42.0 (10.4)	50.7 (12.8)	40.5 (10.3)	49.4 (12.2)
12 weeks	35.2 (7.5)	43.2 (12.6)	36.3 (8.7)	43.4 (10.9)	32.8 (9.2)	44.2 (13.9)
Change	-11%	-14%	-14%	-14%	-19%	-11%
LDL Cholesterol (mg/dl) [a, b, d]						
Baseline	121.4 (31.6)	119.6 (38.0)	116.6 (36.9)	122.4 (36.9)	112.3 (30.4)	130.0 (36.9)

	Became Non-Depressed		Remained Non-Depressed		Remained or Became Depressed	
	Men N=68	Women N=180	Men N=209	Women N=388	Men N=11	Women N=65
12 weeks	92.3 (27.3)	101.5 (38.3)	91.8 (28.7)	104.1 (32.3)	87.1 (25.3)	113.0 (36.2)
Change	-24%	-15%	-21%	-15%	-22%	-13%
Triglycerides (mg/dl)‡ [b, d, g]						
Baseline	200.6 (75.8)	195.7 (129.4)	190.8 (147.0)	189.3 (135.2)	222.9 (115.7)	192.3 (158.9)
12 weeks	167.1 (75.7)	195.5 (118.3)	150.6 (77.8)	179.6 (96.7)	169.7 (80.5)	189.6 (107.0)
Change	-17%	-0%	-21%	-5%	-24%	-1%
Total Cholesterol/HDL ratio [b, d]						
Baseline	5.2 (1.2)	4.4 (1.4)	4.8 (1.5)	4.4 (1.3)	5.2 (1.2)	4.6 (1.5)
12 weeks	4.6 (1.1)	4.4 (1.4)	4.5 (1.2)	4.4 (1.4)	5.0 (1.4)	4.6 (1.3)
Change	-12%	---	-6%	---	-4%	---
Hemoglobin A1c (%) † [b, d, f]						
Baseline	8.5 (2.3)	7.3 (1.4)	7.3 (1.6)	7.7 (1.6)	6.2 (.2)	7.3 (1.5)
12 weeks	7.2 (1.7)	6.7 (1.1)	6.4 (.9)	6.9 (1.1)	5.5 (.1)	7.3 (1.3)
Change	-15%	-8%	-14%	-12%	-11%	---
Depression (CES-D) [a, b, c, e, f, g]						
Baseline	22.1 (6.1)	23.1 (6.4)	6.8 (4.3)	7.2 (4.6)	28.1 (9.6)	24.2 (9.6)
12 weeks	7.6 (4.6)	6.8 (4.3)	4.3 (3.9)	4.3 (4.0)	19.6 (3.3)	22.3 (6.2)
Change	-66%	-71%	-37%	-40%	-30%	-8%
Hostility (Cook-Medley) [a, b, c, e, f]						
Baseline	12.0 (5.2)	8.9 (4.4)	7.7 (4.4)	6.2 (4.2)	13.3 (3.3)	8.9 (4.2)
12 weeks	8.9 (5.0)	6.0 (3.9)	6.5 (4.1)	5.2 (3.7)	10.4 (3.5)	7.6 (3.9)
Change	-26%	-33%	-16%	-16%	-22%	-15%
Perceived Stress Scale [b, c, e]						
Baseline	20.5 (6.8)	22.2 (6.2)	11.8 (6.3)	13.1 (6.5)	24.4 (6.9)	22.5 (7.2)
12 weeks	11.0 (4.8)	11.4 (4.7)	7.6 (4.7)	9.0 (5.0)	19.8 (4.9)	19.5 (6.9)
Change	-46%	-49%	-36%	-31%	-19%	-13%
Quality of Life						
Physical Component Score (SF-36) [b, c, d, e]						
Baseline	45.7 (10.7)	40.5 (10.3)	46.2 (9.1)	44.7 (10.4)	43.4 (11.4)	40.9 (10.6)
12 weeks	50.1 (8.5)	47.7 (9.3)	51.2 (8.7)	50.0 (8.6)	45.0 (10.2)	46.2 (10.4)
Change	10%	18%	11%	12%	4%	13%
Mental Component Score (SF-36) [b, c, e]						

	Became Non-Depressed		Remained Non-Depressed		Remained or Became Depressed	
	Men N=68	Women N=180	Men N=209	Women N=388	Men N=11	Women N=65
Baseline	35.7 (11.5)	37.5 (11.0)	50.3 (10.0)	50.1 (10.0)	34.5 (13.5)	36.8 (12.7)
12 weeks	50.2 (10.3)	53.0 (9.2)	54.8 (9.0)	56.2 (7.5)	40.7 (10.4)	41.4 (11.1)
Change	41%	41%	9%	12%	18%	13%
Lifestyle Behaviors						
Dietary Fat (% of total calories) [b, c, e]						
Baseline	34.2 (9.8)	32.7 (10.1)	30.9 (10.6)	30.2 (10.1)	31.7 (12.8)	30.8 (10.6)
12 weeks	9.6 (2.9)	9.7 (3.0)	9.4 (2.6)	9.8 (3.2)	9.2 (3.1)	10.8 (7.2)
Change	-72%	-70%	-70%	-68%	-71%	-65%
Exercise (hrs per week) [a, b, e, f]						
Baseline	1.3 (1.7)	.8 (1.1)	1.3 (1.9)	1.1 (1.6)	1.0 (1.4)	.7 (1.1)
12 weeks	4.3 (1.9)	3.7 (1.6)	3.8 (1.7)	3.7 (1.4)	4.4 (1.5)	3.3 (1.9)
Change	231%	363%	192%	236%	340%	371%
Stress Management (hrs per week) [b, d, g]						
Baseline	.4 (1.0)	.2 (.8)	.5 (1.4)	.5 (1.4)	.3 (.5)	.3 (1.0)
12 weeks	6.1 (1.8)	6.2 (1.7)	6.3 (2.2)	6.3 (2.3)	7.6 (2.3)	6.0 (2.9)
Change	1425%	3000%	1160%	1160%	2433%	1900%
Group Support Attendance [a, c, f]						
Baseline	---	---	---	---	---	---
12 weeks	95.6 (5.9)	94.6 (6.5)	94.5 (9.5)	94.9 (7.0)	92.0 (6.2)	91.5 (8.2)
Change	---	---	---	---	---	---
Lifestyle Index [a, b]						
Baseline	.33 (.22)	.30 (.16)	.35 (.21)	.35 (.20)	.32 (.17)	.28 (.16)
12 weeks	.92 (.14)	.89 (.13)	.90 (.13)	.91 (.12)	.96 (.10)	.84 (.17)
Change	178%	197%	157%	160%	200%	200%

† For diabetics only.

‡ Winsorizing statistical outliers (i.e., replacing values ± 3 SDs of the mean with "most extreme acceptable values" in the distribution of this variable) did not yield significantly different results.

Note. N ranged from 62-68 for men who became non-depressed, from 157-180 for women who became non-depressed, from 182-209 for men who remained non-depressed and from 342-388 for women who became non-depressed, from 10-11 for men who remained or became depressed and from 55-65 for women who became remained or became depressed, depending on the outcome.

[a] Significant sex effect, [b] Significant time effect; [c] Significant group effect; [d] Significant time-by-sex interaction; [e] Significant time-by-group interaction; [f] Significant sex-by-group interaction; [g] Significant sex-by-time-by-group interaction.

Table 4. Medication Changes from Baseline to 3 Months.

	Became Non-Depressed			Remained Non-Depressed			Remained or Became Non-Depressed		
Medication N (% of Depression Group) *	No Change in Medication	Started Medication	Stopped Medication	No Change in Medication	Started Medication	Stopped Medication	No Change in Medication	Started Medication	Stopped Medication
Anti depressants	157 (98%)	2 (1%)	2 (1%)	384 (97%)	1 (1%)	6 (2%)	33 (94%)	1 (3%)	1 (3%)
Beta blockers	156 (96%)	4 (2%)	3 (2%)	383 (97%)	3 (1%)	6 (2%)	36 (100%)	0	0
Angiotensin-converting enzyme inhibitors	160 (98%)	1 (1%)	1 (1%)	381 (97%)	3 (1%)	8 (2%)	36 (100%)	0	0
Calcium antagonists	158 (98%)	1 (1%)	2 (1%)	376 (96%)	5 (2%)	5 (2%)	35 (100%)	0	0
Diuretics	149 (93%)	1 (1%)	9 (6%)	383 (98%)	1 (1%)	3 (1%)	36 (100%)	0	0
Lipid lowering	156 (96%)	0	7 (4%)	370 (94%)	5 (1%)	18 (5%)	34 (97%)	1 (3%)	0
Oral antiglycemics[1]	69 (93%)	0	5 (7%)	145 (93%)	0	11 (7%)	11 (84%)	1 (8%)	1 (8%)
Insulin[1]	69 (100%)	0	0	152 (98%)	1 (1%)	1 (1%)	13 (100%)	0	0

* Sites that did not collect medication data were excluded from these analyses.
[1] Medication reported for diabetics only.

CHAPTER 8

General Discussion

General Summary of Findings

The aim of this dissertation was to investigate the role of comprehensive lifestyle changes in the prevention and treatment of coronary heart disease (CHD). Lifestyle changes and related coronary and psychological outcomes were investigated in several different patient populations (e.g., patients with CHD, patients with CHD and type 2 diabetes, patients at risk for heart failure, patients at risk for CHD) involving two stages of research [stages III: *Lifestyle Heart Trial (LHT)*, and IV: *Multicenter Lifestyle Demonstration Project (MLDP); Multisite Cardiac Lifestyle Intervention Program (MCLIP)*]. Specifically, the following five questions were addressed in this dissertation: 1.) Can comprehensive lifestyle changes improve psychological well-being in patients with CHD for up to 5 years and are these changes associated with changes in coronary risk factors in the LHT? 2.) Can patients with CHD and type 2 diabetes make comprehensive lifestyle changes experiencing similar improvements in coronary risk factors and quality of life when compared to CHD patients without type 2 diabetes over 1 year in the MLDP? 3.) Can CHD patients at risk for heart failure with a left ventricular ejection fraction (LVEF) ≤ 40% (stage B according to the guidelines of the American College of Cardiology/American Heart Association) make comprehensive lifestyle changes to achieve a similar improvement in medical risk factors and quality of life as those with a LVEF >40% over 1 year in the MLDP? 4.) Is attendance of the intervention's social support groups in the MLDP associated with CHD patients' adherence to the other 3

program components and with improvements in coronary risk factors and quality of life over 1 year? 5.) Can depressed patients at risk for CHD (i.e.., ≥3 coronary risk factors and/or type 2 diabetes) in the MCLIP make comprehensive lifestyle changes over 3 months and benefit in terms of reductions in depression and improvements in coronary risk factors?

In this chapter findings of five empirical studies and one review article are summarized, discussed and are put into perspective regarding future research. Furthermore, strengths and limitations of the five empirical studies are outlined. The main focus of *Chapter 2* was to compare psychological outcomes (psychological distress, anger, hostility, perceived social support) by group (intervention group, n=28; control group, n=20) and time (baseline, 1, 5 years) and examine the relationships of lifestyle changes to coronary risk factors in the LHT. Lifestyle changes (i.e., reductions in dietary fat intake, improvements in exercise and stress management) were maintained in the experimental group relative to controls over 5 years. Reductions in psychological distress and hostility in the experimental group (compared to controls) were observed after 1 year. By 5 years, improvements in hostility tended to be maintained in the experimental group relative to the control group, but reductions in psychological distress were only reported by experimental patients with very high 5 year program adherence. Improvements in diet were related to weight reduction and to decreases in percent diameter stenosis, and improvements in stress management to decreases in percent diameter stenosis at both follow-ups. The findings presented in *Chapter 2* suggest that patients in the LHT may have psychologically adapted or habituated to their new lifestyle. The relative absence of an overall intervention effect on psychological well-being in the experimental group beyond 1 year may have also been due to differences in adherence to comprehensive lifestyle changes within this group. This assumption was, in part, confirmed by results comparing patients in the high program adherence group to the low adherence group. Reductions in psychological distress were maintained over 5 years in patients with very high program adherence. In addition, improvements in diet and stress management were related to medical outcomes (e.g., decreases in percentage diameter stenosis) in all patients over the long-term (i.e., 5 years). Thus, lifestyle changes improve psychological

well-being for 1 year and are associated with improved coronary risk factors over 5 years, illustrating the importance of targeting multiple health behaviors in secondary prevention of CHD.

Chapter 3 reviewed literature on the feasibility of lifestyle interventions in the secondary prevention of CHD in patients with diabetes. Several studies suggested that CHD patients with diabetes seemed to have greater difficulties adhering to and benefiting from standard cardiac rehabilitation compared to those without diabetes, mostly due to a greater adverse risk profile at program entry and an exacerbation of medical problems during the intervention (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004; Suresh, Harrison, Houghton, & Naqvi, 2001; Vergès et al., 2004). However, other evidence suggests that secondary prevention programs emphasizing comprehensive lifestyle changes may not only benefit CHD patients in general, but especially those with CHD and diabetes (Pischke et al., 2006; Sumner et al., 2005, see results of *Chapter 4*). In addition, a review of preliminary evidence on cost effectiveness of lifestyle modification programs indicates cost savings for diabetes prevention programs (e.g., Palmer et al., 2004). Thus, integrating comprehensive lifestyle changes into standard cardiovascular risk modification programs and making them more accessible to a wider public may be the necessary first steps towards improving care for patients with CHD and diabetes.

Chapter 4 examined whether CHD patients with diabetes could make changes in lifestyle with similar improvements in clinical profiles as CHD patients without diabetes over 1 year. Major outcomes included changes in health behaviors, coronary risk factors, and quality of life. The results of *Chapter 4* indicate that, in spite of their worse medical and psychosocial risk factor profile at program entry (also evident in other studies; Banzer, Maguire, Kennedy, O'Malley, & Ballady, 2004; Milani & Lavie; 1996; Suresh, Harrison, Houghton, & Naqvi, 2001), CHD patients with diabetes were able to make comprehensive lifestyle changes similar to non-diabetic CHD patients. At 3 months, improvement in risk factors, lifestyle, and quality of life of patients with diabetes paralleled that of CHD patients without diabetes and was maintained for the entire follow-up. Even women with diabetes, the most medically and psychosocially disadvantaged group in the MLDP, were able to follow the intervention and showed significant improvements in CAD risk factors (e.g., weight, body fat, LDL-C, METs, but no change in

HDL-C and triglycerides) and quality of life. Findings presented in *Chapter 4* underscore the need for more aggressive approaches such as intensive multi-component interventions when targeting CHD patients with diabetes.

Chapter 5 analyzed whether CHD patients at risk for heart failure (HF) with a left ventricular ejection fraction (LVEF) ≤ 40% could make changes in lifestyle with similar improvements in clinical profiles as patients with a LVEF > 40% over 1 year. Our results indicate that comprehensive lifestyle changes are feasible for CHD patients with a LVEF <40%, despite their worse medical history at baseline. These patients were able to make similar changes in lifestyle as those with a LVEF >40% over the course of 3 months, and were able to maintain most of these changes over 1 year. They also showed similar improvements in cardiac outcomes and quality of life. In summary, results of *Chapter 5* indicate that patients with reduced LVEF are able to adhere to comprehensive lifestyle changes, experiencing similar improvements in clinical profile and quality of life compared to those with a LVEF >40%. Thus, comprehensive lifestyle interventions aimed at the modification of major risk factors in CHD should target patients at risk for HF to improve clinical outcomes and prevent further progression and clinical deterioration into the more severe and costly stages of the disease.

Chapter 6 evaluated whether attendance of the intervention's social support groups was associated with CHD patients' adherence to the other 3 program components and with improvements in coronary risk factors and quality of life over 1 year. Changes in coronary risk factors, health behaviors, and quality of life were analyzed by tertiles of social support group attendance among CHD patients in the MLDP. Significant improvements in coronary risk factors, health behaviors, and quality of life were noted at 1 year. Several of these improvements (i.e., systolic blood pressure, health behaviors, quality of life) were related to social support group attendance, favoring those who attended more sessions. The associations between support group attendance to systolic blood pressure and to four quality of life subscales ('bodily pain', 'social functioning', 'mental health', and the mental health' summary score) remained significant when controlling for changes in health behaviors, but dropped to a non-significant level for the quality of life subscales 'physical functioning', 'general health', and 'role-emotional'. These

results suggest an independent relationship of social support group attendance to systolic blood pressure while improvements in quality of life may be in part due to improved health behaviors facilitated by increased social support group attendance.

Chapter 7 focused on depression, a major risk factor for CHD, and examined whether initially depressed patients at risk for CHD (i.e., ≥3 coronary risk factors and/or diabetes) in the MCLIP were able to make comprehensive lifestyle changes and whether they could benefit in terms of reductions in depression. In addition, associations of reductions in depression with reductions in cardiovascular risk factors and improvements in health behaviors, glycemic control, and psychological outcomes were analyzed. At baseline, depressed patients had a more adverse medical (e.g., body-mass, diastolic blood pressure) and behavioral (e.g., dietary fat intake, hostility, perceived stress, SF-36 scores) status than non-depressed patients. Seventy-three percent of the depressed patients became non-depressed at follow-up. These patients reduced dietary fat intake, perceived stress, and hostility and increased exercise and SF-36 Mental Component Scores more than patients who remained or became depressed and non-depressed patients who remained non-depressed. These findings suggest that comprehensive lifestyle changes are related to significant reductions in depression. In patients who became non-depressed, these reductions may have contributed to improvements in health behaviors and psychological well-being.

General Discussion

This dissertation contributed significantly to the body of evidence regarding long-term maintenance of health behavior change and associated health benefits and feasibility of comprehensive lifestyle interventions in patient populations varying in disease severity and risk. It also shed further light on the role of psychosocial factors such as depression, hostility, and social support in the etiology and prognosis of CHD and type 2 diabetes. With the exception of the Lifestyle Heart Trial, a stage III trial (including a control group), all of the studies included in this dissertation were stage IV effectiveness trials (i.e., Multicenter Lifestyle Demonstration Project, Multi-site Cardiac Lifestyle Intervention

Program) demonstrating that comprehensive lifestyle interventions are feasible for CHD patients with diabetes, for patients at risk for heart failure, and for initially depressed patients at risk for heart disease.

The Lifestyle Heart Trial had previously demonstrated long-term maintenance of health behavior change, improvements in cardiovascular risk factors, and reversal of coronary artery stenosis at 1 and 5 years in patients with CHD (Ornish et al., 1990, Ornish et al., 1998). However, long-term psychological benefits had not been analysed before. Findings of this dissertation indicate that improvements in psychological well-being in the experimental group (compared to controls) were maintained for at least 1 year, but were not evident at 5 year follow-up (see *Chapter 2*). However, in patients with very high 5 year program adherence, improvements in psychological well-being were maintained over 5 years. These results are in line with studies reporting relatively short-term (i.e., ≤ 1 year) improvements in psychological well-being (i.e., reductions in psychological distress, hostility, anxiety, and depression) in patients with CHD after participation in cardiac rehabilitation that included psychological or stress management interventions (Blumenthal et al., 2005; Daubenmier et al., 2007; Koertge et al., 2003; Lavie & Milani, 2005; Pischke et al., 2006). Patients in the Lifestyle Heart Trial may have psychologically adapted or habituated to their new lifestyle. Diener (2000) describes this process as hedonic adaptation. People quickly adapt their expectations as they rise in their accomplishments and possessions and therefore no longer derive additional happiness from these accomplishments. Patients in the Lifestyle Heart Trial generally showed very high program adherence. Thus, it is possible that despite their long term maintenance of health behavior change, patients did not maintain improvements in psychological well-being over the long-term. Patients with very high adherence, however, possibly still strived for higher goals [cf. (Diener, 2000)], and maintained improvements in general well-being over the long-term.

To examine which program component may have contributed most to improvements in well-being, we correlated changes in diet, exercise, and stress management with changes in psychological outcomes. Results of this analysis point to an association between improvements in diet and reductions in psychological distress during the 1-year follow-up. Similar associations between dietary changes (high-fat to low-fat, high complex-carbohydrate diet) and reductions in depression and hostility have been reported

by another study (Weidner, Connor, Hollis, & Connor, 1992). In the Multisite Cardiac Lifestyle Intervention Program reductions in dietary fat were related to reductions in perceived stress, especially among those who also increased exercise (Daubenmier et al., 2007). However, it is unclear whether improvements in diet preceeded or followed improvements in depression and hostility. One possible pathway may be that improvements in psychological well-being may have improved eating behavior and then contributed to an increased sense of self-efficacy (Bandura, 1977). Additionally, increases in stress management in the LHT were associated with reductions in trait anger over one year. This latter finding is consistent with a recent study reporting an association between regular yoga practice and reduced anger (Shapiro et al., 2007).

Improvements in healh behaviors in the LHT were also related to 5-year improvements in medical outcomes. Specifically, improvements in diet were related to weight reduction and to decreases in percent diameter stenosis, and improvements in stress management to decreases in percent diameter stenosis. The association between increases in stress management and reductions in percent diameter stenosis could not be explained by dietary changes over the course of 5 years. This finding indicates that alleviating psychological distress by practicing stress management benefited patients' cardiac profile independently from adherence to diet.

Chapters 4 and *5* addressed the feasibility of the intervention for patients with CHD and diabetes and patients at risk for heart failure. Due to their worse clinical profiles, chronically diseased patients with multiple conditions may find it difficult to adhere to long-term lifestyle changes, may have additional psychological barriers to behavior change (Vickers, Nies, Patten, Dierkhising, & Smith, 2006), and may require additional support for health behavior change. Previous research indicated that CHD patients with diabetes seemed to have greater difficulties adhering to and benefiting from standard cardiac rehabilitation compared to those without diabetes (Banzer, Maguire, Kennedy, O'Malley, & Balady, 2004; Suresh, Harrison, Houghton, & Naqvi, 2001; Vergès et al., 2004). Adherence to cardiac rehabilitation programs and related health benefits in patients at risk for heart failure had not yet been investigated. Only a few studies had looked at the effects of structured exercise interventions (as part of standard cardiac rehabilitation) in

patients with chronic heart failure. These studies reported benefits in heart failure symptoms, LVEF, exercise capacity, and quality of life (Dracup et al., 1994; Lloyd-Williams, Mair, & Leitner, 2002; Smart, Haluska, Jeffriess, & Marwick, 2005).

Findings of this dissertation indicate that comprehensive lifestyle changes are feasible for both, CHD patients with diabetes and those at risk for heart failure. Despite their worse medical and psychosocial risk factor profile at program entry (also evident in other studies; Banzer, Maguire, Kennedy, O'Malley, & Ballady, 2004; Milani & Lavie; 1996; Suresh, Harrison, Houghton, & Naqvi, 2001), CHD patients with diabetes were able to make and maintain comprehensive lifestyle changes over 1 year with similar improvements in risk factors and quality of life as CHD patients without diabetes. Even women with diabetes, the most medically and psychosocially disadvantaged group in the MLDP, were able to follow the intervention and showed significant improvements in CAD risk factors and quality of life. Similarly, patients at risk for heart failure (CHD patients with a LVEF $\leq$40%; ACC/AHA stage B) were able to make and maintain similar changes in lifestyle as those with a LVEF >40% over the course of 1 year (despite their worse medical history at baseline). Similar improvements in coronary risk factors and quality of life were evident in both groups at 3 months and 1 year. Thus, reductions in coronary risk factors and changes in health behaviors were comparable in CHD patients with diabetes and without diabetes, and in CHD patients at risk for heart failure with a LVEF $\leq$ 40% and CHD patients with a LVEF>40%. In addition, improvements in patients with CHD and diabetes and in patients at risk for heart failure in the MLDP were similar to those observed in the experimental group of the LHT over the same time period (Ornish et al., 1990, Ornish et al., 1998).

Patients with CHD and diabetes and patients with a LVEF $\leq$40% also showed improvements in quality of life (MOS SF-36 summary scores), similar to CHD patients without diabetes and patients with a LVEF >40% from baseline to 1 year. These improvements reached the *minimally clinically important difference* of 3-5 points (Hays & Morales, 2001). Unfortunately, no assessment of depression was included in the MLDP. However, the MOS SF-36 correlates negatively with measures of depression (Callahan et al., 1997), suggesting that increased quality of life in MLDP patients may also indicate

improvements in depression. Depression is a risk factor for CAD (especially among women with diabetes; Nemeroff & O'Connor, 2000, Clouse et al., 2003), and for the incidence of heart failure, particularly in elderly women (Williams et al., 2002).

Findings of *Chapter 4* take on added significance considering data from the First National Health and Nutrition Examination Survey (NHANES) that suggest that declines in heart disease mortality in the past three decades noted in nationally representative samples of adults are smaller in patients with diabetes than in those without diabetes, particularly in women. In fact, mortality from all causes, heart disease, and ischemic heart disease decreased slightly for men with diabetes between 1971 and 1993 (i.e., 13% vs. 36% in men without diabetes) but increased 23% in diabetic women (compared to a 27% decline in mortality in non-diabetic women; Gu, Cowie, & Harris, 1999). The authors conclude that these smaller declines in mortality may be due to smaller reductions in cardiovascular risk factors and that treatment of heart disease or precursors of heart disease are less effective in diabetics. Results of this dissertation suggest that multi-component cardiac rehabilitation as treatment of heart disease in men and women with diabetes (and in patients at risk for heart failure) is effective in reducing cardiovascular risk factors and may prevent disease progression.

As in any multi-component intervention, we do not know the relative importance of each component. The role of exercise and diet in the prevention of CHD is well established (Ades, 2001; Dubach et al., 1997; Ehsani, Miller, Miller, Ballard, & Schechtman, 1997; Giannuzzi et al., 1997; Oberman et al., 1995). However, some have expressed concerns that a low fat diet, compared to a high-monounsaturated-fat diet, may increase LDL-C and triglyceride levels, and may be associated with a deterioration of glycemic control in patients with diabetes (Garg et al., 1994). However, studies examining the effects of high-carbohydrate, low-fat diets often vary in the amount of fiber, thus confounding the effects of carbohydrates and fat (Hollenbeck & Coulston, 1991). The diet recommended in the MDLP is not only low in fat and high in complex carbohydrates, but also high in fiber. Studies of such diets yield significant improvements in glycemic control among patients with diabetes (Lucus et al., 2003) and improved insulin sensitivity in individuals with normal and impaired glucose tolerance (Liese

et al., 2003). Additional evidence suggests that stress management may be related to reductions in clinical events in patients with CAD (Blumenthal et al., 2002), in hemoglobin A1c in patients with diabetes (Surwit et al., 2002), and may affect diabetes control by facilitating adherence to diet or exercise regimens (Surwit & Schneider, 1993).

Chapter 6 analyzed changes in coronary risk factors, health behaviors, and quality of life by tertiles of social support group attendance among CHD patients in the MLDP. Reductions in systolic blood pressure were found in those who attended >78% of group support sessions (even after controlling for changes in health behaviors). Other studies have reported similarly beneficial effects of social support on blood pressure in CAD patients participating in psychosocial interventions in conjunction with standard cardiac rehabilitation (Gump, Polk, Kamarck, & Shiffman, 2001; Krantz & McCeney, 2002; Linden, Stossel, & Maurice, 1996; Steptoe, Lundwall & Cropley, 2000). The social support received from the group may have helped patients acquire additional coping strategies that alleviated stress, with positive consequences for systolic blood pressure (cf. Uchino, 2006). Support group interventions emphasizing the sharing of emotional experiences (similar to our intervention; Billings, 2000) have been previously shown to be beneficial in reducing anxiety, depression, and stress and improving emotion regulation and even survival in patients with cancer (Kronenwetter et al., 2005; Spiegel et al., 2007). Thus, it is conceivable that stress reductions experienced in the groups may have contributed to the observed improvements in systolic blood pressure in this study.

In regard to health behaviors, 'high attendees' reduced dietary fat intake more and practiced more stress management and exercise compared to 'low attendees'. More frequent participation in group sessions may have allowed patients to share their problems adhering to lifestyle changes with other group members and to learn strategies on how to overcome barriers to health behavior change (Billings, Scherwitz, Sullivan, Sparler, & Ornish, 1996; Boutin-Foster, 2005). Social support may also act as an indirect buffer for a depressive response style. A cluster of social isolation and depression predicted poor prognosis and a higher risk of recurrent cardiac events in patients with CHD (Horsten, Mittleman,

Wamala, Schenck-Gustafsson, & Orth-Gomer, 2000). Thus, engaging patients in group support sessions may decrease depressive symptomatology and facilitate lifestyle changes in patients with CHD.

Patients who attended the most support group sessions also improved quality of life significantly more than their counterparts who were less involved in the patient community. Because of the inverse relationship between the SF-36 subscales and depression (e.g., Callahan et al., 1997; Findler, Cantor, Haddad, Gordon, & Ashman, 2001), clinically meaningful increases in quality of life measured by the MOS SF-36 in the MLDP (Hays & Morales, 2001; Ware, Snow, Kosinski, & Gandek, 1993) may also indicate reductions in depression. Improvements in quality of life were, in part, mediated by improvements in health behaviors. When controlling for changes in health behaviors, associations between group attendance and health-related quality of life (HRQOL) remained significant for 4 subscales of the HRQOL, but rendered non-significant for 3 of the HRQOL subscales. This finding suggests that improvements of some aspects of quality of life seem to be related to improved health behaviors, but others may be independently linked to support group attendance.

Chapter 7 of this dissertation analyzed outcomes of patients at high risk for CHD (i.e., ≥3 coronary risk factors and/or diabetes) in the MCLIP. A worldwide increase in the number of people at high risk for CHD (i.e., with metabolic syndrome: a cluster of multiple coronary risk factors and a precursor of CHD and type 2 diabetes) has been noted over the past two decades resulting from the global epidemic of obesity (Eckel, Grundy, & Zimmet, 2005). Specifically, three questions were addressed in *Chapter 7*: (1) whether depressed patients at high risk for CHD (i.e.., ≥3 coronary risk factors and/or type 2 diabetes) can make comprehensive lifestyle changes over 3 months, (2) whether they can benefit in terms of reductions in depression and (3) whether these reductions in depression are associated with reductions in cardiovascular risk factors and improvements in health behaviors, glycemic control, and psychological outcomes.

All patients, regardless of depression group, met program requirements regarding dietary fat intake, exercise, and stress management at 3 months. Patients who became non-depressed during follow-up reduced dietary fat intake and increased exercise more than patients who remained or became

depressed and those who remained non-depressed over 3 months. No time-by-group-sex interactions were noted for health behavior change. Thus, reductions in depression may have been associated with similar improvements in health behaviors in men and women.

By the 3-months follow-up, 73% of patients who were clinically depressed at baseline became non-depressed. Anti-depressant use remained constant in 98% of patients who became non-depressed during follow-up. It is therefore unlikely that reductions in depression were due to changes in anti-depressant use throughout follow-up. In addition, no sex differences in changes in depression could be noted in our study. This finding is particularly important considering that the prevalence of depression is approximately twice as high in women as in men (Breslau, Schulz, & Peterson, 1995). Contrary to our results, Toobert and colleagues (2007) did not find significant changes in depression in women undergoing comprehensive lifestyle changes compared to a usual care group over 2 years. On the other hand, anti-depressant effects have been reported for cognitive-behavioral therapy and physical activity (Farmer et al., 1988; Georgiades et al., 2007).

To address the question whether alleviating depression in patients participating in lifestyle interventions may potentially facilitate the modification of behavioral and coronary risk factors of the metabolic syndrome, we compared cardiac and psychological outcomes of depressed patients who became non-depressed to patients who remained or became depressed and to those who remained non-depressed over 3 months. Our results show that, all patients, regardless of depression group, significantly improved coronary risk factor profiles, glycemic control (in patients with diabetes), and psychological outcomes over 3 months. Improvements in cardiovascular risk factors in our entire sample were similar to those noted in other lifestyle interventions (Costacou & Mayer-Davis, 2003; Elmer et al., 2006; Hu & Willett, 2002; Kronenberg et al., 2000; Orchard et al., 2005; Stampfer, Hu, Manson, Rimm, & Willett, 2000; The Look AHEAD Research Group, 2007; Toobert, Stryker, Glasgow, Barrera, & Angell, 2005). However, it is noteworthy that, despite their worse clinical profiles at baseline (e.g., weight, bodymass, diastolic blood pressure), depressed patients who became non-depressed improved clinical profiles to a similar degree as non-depressed patients.

We had also hypothesized that patients who became non-depressed would experience greater improvements in cardiovascular risk factors compared to patients in the other two groups. However, our results, similar to findings reported by another study (Georgiades et al., 2007), indicated that reductions in depression were generally not closely linked to changes in cardiovascular risk factors. In regard to psychosocial outcomes, we found that improvements in depression were accompanied by improvements in other psychological outcomes such as hostility, perceived stress, and quality of life. Specifically, depressed patients in our study who became non-depressed also improved hostility, perceived stress, and improved quality of life (i.e., SF-36 Mental Component Score: vitality, social functioning, role-emotional functioning and mental health) more than patients in the other two groups. This finding is consistent with another study linking depressive symptoms to quality of life in primary care patients (Brenes, 2007).

Limitations and Strengths of the Lifestyle Heart Trial, the Multicenter Lifestyle Demonstration Project, and the Multisite Cardiac Lifestyle Intervention Program

The major limitation of the LHT (phase III) was the lack of power due to its small sample size. However, it is noteworthy that, despite the lack of power, significant differences between experimental and control group were detected. In fact, the magnitude of effects was supported by some of the effect sizes exceeding .09, suggesting medium effects (Cohen, 1987). Another limitation of the LHT was that psychological well-being was only assessed at 1- and 5-year follow-up. We therefore do not know whether psychological well-being persisted for more than 1 but less than 4 years. On the other hand, the LHT yielded intriguing findings demonstrating long-term maintenance of health behavior change in patients with CHD (over 5 years; Ornish et al., 1990), a reversal of heart disease (over 5 years; Ornish et al., 1990), and improvements in psychological well-being (over 1 year, Pischke et al., in press). However, as the sample in the LHT was predominantly white and male, these findings were not generalizable to women, patients from a more diverse ethnic background, patients with low socioeconomic status, and patients differing in disease severity.

The phase IV research on the intervention (i.e., *Multicenter Lifestyle Demonstration Project, Multisite Cardiac Lifestyle Intervention Program*) presented a unique opportunity to examine whether this lifestyle intervention worked under real-world conditions (Glasgow, Lichtenstein, & Marcus, 2003), providing us with important information about its feasibility for all the above mentioned subgroups of patients. Phase IV research typically consists of long-term surveillance of an intervention shown to be effective in previous Phase III trials. According to Friedman, Furberg, & DeMets (1998), no control groups are necessary for Phase IV trials. Glasgow, Lichtenstein, & Marcus (2003) also acknowledge decreased experimental rigor during this phase of research. Thus, inferences about the effectiveness of the lifestyle intervention and about causal relationships between lifestyle changes and changes in coronary risk factors and quality of life based on data of the MLDP and MLCIP could not be made. However, the MLDP and the MCLIP were clinical trial evaluations based on insurance data, covering the lifestyle intervention at up to 22 different hospital sites in the U.S. These trials were adequately powered to assess feasibility of the intervention for subgroups of patients (by gender, disease severity, and psychosocial status) in different geographical areas of the U.S. For example, women comprised more than half of the entire sample in the MCLIP. This participation rate is unusually high and may, in part, be explained by the inclusion of support groups and stress management in the program which may be more appealing to women than standard exercise-based cardiac rehabilitation (Moore & Kramer, 1996).

In sum, findings of this dissertation were based on one completed randomized phase III trial (i.e., the LHT) and 2 health-insurance sponsored multi-site demonstration projects (i.e., the completed MLDP and the ongoing MCLIP). The LHT did include a control group and conclusions regarding cause-effect relationships were therefore acceptable. However, this trial was underpowered and predominantly male and white. Thus, generalizations regarding the effectiveness of the intervention in women and more diverse populations could not be made. The following two health-insurance sponsored multi-site demonstration projects did not include a control group but contained a large percentage of women and were slightly more diverse. Results of these two demonstration projects are therefore more generalizable to the general population. However, we still do not know whether comprehensive lifestyle changes are

feasible in underinsured patients or in those without health insurance (16% of the American population; Center on Budget and Policy Priorities, 2008). There is some indication from data of the MCLIP suggesting that patients who were covered by their insurance were able to follow the program recommendations, showing significant reductions in cardiac risk profile and improvements in quality of life, regardless of socioeconomic status (Govil, Weidner, Merritt-Worden, & Ornish, 2007).

Cost-effectiveness of Comprehensive Lifestyle Changes

China, India and the United Kingdom are expected to lose $558 billion, $237 billion, and $33 billion, respectively, in national income due to heart disease, stroke, and diabetes (Daar et al., 2007). These projections include the costs of reduced economic productivity (World Health Organization, 2005; Suhrcke, Nugent, Stuckler, & Rocco, 2006). In the U.S., the cost of heart disease and stroke was projected to exceed $394 billion in 2005: $242 billion for health care expenditures and $152 billion for lost productivity from death and disability (American Heart Association, 2005). Direct health care costs of angina, one of the major symptoms of CHD and a potential cause of disability, reached an average of US $33,695 per person per year (Frattaroli et al., in press; Shaw et al., 2006). In Germany, the expenditures on cardiovascular diseases amounted to 35.4 billion Euros in 2002 (10.8 billion Euros were spent on acute care and 0.99 billion Euros on prevention and rehabilitation) and accounted for approximately 16% of the total costs of diseases (Karoff, Held, & Bjarnason-Wehrens, 2007).

Also, revascularization procedure costs have increased substantially over the years (US $57,140 for coronary artery bypass graft [CABG] and US $27,622 for percutaneous transluminal coronary angioplasty [PTCA] in 2000 to US $85,653 for CABG and US $ 44,110 for PTCA in 2004 [United States Department of Health and Human Services - National Healthcare Costs and Utilization Project, 2006]), while costs for the lifestyle intervention have remained relatively stable (US $7,200 in 2000 and $8100 in 2008 for a 1-year intervention [Ornish, 1998, Highmark Inc., Anna Silberman, personal communication, March 2008]). The cost savings for the intervention group (1-year intervention) of the MLDP compared to their matched controls in a 3-year follow-up (Ornish, 1998) amounted to US $29,529 per person in

1998 (Ornish, 1998). Similarly, Blumenthal and colleagues reported that a 4-month stress management intervention in male CHD patients resulted in a significant reduction of medical costs over a 5-year period compared to a usual-care control group (Blumenthal et al., 2002). In addition, cost-utility analysis based on three major diabetes prevention trials, the Da Qing study (40% reduction of diabetes incidence), the Finnish Diabetes Prevention Study (58% reduction), and the Diabetes Prevention Program (58% reduction), showed that the costs of one case of diabetes prevented amounted to $15,700 (Wylie-Rosett, Herman, & Goldberg, 2006). Thus, considering the medical costs of diabetes complications and the costs of surgical procedures associated with CHD, preventive measures such as lifestyle changes may represent cost-efficient strategies for the prevention of chronic disease and could potentially reduce the economic burden of heart disease, stroke, and diabetes.

Future Research

More translational research is needed to investigate whether comprehensive lifestyle changes work under real world conditions (e.g., in low SES populations; Govil, Weidner, Merritt-Worden, & Ornish, 2007). As of 2007, the U.S. Centers for Medicare and Medicaid Services have included this lifestyle intervention as a defined cardiac rehabilitation benefit for Medicare beneficiaries with CHD (U.S. Department of Health and Human Services - Centers for Medicare and Medicaid Services, 2008). Medicare is a US government health insurance plan that provides hospital, medical, and surgical benefits for persons age 65 and older and people with certain disabilities. Employer and employee typically pay 1.45% each on all earnings towards this health insurance plan (Social Security Online, 2008). Medicare Part A provides basic hospital insurance and Medicare Part B provides benefits for physicians' professional services.

However, “only 19% of 267,427 Medicare eligible patients >65 years of age who experienced a CHD event (myocardial infarction or coronary artery bypass graft surgery in this case) in 1997 actually participated in a cardiac rehabilitation/secondary prevention program, a number that probably has not improved much over the past 15 years” (p. 1644, Thomas, 2007; Ades, Waldmann, McCann, & Weaver,

1992, Thomas et al., 1996). Participation was particularly low in older patients, women, patients with nonwhite racial /ethnic status and lower socioeconomic status, and in those with significant comorbid conditions (Thomas, 2007). Thus, our knowledge on the effects of lifestyle changes in these populations is still limited.

Reasons for the underuse of cardiac rehabilitation programs can be found on multiple levels. Less than 50% of patients referred to a cardiac rehabilitation program actually enroll in the program (Thomas, 2007; Witt, Thomas, & Roger, 2005). Patients themselves are not informed about the benefits of cardiac rehabilitation. Group exercise programs are often too far from home, too expensive and time-consuming. There may also be provider barriers to the underuse of cardiac rehabilitation. Healthcare professionals often do not refer patients because they are not sure whether patients are eligible for cardiac rehabilitation, whether they will benefit from cardiac rehabilitation or simply forget to refer patients due to their own time constraints. Interestingly, the physician's endorsement of the effectiveness of an intervention was the main predictor of referral to cardiac rehabilitation (Jackson, Leclerc, Erskine, & Linden, 2004). Thomas (2007) also identifes system barriers and community barriers. For example, resouces at the healthcare-system level may be assigned to acute care settings instead of chronic care and preventive services like cardiac rehabilitation. On the community-level public policies such as smoking bans or banning trans-fats, and improving local infrastructures (e.g., access to grocery stores; Kristenson, Erikson, Sluiter, Starke, & Ursin, 2004) and making neighborhoods safer may be important issues to address when implementing cardiac rehabilitation programs for a wider public.

In most European countries, cardiac rehabilitation is delivered in an outpatient setting lasting 12 weeks and more. However, in Germany and Austria cardiac rehabilitation is delivered in an inpatient setting lasting for 3-4 weeks (Bjarnason-Wehrens, Grande, Loewel, Völler, & Mittag, 2007; Karoff, Held, & Bjarnason-Wehrens, 2007). As cardiac rehabilitation is covered by the health insurance or pension plan for almost all patients and mostly delivered in an inpatient setting in Germany, barriers to participation, such as co-morbidity and transportation, which are especially relevant to the participation of women, are eliminated (Grande, Leppin, Romppel, Altenhoener, & Mannebach, 2002).

It is therefore surprising that cardiac rehabilitation is still underused in Europe (Karoff, Held, & Bjarnason-Wehrens, 2007). More than 55% of patients with heart disease are not recommended to participate in cardiac rehabilitation (EUROASPIRE II Study Group, 2001). One of the reasons for this shortcoming may be that heart disease is still perceived as a "male" disease. Bjarnason-Wehrens and colleagues (2007) point out that "cardiac rehabilitation was developed in the 1960s in Germany with special regard to the needs of middle-aged men to avoid invalidism and to improve return to work" (p.164).

Traditional cardiac rehabilitation mostly focuses on exercise. Older women may be suffering from co-morbidities such as arthritis, osteoporosis, or urinary incontinence that inhibit exercise behavior (Weiss, 1998; Nihiria & Henderson, 2003). Women may also have time constraints due to their gender roles (Conn, Tripp-Reimer, & Maas, 2003). Women may feel more responsible for their partnerships and household tasks (Jackson, Leclerc, Erskine, & Linden, 2004). It is known that being married decreases attendance of cardiac rehabilitation in women, but not in men (Conn, Tripp-Reimer, & Maas, 2003).

Women may also feel uncomfortable in men-dominated group exercise settings. Especially older women may have very little experience with exercise. In addition, women are more likely to experience anxiety and depression, and particularly low levels of self-efficacy after a first cardiac event (Karoff, Held, & Bjarnason-Wehrens, 2007). Thus, future interventions should incorporate solutions to these women-specific needs (e.g., special retreat areas, emotional interactions and support). The inclusion of psychological interventions such as group support sessions may be particularly helpful to women coping with stressful social environments and emotional responses (e.g., depression; Kuper, Marmot, & Hemingway, 2002). Future research should also evaluate whether modifications of standard cardiac rehabilitation yields similar attendance and adherence rates of cardiac rehabilitation in women and men.

Future studies should also include follow-up assessments beyond 5 years. Maintenance of behavior change (beyond the time of the intervention) in self-directed communities is a major issue, particularly in women (Daly et al., 2002). New technologies may help assist in monitoring and supporting

patients in long-term maintenance of health behavior change (Koskinen & Salminen, 2007; Norman et al., 2007; Williams, Lynch, & Glasgow, 2007).

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Appendix

(On CD-ROM)

a.) Pdf-File of this Dissertation (for a summary of the results in German see section III "Zusammenfassung")

b.) Curriculum Vitae

c.) Erklärung

Aus Datenschutzgründen wird mein Lebenslauf in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Erklärung

Hiermit versichere ich, dass ich die vorliegende Arbeit selbstständig verfasst habe. Andere als die angegebenen Hilfsmittel habe ich nicht verwendet. Die Arbeit ist in keinem früherem Promotionsverfahren angenommen oder abgelehnt worden.

Sausalito, 8.April, 2008 Claudia Ruth Pischke