Title
Health related quality of life over ten years after acute myocardial infarction

Author
Lau Kee, Laura-Ann,

Publication Date
1997

Health-Related Quality of Life Over Ten Years After Acute Myocardial Infarction

by

Laura-Ann Lau Kee

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

NURSING

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA

San Francisco

[redacted]

This is dedicated to my dear husband, Daryl F. Browne,
whose unwavering patience, understanding, love, and support
makes reaching the stars possible

ACKNOWLEDGEMENTS

This dissertation was a major undertaking, accomplished with the help of many people. First, I would like to express my gratitude to my dissertation committee, Drs. Erika Froelicher, Nancy Stotts, and Sandra Weiss.

I am deeply indebted to Erika Froelicher who served as the chairperson of the committee. I am honored to have been given the opportunity to analyze the multitude of data that she has collected over the years. Without her generous offer of access to the extremely valuable data on quality of life, this project would not have been possible. Beyond data, Erika also has shared her wealth of knowledge with me, offering me invaluable guidance with her expertise and wisdom. She gave me continuous support, encouragement, and a display of confidence in me, helping me to believe that I could accomplish this daunting task, all the while being sensitive to my trials and tribulations.

I also want to express my gratitude to Nancy A. Stotts for many years of support and gentle encouragement. It was Nancy who planted and fertilized many years ago the seed that grew into this project.

I owe thanks to Sandra Weiss who continuously provided me with the global thinking and vision that led me far beyond what I had ever envisioned.

My thanks also go out to Dr. Steve Paul who never tired of my statistical bewilderment and who was so adept at setting me straight over the many years. In addition, I wish to acknowledge the research team of CSECR, the original study, who meticulously gathered and recorded the data. Without their hard work, this project would not be possible.

Projects of such large undertaking are rarely possible without the support of friends. My doctoral student colleages, Dr. Deidre Wipke-Tevis and Dr. Teresa Juarbe went beyond the call of friendship and collegial support, especially when I was flat on my back.

And last, but not least, I owe unending thanks to my family. My husband, Daryl Browne, provided me with unwavering patience, understanding, love, and support that sustained me through the years. My daughter, Rachel, wise beyond her young years, was understanding of my need for time and endless drawings of hearts and rainbows that kept my spirits up.

Health-Related Quality of Life Over Ten Years After Acute Myocardial Infarction

Laura-Ann L. Kee, R.N., Ph.D.
University of California, San Francisco

Abstract

Longitudinal research on health-related quality of life (HRQOL) can provide justification for allocation of limited health care resources and can assist in setting priorities for research and interventions. Yet, there are few studies evaluating HRQOL after acute myocardial infarction (AMI) for a period beyond one year.

The study is a secondary analysis of longitudinal data from a prospective cohort. The purposes of this study were to describe changes in HRQOL over ten years after AMI, to estimate the prognostic values of clinical and exercise test variables on HRQOL, and to estimate the prognostic value of HRQOL at 6 months on survival over 10 years. The Sickness Impact Profile (SIP) was used to evaluate HRQOL, physical and psychosocial dimensions, and 12 separate HRQOL-related categories. Patients (n=258) completed the SIP at baseline, 3 and 6 months, and 10 years after AMI. Data were analyzed with descriptive and non parametric tests (Wilcoxon Matched-Pairs, McNemar, and Mann Whitney U tests) and survival analyses (Cox Proportional Hazards Modelling).

Total SIP and physical dimension scores showed that patients' dysfunction were similar at baseline and 3 months, improved at 6 months, then worsened by 10 years. Psychosocial dysfunction was greatest at baseline, improved by 3 months, then remained constant thereafter. Six month scores of total SIP, physical dimension, and individual categories of Home Management,

Mobility, and Work were predictive of increased risk of death when adjusted for age and sex. Age was a statistically significant covariate.

Data show that overall HRQOL and physical dysfunction persist between baseline and 3 months with improvement not seen until 6 months. In addition, patients are at greatest need of psychosocial support and nursing intervention at the time of the AMI. Despite improvements at 6 months, overall HRQOL and physical dysfunction are predictors of increased risk of death over ten years. Understanding how HRQOL changes over time after AMI can give insight to clinicians in determining appropriate interventions and resources at times most beneficial to patients. In addition, the results provide information to scientists in setting priorities for research.

Erika S Froelich

Erika S. Froelicher, R.N., Ph.D.
Dissertation Chairperson

TABLE OF CONTENTS

ACKNOWLEDGEMENT iv

ABSTRACT vi

TABLE OF CONTENTS viii

LIST OF TABLES xi

LIST OF FIGURES xiii

CHAPTER ONE: THE STUDY PROBLEM

- Introduction 1
- Problem 2
- Purpose 2
- Significance of the Study 3

CHAPTER TWO: CONCEPTUAL FRAMEWORK AND LITERATURE REVIEW 6

Conceptual Framework

- Biopyschosocial Model of Health 6
- Quality of Life in AMI Patients 7

Review of Literature

- Health-Related Quality of Life As a Concept 9
- Health-Related Quality of Life In Patients with Coronary Artery Disease 22
- Research on Health-Related Quality of Life In Patients with Coronary Artery Disease 32
- Important Confounders in the Study of Quality of Life as an Outcome 34
- Measurement of Health-Related Quality of Life 42
- Limitations of Current Knowledge 47

TABLE OF CONTENTS (continued)

CHAPTER THREE: METHODOLOGY 49

- Dissertation Study Design 49
- Objectives 49
    - Original study 49
    - Follow-up study 50
    - Present study 50

- Study Population

    - Original study 51
    - Follow-up study 53
    - Present study 53

- Sources of Data

    - Original study 54
    - Follow-up study 56
    - Present study 56
- Instrument: Sickness Impact Profile 57
- Data Management 64
- Power Estimates 65
- Data Analysis 66
- Human Investigations Approval 73

CHAPTER FOUR: STUDY RESULTS 74

- Analysis 1 76
- Analysis 2 87
- Analysis 3 90
- Analysis 4 95
- Analysis 5 96
- Analysis 6 100

TABLE OF CONTENTS (continued)

Summary of Results 107

CHAPTER FIVE: DISCUSSION AND CONCLUSIONS 109

Changes in HROQL After AMI Over 10 years 110

HRQOL as a Predictor for Increased Risk of Mortality 115

Sensitivity of Sickness Impact Profile to Change 117

Conclusions 118

Clinical and Policy Implications 118

Strength and Limitations 119

Future Research 121

REFERENCES 122

APPENDIX 141

LIST OF TABLES

3-1. Study Sample and Categories of Exclusions of CSECR 52

3-2. Clinical Application of Sickness Impact Profile in Research 62

3-3. Summary of Data Analysis Plan 67

3-4. Operational Definitions of Predictor Variables 71

4-1. Baseline Characteristics of Subjects Enrolled into CSECR 75

4-2. Baseline Demographic Characteristics of Subjects Completing SIP 77

4-3. Baseline Clinical and Exercise Test Characteristics of Subjects Completing SIP 78

4-4. SIP and Dimension Scores at Baseline, 3 Months, 6 Months, and 10 Years 82

4-5. Category Scores for Baseline, 3 Months, 6 Months, and 10 Years 83

4-6. SIP Categories and Items Endorsed by Greater Than 10 Percent of Subjects at 10 Years 86

4-7. Baseline Characteristics of Subjects by Treatment Groups at 10 Years 88

4-8. Comparison of Groups Differences in SIP at 10 Years Using the Kruskal Wallis Test 89

4-9. Baseline Demographic Characteristics of Subjects Completing SIP at Both 6 Months and 10 Years 91

4-10. Comparison of Total SIP and Dimension Scores Using the Wilcoxon Matched-Pairs Sign Test 92

4-11. Comparison of Proportion of Subjects with Changes in Total SIP and Dimension Scores Using the McNemar Test 94

4-12 Comparison of 6 Month SIP Scores Between Survivors and Nonsurvivors Using the Mann Whitney U Test 97

4-13. Relative Risk of Death by 10 Years with Dysfunction at Baseline, 3 Months, or 6 Months 99

LIST OF TABLES (continued)

4-14. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Total SIP Score at 6 Months 102

4-15. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Physical Dimension Score at 6 Months 102

4-16. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Psychosocial Dimension Score at 6 Months 102

4-17. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for 5 Category Scores at 6 Months 104

4-18 Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for 12 Category Scores at 6 Months 104

4-19. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Clinical Variables and SIP at 6 Months 106

4-20. Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Clinical Variables, Exercise Test Variables, and SIP at 6 Months 106

LIST OF FIGURES

1-1. Conceptual Framework of Health-Related Quality of Life in AMI Patients 10

1-2. Model of Health-Related Quality of Life 23

4-1. Distribution of Total SIP Scores at Baseline, 3 and 6 Months, and 10 Years (n=119) 80

4-2. Frequency Distribution of Sickness Impact Profile Score at Baseline 81

CHAPTER ONE: THE STUDY PROBLEM

Introduction

Over the years, advances in technological development have changed the direction and priorities of medical care. The diminished presence of communicable diseases in the developed world and increased longevity of patients have led clinicians to focus their attention on chronic illnesses and their effects on patients' lives. In addition, as the economic climate worsens and the realization that the expenditures used for chronic illnesses are disproportionate to the number of persons using them, the need to determine where the limited resources would be best directed has become the focus of public policy administrators and organizational managers (Hoffman, Rice, & Sung, 1996).

The issue of quality of life has gained attention in the recent years as the prevalence of patients with chronic illnesses has increased. Care of the chronically ill focuses less on cure than on minimizing symptoms and improving the life of the individual. The goal of therapeutic interventions for chronic illnesses is to maximize the person's quality of life and improve subsequent prognosis. The important issue to consider when prescribing pharmacological and technological treatments depends in part on its effect on patients' physical health, daily functioning, and sense of well-being. Health care providers and clinical investigators are increasingly aware of the importance of including quality of life as an outcome of treatment and clinical research. The evaluation of costs and benefits of treatments is essential in providing the best possible outcomes for chronically ill patients.

Factors that influence quality of life extend far into social and environmental issues of interest to social scientists. Education, job satisfaction, housing, neighborhood, and standard of living affect one's perception of quality of life. Quality of life is too broad to address across its breadth. However, it is possible to focus on one aspect of quality of life. This study focuses particularly on the concept of quality of life of interest to health care givers, health-related quality of life, in other words, quality of life as an outcome of illness and/or treatment.

Problem

The literature on the quality of life in patients with acute myocardial infarction (AMI) primarily focuses on quality of life as an outcome of specific pharmacological, technological, and program evaluation perspectives. At least half of the research studies that focus on quality of life in cardiac patients fail to define quality of life as a concept (Kinney, Burfitt, Stullenbarger, Rees, & DeBolt, 1996). This omission has lead to inconsistencies in the measurement of the concept. Many studies use instruments developed by investigators with little or no evidence of reliability, validity, or sensitivity to detect change (Kinney, et al., 1996).

In addition, the majority of the researchers measure quality of life at one point in time, or, if longitudinally, the studies have focused on up to three months (Kinney et al., 1996). Little is known about how HRQOL changes for the patient beyond the first year after AMI as there are no prospective longitudinal studies that evaluate the long term HRQOL in patients after AMI. This study describes HRQOL as an outcome of AMI over a ten year period. It also examines HRQOL as a predictor of mortality.

Purpose

The purposes of this prospective longitudinal secondary analysis are 1) to provide information about long term HRQOL in AMI patients, 2) to evaluate the effects of clinical variables on HRQOL as an outcome, and 3) to determine the effect of HRQOL as a predictor of mortality.

The aims of this study are to:

1. describe HRQOL in patients ten years after experiencing an AMI, according to the following dimensions and categories:
    a) overall HRQOL;
    b) physical dimension of HRQOL;
    c) psychosocial dimension of HRQOL;
    d) 12 sickness-related behaviors influencing HRQOL:
        i) ambulation; ii) mobility; iii) body care and movement; iv) emotional behavior; v) social interaction; vi) alertness behavior; vii) communication; viii) working; ix) recreational and pastimes; x) home maintenance; xi) sleep and rest; xii) eating.
2. estimate the effect of three cardiac rehabilitation treatments used early after AMI on HRQOL in patients 10 years after AMI.
3. estimate the changes in HRQOL of patients with AMI over the ensuing 10 years.
4. estimate the predictive value of baseline clinical and exercise test variables for HRQOL at 10 years.
5. estimate the difference in the 6 month SIP scores between subjects who survived 10 years and those who died.
6. estimate whether HRQOL at 6 months is predictive of mortality .

Significance

Every year, over one million Americans suffer AMI. With substantial pharmacological and technological advances and increased knowledge about the benefits of risk factor reduction over the years, mortality from AMI has decreased, with patients surviving a first or subsequent AMI. Based on statistics for 1994, it is estimated that 6.9 million persons, or 2.9% of the population, have coronary artery disease (CAD) (Adams & Marano, 1995). About 800,000 persons had new AMIs while 450,000 had recurrent attacks (Kannel & Thom, 1994). Despite the decline in mortality, CAD is a leading cause of permanent disability in the United States, and the economic impact of medical care and disability payments of patients with CAD continues to rise. Thus, CAD is a major public health problem and social and economic concern in the United States.

It is important to learn more about HRQOL after AMI so that clinicians can have a greater understanding about the impact of cardiovascular disease. Research on HRQOL could assist in refocusing the goals for health care delivery to include issues of patient outcome in addition to those of traditional biomedical science. It is important to look beyond pharmacological and technological treatments and program interventions to find areas which may have a greater impact on HRQOL than those previously studied (Najman & Levine, 1981).

Results from a longitudinal study on HRQOL in AMI patients can provide justification for allocating limited health care resources. Chronic diseases progress gradually leading to functional impairment. It is important to learn about the nature and extent of problems that patients face at various stages of illness. Early appropriate and continuous interventions can minimize the progression of the disease and the occurrence of severe illness and disability. Obtaining information on HRQOL after AMI can assist in the decision making process for the utilization of resources. Long term outcomes are taking an increasingly important role in an era of managed care.

While many researchers have evaluated HRQOL of interventions and treatments, changes in HRQOL during the course of recovery after AMI is unknown. Evaluating HRQOL and its dimensions and potential predictors of HRQOL in AMI patients over a 10 year span can give insight to clinicians in determining utilization of appropriate interventions and resources at times most beneficial to patients and to nurse researchers in setting priorities for research.

CHAPTER TWO: CONCEPTUAL FRAMEWORK AND LITERATURE REVIEW

This chapter begins with a presentation of the conceptual framework and review of literature that guided the research questions. The conceptual framework is composed of the biopsychosocial model of health and health-related quality of life (HRQOL) in patients with acute myocardial infarction (AMI). The review of the literature includes the definition and conceptualization of HRQOL and a review of research of HRQOL in patients with CAD, particularly in those who have had AMI.

Conceptual Framework

Biopsychosocial Model of Health

For many years, nurse scholars have debated and shifted between views of health focused on the biomedical model and those focused on social and behavioral sciences. The pendulum swung from early usage of theories of the physical sciences, such as physiology and biochemistry, to describe complex phenomena of human health to primarily using theories found in disciplines such as psychology and sociology. However, each model leaves gaps in its attempts to explain human responses to health and illness, the focus of nursing.

More recently, the majority view purports that both the biological and psychosocial dimensions of the human being provide a more comprehensive view of a person than one model alone can. Engle (1977) was among the first to promote the need to view the patient as a whole, expressing the concern that biomedical research focused on the person in a cold and impersonal way without sensitivity to personal needs of patients and families. To separate disease from the human aspects of the person creates a world which views the disease apart from the patient and out of the social context in which he or she lives. Biochemical and physiological changes are manifested differently in each individual depending on the acceptance of the sick role, the individual's personal characteristics, and the social and cultural expectations and pressures. On the other hand, considering only the psychosocial aspects of the patient removes the patient from the disease. The disease process and treatments produce physical symptoms to which the individual will respond both physically and emotionally.

The biopsychosocial model evaluates all factors "which contribute to illness and patienthood" (Engle, 1977, p. 133). The emphasis is not on biological factors nor psychosocial factors alone. A person is influenced by personal factors, behaviors, signs and symptoms of disease and illness, and environmental factors in his or her physical and social interaction with the environment. A clinician must evaluate and weigh all factors which contribute to patients' dysphoria and dysfunction. The interrelationship of the factors supports the biopsychosocial model as the appropriate and comprehensive perspective to evaluate the responses of patients with coronary artery disease to health and illness.

Quality of Life in AMI Patients

Patients who have had an AMI are faced with the knowledge of having a chronic disease. Typically, chronic diseases follow a predictable trajectory, beginning with onset and diagnosis of the disease, followed by disease progression and ultimately death (Strauss, 1975). Patients with AMI most often present with acute chest pain and shortness of breath in emergency departments. As patients adjust to the changes in myocardial function, patients may experience few symptoms to severe symptoms of heart failure. The disease progresses despite treatment due to clinicians' inability to eliminate atherosclerotic plaque, completely arrest the progression of plaque formation, and cure patients of the disease. To minimize progression of disease, clinicians recommend changes in a patient's lifestyle, such as diet, exercise, smoking, and control of diabetes and hypertension. The course of the disease is affected by the patient's pathophysiology, treatment, and responses to treatment. Unique to the trajectory of cardiac disease compared to other chronic diseases is the always present possibility of sudden death from coronary occlusion or arrhythmias (Rizzuto, 1983).

Quality of life in AMI patients is dependent upon patients' physical and emotional responses to ischemic heart disease and the management of the disease. Factors which influence quality of life continually influence each other in a cyclical manner. Clinicians assess physical symptoms due to the disease to determine treatment with medications and/or interventions such as angioplasty or cardiac surgery. The treatment evokes both physical and psychological responses which continue to be in constant flux as clinicians alter treatment in order to address changes in symptoms and the disease process. The individual often responds to the disease with changes in his or her interaction with the environment. In addition, the cultural value and meaning of the heart often place the individual with cardiac disease in a protected place in society. Such responses usually have an effect on the social interaction of the individual in the family, at work, and in the community. Changes are ongoing as "new experiences are incorporated, integrated, and as the individual, both consciously and unconsciously, reevaluates" the experiences and illness (Croog, 1983, p.324).

To assess quality of life in AMI patients, comprehensive evaluation of physical, psychological and social health and general feelings of well-being in relation to the disease and treatment is needed. The biopsychosocial framework and the framework for quality of life in patients after AMI both incorporate similar components to evaluate patient responses to the disease and therapy. A model viewing the biopsychosocial model applied to patients with AMI is presented (Figure 1-1). From the onset of symptoms of disease to death, quality of life is continually affected by the physical and psychosocial responses to the disease and treatment. Because patients with AMI may experience sudden death from coronary occlusion or arrhythmias, the risk of sudden death is present. The potential for unexpected events in AMI patients is not a typical concern of patients with other chronic diseases. The interplay in the circular area in Figure 1 may continue for a long time or may end suddenly with sudden death due to coronary occlusion or arrhythmias. Over the course of the disease, different components of this model prevail based upon the changes in health and illness of the patient. Because of this, no element of time was included in the model. With growing awareness of the interactions of the various dimensions of the patient and demand for more knowledge about the complete response to illness, investigators are including inquiries about quality of life in their research studies.

Review of Literature

The following review of literature will begin with a discussion of health-related quality of life as a concept, followed by a presentation of HRQOL in patients with CAD. Literature on the issues of measurement and instruments of HRQOL is also presented.

Health-Related Quality of Life as a Concept

Before the term quality of life became popular, few health care providers were concerned with more than the functional effects of diseases, illnesses and treatments on patients. In 1948, the World Health Organization defined health as "a state of complete physical, mental, and social well-being and not

Figure 1-1

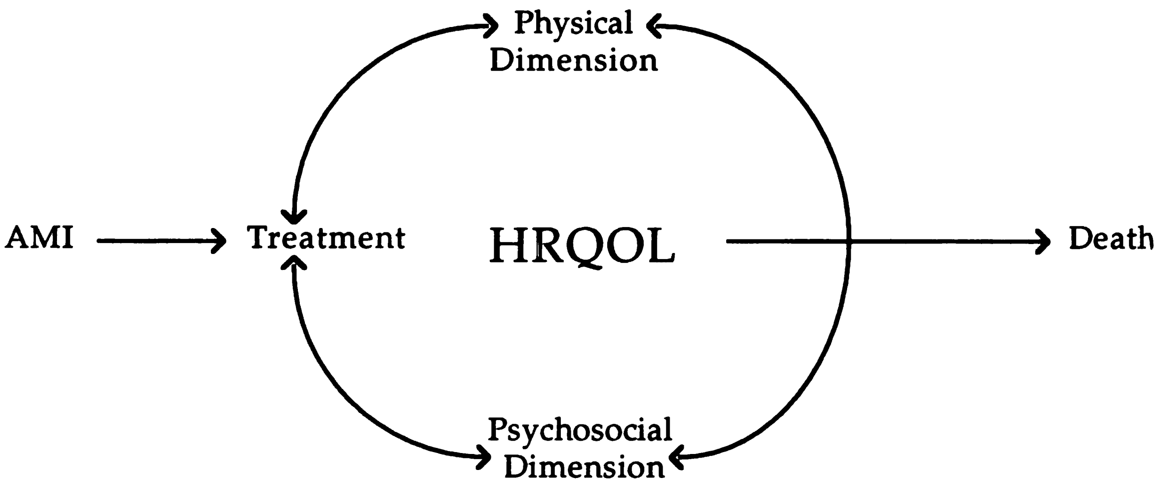


Figure 1: Conceptual Framework of health-related quality of life in patients after acute myocardial infarction.

merely the absence of disease and infirmity" (WHO, 1947). While most thought the definition to be utopian, it was instead visionary. Not until 30 years later did health care workers begin to perceive health as related to more than disease. Health is no longer thought of purely as the absence of disease; authorities agree that the basic dimensions of health include physical, mental, and social aspects of life (Spitzer, 1987).

In the last two decades, there has been a shift in the concerns about the impact of diseases and medical care on patients' health. The focus of health care is moving away from emphasizing only disease to including health, functioning, and well-being (Greenfield & Nelson, 1992). In addition, outcomes measuring the impact of disease and medical care has shifted from morbidity and mortality to also include a focus on patients' views on their quality of life.

The reluctance of most health care providers and researchers to include quality of life in their work has been due to their lack of familiarity and discomfort with subjective data which could not be easily measured with precision. In addition, many believed that the main thrust of energy should be directed towards assessing physiologic mechanisms of illness rather than psychosocial variables (Schipper, Clinch, Olweny, 1996).

Pioneers such as Karnofsky and Katz developed measures of functional status which departed from traditional physiologic assessments. Karnofsky (1948) conducted one of the first studies which measured the subjective as well as objective response to treatment. The Karnofsky Performance Scale measures symptom status and the ability to perform work and self-care activities on a graded scale from 100 (normal) to 0 (dead) (Karnofsky, Abelmann, Craver, & Burchenal, 1948). The Katz Index of Activities of Daily Living rated six functional activities which reflected levels of independent living: bathing, dressing, toileting, transfer, continence, and feeding (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963). While the index is useful in measuring patients' needs in long term care settings, it relies on a narrow definition of functional living. Western society places great value on the ability to be independent, thus the emphasis on a functional existence is reflected in the priorities given to the initial stages of instrument development.

Definition

In recent years, the use of the term "quality of life" has grown considerably. Since it was entered into the Index Medicus in 1975, quality of life is described in a multitude of ways with each author using dimensions appropriate for the particular disease or treatment being studied (van Dam, Somers, van Beek-Couzijn, 1981). Most often, quality of life is not defined, and the reader must deduce a definition from the report (van Dam et al., 1981; Bergner, 1989). Patrick and Erickson (1987) define quality of life as representing "a broad spectrum of dimensions of human experience ranging from those associated with the necessities of life, such as food and shelter, to those associated with achieving a sense of fulfillment and personal happiness" (p. 11).

The concept of HRQOL is extremely complex eluding a universally acceptable definition. The word "quality" is defined in Webster's dictionary as a "characteristic" and "attribute" of something (Webster, 1996). This implies that a judgment is required to determine the value of the object or concept being discussed. Because precision in the measurement of variables requiring value judgments is difficult, early definitions of quality of life focused on objective indicators which were easily obtained. For example, HRQOL as an outcome after illness and treatment was initially measured in terms of mortality and the extent of morbidity. As clinicians became more aware of the lack of ability to significantly extend the life of the chronically ill and the need to address other issues influencing the HRQOL of the patients, more researchers began to undertake the challenge of studying the concept including the individual's perspective on the effects of illness. The concept of HRQOL has broadened to include daily functioning, emotional and social functioning and a general sense of well-being, in addition to physical health (Ware, 1991).

As researchers' view of health broadened, the terms "health status" and "quality of life" became popular and are used interchangeably (Spitzer, 1987). However, controversy remains as to whether interchanging the two terms is appropriate (Spitzer, 1987; Bergner, 1989). While "health status" and "quality of life" overlap in many areas, the difference in the terms centers on the focus of the assessment. Quality of life focuses on an individual's perception of well-being while health status focuses on the state of health of an individual. An alternative to "quality of life" which is too broad and "health status" which implies a focus on the state of health is the term "health-related quality of life." Health-related quality of life (HRQOL) narrows the focus of quality of life to include aspects of quality of life directly affected by health. Health-related quality of life will be used throughout the remaining chapters to refer to quality of life as impacted by health.

Conceptual Issues

Despite the lack of consensus on a definition, authors agree upon the properties of the concept: that it is multidimensional, subjective, and variable with time (van Dam et al., 1981; Schipper et al., 1991). The major dimensions which affect one's assessment of overall HRQOL are the physical, emotional, and social dimensions, and general perceptions of well-being. The multidimensional quality of the concept of HRQOL leads to the use of complex instruments that address the many dimensions in one instrument or the need to use multiple instruments to measure quality of life, depending upon the definition used by the author.

Health-related quality of life is subjective in nature. Objective indicators of HRQOL are used frequently because of the availability of the information and ease of measurement; however, most agree that the best judgment on one's quality of life is made by the individual (Berzon, Hays, & Shumaker, 1993). The patient's experience and perspectives of the illness and treatment influence the report of quality of life. Debates on the use of subjective or objective indicators (for example, mortality and physiological measurements) center primarily on the discomfort that some investigators have with subjective data.

Health-related quality of life is temporally related. How one feels and reports experiences may change over time; a person may adjust expectations upward or downward during the course of illnesses or as a result of aging. For example, the inability to work may affect a patient who is forty years old differently from one who is sixty and preparing for retirement. Measurements of quality of life can be made at various points in time. Many studies evaluate patients' quality of life at one point in time (Dracup, Walden, Stevenson, Brecht, 1992) or a few times over a period of a year (Croog et al, 1986). Few studies have followed patients for periods of time beyond one year, leaving a gap in knowledge about how quality of life changes over long periods of time in chronically ill patients whose disease is likely to be progressive.

Theoretical Foundation for Quality of Life

Health-related quality of life is conceptualized in various ways. Experts have agreed that HRQOL includes four basic dimensions: physical function and emotional health, social interaction, and general perceptions of well-being (Berzon et al., 1993). However, differences in conceptualization occur primarily in the identification and method of categorizing the indicators of the dimensions.

Levine and Croog (1984) include five major elements in the measurement and analysis of quality of life: performance of social roles, physiologic state, emotional state, intellectual functioning, and general satisfaction and well-being. In measuring quality of life, the authors examined general well-being, physical symptoms, sexual function, sleep, and cognitive dysfunction, work performance, life satisfaction, and social participation using a variety of instruments (Croog et al, 1986).

Wenger conceptualizes quality of life with three major components: functional capacity, perceptions, and symptoms (Wenger, Mattson, Furberg, & Elison, 1984). Functional capacity consists of five sub-components: the ability to conduct activities of daily living, social function, intellectual function, emotional function, and economic status. Perceptions are the person's view of his or her general health status, level of well-being, and satisfaction with life. Symptoms may be induced by disease or treatment, or reduced or alleviated by interventions.

Ware (1986) conceptualizes quality of life to include physical, mental and social functioning and well-being, and general perceptions of health and well-being. However, in the development of the Medical Outcomes Study, in which Ware provided major leadership, social functioning and general perceptions of well-being were incorporated into the central categories of physical and mental health (Stewart, 1992).

In addition to physical and occupational function, psychological function, and social interaction, Schipper (1996) includes somatic sensation as a domain. Somatic sensation refers to feelings of discomfort experienced by the patient, such as pain, nausea, and shortness of breath. Unpleasant feelings and symptoms can have a negative impact upon one's quality of life. Duration and intensity of symptoms may influence the degree of impact.

One of the first instruments developed to measure quality of life, the Sickness Impact Profile (SIP) was developed by Bergner (Gilson et al, 1975). Literature regarding the conceptualization was published after the development of the instrument. Bergner presents a global view of health and factors which influence health. Bergner (1985) used the term "health status" in reference to an individual's health and the factors that may influence it. She identifies five dimensions of health status, none of which are independent of the others: genetic foundation; biologic, physiologic, anatomic condition; functional condition; mental condition; and health potential. The cumulative and interactive effects of the dimensions affect health potential, the dimension most clearly related to all the other dimensions (Bergner, 1985). Unique to Bergner's conceptualization is the inclusion of the dimensions of genetic foundation which refers to inherited characteristics of an individual and health potential which includes longevity, health potential, prognosis, and disability among the dimensions. While Bergner's conceptualization is comprehensive, consistent with her use of the term "health status," it focuses on the state of health versus the quality of life affected by health. However, many investigators have subsequently used the SIP to measure HRQOL rather than health status

(Arfvidsson, Karlsson, Dahllof, Lundholm, & Sullivan, 1993; Deyo, Inui, Leininger, & Overman, 1983; Fletcher et al, 1988; Ott, Sivarajan, Newton, Almes, Bruce, Bergner, & Gilson, B., 1983; Tandon, Standen, & Schwartz, 1989).

Dimensions of Health-Related Quality of Life

The fundamental dimensions of quality of life include physical health, mental health, social functioning, and general satisfaction and well-being. They are further described by indicators which are used to operationally define the dimensions.

Physical health is related to physical abilities of the body. It is most commonly described in terms of the strength, energy, and ability to function in daily activities, mobility, and physical activities. Daily activities include activities basic to all individuals, thus separating the social role function from the physical capabilities (Stewart & Kamberg, 1992). Clinicians are interested in whether the individual needs assistance with self care activities such as bathing, dressing, grooming. In addition, basic activities common to movement, such as climbing stairs, lifting, and walking are considered part of physical functioning. Interest also lies in knowing whether a person's mobility is affected by his or her physical health. Major issues of mobility include the ability to ambulate freely, the need for assistance, confinement to limited areas due to physical limitations. Measures of symptoms, such as pain and the ratings of and limitations caused by discomfort, are sometimes included, particularly in disease-specific instruments and studies.

Many psychological variables have an impact on quality of life. Psychological distress/well-being, anxiety/depression, and behavioral/emotional control are positive and negative affective states which are indicators of emotional health, or psychosocial functioning

(Stewart, Ware, Sherbourne, Wells, 1992). Cognitive functioning, considered a dimension of mental health, includes concepts such as memory, intelligence, mental alertness, perception, comprehension and problem solving and judgment. Mental health includes the biological functioning of an individual in addition to the psychosocial functioning considered when evaluating one's emotional health. Psychometric measures may be simple, asking direct questions about mood, anxiety or depression, or may use large psychometric scales in literature, such as the Minnesota Multiphasic Personality Index (also known as the MMPI) (Schipper et al, 1996). Schipper believes that simple, direct questions serve the purpose, particularly since the large psychometric tests were developed for specific populations with psychiatric conditions.

Social interactions are central to living with and among others. There are three aspects to social functioning: social interaction, role functioning and sexual functioning. The ability to carry out social interactions without interference from effects of illness or treatments is of primary importance to most persons. Indicators of social functioning focus on changes in one's normal social interaction. Illness can affect the individual's ability to maintain the frequency of interpersonal contacts with friends and relatives, the number of visitors, the amount of visiting, and/or telephone contacts. The quantity of social contacts can be measured by such information, however, the quality of contacts is not determined. Assessment of this domain has experienced tremendous growth since the 1977's when studies began to suggest that low perceived social support is an important psychosocial risk factor (Jenkinson, Madeley, Mitchell, & Turner, 1993; Ruberman, Weinblatt, Goldberg, & Chaudhary, 1984).

Role functioning refers to the ability to function in social roles such as spouse, parent, or employee. Participation in interactions and activities that are a normal part of the individual's roles at home, at work and/or in the community can be affected by illness. Factors which affect role functioning include changes in physical health, attitudes about particular roles, attitudes of people close to the patient, and personal satisfaction with the roles (Sherbourne, Stewart, & Wells, 1992).

Sexual functioning, which can be affected by diseases and their treatments, is included in the social dimension by some authors (Bergner, Bobbitt, Pollard, Gilson, & Morris, 1976; Sherbourne & Kamberg, 1992). Indicators of sexual dysfunction are the lack of sexual interest, inability to perform sexually, and decreased enjoyment from sexual activities.

The relationship of sense of well-being and satisfaction to psychological well-being is close. However, the influence of different factors dictates the need for separate dimensions. General satisfaction and well-being refers to the overall feeling a person perceives about his or her current health status. It is not only influenced by patients' outlook on their health at the time of inquiry, but also by their perceptions of health in general. Emotional adaptation to the presence of chronic diseases may feed into optimism or pessimism affecting the individual's sense of well-being. Patients may report decreased functioning in specific areas of their life, however, their report of their general sense of well-being may not reflect poorer functioning. Reports from patients who have adapted to the chronic presence of a disease may reflect relative changes in their symptoms rather than the fact that they have a disabling chronic illness. On the other hand, an observer of the same patient may not be able to conceive of how the patient can have a positive sense of well-being. The benefit of self report is supported by factors that influence general satisfaction and well-being.

Models of Health-related quality of life

Few models of quality of life, defining the relationship of the dimensions to one another, have been proposed. Four models that were evaluated include basic dimensions of HRQOL, although in different formats. Rice and Miller (1990) and, in a pilot study, Cowan, Graham, and Young (1992) developed models of HRQOL with perceptions of quality of life as the final outcome. Rice and Miller (1990) proposed that social support, disability, and physical symptoms determine the perceptions of quality of life which is indicated by sense of well-being, satisfaction and activities. However, the relationship of perceptions to the determinants and indicators is not clearly defined. Cowan and Graham (1992) developed a model of quality of life, identifying various antecedent variables (severity of disease, aggressiveness of treatment, and socioeconomic level) directly affecting mediating variables (manifestation of symptom distress, functional alterations, and cognitive adaptations) which ultimately affect perceived quality of life in a positive or negative manner. The relationships of various factors identified in the model appear to be unbalanced, with some having a direct and others an indirect effect on perceived quality of life. The model does not include psychological functioning nor social interactions. The studies by Rice and Miller (1990) and Cowan and her colleagues (1992) reported the pilot studies from the preliminary testing of the models. Their lack of additional progression is an indication of a transient interest in this topic and a lack of a rigorous approach to this problem. The need for further testing remains.

Ware (1984) and Bergner (1985) presented comprehensive models of health status. Ware (1984) provided a basic framework for discussing disease and its impact. Disease, the central issue to both the health care provider and the patient, is centrally located and surrounded by personal functioning, psychological distress/well-being, general health perceptions, and social/role functioning, placed in a series of squares, one enclosing the next. The proximity of a dimension to "disease" is affected by the strength of the impact of disease on it. Ware suggests there are priorities of health care outcome assessment and that there is a sense of order to individuals' experiences of disease, treatment, and changes in health over time (Ware, 1984). The display of the model in a linear manner may be restricting when evaluating the impact of disease and its treatment. The multidimensional nature of quality of life lends to overlapping of the attributes of the concept. Ware's model prioritizes the components of health status whereas other models do not. Prioritizing the components places limitations on the relationships of the components by implying a sense of order to individual's experiences of illness.

Bergner (1985) developed a model which identifies broad relationships between dimensions of health status and factors that may directly or indirectly affect health status. Personal factors include personal health care, social network, coping skills, and resources; social and familial factors incorporate personal health care and resources; societal factors consist of housing, crowding, sanitation, environmental quality; the availability and accessibility of health care indirectly affects the health status of individuals.

Bergner (1985) does not draw relationships between the dimensions of health status. She presents health status and factors which affect health status separately and as broad categories, minimizing controversy on direction and degree of the relationship of specific components. Bergner's model is comprehensive while providing for relationships unique to individuals.

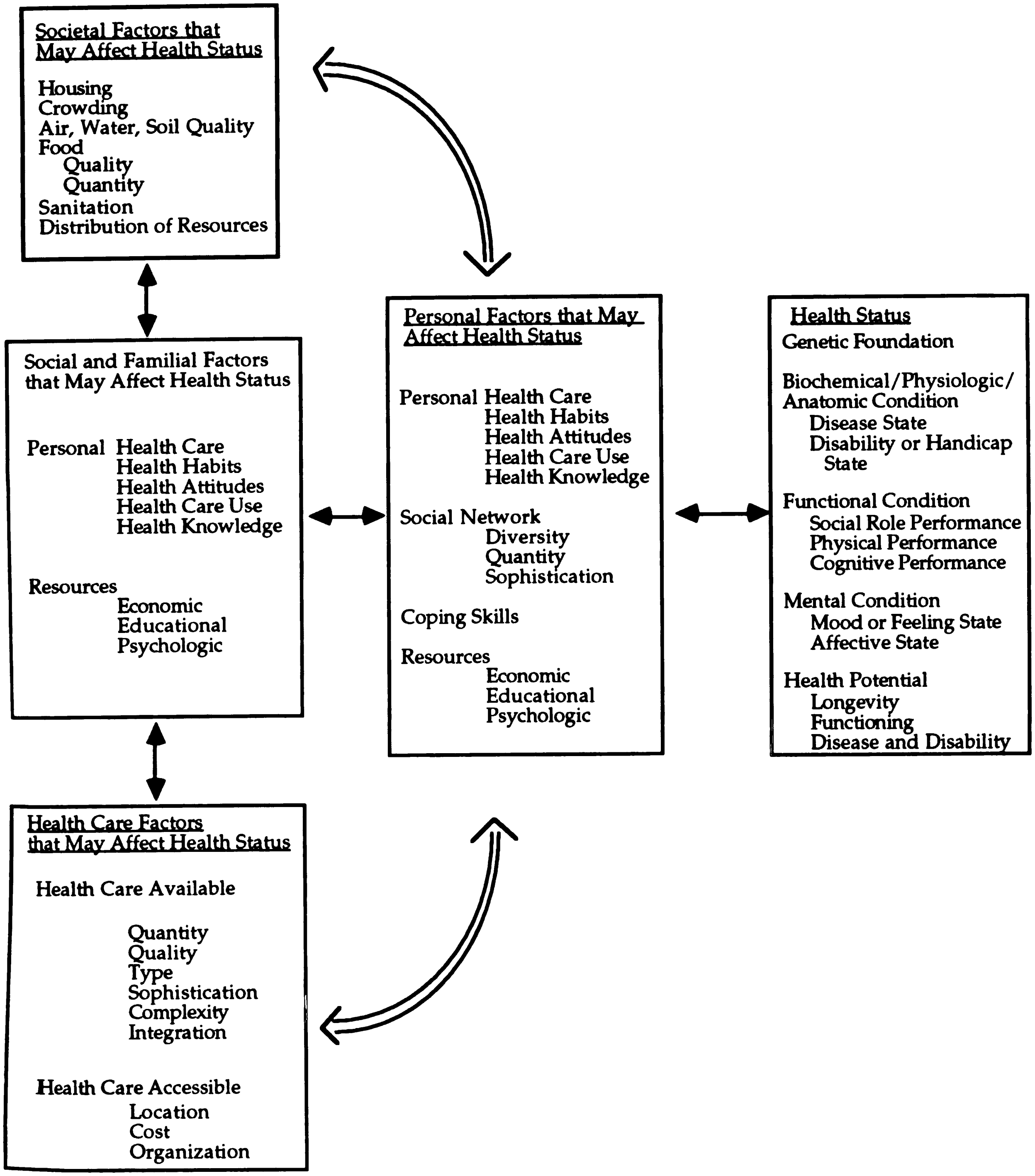
In an attempt to synthesize the various models, this author modified Bergner's model by establishing a direct relationship between personal factors and societal and health care system factors, providing additional avenues for interaction between health status and the various factors (Figure 1-2). The factors are not only interrelated, but are also dynamic, constantly changing with time.

Health-Related Quality of Life in Patients with Coronary Artery Disease

This section will begin with a presentation of HRQOL, organized by physical health, mental health, and social functioning, as it relates to populations of patients with CAD in general. This is followed by a review of HRQOL in the largest subset of CAD population, namely the AMI population with angina and clinical heart failure. The relevant quality of life issues which can differ for patients in the acute setting and those with chronic illness will be presented. In addition, factors which confound quality of life as an outcome for patients with AMI will be discussed. These include aging and treatment for CAD.

Quality of life is continuously affected by treatment, progression of disease, regression in a very few, and phases of illness and by psychosocial factors. The goals of management of patients with ischemic heart disease are to minimize symptoms with pharmacological and non pharmacological interventions and, if possible, to prolong life, while maintaining a satisfactory level of quality of life. Patients who have AMI have many physical, emotional, and social experiences and responses, depending on the course of the illness. Quality of life attributes are different for various

Figure 1-2



From "Measurement of health status" by M. Bergner, 1985, <u>Medical Care</u>, <u>23</u>, p. 699. Copyright 1985 by Lippincott-Raven Publishers. Adapted by permission.

subgroups of patients with coronary artery disease. The concerns and responses of patients with stable angina (predictable exertional chest discomfort) differ from those with unstable angina (frequent chest discomfort, chest discomfort at rest, death). When treatments for CAD have marginal differences in morbidity and mortality as measures of outcome, assessment of quality of life issues may be more helpful in guiding the choice of therapy (Wenger, 1988). Literature on patients' responses and preferences to particular treatments for CAD is growing, however, further research on comprehensive evaluation of patients' physical, psychological and social health and general feelings of well-being in relation to the disease and treatment are needed.

Physical Health

Physical health, the strength, energy, and ability to function in daily activities, mobility, and physical activities, is directly affected by the symptoms of CAD. Coronary artery disease is a progressive, chronic condition in which symptoms occur in varying degrees of intensity and frequency throughout the course of patients' lives. The impact of clinical symptoms of angina and heart failure on the ability to function is the most common concern of the patient.

Angina pectoris, chest discomfort due to myocardial demands for oxygen which exceed the supply, is the most common clinical symptom of CAD. While about 30% of AMI do not experience angina (O'Rourke, 1994), most others report chest discomfort (pain, pressure, or tightness) with physical exertion or emotional stress. The experience of angina varies between patients, but is usually consistent in the individual patient.

The experience of angina impacts on patients' physical and psychological functioning and well-being. As symptoms evolve, patients adjust their physical activity and change lifestyles to minimize occurrence or intensity of anginal discomfort. Many reduce or cease participation in activities such as work, hobbies, and sexual activity. Researchers have demonstrated that a decrease in the frequency of anginal attacks that patients experience can lead to improvement of quality of life (p=0.03) (Wilson, Wiklund, Lahti, & Wahl, 1991).

VandenBurg (1988) describes an increase in functional impairment in patients with angina compared with healthy volunteers. The level of significance was not reported. However, the degree of disability in patients is difficult to quantify due to the lack of reliable instruments. Researchers have reported variability with visual analog scales and the lack of correlation between exercise stress tests and reports of quality of life in patients with angina (Wiklund, Comerford, Dimenas, 1991).

Heart failure, a pathophysiological state in which the heart is unable to pump blood to meet the metabolic needs of the body, most often results in activity-limiting symptoms. Symptoms arising from pulmonary and systemic congestion due to inadequate cardiac function include fatigue and dyspnea, peripheral edema, and pulmonary edema. The symptoms lead to a decrease in exercise capacity and diminished ability to perform activities of daily living. Researchers identified symptoms affecting the ability of heart failure patients to function, including chest pain, fatigue, dyspnea, and sleeplessness (Grady, Jalowiec, Grusk, White-Williams, & Robinson, 1992; Rector & Cohn, 1992; Tandon, Stander, & Schwartz, 1989).

Grady et al. (1992) examined symptom frequency and distress in 175 heart transplant candidates in advanced stages of heart failure. They found that patients who reported more symptom distress reported more total functional disability (r=0.58, p<0.0001) and more physical disability (r=0.50, p<0.0001).

Dracup, Walden, Stevenson, & Brecht (1992) studied 134 patients with advanced heart failure and found that activity tolerance was related to the self report of symptoms (fatigue, weakness, shortness of breath, chest pain) and was negatively correlated to functional class-of the individual (r= -0.31, p<0.001).

The goals of treatment of patients with CAD are to minimize symptoms and improve cardiac function through pharmacological therapy and/or revascularization therapy. The results and/or side effects of treatments can improve or worsen patients' quality of life. The impact of therapy can reduce or eliminate symptoms of angina and/or improve cardiac function, resulting in improved HRQOL. However, adverse effects of the treatment can negatively impact patients' lives. If adverse effects overwhelm beneficial effects of the medication, patients' quality of life can diminish.

Mental Health

Long term psychological effects of AMI on patients and families have been identified and described (Conn, Taylor and Wiman, 1991; Mayou, Foster, & Williamson, 1978; Wiklund, Sanne, Vedin, & Wilhelmsson, 1984). Adjustments to the illness involve a succession of emotional adaptations in the individual, the family, and the patient's social network.

Pain, anxiety, stress of hospitalization in the coronary care unit (CCU), and fear of death overwhelm patients with AMI. With the development of CCUs during the 1960s and 1970s, and before the term quality of life was coined, researchers evaluating the psychological responses of patients during the acute phase of AMI found that denial, anxiety, and depression were the most common responses (Froese, Hackett, Cassem, Silverberg, 1974; Hackett, Cassem, Wishnie, 1968; Stern, Pascale, Ackerman, 1977). Psychosocial maladjustment can continue past one year after the AMI depending on the relationship between the nature of the illness and the psychological attributes of the individual (Byrne, 1982; Stern et al., 1977; Wiklund et al., 1984)

Denial has been described as both an adaptive and maladaptive defense mechanism to overcome the high level of anxiety that patients with AMI experience (Froese et al., 1974). Froese, Hackett, Cassem & Silverberg (1974) found that patients with denial experienced decreased anxiety and lower mortality rates than other patients. However, denial can lead to delayed medical care, lower levels of compliance in medical regimen, and inadequate risk factor modifications.

Anxiety is experienced universally in patients with AMI (Faller, 1990; Mayou et al., 1978). While anxiety is most pronounced during the acute phase of AMI, there is evidence that patients may be anxious, with concerns such as the loss of vitality and the possibility of sudden death, up to one year after AMI (Mayou et al., 1978; Wiklund et al., 1984). Anxiety in patients with AMI has been associated with more complications (Lown & DeSilva, 1978) and poorer recovery as measured by return to work and social activities (Philip, Cay, Vetter, & Stuckey, 1979; Stern et al., 1977; Winefield & Martin, 1981).

Depression frequently coexists with anxiety in patients with AMI (Faller, 1990). Depression is also associated with less than satisfactory outcomes, with greater numbers of complications and higher mortality than AMI patients without depression (Jenkinson, Madeley, Mitchell, Turner, 1993). Patients who are depressed early after AMI are more likely to remain depressed for a long period of time and have greater difficulty in resuming previous vocational and social activities (Stern et al., 1977).

Conn, Taylor and Wiman (1991) studied the relationship between anxiety, depression, quality of life, and self-care behaviors among 94 survivors of AMI

65 years and older. They used the Perceived Quality of Life scale to measure quality of life and the Profile of Mood States to measure anxiety and depression. They found that depression is a significant predictor of quality of life ($p<0.0001$). The performance of self-care behaviors, such as taking medications and smoking cessation, were also affected by depression ($p<0.05$). Anxiety failed to have similar affects on quality of life. The results suggest that interventions aimed at reducing depression could be useful in increasing quality of life and improving self care behaviors.

Cognitive functioning is an element of mental health which is not often evaluated in quality of life studies of CAD patients. A few studies evaluated cognitive and memory function in the pharmacological treatment of hypertensive patients (Lichter, Richardson, & Wyke, 1984; Solomon et al., 1983; Streufert, et al, 1988). The Studies of Left Ventricular Dysfunction (SOLVD) investigators obtained baseline measurements of cognitive functioning in heart failure patients through assessment of vocabulary, Digit span test, and the Trail Making Test, a concentration test (Gorkin et al, 1993). The patients were divided into two groups by the New York Heart Association (NYHA) functional classification system: class I (least functional impairment) and classes II and III. There were too few subjects in class IV (most impairment) to provide data for analysis. There were no differences between class I and classes II-III in the Vocabulary test or in the part of Trail Making Test requiring more concentration. However, significant differences between the two groups (I vs II-III) became apparent in the Digit Span, an attention-concentration task and the less complex part of the Trails Making Test ($p<0.05$). The results were mixed with no relationship between the functional capacity of heart failure patients to the level of cognitive functioning required for a test. Further research is needed in the area of cognitive functioning of patients with AMI.

Social Functioning

Physical and psychological well-being affect social functioning. Serious illnesses such as AMI cause major changes in patients' social interactions. One's ability to carry out social functioning is measured through comparison to one's normal pattern of social activities. Social roles and relationships constitute major aspects of social functioning.

Social relationships can be affected by the event of AMI, during early recovery and late in the course of the disease. Changes in the frequency and quality of social interactions can be indicative of changes in physical and mental health (Sherbourne, 1992). Mayou, Foster, and Williamson (1978) found that 24% of their subjects (n=100) perceived improvements in their marriage and family interactions after the patient's illness, reportedly due to deliberate efforts to show more tolerance and consideration for their family members. At the same time, 11% experience slight and 7.6% moderate deterioration of spouse and family interactions.

Role functioning refers to the ability to function in social roles, for example, as a spouse, parent, or employee. Changes in patients' social roles begin immediately during the acute phase when patients are dependent upon others for their care and to meet their needs. Decrease in functional capability may affect one's ability to perform social roles and the psychological health of the patient. In addition, changes in the ability of the patient to return to previous activities at home, work, and community will affect the role of the individual in the family, community, and workplace.

Research on AMI and social roles has focused on rates of patients returning to work and activities (Froelicher, Kee, Newton, Lindskog, &

Livingston, 1994; Dennis et al, 1988). Return to work has been viewed as a marker for recovery from myocardial infarction . The literature suggests that from 50% to 89% of patients who were previously employed return to work after AMI (Abbott & Berry, 1991; Burgess, Lerner, D'Agostino, Vokonas , Hartman, Gaccione, 1987; Saeterhaug, & Nygaard, 1989). The rate at which patients return to work ranges from 35% within about two months after discharge, 50% to 79% by 3 to 4 months, and 56% to 79% by one year (Froelicher et al., 1994; Abbott & Berry, 1991; Burgess et al, 1987; Smith & O'Rourke, 1988).

Patients who have suffered AMI are concerned with resumption of other activities besides work. Few studies address the ability of AMI patients to return to activities such as walking, stair climbing, lifting objects, household chores, and social visits. Wiklund and colleagues (1984) found that patients decreased activities related to convalescence over the first year after AMI while increasing activities out of the home. Gulanick, Kim, and Holm (1991) interviewed and gave questionnaires about the resumption of home activities to 40 patients recovering from AMI with or without coronary angioplasty or coronary artery bypass surgery. They found that almost all patients resumed their previous level of driving, walking, climbing stairs, lifting, and social activity by 9 weeks of recovery. Several investigators addressing the return to driving after AMI (Bertie, King, Reed, Marshall, & Ricketts, 1992; Froelicher et al., 1994) consistently showed that patients in exercise and/or education-counseling groups resume driving early after AMI, similar to patients in control groups.

There is overall agreement in the literature that many but not all patients return to work, sexual activity, driving, and other activities after AMI. Most often, patients return to activities, but at a reduced level compared to the level carried out before their AMI. The effect of the changes in social activities on quality of life remains unknown.

Sexual functioning, which can be affected by diseases and their treatments, is one aspect of social functioning (Sherbourne & Kamberg, 1992). The psychological impact of AMI as well as the physiological effects of the illness and medications can have a major effect on patients' ability to resume sexual activity. Indicators of sexual dysfunction are sexual interest, ability to perform sexually, and level of enjoyment from sexual activities. Anxiety and fear of another heart attack by the patient or partner often lead to reduced sexual activity or sexual dysfunction after AMI (Cassem & Hackett, 1973; Mann, Yates, & Raferty, 1981; Papadopoulos, 1978). For many years, refraining from sexual activity after AMI for many months was advocated due to the belief that the energy demands would place an excessive burden on the cardiovascular system after AMI. In 1970, Hellerstein and Friedman's classic study (1970) demonstrated that patients who suffered AMI did not have any greater physiological demand on the heart during coitus than healthy persons. Since then, greater attention has been paid to counseling regarding sexual activity (Scalzi & Burke, 1989; Seidl et al., 1991).

There are many reports in the literature of reduced sexual activity after AMI (Froelicher et al., 1994; Bertie et al, 1992; Hellerstein & Friedman, 1970; Mayou, Foster, and Williamson, 1978; Papadopouos, 1978). Not only do patients fail to resume sexual activity after AMI, but for those who do resume sexual activity, the frequency of coitus usually decreases. These changes are attributed to anxiety, depression, loss of libido, impotence, cardiac symptoms, and partners' decisions to protect the patient (Mann, Yates, & Raferty, 1981; Papadopoulos, 1978). The psychological aspects of sexual dysfunction are thought to have a greater effect than the physiological (Papadopoulos, 1989).

Research on Health-Related Quality of Life in Patients with Coronary Artery Disease

In recent years, literature on HRQOL in patients with CAD has grown rapidly. Many researchers have studied specific aspects of HRQOL, such as functional capacity, symptoms, and psychological health. However, the narrow focus of the research minimizes the potential of obtaining a broad perspective of patients' HRQOL. The following review consists of studies which provide comprehensive assessments of patients over all the dimensions of HRQOL.

Few studies specifically examine the question of HRQOL in patients with angina pectoris; instead, most primarily focus on the outcome of treatments for angina. Traditionally, researchers have used exercise tests, angina severity, return to work or psychosocial questions to determine the benefit of treatment. However, information on the impact of angina on the quality of patients' lives is then limited to those particular issues, with the unfounded expectation that the issue correlates with quality of life. Visser, Fletcher, Parr, Simpson, and Bulpitt (1994) conducted a study with the primary purpose of comparing three different global quality of life instruments, the Sickness Impact Profile (SIP), Nottingham Health Profile (NHP), and the Quality of Well Being Index (QWB) in patients with angina. They found that impairment determined by SIP and NHP scores of the 59 patients with angina increased with higher NYHA classification of subjects' angina given by their general practitioner ($p<0.05$). The results suggest patients have decreased quality of life due to anginal pain and diminished function.

The degree of myocardial damage after the AMI will influence the development of heart failure. The Framingham study estimates that coronary artery disease is the etiology of heart failure in 46% of men and 27%

women with failure (Kannel & Belanger, 1991). The prevalence and incidence increase dramatically with each decade of age. The end-stage of heart disease, heart failure has a high mortality with 37% men and 33% women dying within two years (Kannel & Belanger, 1991). The long term-survival is poor such that improving the quality of life becomes the central issue in treatment, rather than increasing longevity.

Dracup, Walden, Stevenson, and Brecht (1992) measured the quality of life in 134 patients with advanced heart failure awaiting heart transplant. They measured functional status with the 6 minute walk test, physical symptoms with the Heart Failure Functional Status Inventory, and the emotional state and psychosocial adaptation using the Multiple Affect Adjective Checklist, and the Psychosocial Adjustment to Illness Scale. They found that all subjects considered themselves to be severely compromised in functional capacity with the mean distance walked by their subjects to be less than subjects in other studies who were classified as less impaired. Subjects reported psychological distress with moderate to severe depression and moderate anxiety and hostility. Domestic relationships remained stable, however, relationships with friends and extended families deteriorated.

Gorkin et al. (1993) reported on a quality of life substudy from the baseline data of the Studies of Left Ventricular Dysfunction (SOLVD). A subgroup of 318 patients with heart failure were given several instruments measuring different domains of quality of life (Gorkin et al, 1993). The measures included the 6 minute walk test, Dyspnea scale, Living with Heart Failure, Physical Limitations, Psychologic Distress and Health Perceptions, and three tests of cognitive functioning (vocabulary, Digit Span, and Trail Making tests). Comparing patients with class II and III NYHA classification to Class I patients, the researchers found diminished quality of life in all areas except social support and two cognitive functioning tests ($p<0.05$).

A follow-up study for the SOLVD study population examined the relationship of domains of HRQOL to mortality and congestive heart failure (CHF) -related hospitalizations (Konstam et al, 1996). They found that activities of daily living, general health, and social functioning were independently predictive of increased risk of death and CHF-related hospitalizations ($p<0.001$). In the multivariate model, heart failure symptoms were predictors of mortality and CHF-related hospitalizations ($p<0.05$) instead of social functioning, after adjusting for ejection fraction, age, treatment, and New York Heart Association classification. The studies confirm that quality of life issues are central to the management of heart failure patients.

Important Confounders in the Study of Quality of Life as an Outcome for Patients with Coronary Artery Disease

Health-related quality of life of patients with CAD is most frequently impacted by symptoms of angina and heart failure. Angina and heart failure have a direct effect on patients' perceptions and report of HRQOL. However, there are other factors which have an indirect effect that confound the issue of patients' HRQOL: treatments of CAD and the aging process. The multitude of treatment modalities can negatively or positively affect patients' symptoms and function which can alter perceptions of HRQOL. In addition, aging is an ongoing process which can alter physical and psychological responses to illness. The effect of treatment of CAD and aging are presented in the following section.

Treatments

Two major types of treatment are available to patients with CAD: pharmacological and revascularization therapy. Some patients can be managed with one type of treatment or the other, while others require combinations of treatment. Balancing the beneficial and adverse effects of treatment is the primary goal of clinicians. A discussion of the effect of treatment of CAD on HRQOL follows.

Several groups of pharmacological agents are available to treat patients with various symptoms of coronary artery disease. The major groups of agents prescribed are nitrates, beta-adrenergic blockers (B-blockers), calcium channel blockers, and angiotensin converting enzymes (ACE inhibitors), each with different mechanisms to reduce the myocardial demands. Studies of Left Ventricular Dysfunction, a large multicenter study (SOLVD Investigators, 1992) provides evidence that the addition of ACE inhibitors to diuretic therapy reduces mortality with moderate and severe heart failure and improves heart failure symptoms and exercise tolerance. The results have led clinicians to include the agents as part of the routine treatment for heart failure patients.

While agents may decrease symptoms of angina and heart failure, side effects of the medications may affect other aspects of patients' lives. A growing number of researchers have evaluated the effects of pharmacological agents and include quality of life as an outcome measure (Gorkin et al, 1993; Rector & Cohn, 1992; Rogers et al, 1994). The SOLVD study used several measures to evaluate quality of life in heart failure patients randomized to treatment with Enalapril, an ACE inhibitor, and placebo (Gorkin et al, 1993). Rogers et al (1994) reported the two year follow-up of the quality of life of these patients. The results demonstrated slight improvement in functional status and improvement in quality of life categories of "social functioning" at 6 weeks and 1 year and in "general health" at 6 weeks only. No significant differences were found in 12 of the 14 scales of a quality of life questionnaire. Significantly better scores in the dyspnea and social functioning scales were found in patients who were treated with Enalapril than those given placebo at 6 weeks and 1 year ($p<0.05$). However, as the investigators reported, there was a significant amount of missing data, about 50%, by 2 years. They found that the lack of response to the questionnaire was related to the severity of heart failure. Therefore, it is difficult to ascertain whether the few benefits of quality of life found in this group of patients are related to the missing data or an actual lack of benefit. In addition, there is lack of information regarding the validity and reliability of the HRQOL questionnaire that was compiled from individual items and subscales of established sources.

Critics caution clinicians and researchers that while ACE inhibitors are an advance in pharmacological therapy, there are limitations in their benefit, with a decrease in mortality of 5 to 8 months and limited improvements in HRQOL (Townend & Littler, 1992). The prolongation of life with heart failure is not without drawbacks unless greater gains in quality of life are made. Further research on other pharmacological and biomechanical treatments needs to be conducted.

Revascularization procedures are used to reestablish flow through or around the occluded coronary artery vessel(s) to areas at risk for infarction. Currently, there are three primary methods for revascularization: thrombolysis, percutaneous transluminal coronary angioplasty (PTCA), and coronary artery bypass (CABG) surgery. Each requires an invasive procedure of varying complexity, from arterial cannulation for thrombolysis and PTCA, to major surgery for CABG.

Few studies assess quality of life after thrombolytic therapy. Simoons, Vos, and Martens (1991) found 14% mortality in patients who received thrombolytic therapy and 22% mortality in those who received conventional treatment. Levin and Jonsson (1992) used the Nottingham Health Profile to determine differences in quality of life one and twelve months after administration of intravenous thrombolytic therapy (n=153) and placebo (n=160). They found that patients who underwent thrombolysis had slightly higher (worse) scores, although not statistically significant, in all dimensions except sleep at one month. Twelve months later, the differences were no longer present.

Long-term benefits of PTCA such as a reduction of angina, improved exercise capacity, and more rapid return to work have been documented (Parisi, Folland, & Hartigan, 1992; Gruentzig, King, Schlumpf, & Siegenthaler, 1987; Holmes et al, 1984). Several studies evaluating quality of life after PTCA demonstrate that patients who have undergone PTCA have significant improvements in function and in perceived quality of life and health-related quality of life from six weeks to one year later (Faris and Stotts, 1990; Bliley and Ferrans, 1993; McKenna et al, 1994).

Several large prospective, randomized studies have compared the benefits of medical versus surgical treatment for patients with stable angina (Rogers et al., 1990; Veterans Administration, 1984). In the initial five to seven years, mortality was lower in patients who had undergone CABG surgery; however, at 10 to 11 years, there was no difference between medical versus surgical treatment (Rogers et al., 1990; Veterans Administration, 1984).

Quality of life in patients who have undergone CABG has been primarily measured in terms of relief from angina and return to work (King, Porter, Norsen, & Reis, 1992, Peduzzi, Hultgren, Thomsen, & Detre, 1987). Two studies reported improvements in mood, perceptions of family life, work, and sexual satisfaction after surgery (Jenkins et al, 1983 Kornfield, Heller, Frank, Wilson, & Malm, 1982). King and her colleagues (1992) measured life satisfaction, affect, functional disruption, and severity of angina in 155 patients before and one year after surgery. Patients who perceived improvement in functional capacity felt surgery was worth having; those who saw it as an alternative to death focused on the emotional aspects of recovery.

A large multicenter prospective randomized study was conducted to evaluate the relative benefits of medical versus surgical treatment for patients with coronary artery disease (CASS Investigators, 1983). Quality of life, measured in terms of chest pain, heart failure symptoms, graded exercise test results, activity limitations, employment status, and recreational status, was compared in 780 patients randomized to medical and surgical treatment groups at 6, 18, 60, and 120 months after entry into the CASS study. At 5 years follow-up, patients in the surgically treated group had significantly less chest pain, fewer activity limitations, and less exercise induced angina, and longer exercise test time than the medically treated group ($p<0.05$). There was no significant difference in heart failure symptoms, employment status, and recreation status. However, at 10-year follow-up, the advantages to surgery became less apparent (Rogers et al., 1990). The investigators attribute the absence of a difference due to the return of symptoms to patients in the surgical group and the performance of surgery to patients in the medical group. Similar patterns of significant differences in the early follow-up period (one year) with no significant differences at the later follow-up period (three and five years) were obtained by the Veterans Affairs Cooperative Study Group (Booth et al, 1991). These studies are among the first to report to evaluate the quality of life in patients with coronary artery disease over a period of greater than one year (five to ten years.) However, the studies fail to define "quality of life," and they use only measures of symptoms to represent quality of life.

Papadantonaki, Stotts, and Paul (1994) measured quality of life in patients who had undergone CABG (n=44) and PTCA (n=32), before revascularization and 3 weeks after discharge. Using Quality of Life Index, the Profile of Mood States (POMS), and a physical functioning questionnaire, they found no significant difference in quality of life, mood state, and physical functioning between the two groups before the procedures. Overall quality of life did not change significantly from baseline results. There were significant improvements in mood state and physical functioning in both groups, with greater improvements occurring in the patients undergoing PTCA ($p<0.001$). The measurement of quality of life three weeks after the procedure may have masked the ultimate improvements in quality of life in patients after CABG surgery since the recovery period from CABG is typically much longer than from PTCA. Evaluating the patients over longer periods of time would give more comprehensive results on the long term effect of the two procedures on quality of life.

The goals of management of patients with ischemic heart disease are to minimize symptoms with pharmacological and nonpharmacological interventions and to prolong life, while maintaining a satisfactory level of quality of life. Patients who have had an AMI have many physical, emotional, and social experiences and responses, depending on the course of the illness. When treatments for CAD have marginal differences in morbidity and mortality as measures of outcome, assessment of quality of life may be more helpful in guiding the choice of therapy (Wenger, 1988).

Literature on patients' responses and preferences to particular treatments for CAD is growing, however, further research on comprehensive evaluation of patients' physical, psychological and social health and general feelings of well-being in relation to the disease and treatment are needed and have become mandate for most clinical trials.

Aging

Many normal physiological changes affecting physical and psychosocial well-being occur throughout all phases of life. Many age-related changes are not manifested until stresses in the environment result in imbalance of the basal state of the person. Lower reserve capacity for responses to stress distinguishes older persons from younger persons (Tobin, 1975). In addition to expected age-related changes, the prevalence of chronic diseases is higher in elderly populations. It is important to make the distinction between the effects of normal physiologic aging and effects of disease.

Aging is a natural process that occurs throughout the life span and is not limited to a specific period. In a report of the first 23 years of a longitudinal study of physiologic aging in 1142 healthy men, researchers described a general decline in physiological measures, such as basal metabolic rate, conduction velocity, glomerular filtration rate, vital capacity, functional aerobic capacity, and cardiac index with increasing age (Shock et al., 1984). Different functions and organ systems appear to decline at different rates.

Although there is evidence that general physiological decline occurs, cardiovascular function at rest does not decrease substantially with normal aging processes (Shock et al, 1984; Schulman & Weisfeldt, 1994). However, age-related changes in the cardiovascular system are manifested in the response to physical or emotional stress. As age increases, cardiac indices measured during exercise, such as cardiac output, maximum aerobic capacity, stroke volume, and heart rate, decline. The ability of the myocardial muscle fibers to develop tension does not diminish. However, four major factors contribute to the changes in left ventricular function: 1) prolonged relaxation or contraction duration of cardiac muscle, 2) decreased sympathetic responsiveness, 3) decreased left ventricular diastolic compliance, and 4) increased impedance to left ventricular contraction (Weisfeldt, 1980).

Individuals are affected not only by the natural aging processes that occur, but also diseases that affect them as they age, particularly CAD. While atherosclerotic changes occur throughout life, the effects of the disease are manifested more often in the elderly when the degree of plaque accumulation in the coronary arteries can advance to a degree that symptoms begin to manifest.

Many psychosocial changes occur during the life span. Roles in the family, at work, and in the community go through transitions as the degree of participation in the setting changes. Changes in social roles can affect an individual's emotional health. For example, a reduction in self esteem from unemployment due to retirement or disability or the loss of family and friends could lead to depression.

Life satisfaction in older Americans has been found to be greater than in younger persons (Herzog & Rogers, 1986). Herzog and Rodgers (1986) found this relationship to be stronger for specific domains such as family life, job, and standard of living, rather than general concerns, such as life satisfaction or happiness. They also found that satisfaction with environmental domains of life (housing, community of residence, standard of living, work) had a stronger relationship with age than person oriented domains (family life, marriage, friendships). Greater life satisfaction in older persons has been attributed to increasing satisfaction with declining aspirations due to feelings of resignation or realistic expectations, reluctance to admit to anything that sounds like an inability to cope, preference to deny unpleasant or anxiety provoking facts, and more time to become used to the circumstances in life. Herzog and Rodgers concluded that there was a general positive relationship present across all domains except health. Satisfaction with health diminished with increasing age. Because many clinical studies previously have excluded elderly persons by setting an age exclusion, there is little information available about the relationship of quality of life measures in the advanced age categories.

Measurement of Health-related quality of life

As researchers broaden their focus to include HRQOL in their studies, the need to develop new instruments to measure health arose in the 1980s. Initially, traditional physiologic measurements and measurements of mortality and morbidity were used to determine quantity rather than quality of life. With advances in technology, researchers became more comfortable with technical endpoints that were physiological, chemical, and anatomical in nature. Objective measures, however, do not always correlate with patients' functional capacity, their perceptions of changes in their health status and to their sense of well-being (Read, 1987). In addition, patients have different responses despite the same clinical criteria and treatment (Guyatt, Feeny, & Patrick, 1993). In medical research, mortality continues to be included as an outcome measure of interest. The measure of quality of life is frequently seen as a secondary outcome. Many researchers are turning to instruments developed to encompass the various dimensions of health to determine the impact of disease and the impact of treatment on patients.

Health-Related Quality of Life as an Outcome

While progress has been made with investigators including HRQOL more frequently in their studies, the lack of conceptualization in the reports has been a problem. Conceptualization of HRQOL affects development of instruments and researchers' choice of instruments for their studies. In order to obtain data appropriate to the research question, the conceptualization of HRQOL and the purpose of the research must match the content of the instrument. Guyatt and his colleagues (1989) found that researchers reporting results of quality of life studies in three major journals in 1986 did not always measure quality of life with relevant and valid instruments.

Kirshner & Guyatt (1985) developed a methodological framework for assessing health indices based on the purpose of inquiry. They presented three broad purposes of using tests or measures in clinical or social science research: to discriminate between subjects, predict prognosis or the results of other tests, and evaluate change over time. Identifying the purpose of new tests is not necessary in most clinical situations. For example, physiological measurements can be used to distinguish between subjects, predict prognosis, and evaluate change in an individual over time. However, it is difficult to develop an instrument measuring quality of life which aims to comprehensively discriminate, predict, and evaluate at the same time. Therefore, the need to make distinctions between the purposes of measurement becomes essential. A discriminative index is used "to distinguish between individuals or groups on an underlying dimension when no external criterion or gold standard is available for validating these measures" (Kirshner & Guyatt, 1985, p. 27). An example is the intelligence test which is used to distinguish between individual's learning abilities. When gold standards are available, a predictive index can be used to classify individuals into separate categories, identifying persons that will develop a specific condition or outcome. An example of a predictive index is the Denver Development Screening Test, designed to identify children with learning disabilities. An evaluative index is used to measure the extent of change of an individual or group over a period of time. Evaluative instruments are used particularly in HRQOL studies which focus on the impact of treatments on subjects. HRQOL is the overall outcome of interest when comparing interventions that differ little in the effect on mortality, but may have an impact on functional capacity and symptoms and indirectly affect emotional and social function. The process of instrument development needs to focus on item selection, scaling, and reduction as well as discrimination, prediction, and evaluation.

Health-Related Quality of Life Instruments

The impact of illness and medical interventions on the quality of life has led to the development of many instruments measuring health status or HRQOL. They can be categorized into disease specific and generic instruments. Disease specific instruments focus on particular disease states, problems, or patient populations while generic instruments focus on wide spectrum of issues, provide a summary of health-related quality of life (Guyatt, Feeney, & Patrick, 1991).

Disease specific instruments focus on being able to detect small, clinically significant changes unlike general health surveys. Investigators find validated disease-specific instruments are useful, but the applicability of disease-specific instruments is limited. For example, instruments for cancer patients (Spitzer et al., 1981), heart disease (NYHA, 1978), and arthritis (Meenan, Gertman, & Mason, 1980) address issues related only to the particular population for which the instrument was developed. Such instruments use non physiological assessments to investigate specific issues. The advantages of disease-specific instruments are their focus on particular problems of interest and the responsiveness of the measures to change within individuals. However, the broad scope of generic measures leads to stability of the measures, and the appropriateness of the measure and generalizability of results to a wide variety of populations. Approaches to measurement of HRQOL depend on the resources of the researchers, clinicians, and patients. Administration of single measures is ideal for simplicity, cost, and patient burden. However, the selection of measures largely depend upon the conceptualization of HRQOL and the objective(s) of measurement.

Generic instruments are designed to cover a wide spectrum of conceptions of HRQOL and to allow global assessments of subjects. They can be used with a wide variety of populations, allowing direct comparisons of different groups (Bergner & Rothman, 1987). Generic instruments have two major classes: single indicators and health profiles. Single indicators are instruments with one score given to represent quality of life. The various domains are incorporated into one general assessment of the subject's perception of quality of life. For a long time, mortality was the main endpoint in determining quality of life. Mortality rates are routinely collected and easily obtained. However, mortality is limited to information on subjects' death, with little information on the benefit of interventions (Kaplan & Anderson, 1987). As the prevalence of chronic diseases increases, the usefulness of mortality rates in distinguishing cause of death has diminished. Morbidity statistics do not clearly define health status or quality of life. A single indicator resulting in information on HRQOL is designed as a single question asking the subject to rate his or her health or quality of life on a Likert-type scale. This method can be used to determine a subject's perception of his/her well-being, as the individual incorporates values and emotions while processing the answer. However, information about specific aspects of health are eliminated in the specified response. Cunny and Perri (1991) demonstrated that a single item measure with five response options ("In general, would you say your health is Excellent, Very Good, Good, Fair, or Poor") correlated well with the overall score for the 20-item Short-form General Health Survey (r=0.86) and concluded that single item measures are valuable tools for the researcher or clinician with limited resources.

The advantage of the single indicators is the simplicity of administering one question. However, the single indicator will not reveal the dimensions affecting quality of life. In addition, instruments usually need to be adapted to each set of study questions.

Health profiles are often obtained by using single instruments that cover a broad range of quality of life issues. The primary dimensions include physical, mental, and social function. The various dimensions share a scoring system that can be grouped into several smaller sections or into one total score that summarizes all components. The advantages of using a health profile is that one single instrument rather than multiple instruments can be administered, saving time of both patients and investigators. In addition, incorporation of many dimensions of QOL into one instrument contribute to its utility in many situations. In fact, the breadth of the instrument leads to the potential of uncovering unexpected findings (Rockey & Griep, 1980). The disadvantage of health profiles is that the instrument may not focus on the specific interest of quality of life. The lack of specific focus can result in unresponsiveness, particularly if the intervention does not specifically affect an area of quality of life measured by the instrument (Guyatt, Van Zantan, Feeny, & Patrick, 1989).

Limitations of Current Knowledge

While the literature about HRQOL in AMI patients is growing, there are major deficiencies in the studies reported (Kinney et al., 1996). In many studies, HRQOL is measured as a unidimensional concept rather than as multidimensional concept. Literature on patients' responses and preferences to particular treatments for CAD is growing; however, further research on comprehensive evaluation of patients' physical, psychological and social health and general feelings of well-being in relation to the disease and treatment are needed and have become mandated for most clinical trials. Endpoints such as angina, symptoms, return to work, or physical functioning are often used, and subjective indicators are frequently lacking. Few studies utilized comprehensive assessment tools to measure HRQOL. Many investigators measure HRQOL with instruments developed for their studies usually lacking adequate evidence of validity, reliability, or sensitivity to change.

There is also a paucity of longitudinal studies which are longer than three months. Kinney et al. (1996) evaluated 84 studies of cardiac patients that identify quality of life as an outcome of interest. They found that 98.9% of the studies used a longitudinal design, but for a period of three months or less. A few studies report some dimension of HRQOL at five years after an event, but HRQOL data was obtained at only one point in time (Rosenblum, Rosen, Pine, Rosen, & Borg, 1993; Wiklund, Herlitz, & Hjalmarson, 1989). In addition, the literature on the value of HRQOL in predicting subsequent mortality is extremely limited.

The current study addresses the issues presented above. This longitudinal study used a comprehensive instrument that includes physical and psychosocial dimensions and has longstanding evidence of validity, reliability, and sensitivity to changes to measure HRQOL of patients over ten years after AMI. The study gives an unprecedented view of how HRQOL changes for patients after AMI. In addition, it provides further information on the use of HRQOL as a predictor of mortality in the AMI population.

CHAPTER THREE: METHODOLOGY

This chapter will present the design and methods used in the present study. This study is a secondary analysis of existing data. Therefore, to facilitate an understanding of the sample, methods, design, and measurements, a description of the original and the follow-up studies is given in order to be able to place this historical longitudinal study into context. The methods of obtaining data in the 10 year follow-up study are then described. Lastly, the methods of performing the secondary analysis on the data are presented.

Design

A secondary analysis of an existing database was used to answer the aims of this study. A historic prospective longitudinal study design was used to obtain the data. The data were previously collected as part of a randomized clinical trial (original study) and during the 10 year data collection period (follow-up study.)

Objectives

Original Study

The original study was a randomized clinical trial entitled "Controlled Study of Earlier Cardiac Rehabilitation" (CSECR) conducted at the University of Washington, Seattle, Washington and funded by the Department of Health, Education, and Welfare (#5 RO1-NU-00589-04) (Sivarajan & Bruce, 1981; Sivarajan et al., 1981, 1982, 1983; Ott et al, 1983; Sivarajan & Newton, 1984;). Louise W. Mansfield, R.N., M.S., Robert A. Bruce, M.D., and Erika S. Sivarajan, R.N., M.A. (aka Froelicher) were co-investigators.

The primary objective of the CSECR study was to evaluate the effects of three different rehabilitation treatments on physical and psychosocial

outcome measures in patients soon after myocardial infarction. This included an assessment of quality of life using the SIP instrument.
The three groups were Group A which received usual care, Group B1 which received usual care plus an exercise program, and Group B2 which received usual care, an exercise program, plus an education-counseling program.

Follow-up Study

Subsequently, Sivarajan Froelicher followed the cohort prospectively over a period of ten years as part of her doctoral work at University of California, Los Angeles (Sivarajan Froelicher, 1989). The primary objective of the 10 year follow-up study was to investigate the 10 year prognostic value of exercise test variables in patients early after AMI in predicting cardiovascular death. The follow-up study was funded by a National Research Service Award from the National Institutes of Health, Center for Nursing Research (#US HHS1F31 NRO6312-01). The actual follow-up period ranged from eight to ten years (average 9 years) after AMI. The follow-up period will be referred to as 10 years.

Present study

The present study is a secondary analysis of a prospective study using longitudinal data for the measurement of baseline demographic and clinical information and quality of life from the original and follow-up studies. The use of data from the original and follow-up studies provided an opportunity to examine quality of life in acute myocardial infarction patients over ten years without the immense costs typically required for such prospective follow-up studies and the necessary time to elapse to accumulate such information for data collection.

Study Population

Original Study

All consecutively admitted patients 70 years of age or younger at the time of the index AMI, with the diagnosis of AMI admitted to coronary care units of seven participating hospitals in Seattle were screened for inclusion in the original study. Two of the hospitals were teaching hospitals, two were health maintenance organizations, and three were private hospitals. Patients were enrolled into the study between September 1, 1977 and December 2, 1979. The six-month follow-up of the last patient was completed by May, 1980.

Inclusion Criteria

Patients were considered for inclusion into the study if they 1) had a primary diagnosis of myocardial infarction (transmural or subendocardial) by any two of the following three criteria: history of acute prolonged chest pain, electrocardiographic changes characteristic of myocardial infarction, and, typical enzyme changes; 2) were free of complications for a minimum of 24 hours within seven days of hospital admission; 3) able to walk without aid; 4) able to speak and read English, 5) were free from serious non cardiac complications prior to this admission,; 6) were free of cardiac complications or limitations resulting in New York Heart Association Classification Class III or IV before this admission; and 7) resided within a 50 mile radius of the University of Washington.

Of the 6561 patients admitted to the coronary care units during the enrollment period, 506 were eligible for the study and 258 of these were enrolled. Reasons patients were excluded from the study are listed in Table 3-1.

Table 3-1

Study Sample and Categories of Exclusions from
September 1, 1977 to December 2, 1979

Category	No. of Patients	
Admissions to hospital	6561	
Confirmed myocardial infarction	1481	(22)*
Exclusion from study	912	(64)*
Age over 70 years	460	(32.4)
Prolonged complications	136	(9.6)
Physical limitations	63	(4.4)
Noncardiac diseases	61	(4.3)
Other cardiac diseases	42	(3.0)
Distance over 80km	42	(3.0)
Communications	11	(0.8)
Other reasons (e.g., massive obesity, psychological problems, etc.)	70	(4.9)
More than one reason	27	(1.9)
Eligible for study	506	(36)*
Physician's refusal	80	(16)*
Physician's permission granted	426	(84)*
Patient's refusal	168	(39)*
Enrolled in study	258	(61)*

From "In-hospital exercise after myocardial infarction does not improve treadmill performance" by E. S. Sivarajan, R. A. Bruce, M. J. Almes, B. Green, L. Belanger, B. D. Lindskog, K. M. Newton, L. W. Mansfield, 1981, New England Journal of Medicine, 305, p. 359. Copyright 1981 by New England Journal of Medicine. Reprinted by permission.

Follow-up Study

The ten-year follow-up was conducted between December, 1987 and April, 1988. To locate patients who had participated in CSECR, several resources were used (Froelicher, 1996). A letter was sent to subjects at the last known address with the purpose of reintroducing the investigator to the patient and allowing the patient the opportunity to plan the telephone contact by the investigator. If a patient was not interested in further contact, he/she were to return the provided self-addressed postcard to decline. Each envelope was stamped with "Forward and Address Correction" to maximize patients receipt of letters and to obtain updated addresses for patients who had moved during the last six months.

Most of the patients who were not located by the method described above were found by examining vital records in the State of Washington Vital Records Department which maintains records of death certificates. Additionally, telephone directories, and patient registration files were also used in some instances. In addition, property tax rolls of King County and Pierce County Assessors Offices, poll directories, voter registration in Washington, physicians' offices, relatives or friends, and door to door house calls were used to provide clues or information on the location of remaining subjects' whereabouts. These methods are outlined in detail elsewhere (Froelicher, 1996).

Present Study

The sample was limited to the patients who were alive and available during the 10 year follow-up and who were willing to complete the SIP. Of the 258 patients who participated in CSECR, 65% (n=167) patients completed the SIP 10 years after enrollment into the study. Of the 91 patients who did not complete the SIP, 78% (n=71) were recorded as having died by the time of the 10 year followup study, 20% (n=18) refused to be interviewed, 2% (n=2) did not return the SIP, and one of the returned forms had no identification number on the form and thus, was not be used in the analysis of comparisons over time.

Sources of Data

Original Study

After informed consent, 258 subjects were randomly assigned into one of three groups. Group A received usual care. Group B1 received usual care plus an exercise program. Group B2 received usual care, an exercise program, plus an education-counseling program (Sivarajan et al., 1982).

Group A, the control group, received conventional medical and nursing management throughout all phases of hospitalization and convalescence at home. In addition to receiving conventional care, subjects in group B1 participated in an inpatient exercise program and received a home exercise program and prescriptions from the research staff based on low-level treadmill tests before discharge. For three months after discharge from the hospital, the subjects had weekly 30 minute outpatient appointments with a research nurse, occupational therapist, or physical therapist to review the prior week's activities and responses to daily activities carried out at home. Subjects were given a renewed exercise prescription each week.

Subjects in group B2 received the same care as those in B1 plus attended a series of twelve one-hour group education-counseling sessions concerning the following eight topics: cardiac anatomy and physiology of myocardial infarction, coronary artery disease risk factors, nutrition, dietary changes, activities and exercise, stress and relaxation, issues related to the resumption of sexual activity and work, and emotional reactions to myocardial infarction. Two research staff cardiovascular clinical nurse specialists led the classes, and the physical therapist who is specially trained in methods of relaxation therapy conducted the relaxation sessions, providing 20 to 40 minutes of content with liberal time for questions and answers, discussion and problem solving. Spouses and friends were encouraged to attend the sessions with the patients to develop knowledge and skills, to assist with problem solving, and to provide family support and tangible support, such as driving the patient to the appointments. No formal teaching was done in the hospital by the research staff, who were instructed to offer only advice for the exercise program. The teaching and counseling program was offered only after hospital discharge in order to minimize any crossover contamination by the hospital medical and nursing staff between patients in group A, B1, and B2 in the hospital phase of the study (Ott et al., 1983). The patient assignment of group A, B1, or B2 was not revealed until the time of hospital discharge to minimize bias.

Baseline data on the Sickness Impact Profile were collected within one week of entry into the study (Ott et al., 1983). The instruction given to subjects was to answer the questions "*pertaining to the week before hospital admission..*" This decision was made in consultation with Betty Gilson, M.D. and Marilyn Bergner, PhD, the developers of the instrument. Instructions for information differs from instructions during standard administration of the questionnaire when the subject is guided to respond to the question as the item pertains to them "today" and because of their illness. Although recall difficulties compounded by the stress of the myocardial infarction and hospitalization could influence the results of the questionnaire, it was considered necessary to obtain a measure to determine the patient's function before admission as a baseline and to allow evaluation of patients' return to their previous levels of functioning. Recall bias can be assumed to be equal across all three group assignments, thus allowing a fair comparison. Administration of the SIP was done as soon after enrollment as possible to ensure the best recall. The SIP was also administered at 3 months (at the conclusion of the intervention) and at the 6 month follow-up clinic visit. The SIP was self administered after subjects received instructions by a masters prepared research nurse (Ott et al., 1983).

Follow-Up

In the 10 year follow-up, SIP questionnaires were sent to the subjects who agreed to complete them. After the subjects filled them out, they sent them back in a stamped self-addressed envelope to the investigator. Although patients had previously completed the SIP three times, they were instructed on how to complete the questionnaire during the phone contact made by the principal investigator at the time of the 10 year follow-up evaluation telephone call (Froelicher, 1994, 1996; Sivarajan Froelicher, 1989).

In addition to the SIP questionnaire, a formally structured telephone interview was conducted. A questionnaire was developed to obtain demographic data and subjects' general perceptions of their current physical and psychological health. It was administered in a standardized format to each consenting patient, using a written scripted interview data collection form.

Present Study

The raw data of the original study were available on the original questionnaires, on ASCII files on magnetic tapes and in SAS Database format on computer diskettes. The original SIP questionnaires completed by the subjects were used to develop the database of responses from baseline, 3 month, 6 month and 10 year administrations of the questionnaire. The data were entered into and analyzed by the SPSS statistical analysis program

(SPSS, 1994). Scores of the SIP were calculated using the standard method for the instrument (Damiano, 1996). The method of calculating the scores is described in the next section.

Instrument

Sickness Impact Profile

The Sickness Impact Profile (SIP) was one of the first instruments developed to measure quality of life. It was developed to provide a measure of outcome capable of assessing the effects of clinical interventions (Bergner et al., 1976). Gilson and Gilson's observations that improvement in patients' functional capacity often did not coincide with changes in their medical condition or pain and symptoms led to the development of the behaviorally based questionnaire to determine the impact of disease and treatment for both chronic and acutely ill patients (Gilson et al., 1975).

A model of sickness-related behavior was developed in which "sickness" which refers to a person's experience of illness, as "one's own perception of his or her health" (Bergner et al., 1976). The authors conceptualize the impact of sickness as changes in one's behavior associated with performing daily activities, manifested through changes in behavior, performance, feelings, or symptoms. The change in behavior is called a health-related dysfunction, whether the change represents an improvement or deterioration in health. Changes towards better health originate from impaired performance, thus the term "dysfunction" is applicable.

The SIP was developed as a behaviorally based measure because performance or behavior can be measured directly or by an observer, it may be affected by medical treatment even though the disease is unaffected, and measurement is not affected by diverse definitions of health and illness during measurement (Bergner et al., 1976). The statements of health-related behavioral dysfunction are worded to elicit "yes" or "no" responses that can be obtained by the subject or an observer. Examples of statements include, "I sit during much of the day" or "I walk shorter distances or stop to rest often".

The 136 item SIP is organized with seven main dimensions made up of twelve categories (Bergner et al., 1976). The physical dimension consists of three categories: ambulation, mobility, and body care and movement. Psychosocial dimension consists of four categories including social interaction, alertness behavior, emotional behavior, and communication. Five dimensions are also categories, independent from the physical and psychosocial dimensions and from each other, including sleep and rest, eating, work, home management, and recreation and pastimes. The statements of health-related behavioral dysfunction are worded to elicit "yes" or "no" responses that can be obtained by the subject or an observer. Examples of statements include, "I sit during much of the day" or "I walk shorter distances or stop to rest often".

To provide the ability to discriminate between patients with varying degrees of severity of dysfunction, a group of 25 health care students and professionals rated each item within each category on an 11-point and 15-point scale from "minimally dysfunctional" to "severely dysfunctional." There was high agreement among the judges during both times. The items were then assigned weights reflecting severity of dysfunction the judges identified (Gilson et al., 1975).

To obtain a total score for the SIP, the weighted scale values of all statements checked by the respondent are summed and divided by the total scale values for the whole questionnaire (Damiano, 1996). Dimensions and category scores are obtained in a similar fashion, totaling the values of items checked in the specific dimension or category and dividing the sum by the total dimension or category values. Scores are multiplied by 100 to convert it to a percentage. The scores can range from 0 to 100 with 0 representing no dysfunction and 100 representing maximum dysfunction. A subject who does not check or "endorse" any items receives a score of 0 while a subject who endorses every item would received a score of 100. The higher the score on the SIP, the greater the impact on the health of the respondent.

Reliability tests were reported for the early 235-item version of the SIP (Pollard, Bobbitt, Bergner, Martin & Gilson, 1976) and for the final 136-item version (Bergner , Bobbitt, Carter, & Gilson, 1981). The investigators administered the SIP twice in a 24 hour period to four subscales of patients with various degrees of sickness and dysfunction: rehabilitation medicine inpatients and outpatients, speech pathology patients, outpatients with chronic health problems, and healthy enrollees in prepaid health plans. Different interviewers, forms, and administration procedures were used. Test-retest reliability for the overall score of the SIP ranged 0.88 to 0.92 in three field trials (Bergner et al., 1981; Pollard et al., 1976). Correlation coefficients for individual items ranged from 0.45 to 0.60, and 0.82 for the 12 categories. Testing for internal consistency resulted in Cronbach's coefficient alpha 0.97 for the early 235-item version, 0.94 for the final 136-item version, and 0.81 for a mailed self-administered version.

The investigators evaluated three methods of administration: interviewer administration (I), interviewer-delivered, self-administration (ID), and mail-delivered, self-administration (MD). Test-retest reliability coefficient and Cronbach's coefficient alpha for internal consistency was high for both I (.97 and .94, respectively) and ID (.87 and .94 respectively). No retests were obtained on MD, and lower internal consistency was demonstrated (.81). The results suggest that self-administration method accompanied by an interviewer's guidance for comprehension and adherence to instructions may be more reliable than interviewer-administered method. In addition, the presence of an interviewer may improve the reliability of the data obtained. The researchers suggest that MD administered SIP requires careful follow-up and monitoring to assure reliability and validity (Bergner et al, 1981). In the original study of this proposal, the SIP was administered by ID while the SIP was mailed to subjects in the follow-up study. However, the primary investigator of the follow-up study reviewed instructions for the SIP during phone contact.

The developers of the SIP tested construct validity in several field trials by comparing the SIP constructs of dysfunction and sickness with self assessments of dysfunction and sickness (Bergner et al., 1981). Correlation between SIP score and self assessment of dysfunction was 0.69 and between SIP score and self assessment of sickness was 0.63. Correlations between SIP and clinicians' assessment of patients' dysfunction and sickness were lower. This finding supports the opinion that the best judgment on one's quality of life is made by the individual, with the patient's experience and perspectives of the illness and treatment influencing the report of quality of life (Berzon, Hays & Shumaker, 1993).

The relationships of the SIP and each of the criterion variables were analyzed by the multitrait-multimethod technique. High correlations of category scores to total scores (r=0.82) demonstrated the importance of each category to the total instrument and low correlations between the categories (r=0.32-0.40) assured minimal overlap among categories (Bergner et al., 1981). Convergent and discriminant validity were demonstrated (Bergner et al., 1981).

Clinical validity was tested to evaluate the relationship between the SIP and existing clinical measures. The developers administered the SIP to patients with hip replacements, hyperthyroid patients, and patients with rheumatoid arthritis (Bergner et al., 1981). The relationship between appropriate clinical measures ranged from moderate (thyroid T4 test vs overall SIP, r=0.41) to high (Harris analysis of hip function versus physical dysfunction categories of SIP, r=0.94) (Bergner et al., 1981).

The SIP has been used with populations of patients after myocardial infarction (Ott et al., 1983), patients who survived cardiac arrest (Bergner et al., 1984; Bergner et al., 1985), and patients with rheumatoid arthritis (Deyo, Inui, Leininger & Overman, 1983) intermittent claudication (Arfvidsson, Karlsson, Dahllof, Lundholm & Sullivan, 1993), chronic obstructive pulmonary disease (Schrier, Dekker, Kaptein, & Dijkman, 1990), low back pain (Deyo & Diehl, 1983), inflammatory bowel disease (Drossman, Patrick, Mitchell, Zagami & Appelbaum, 1989), pneumonia (Hasley, Brancati, Rogers, Hanusa & Kapoor, 1993), and sarcoma (Sugarbaker, Barofsky, Rosenberg & Gianola, 1982) (Table 3-2). The results demonstrate the instrument is applicable to broad use in patients with chronic conditions.

As with other health profiles, the SIP's sensitivity, or responsiveness, to change has been questioned. Responsiveness is the ability of an instrument to detect small but important changes over time (Guyatt, Walter & Norman, 1987). Characteristics that could affect responsiveness of instruments include ceiling and floor effects. A ceiling effect occurs when an instrument cannot detect improvement in patients with the best possible score; conversely, a floor effect is when an instrument cannot detect deterioration in patients with the worst possible score (Guyatt, Feeny & Patrick, 1991).

Table 3-2

Clinical Application of Sickness Impact Profile in Research

Population	Investigators	Year	n	% Women	Mean FU
AMI	Ott & Sivarajan	1983	258	15	6mos
Angina	Fletcher	1988	427	0	8wks
	Visser	1994	59	27	once
Cardiac Arrest	Bergner, L.	1984	424	NR	6mos
	Bergner, L.	1985	308	NR	6mos
	Hillis	1993	29	NR	6mos
Intermittent Claudication	Arfvidsson	1993	148	35	once
Low Back Pain	Deyo	1983	80	62	3 wks
Pneumonia 6wks	Hasley	1993	80	24	once at
Pulmonary Disease	Schrier	1990	70	51	once
Rheumatoid Arthritis	Deyo	1983	79	29	6mos
Sarcoma	Sugarbaker	1982	26	NR	1 - 3yrs
Thyroid	Rockey	1980	14	78	5 - 52wks

Legend: AMI=Acute myocardial infarction; NR=Not reported
wks=weeks; mos=months; yrs=years

Researchers have presented conflicting results on the responsiveness of the SIP to change. MacKenzie, Charlson, DiGioia, and Kelly (1986) compared improvement or deterioration detected by the SIP to the changes in a "transition index", a five point self assessment scale (much better, better, same, worse, much worse) in a small sample of 22 medical patients and 21 vascular or orthopedic surgical patients. They reported no significant differences in the total SIP score between the baseline and four succeeding assessments at 1, 2, 4, and 6 weeks after discharge. However, there were statistically significant changes in the physical and psychosocial dimensions ($p<0.001$). Differences in SIP scores obtained at the different transition index levels were significantly different ($p<0.001$). They concluded that the SIP was most sensitive to deterioration in patients who were least impaired and improvement in those most impaired. However, the magnitude of change in scores was greater with deterioration than with improvement, suggesting a ceiling effect.

Deyo tested the responsiveness of the SIP in patients with rheumatoid arthritis (Deyo, Inui, Leininger & Overman, 1982; Deyo et al., 1983) and low back pain (Deyo & Diehl, 1983). In all three studies, he found that the SIP was able to discriminate between patients who improved and those who did not. However, the sensitivity of the SIP to clinical change was not conclusive in the two patient populations. Others, however, have reported changes over time in small specific populations that corresponded to changes in subjects' scores on other instruments (Ahlmen, Bengtsson, Sullivan & Bjelle, 1990; Nielson et al., 1990; Ott et al, 1983; Sullivan, Ahlmen & Bjelle, 1990).

No gold standard of what constitutes real change exists. It is not known what SIP scores or magnitude of change in scores are normal or are clinically significant. However, changes in scores can be used to evaluate patient progress. Findings suggest that the instrument is not sensitive to small daily changes, but is better at reflecting changes occurring over longer periods of time (deBruin, deWitte, Stevens & Diederiks, 1992).

The clinical and exercise test variables collected for the purposes of the original study at baseline were used in various analyses in this study. The decision on which variables to include in the analyses was based on a review of the literature (Kelly, 1985) and the findings of the follow-up study (Froelicher, 1994). Four clinical variables (digoxin use, history of prior AMI, history of systemic hypertension, and angina) and three exercise test variables (inadequate blood pressure response to exercise, ST-segment depression, and ST-segment elevation) were strong predictors of cardiovascular death after controlling for age and sex (Froelicher, 1994). Therefore, they were included in the models for the present study. The absences of stress was also found to be a strong predictor of cardiovascular death; however, it was eliminated as a variable in this study due to the instability the variable exhibited in previous analyses. The Killip classification for heart failure and arrhythmias were not included because they were not statistically significant in the previous follow-up study, and a parsimonious model was desired.

Data Management

The data management phase of the research was a major challenge of the project. The initial task involved organizing the materials from both the original study and follow-up study: the code book, original questionnaires, data tapes, and diskettes. Time was required to investigate methods of transferring data from the original format to a microcomputer format and carrying out the transfer. The principal investigator decided to reenter the SIP data from all four data points (baseline, 3 month, 6 month, and 10 year follow-up) to minimize the time needed to transfer the data for analysis from mainframe tapes and to familiarize herself with the data collected by the previous investigators. During the data entry process, she continually checked for errors and missing values. Data was rechecked for errors after all the data had been entered. Since each item of the SIP had a specific weighted score, data entry errors were identified by evaluating the minimum and maximum values and frequencies for each item. In addition, random checks of data entered for entire questionnaires were performed. Data analysis followed the completion of data entry.

Power Estimates

Since the present study uses a secondary data set, the available sample size is fixed. Preliminary informal power calculations were computed during the planning of the 10 year follow-up. A power estimate is required to determine adequacy of the sample size to estimate significant differences in changes in SIP score from baseline to 10 years. Since there are no power calculation formulas developed for paired nonparametric comparison, the unpaired x^2 was used to obtain an estimate for expected proportions. Sivarajan reported 37% to 46% improvement in SIP scores 3 months after AMI among three groups of randomized subjects and 46% to 63% improvement from baseline to 6 months after AMI (Ott et al., 1983). Using the changes Sivarjan detected as proportions, a sample of 169 subjects is necessary to detect a change of 15% from three months to 10 years with an alpha of 0.05 (two-tailed), beta of 0.20, and power of 80%. Using the unpaired x^2 statistic, it is evident that there is at least 80% power to detect a change of 15% in the scores. If the power requirements for independent group tests are satisfied, power requirements for paired analysis will be more than satisfied. This provides confidence that the data provided will answer the research questions.

Data Analysis

The statistical methods used to accomplish the objectives were descriptive, nonparametric and parametric statistics. To maximize the information that could be obtained from the data set, more than one statistical method was utilized for some of the aims. Table 3-3 outlines the data analysis plan used for this study.

Aim 1

To describe the quality of life in patients over the ensuing 10 years after an AMI in terms of the overall quality of life, physical and psychosocial dimensions and the following 12 sickness-related behaviors: ambulation, mobility, body care and movement, emotional behavior, social interaction, alertness behavior, communication, working, recreational and pastimes, home management, sleep and rest, and eating.)

The first aim is focused on describing the overall quality of life, physical dimension, psychosocial dimension, and the 12 sickness-related behaviors over the 10 years after AMI. Descriptive statistics including frequency distributions,

measures of central tendency (means, medians, and modes), and measures of dispersion (ranges, quartiles, standard deviations) were used to accomplish the objectives. Previous analysis of SIP scores three months after AMI in this sample demonstrated a skewed distribution with scores centered around low SIP scores reflecting little dysfunction (Ott et al., 1983). The presence of skewed distributions required use of nonparametric statistical methods for further analyses (Table 3-3).

Table 3-3

Summary of Data Analysis Plan

AIMS	DESCRIPTIVE	NONPARAMETRIC		PARAMETRIC	VARIABLES
		Continuous	Dichotomous		
1: Describe HRQOL	Measures of central tendency and dispersion				SIP scores
2: Effect of Rehab rx on SIP 10 yrs		Kruskall-Wallis			D: SIP scores I: Rehab rx
3: Change in SIP 6 mo and 10 yrs		Wilcoxon Matched-Pairs	McNemar		SIP scores: 6 mo & 10 yrs
4: Estimate predictive value of clinical var for HRQOL (SIP 10yrs)				Logistic regression	D: SIP score I: Clinical variables Exercise variables
5: SIP 6 mo survivors vs non survivors		Mann Whitney U test	Odds ratio		
6: Predictive value of SIP 6 months for death				Cox P.H.	D: survival I: Clinical variables Exercise variables

D = Dependent variable; I = Independent variable; SIP = Sickness Impact Profile;
Cox P.H. = Cox Proportional Hazards Regression

Aim 2

To estimate the effect of three cardiac rehabilitation treatments used early after AMI on HRQOL in patients 10 years after AMI.

Ho: There is no significant difference in the 10 year SIP scores between subjects in the three cardiac rehabilitation treatment groups (A, B1, and B2).

The next analysis was performed for two reasons: 1) to evaluate if the long term effects of the original group persisted over 10 years and 2) to determine whether group differences were present at 10 years. To measure the effect of three cardiac rehabilitation treatment groups on the SIP score at ten years, the Kruskal-Wallis test for several independent groups was conducted. The total SIP, Physical and Psychosocial dimension, and category scores were compared between Groups A, B1, and B2. The finding that there are no group differences allows the data to be pooled into one sample and analyzed across the groups.

Aim 3

To estimate the changes in HRQOL of subjects with AMI over the ensuing 10 years.

Ho: There is no significant difference between the median scores of the total SIP score and the Physical and Psychosocial Dimension scores obtained at the different time periods after AMI.

The research hypothesis was analyzed using two different approaches, depending on whether the SIP scores were treated as paired tests of continuous data or the proportion of the sample was dichotomized to one of two SIP outcomes. The identification of a skewed distribution of scores in the previous analysis of SIP data by the investigators of the original study precluded the use of statistical methods that require normal distributions (Ott et al., 1983). Pairing the scores from two time periods to compare their differences, the nonparametric statistical method of Wilcoxon Matched Pair Signed-Rank test was applied. The statistical method tested the null hypothesis that the medians, rather than the means, are equal in the two paired samples. The SIP scores were ranked and given the same sign as the original difference. The ranks of the SIP scores were then treated like observations with a mean and standard deviation computed from them.

> **Ho: There is no significant difference between the proportions of subjects that have worsening dysfunction and those with less dysfunction across the four data collection points.**

A parallel analysis was conducted using McNemar's test to compare proportions of dichotomous measures on the same subjects to measure change. The nonparametric statistical method was used to estimate the significance of proportions of subjects with dysfunction at the different data collection periods. Subjects with SIP scores of zero were classified as having no dysfunction and those with SIP scores greater than 0 will be classified as having dysfunction. The McNemar's formula for testing an association in a 2x2 table when samples are matched is not concerned with the similarities, but the discordant pairs. The underlying null hypothesis of no difference between matched samples with respect to the attribute, x^2 has a distribution of 1 degree of freedom.

Aim 4

To estimate the predictive value of baseline clinical and exercise test variables for HRQOL at 10 years.

Ho: In patients who have had an AMI, after controlling for age and gender, the clinical and exercise test variables will not be independently predictive of SIP scores at 10 years.

Because of a skewed distribution, the use of multiple regression would violate assumptions of normal distribution. Therefore, logistic regression was used to analyze the data estimating the predictive value of baseline clinical variables for quality of life at 10 years. Logistic regression analysis tests the relationship between multiple independent variables and categorical dependent variables without the need to meet the assumption that the data are normally distributed (Lee, 1992). The statistical method presents the probability of an event occurring when associated with another event. Clinical variables (digoxin, history of hypertension, previous AMI, angina, age, and sex) and exercise test variables (systolic blood pressure, ST-segment depression, and ST-segment elevation) were the predictor variables that were be examined (Table 3-4) and the SIP score (SIP=0 or SIP>0) was the outcome.

Aim 5

To estimate the difference in the 6 month SIP score between subjects who survived 10 years (survivors) and those who died by 10 years (nonsurvivors).

Ho: There is no significant difference in the 6 month SIP score between survivors and nonsurvivors.

As with Aim 3, the data could be analyzed using two approaches, depending on how the SIP scores were utilized. Both methods of analyzing Aim 5 were used. The Mann Whitney U test, a nonparametric statistical method, tests the equality of the medians of two independent groups rather than the means. The three month SIP score was the dependent variable

Table 3-4

Operational Definitions of Predictor Variables

Clinical variables

Digoxin - Taking digoxin the day of exercise test.

History of hypertension - The patient had a history of hypertension before admission to hospital for index myocardial infarction.

Previous MI - The patient had a history of one or more confirmed myocardial infarction(s) before admission to hospital for index myocardial infarction.

Angina - The patient had a history of angina pectoris before admission to hospital for index myocardial infarction. Note exercise-induced angina at time of exercise test has been called pain.

Age - Age at time of entry into the original study between 1977 - 1979.

Sex - Gender of subject

Exercise test variables

Exercise-induced systolic blood pressure response (Systolic blood pressure) - A drop in systolic blood pressure below the usual resting level, or a failure of the pressure to raise at least 10mmHg. The predictor variable is inadequate systolic blood pressure in response to exercise versus absence of this finding.

Exercise-induced ST-segment depression (ST-segment depression) - ST-segment depression measured 0.08msec after the J point from baseline. Down sloping or horizontal ST-segment depression in response to exercise greater or equal to one millimeter (mV). The predictor variable is the presence versus absence of this abnormality.

Exercise-induced ST-segment elevation (ST-segment elevation) -ST-segment elevated greater or equal to 1mm when measured 0.08 msec after the J point from baseline. The predictor variable is the presence versus absence of this abnormality (ordinal scale) and the vital status (dichotomous: survivor versus nonsurvivor) was the independent variable. Observations (SIP scores) were ranked, ignoring the group (dead vs alive) to which an observation belongs. A *t* -statistic for each of the two independent groups was then calculated using the calculation for the ranks, rather than the original observations.

Ho: There is no significant relationship between the six month SIP score and the risk of death from all causes by 10 years (odds ratio = 1).

An odds ratio using a case control methodology was also used. Odds ratio is a measure of the relationship between two nominal characteristics (Fleiss, 1981). Patients who were deceased at 10 years were classified as "cases" and those who survived 10 years will be "controls." Using the six month SIP data as the predictor variable (SIP>0 vs SIP=0) and vital status as the outcome variable (dead vs alive), the odds ratio and 95% confidence interval for the estimate were calculated. The odds ratio presented the probability of survival at 10 years occurring over the probability of it not occurring given that the subject had dysfunction at baseline or not.

Aim 6

To estimate whether HRQOL at 6 month is predictive of mortality at 10 years.

Ho: In patients who have had an AMI, after controlling for age and gender, the SIP scores at 6 months and clinical and exercise variables will not be independently predictive of subsequent death.

To estimate the effects of the 6 month SIP scores on survival, multivariate survival analyses with Cox Proportional Hazards regression analysis were performed. Various models including the total SIP, Physical and

Psychosocial Dimension, and category scores and the baseline clinical and exercise test variables were used. The variables for the follow-up study of the CSECR were chosen based on the literature that identified clinical predictors that place a person at risk for cardiovascular mortality and the availability of the variables in the data. The clinical and exercise test variables for the current study used the definitions of the follow-up study (Table 3-4). Killip classification for heart failure and arrhythmias were eliminated from the follow-up study variables because they were not statistically significant in the model predicting cardiovascular death. In addition, stress was eliminated because of instability the variable exhibited in previous analyses.

Human Investigations Approval

The Human Subjects Review Committee requirements for informed consent were observed for the CSECR (Sivarajan & Bruce, 1981). The 10 year follow-up study used survey research methods to determine current health status, cardiac events since the six month follow-up visit, and general quality of life. Therefore, an application to the University of California, Los Angeles, School of Public Health for "Statement of Exemption from Review by Human Subjects Protection Committee" was made and approved (Froelicher, 1994; Sivarajan Froelicher, 1989). The present study was approved as meeting the criteria for an exemption by the Human Subjects Committee, University of California, San Francisco (Appendix A).

CHAPTER FOUR: RESULTS

There were 258 subjects enrolled into the original study, Controlled Study of Early Cardiac Rehabilitation (CSECR). Subjects were randomized into three treatment groups with 84 subjects assigned to the control group (A), 88 to the exercise group (B1), and 86 to the exercise and teaching-counseling group (B2).

Of the original 258 subjects, the age at entry to CSECR ranged from 30 to 70 years with a mean age of 56.2 (±8.4) years. Most of the population were male (84.9%), and Caucasian (88.4%). The average length of education was 13.9 years with an average income of $23,000 (range: 3,000 to 100,000). The majority of subjects did not have heart failure (77.8%), previous AMI (84.4%), did not report stress (87.5%), nor have abnormal exercise test variables (81.6-93.9%). The baseline characteristic of the 258 subjects are listed in Table 4-1. Previous analysis showed there were no differences in the demographic data for the three groups (Ott et al, 1983).

The number of SIP returned at each data collection period varied. Of the 258 subjects originally enrolled into CSECR, 94% (245) completed the SIP at baseline, 84% (217) at 3 months, 79% (206) at 6 months, and 53% (139) at 10 years. Forty-six percent (n=119) of all the subjects completed the SIP at all four time periods.

Through methods described in the 10 year follow-up study, it was determined that 72% (n=187) of the subjects were alive ten years after their AMI and 28% (n=71) of the subjects had died (Froelicher, 1996). Of the 187 survivors to whom the SIP was sent at 10 years, 74% (n=139) of the subjects returned the questionnaire. One questionnaire that was returned did not have an identification number on it making it unusable in the data analysis

TABLE 4-1: Baseline Characteristics of Subjects Enrolled into CSECR

	n	% or S.D.
Demographics (n=258)		
Age (years)	56.2	±8.4
Sex		
Male	219	84.9
Female	39	15.1
Race		
Caucasian	228	88.4
Other	30	11.6
Marital Status		
Married	209	81.0
Other	49	19.0
Clinical Variables (n=258)		
Digoxin when tested		
no	219	89.4
yes	26	10.6
Previous MI		
none	217	84.4
any	40	15.6
Hypertension		
no	149	58.0
yes	108	42.0
Angina		
no	160	63.5
yes	92	36.5
Exercise Test variables (n=245)		
Systolic blood pressure		
>/= 10mmHg	230	93.9
< 10mmHg	15	6.1
ST-segment depression		
no <1mm	200	81.6
yes >/= 1mm	45	18.4
ST-segment elevation		
no <1mm	217	88.6
yes >/= 1mm	28	11.4

of those who returned the questionnaire and is included as one that was not returned. Therefore, data of the remaining 138 subjects were used in the ten year analyses. Of the 120 subjects who did not return the SIP questionnaire, 59% subjects (n=71) died, 15% (n=18) declined to participate in the study follow-up interview and hence, were not sent the SIP, and 26%(n=31) did not return the questionnaire that was sent to them.

The baseline characteristics of the subjects who completed the SIP at each of the four data collection points are listed in Tables 4-2 and 4-3. The changes in sample sizes at the four data points were not due to progressive drop out of subjects; subjects who returned the SIP at each data point were not always a subset of those who returned the SIP at the previous data point. Therefore, statistical comparisons of the baseline characteristics were not valid. Visual inspection of the differences in the proportions across the subsets showed that the baseline characteristics do not appear to be different, although there appears to be a trend towards slightly better baseline clinical status in subjects who completed the SIP at 10 years (Table 4-3).

Analysis 1

The aim of the first analysis is as follows:

> To describe the quality of life over 10 years after an AMI including the overall quality of life, physical dimension, psychosocial dimension and 12 sickness-related behaviors (ambulation, mobility, body care and movement, emotional behavior, social interaction, alertness behavior, communication, working, recreational and pastimes, home management, sleep and rest, and eating.)

The analyses for Aim 1 were conducted on the SIP questionnaires returned during the four different data collection periods: at baseline, 3 and 6 months,

TABLE 4-2: Baseline Demographic Characteristics of Subjects
Completing SIP at Each Data Point

	Baseline		3 Month		6 Month		10 Year		All	
	n=245		n=217		n=206		n=138		n=119	
Variables	n or %		n or %		n or %		n or %		n or %	
Demographics										
Age (years)	56.2	± 8.5	55.8	±8.7	56.3	±8.2	56.1	±7.9	56.1	8.0
Sex										
Male	208	84.9	184	84.8	177	85.9	116	84.1	100	84.0
Female	37	15.1	33	15.2	29	14.1	22	15.9	19	16.0
Race										
Caucasian	218	89.0	193	88.9	184	89.3	126	91.3	109	91.6
Other	27	11.0	24	11.1	22	10.7	12	8.7	10	8.4
Marital Status										
Married	199	81.2	177	81.6	167	81.1	115	83.3	99	83.2
Other	46	18.8	40	18.4	39	18.9	23	16.7	20	16.8

Baseline → Within one week of entry into original study.

3 month, 6 month, 10 year = 3 months, 6 months, or 10 years after entry into originalstudy

All = Subjects who completed SIP at all four data points.

n = number of subjects who completed the SIP.

TABLE 4-3: Baseline Clinical and Exercise Test Characteristics of Subjects Completing SIP at Each Data Point

	Baseline		3 Month		6 Month		10 Year		All	
	n=245		n=217		n=206		n=138		n=119	
Clinical Variables	n or %		n or %		n or %		n or %		n or %	
Digoxin when tested										
no	213	90.3*	192	91.4*	178	89.4*	122	92.4*	107	89.9
yes	23	9.7	18	8.6	21	10.6	10	7.6	9	7.6
Previous MI										
no	209	85.3	185	85.3	176	85.4	127	92.0	111	93.3
yes	36	14.7	32	14.7	30	14.6	11	8.0	8	6.7
Hypertension										
no	138	56.3	126	58.1	119	57.8	85	61.6	69	58.0
yes	107	43.7	91	41.9	87	42.2	53	38.4	50	42.0
Angina										
no	153	64.0	138	65.4	134	66.7	99	73.3	90	75.6
yes	92	36.0	79	34.6	72	33.3	39	26.7	26	21.8
Exercise test variables	n=236		n=210		n=199		n=132		n=116	
Systolic blood pressure										
>/= 10 mmHg	222	94.1	198	94.3	188	94.5	129	97.7	113	95.0
< 10 mmHg	14	5.9	19	5.7	11	5.5	3	2.3	3	2.5
ST-segment depression										
no <1 mm	192	81.4	168	80.0	157	78.9	112	84.8	96	80.7
yes >/= 1mm	44	18.6	49	20.0	42	21.1	20.0	15.2	20	16.8
ST-segment elevation										
no <1 mm	210	89.0	189	90.0	177	88.9	121	91.7	106	89.1
yes >/= 1mm	26	11.0	21	10.0	22	11.1	11	8.3	10	8.4

*n=same as exercise variables

Baseline = Within one week of entry into original study.
3 month, 6 month, 10 year = 3 months, 6 months, or 10 years after entry into originalstudy
All = Subjects who completed SIP at all four data points.
n = number of subjects who completed the SIP.

and 10 years after AMI. The descriptive data for each data collection period are for all the questionnaires completed at that particular time period, with differing sample sizes.

The possible total, dimension, and category scores for the SIP can range from 0 to 100. The baseline distribution for the total SIP, Physical dimension, and the Psychosocial dimension scores are positively skewed with most of the scores near zero. Figures 4-1 and 4-2 illustrate the skewed distributions of the total SIP scores at the four data points due the frequent scores close to or equal to zero. The skewed distributions are similar to the distributions for the dimension, and category scores. This finding substantiates the need to utilize statistical analysis procedures which are appropriate for populations with skewed distributions.

The means of the scores obtained at each time period ranged from 4.04 to 5.25 for the total SIP score, 1.28 to 2.44 for the Physiological dimension, and 3.44 to 5.75 for the Psychosocial dimension. The lowest scores were obtained at 6 months in each case (Table 4-4). The minimum scores consistently were zero, representing no dysfunction. The maximum scores ranged from 4.04 to 5.25 for the SIP, 1.28 to 2.44 for the Physical Dimension, and 3.44 to 5.75 for the Psychosocial Dimension. The median scores were lower than the mean scores, ranging from 2.05 to 3.91 for the SIP, 0 to 0.84 for the Physical Dimension, and 0.98 to 1.7 for the Psychosocial Dimension. Since the mean and median scores are far apart, these data are very skewed. This is due to the high number of subjects with little or no dysfunction.

The scores of the twelve individual categories were also analyzed. The distribution of the scores were positively skewed with most scores ranging between zero and 20 (Table 4-5). Most of the medians of the categories were

Figure 4-1

Distribution of Total SIP Scores

at Baseline, 3 and 6 Months, and 10 Years (n=119)

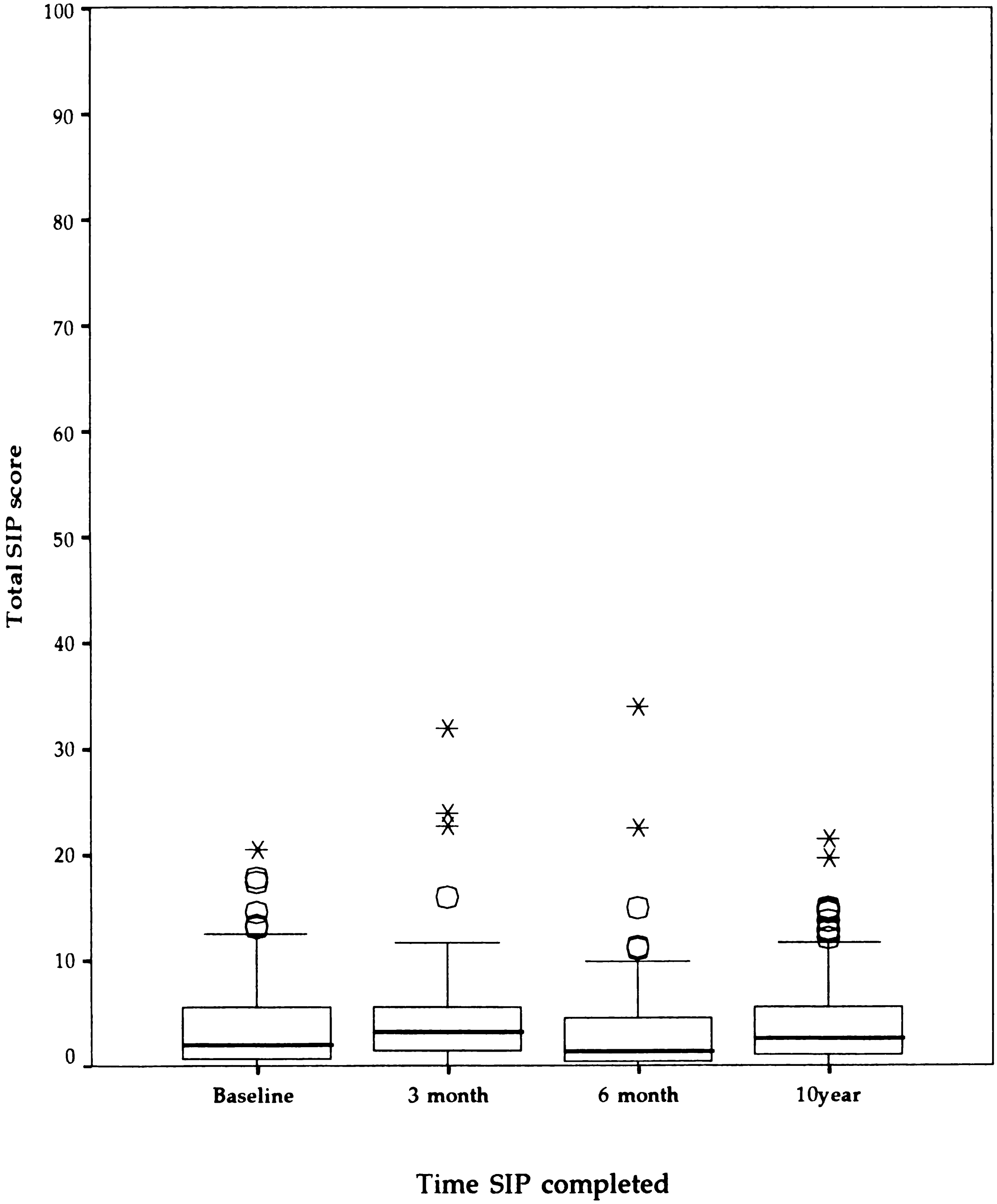


Figure 4-2

Frequency Distribution of SIP Score at Baseline

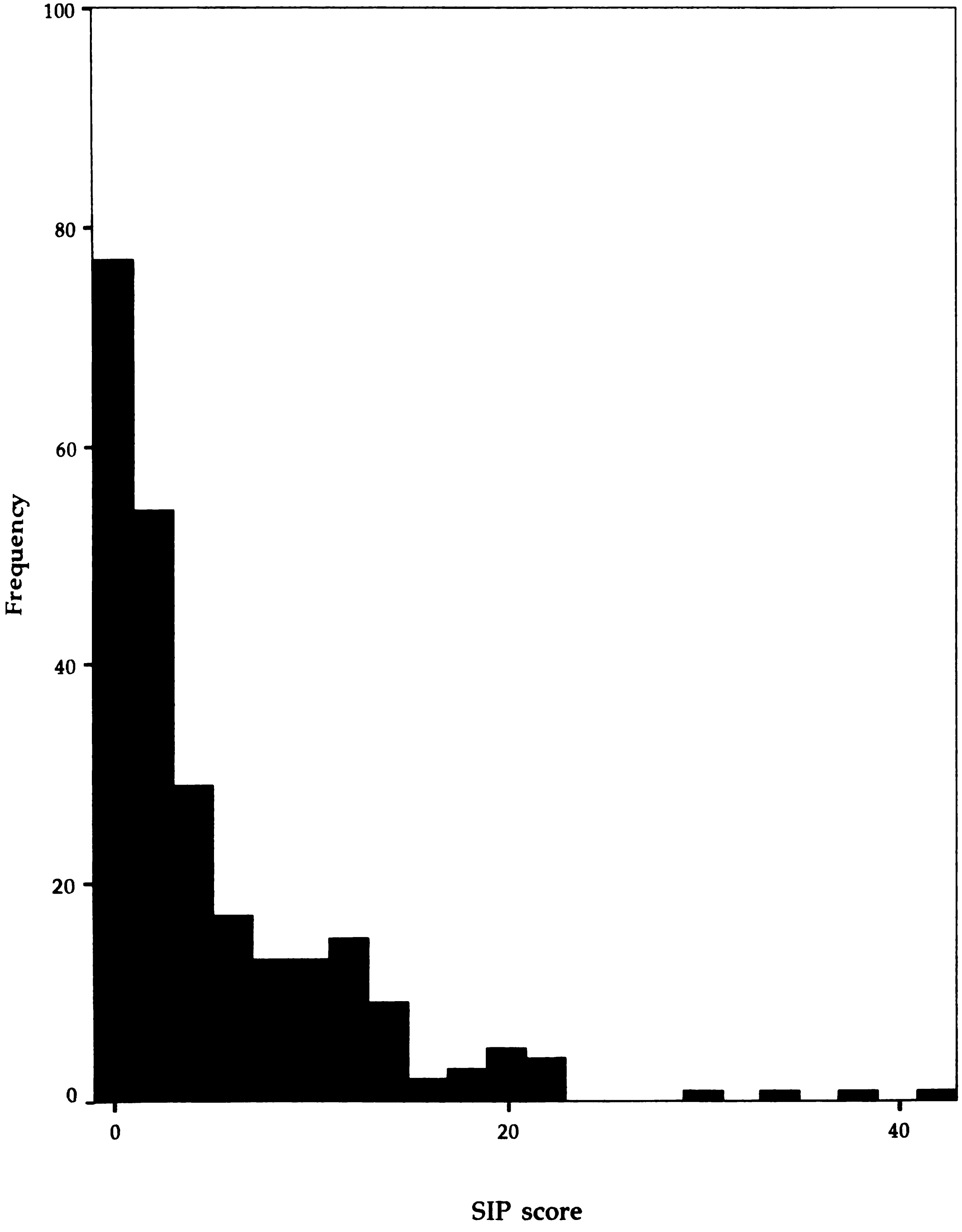


TABLE 4-4: SIP and Dimension Scores at Baseline, 3 Months, 6 Months, and 10 years

	Baseline n=245	3 Month n=217	6 Month n=206	10 Year n=138
SIP				
Mean	5.25	5.20	4.04	4.51
Standard Deviation	6.77	5.44	5.39	5.13
Median	2.54	3.91	2.05	2.86
Maximum	41.14	32.40	40.77	29.36
% with score > 0	79.2	92.6	87.4	88.4
Physical Dimension				
Mean	2.44	2.08	1.28	2.25
Standard Deviation	4.41	3.35	2.48	3.74
Median	0.00	0.84	0.00	0.00
Maximum	24.21	20.23	16.30	19.51
% with score > 0	44.9	50.7	40.3	48.6
Psychosocial Dimension				
Mean	5.75	3.81	3.44	3.78
Standard Deviation	9.25	7.16	7.50	6.19
Median	1.70	1.40	0.98	1.40
Maximum	52.48	49.82	62.90	38.42
% with score > 0	56.7	57.6	50.5	64.5

SIP = Sickness Impact Profile
Baseline = within one week of entry into original study.
3 month, 6 month, 10 year = time after entry into original study.

Table 4-5: Category Scores for Baseline, 3 Month, 6 Month and 10 Years

	Baseline n=245	3 month n=217	6 month n=206	10 year n=138
Sleep & Rest				
Mean	10.96	9.03	6.88	7.89
Std deviation	16.75	12.74	12.69	12.18
Median	9.82	0.00	0.00	0.00
Maximum	100.00	87.78	100.00	83.37
% with score > 0	50.40	48.90	38.40	45.70
Emotional Behavior				
Mean	6.97	3.93	3.47	3.92
Std deviation	10.63	9.60	9.228	7.99
Median	0.00	0.00	0.00	0.00
Maximum	48.23	60.43	80.57	40.00
% with score > 0	41.60	24.00	21.40	26.10
Body Care & Movement				
Mean	1.74	0.81	0.77	1.26
Std deviation	4.31	2.37	1.93	3.03
Median	0.00	0.00	0.00	0.00
Maximum	27.51	14.48	10.58	17.87
% with score > 0	27.80	18.00	18.40	22.50
Home Management				
Mean	6.88	10.32	5.97	5.61
Std deviation	11.16	12.00	10.96	9.64
Median	0.00	6.59	0.00	0.00
Maximum	75.90	57.49	77.1	63.02
% with score > 0	40.80	59.90	33.00	40.60
Mobility				
Mean	2.31	2.76	1.31	1.60
Std deviation	6.26	6.80	3.96	4.73
Median	0.00	0.00	0.00	0.00
Maximum	57.86	41.03	26.14	30.18
% with score > 0	19.20	19.80	12.60	15.20
Social Interaction				
Mean	6.01	4.88	4.19	4.50
Std deviation	10.34	8.68	8.82	7.49
Median	0.00	2.48	0.00	3.52
Maximum	78.07	75.52	75.52	48.76
% with score > 0	43.30	50.20	40.30	55.10

Table 4-5 (cont.): Category Scores for Baseline, 3 Month, 6 Month and 10 Years

		Baseline	3 month	6 month	10 year
		n=245	n=217	n=206	n=138
Ambulation					
	Mean	4.23	4.52	2.47	5.15
	Std deviation	7.07	7.01	5.07	8.70
	Median	0.00	0.00	0.00	0.00
	Maximum	30.88	35.39	29.45	40.14
	% with score > 0	33.90	40.60	26.70	39.90
Alertness Behavior					
	Mean	6.56	3.87	4.24	4.37
	Std deviation	16.58	11.48	13.14	8.80
	Median	0.00	0.00	0.00	0.00
	Maximum	100.00	90.35	100.00	53.54
	% with score > 0	25.30	18.00	17.50	28.30
Communication					
	Mean	3.16	1.49	1.05	1.60
	Std deviation	9.32	5.09	4.42	5.47
	Median	0.00	0.00	0.00	0.00
	Maximum	67.72	40.41	39.17	40.41
	% with score > 0	15.90	9.70	7.30	10.90
Work					
	Mean	10.70	17.02	14.96	17.07
	Std deviation	21.16	25.22	24.65	28.46
	Median	0.00	0.00	0.00	0.00
	Maximum	80.78	86.99	71.65	78.45
	% with score > 0	32.70	47.50	42.20	35.50
Recreation & Pastime					
	Mean	12.64	15.94	12.33	10.69
	Std deviation	18.33	17.35	16.50	15.47
	Median	0.00	10.19	8.18	7.82
	Maximum	80.10	80.10	76.78	70.85
	% with score > 0	46.30	63.60	51.90	50.70
Eating					
	Mean	2.90	5.59	4.26	3.46
	Std deviation	5.16	2.78	5.04	3.82
	Median	0.00	6.10	5.25	0.00
	Maximum	35.75	17.02	27.38	11.35
	% with score > 0	32.00	64.1	51.00	49.30

zero with the highest medians in Recreation and Pastime. The differences between the mean and median scores reflect the skewed distribution of the category scores. The proportion of subjects reporting any dysfunction in each category ranged from 7.3% (Communication at 6 months) to 59.9% (Home Management at 3 months). More commonly, 20% to 50% of the subjects reported some dysfunction in each category in every time period (Table 4-5).

Median scores were unchanged for all category scores at 6 months and 10 years except for social interaction, which increased at 10 years (more dysfunction), and Eating, which decreased at 10 years (less dysfunction). However, a greater proportion of subjects reported dysfunction in all categories at 10 years than at 6 months. At 10 years, the means of all category scores except Home Management, Recreation and Pastime, and Eating for the 138 subjects were higher than the means of the subjects completing the SIP at 6 months (n=206). The mean and median scores and proportion reporting dysfunction is higher in all categories (except Alertness Behavior) at 3 months than at 6 months demonstrating that further recovery takes place between 3 and 6 months after AMI.

Certain items were checked or endorsed frequently by subjects. Those endorsed by more than 10 percent of the subjects include items from the categories of Sleep and Rest (3 of 7 items), Home Management (3 of 10 items), Social Interactions (3 of 20 items), Ambulation (3 of 12 items), Alertness Behavior (1 of 10 items), Work (2 of 9 items), Recreation and Pastime (5 of 9 items), and Eating (2 of 9 items). The items suggest that individuals have decreased endurance for social activities, participating less in personal, family, and community activities. In addition, sleep and rest patterns are frequently altered (Table 4-6).

TABLE 4-6: SIP Categories and Items Endorsed by Greater Than 10 Percent of Subjects at 10 years

Category	Item No.	Item	yes (%)
Sleep and rest			
	2	I sit during much of the day.	11.6
	6	I sleep less at night, for example, wake up too early, don't fall asleep for a longtime, awake frequently.	26.1
	7	I sleep or nap more during the day.	18.1
Home management			
	1	I do work around the house only for short periods of time or rest often.	14.5
	2	I am doing less of the regular daily work around the house than I would usually do.	23.2
	9	I am not doing heavy work around the house.	25.4
Social Interaction			
	1	I am going out less to visit people.	14.5
	6	I am doing fewer social activities with groups of people.	16.7
	9	My sexual activity is decreased.	43.5
Ambulation			
	1	I walk shorter distances or stop to rest often	26.1
	2	I do not walk up or down hills.	10.9
	12	I walk more slowly.	29
Alertness Behavior			
	7	I forget a lot, for example, things that happened recently, where I put things, appointments.	16.7
Work			
	1	I am not working at all.	11.6
	5	I am working shorter hours.	11.6
Recreation & Pastime			
	1	I do my hobbies and recreation for shorter periods of time.	17.4
	2	I am going out for entertainment less often.	22.5
	5	I am doing more inactive pastimes in place of my other usual activities.	13.9
	6	I am doing fewer community activities.	13.8
	7	I am cutting down on some of my usual physical recreation or activities.	25.4
Eating			
	1	I am eating much less than usual.	13.8
	3	I am eating special or different food, for example, soft food, bland diet, low-salt, low-fat, low-sugar.	44.2

Analysis 2

To estimate the effect of three cardiac rehabilitation treatments used early after AMI on HRQOL in patients 10 years after AMI, the following null hypothesis was tested:

> Ho: There is no significant difference in the 10 year SIP scores between subjects in the three cardiac rehabilitation treatment groups (A, B1, and B2).

Subjects who completed the SIP at 10 years were included in this analysis (n=138). Of the 138 subjects, 46 were in Group A, 42 were in Group B1, and 50 were in Group B2. The baseline characteristics for the three groups were not significantly different (Table 4-7).

To measure the effect of three cardiac rehabilitation treatment groups on the SIP score at ten years, the Kruskal-Wallis test for several independent groups was conducted. When scores for the SIP, and Physical and Psychosocial dimensions were compared for Groups A, B1, and B2, no significant differences were found between the three groups (Table 4-8). Since cardiac rehabilitation treatments may have effects on particular areas of HRQOL, additional analyses were performed to determine whether there were group differences in the category scores. No significant differences were found. Therefore, the null hypothesis was not rejected.

This data set came from an original randomized clinical trial of three groups. There were no significant differences between the groups in the original study (except for social interaction). This research question was tested and there were no significant differences between groups at baseline or at 10 years. This justifies the pooling of the data across the three groups as one group in the analyses for the remaining research questions of the present study.

Table 4-7: Baseline Characteristics of Subjects in Treatment Groups at 10 Years

	Group A (n=84)		Group B1 (n=88)		Group B2 (n=86)		
Demographics	n	% or SD	n	% or SD	n	% or SD	
Age (years)	57.1	7.5	55.6	9.0	56.3	8.7	ns
Female	14	16.7	11	12.5	14	16.3	
Caucasian	76	90.5	77	87.5	75	87.2	ns
Married	68	81.0	72	81.8	69	80.2	ns
Clinical Variables							
Digoxin when tested							
No	69*	87.3	75*	89.3	75	91.5	ns
Yes	10	12.7	9	10.7	7	8.5	
Previous MI							
No	64	77.1	77	87.5	76	88.4	ns
Yes	20	22.9	11	12.5	10	11.6	
Hypertension							
No	48	57.8	50	56.8	51	59.3	ns
Yes	36	42.2	38	43.2	35	40.7	
Angina							
No	50	61.7	57	65.5	53	63.1	ns
Yes	34	38.3	31	34.5	33	36.9	
Exercise test variables	n=79		n=84		n=82		
Systolic blood pressure							
>/= 10mmHg	74	93.7	80	95.2	76	92.7	ns
< 10mmHg	5	6.3	4	4.8	6	7.3	
ST-segment depression							
no <1mm	63	79.7	69	82.1	68	82.9	ns
yes >/= 1mm	16	20.3	15	17.9	14	17.1	
ST-segment elevation							
no <1mm	73	92.4	71	84.5	73	89.0	ns
yes >/= 1mm	6	7.6	13	15.5	9	11.0	

*n=same as for exercise test variables

Table 11: Comparison of Group Differences in SIP at 10 Years
Using the Kruskal Wallis Test

	Group A mean rank*	Group B1 mean rank*	Group B2 mean rank*	Chi-Square	D.F.
SIP Total	68.51	69.04	70.80	0.0868	2
Physical Dimension	70.17	61.33	75.74	3.4542	2
Psychosocial Dimension	67.63	72.73	68.51	0.427	2
Categories:					
Sleep & Rest	64.77	72.67	71.19	1.1957	2
Emotional Behavior	69.86	72.83	66.37	1.0103	2
Body Care & Movement	68.98	65.31	73.50	1.8167	2
Home Management	68.23	69.12	70.99	0.1527	2
Mobility	69.48	69.21	69.76	0.0109	2
Social Interaction	71.14	72.49	65.48	0.9156	2
Ambulation	69.53	60.81	76.77	4.655	2
Alertness Behavior	67.01	66.24	74.53	1.9846	2
Communication	71.26	67.05	69.94	0.8681	2
Work	68.87	74.00	66.30	1.1943	2
Recreation & Pastime	66.78	70.29	71.34	0.3808	2
Eating	63.59	73.60	71.50	1.9015	2

* mean rank is calculated by ranking all observations as one group in ascending order. The mean of ranks of each treatment group is calculated.

Analysis 3

To determine whether there is a difference in the SIP scores at different time periods, the null hypothesis tested in analysis 3 is as follows:

> Ho: There is no significant difference between the total SIP score and Physical and Psychosocial Dimension scores obtained at 6 months and 10 years after AMI.

The subjects who completed the SIP at both 6 months and 10 years were included in this analysis of change over time. Of the 138 subjects who completed the SIP at 10 years, 121 of them completed the questionnaire at 6 months and 10 years. Of the 121 subjects who returned the SIP at both 6 months and 10 years, the mean age at entry to CSECR was 56.1 (±7.9) years, 83.5% (n=101) were male, 91.7% (n=111) were Caucasian, and 82.6% (n=100) were married. There were no significant differences in the baseline characteristics between subjects who returned the SIP and those who did not (n=137) (Table 4-9).

To compare the total SIP and dimension scores of the two data points, the Wilcoxon Matched-Pairs Sign test was performed on the scores of the 121 subjects. At ten years, there was a significant increase of the total SIP score ($p<0.01$) and Physical Dimension score ($p<0.0001$) compared to the six month score. The higher score indicates greater dysfunction. There was no statistically significant change in the Psychosocial Dimension score (Table 4-10). Therefore, the null hypothesis is rejected.

Additional analyses were performed, comparing data from all data collection points with each other. The six month score of the total SIP was significantly lower than the three month and ten year scores ($p<0.0001$ and $p<0.01$, respectively), indicating less dysfunction overall at six months among the survivors. The six month score of the Physical Dimension was

Table 4-9: Baseline Characteristics of Subjects Returning SIP at Both 6 Months and 10 Years

Demographics	Returned (n=121)		Not Returned (n=137)	
	n or SD		n or SD	
Age (years)	56.2	±8.4	56.2	±9.29
Sex				
Male	101	83.5	118	86.1
Female	20	16.5	19	13.9
Race				
Caucasian	111	91.7	117	85.4
Other	10	8.3	20	14.6
Marital Status	100	82.6	109	79.6
Married	21	17.4	28	20.4
Other				

Table 4-10: Comparison of Total SIP and Dimensions Scores
Using the Wilcoxon Matched-Pairs Sign Test

Comparison	n	z score	Significance	Differences in Scores
SIP Total score				
Baseline vs 3 month	213	-1.9163	p=0.055	Baseline worse than 3 month
Baseline vs 6 month	203	-1.8774	p=0.060	Baseline worse than 6 month
Baseline vs 10 year	134	-1.3544	ns	No difference
3 month vs 6 month	201	-6.5169	p<0.001	3 month worse than 6 month
3 month vs 10 year	127	-0.6613	ns	No difference
6 month vs 10 year	121	-2.7218	p<0.01	10 year worse than 6 month
Physical Dimension				
Baseline vs 3 month	213	-0.0376	ns	No difference
Baseline vs 6 month	203	-3.7220	p<0.005	Baseline worse than 6 month
Baseline vs 10 year	134	-1.0570	ns	No difference
3 month vs 6 month	201	-4.5093	p<0.001	3 month worse than 6 month
3 month vs 10 year	127	-1.4368	ns	No difference
6 month vs 10 year	121	-4.4063	p<0.001	10 year worse than 6 month
Psychosocial Dimension				
Baseline vs 3 month	213	-3.0416	p<0.005	Baseline worse than 3 month
Baseline vs 6 month	203	-0.4212	p<0.001	Baseline worse than 6 month
Baseline vs 10 year	134	-1.2577	ns	No difference
3 month vs 6 month	201	-0.1803	ns	No difference
3 month vs 10 year	127	-0.7661	ns	No difference
6 month vs 10 year	121	-1.6836	ns	No difference

significantly lower (less dysfunction) than at Baseline ($p<0.005$), three month ($p<0.0001$), and ten years ($p<0.0001$). The baseline Psychosocial Dimension score was significantly higher (more dysfunction) than at three months ($p<0.005$) and six months ($p<0.0001$). The results of these comparisons are in Table 4-10.

To test the proportions of subjects with improving or worsening dysfunction at each data collection point, the following null hypothesis was tested:

> Ho: There is no significant difference between the proportions of subjects that have worsening dysfunction and those with less dysfunction at each data collection period.

Data were analyzed with the McNemar test to examine the proportions of subjects that have greater or less dysfunction at one data point than another. As previously described, the SIP dimension score was dichotomized (dysfunction= SIP or dimension score> 0; no dysfunction=SIP or dimension score=0). Analysis with the McNemar test is based on the discordant pairs in a 2x2 table.

The results demonstrated statistically significant differences in several of the analyses. At 3 months, 6 months, and 10 years, a greater proportion of subjects' overall dysfunction worsened than improved when compared to baseline ($p<0.0001$, $p<0.05$, and $p<0.05$, respectively). At 6 months, the proportion of subjects who had improved physical dysfunction is greater than the proportion of subjects who had worsened when compared to the 3 month scores ($p<0.005$). At 10 years, a greater proportion of subjects' physical and psychosocial dysfunction had worsened than had improved when compared to 6 month scores ($p<0.05$, $p<0.005$, respectively) (Table 4-11).

Table 4-11: Comparison of Proportion of Subjects with Changes in Total SIP and Dimension Scores
McNemar Test

Comparison	n	Chi-square	Significance	Change
SIP Total Score				
Baseline vs 3 month	213	17.52	p<0.001	3 month worse
Baseline vs 6 month	203	5.69	p<0.05	6 month worse
Baseline vs 10 year	134	4.36	p<0.05	10 year worse
3 months vs 6 month	201	3.70	p=0.054	6 month improved
3 month vs 10 year	127		p=0.057	10 year improved
6 month vs 10 year	121	5.02	NS	no difference
Physical Dimension				
Baseline vs 3 month	213	2.88	NS	no difference
Baseline vs 6 month	203	0.55	NS	no difference
Baseline vs 10 year	134	1.88	NS	no difference
3 months vs 6 month	201	8.20	p<0.005	6 month improved
3 month vs 10 year	127	0.02	NS	no difference
6 month vs 10 year	121	5.02	p<0.05	10 year worse
Psychosocial Dimension				
Baseline vs 3 month	213	0.05	NS	no difference
Baseline vs 6 month	203	1.33	NS	no difference
Baseline vs 10 year	134	2.91	NS	no difference
3 months vs 6 month	201	3.70	p=0.055	6 month improved
3 month vs 10 year	127	3.44	p=0.06	10 yr worse
6 month vs 10 year	121	9.19	p<0.005	10 year worse

Analysis 4

To determine the predictive value of baseline clinical variables and exercise variables for the SIP at 10 years, the following null hypothesis was tested:

> Ho: In patients who have had an AMI, after controlling for age and gender, the clinical and exercise variables will not be independently predictive of SIP scores at 10 years.

Data of 138 subjects who completed the SIP questionnaire at 10 years were included in this analysis. The baseline characteristics of the 138 subjects have been previously described (Table 4-2).

Logistic regression analysis had been planned to test the null hypothesis. The dependent variable, SIP score at 10 years, was dichotomized to 0 for those subjects whose total SIP scores equaled zero and "1" for those subjects whose SIP scores were greater that zero. The predictor variables of the model used in this analysis were four baseline clinical (digoxin when tested, previous AMI, hypertension, and angina) and three exercise variables systolic blood pressure, ST-segment elevation, and ST-segment depression (Table 3-4). The model was adjusted for age and sex. All the variables were entered in a single step. However, this model for 138 subjects does not provide the necessary data for logistic regression. There were cells with insufficient number of observations in all variables except for hypertension. Therefore, logistic regression was not performed and further analysis of Aim 4 was discontinued.

Analysis 5

To estimate the prognostic value in the 6 month SIP score between patients who died and those who survived 10 years, the following null hypothesis was tested:

> Ho: There is no significant difference in the 6 month SIP score between patients who died and those who survived 10 years.

The data of the 206 subjects who completed the SIP at 6 months were used in this analysis. Of the 206 subjects, 76.7%(n=158) survived and completed the SIP (survivors) and 23.3% (n=48) had died by 10 years (non survivors). The baseline characteristics for the 206 subjects are listed in Table 4-2.

The Mann Whitney U test for parametric data was used to estimate the differences in the SIP 6 month scores between the survivors and the non survivors. In this statistical method, the scores for the 206 subjects are ranked in ascending order. A t statistic for the two independent groups of survivors versus the non survivors was determined, using the mean calculations for the ranks, not the original observations. There was a significantly higher total SIP score ($p<0.005$), and Physical dimension score ($p<0.05$) at six months among non-survivors compared to the survivors. The mean rank was consistently higher among the non survivors representing the presence of more dysfunction (Table 4-12). In addition, at three months, the total SIP score ($p<0.05$) and Physical Dimension score ($p<0.005$) were also significantly higher for non survivors than survivors.

Table 4-12: Comparison of Differences in 6 Month SIP Score Between Survivors and Nonsurvivors
Mann Whitney U Test

	Mean Rank			Signficance
	Nonsurvivors	Survivors	Z score	Corrected for ties
SIP				
Baseline	134.6	118.8	-1.55	ns
3 Months	124.6	104.4	-1.98	p<0.05
6 Months	124.9	97.0	-2.85	p<0.005
Physical Dimension				
Baseline	133.6	119.2	-1.54	ns
3 Months	130.5	102.7	-2.90	p<0.005
6 Months	117.9	99.1	-2.15	p<0.05
Psychosocial Dimension				
Baseline	124.3	122.5	-0.18	ns
3 Months	121.2	105.5	-1.60	ns
6 Months	115.5	99.8	-1.70	ns

To estimate the difference in the relative risk of death if a subject reports dysfunction at 6 months, the following null hypothesis was tested:

> Ho: There is no significant relationship between the six month SIP score and the risk for death by 10 years (risk ratio = 1).

Using an odds ratio method, the vital status of subjects at ten years (dead or alive) was the outcome variable and the SIP and dimension scores at each data collection period were the predictor variables. Subjects who survived ten years were "controls" and were recoded "0" and those who were deceased at ten years were "cases" recoded "1". The SIP and dimension scores at six months were recoded to "0" if the score equaled zero and "1" if the score was greater than zero.

The number of subjects evaluated at each data collection period varied with data of 245 subjects available at baseline, 217 at three months, and 206 at six months. Baseline characteristics have previously been described (Table 4-2).

The results demonstrate that if a subject has a Physical Dimension score at three months that is greater than zero (dysfunction present), the estimated relative risk that the subject will be dead by ten years is 1.17 (CI=1.03-1.37), a small beut significant difference. There is no statistically significant risk of death when a subject reports dysfunction for the total SIP, Physical or Psychosocial Dimension at the other data collection periods (Table 4-13).

Table 4-13: Relative Risk of Death by 10 Years with Dysfunction at Baseline, 3 Months, or 6 Months

	Relative Risk	95% Confidence Bounds	
SIP			
Baseline	1.12	0.95	1.32
3 months	0.80	0.54	1.17
6 months	1.11	0.93	1.35
Physical Dimension			
Baseline	1.11	0.95	1.30
3 months	1.18	1.02	1.37
6 months	1.13	0.96	1.33
Psychosocial Dimension			
Baseline	1.00	0.86	1.16
3 months	1.12	0.97	1.29
6 months	1.15	0.99	1.35

n: Baseline=245; 3 month=217; 6month=206

Analysis 6

To estimate the effects of the 6 month scores of the SIP on death, the following null hypothesis was tested:

> Ho: In patients who have had an AMI, after controlling for age and gender, the SIP scores and clinical and exercise test variables will not be independently predictive of subsequent death.

The subset of data evaluated in this analysis included data from the 206 subjects who completed the SIP at six months. Baseline characteristics of these subjects have previously been described (Table 4-2). To answer the research question, multivariate analyses with Cox regression analysis were performed on several models. Various models were constructed in this study with the choice of the models guided by the sample size since the standard recommendation is to have at least ten subjects for ever variable (Lee, 1992). The models included the total SIP, dimension, and category scores and the baseline clinical and exercise test variables. The outcome of interest was death from all causes. The results of the analyses are presented in the tables with the following format: the estimated beta coefficient, the standard error for the coefficient, the hazards ratio, and the 95% confidence intervals. The results are given in Tables 4-14 through 4-20 for the models using death from all causes as the outcome.

Model I:

In the first model, the total SIP score at six months was plotted against the outcome death from all causes. There were 48 non-censored values and 158 censored values. The log likelihood (LL) chi square statistic was obtained by multiplying the difference between the LL chi-square for the initial model and the current model by two. The overall chi-square, entering the appropriate degrees of freedom, was used to obtain a p-value and tested the null hypothesis that all the hazards are proportional. Model I had a significant chi-square of 11.57 ($p<0.01$) and thus, the null hypothesis was rejected (Table 4-14).

Among the three variables in Model I, the 6 month SIP score was a statistically significant predictor of increased risk of death after AMI. Age when the subjects were enrolled into the original study (62-70 years vs 30-61 years) also had a statistically significant association with increased risk of death. This association with age is expected when examining the risk of death over ten years. Sex was not associated with increased risk of death.

Model II

Model II included the Physical Dimension scores corrected for age and sex. There were 48 non-censored values and 158 censored values. The significant chi-square indicated that the global model is significant and the null hypothesis was rejected ($p<0.005$) (Table 4-15). Of the three variables, the 6 month Physical Dimension score was a statistically significant predictor of increased risk of death. Age when the subjects were enrolled into the original study (62-70 years vs 30-61 years) also had a statistically significant association with increased risk of death.

Model III

Model III included the 6 month Psychosocial Dimension scores corrected for age and sex. There were 48 non-censored values and 158 censored values. The chi-square was not significant indicating that the global model was not significant, and the null hypothesis was not rejected (Table 4-16). Of the three variables, the 6 month Psychosocial Dimension score had a borderline association with an increased risk of death. Age when the subjects were enrolled into the original study (62-70 years vs 30-61 years) also had a

Table 4-14: Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Total SIP Score at 6 Months

				95% CI	
Model I Variables	B	S.E.	Exp(B)	Lower	Upper
SIP, total	0.046	0.017	1.047	1.012	1.083
Age	0.584	0.296	1.793	1.004	3.199
Sex	0.440	0.475	1.553	0.612	3.942

Note: 48 non-censored values, 158 censored values.
Global chi-square = 11.565, df = 3, $p < 0.01$

Table 4-15: Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Physical Dimension Scores at 6 Months

				95% CI	
Model II Variables	B	S.E.	Exp(B)	Lower	Upper
Physical Dimension	0.119	0.040	1.126	1.04	1.22
Age	0.613	0.297	1.846	1.03	3.30
Sex	0.510	0.474	1.665	0.66	4.22

Note: 48 non-censored values, 158 censored values.
Global chi-square = 13.106, df = 3, $p<0.005$

Table 4-16: Estimates of Coefficients, Hazard Ratios, and Confidence Intervals for Psychosocial Dimension Scores at 6 Months

				95% CI	
Model III Variables	B	S.E.	Exp(B)	Lower	Upper
Psychosocial Dimension	0.184	0.141	1.019	0.99	1.05
Age	0.560	0.295	1.750	0.93	3.12
Sex	0..4549	0.475	1.576	0.62	4.00

Note: 48 non-censored values, 158 censored values.
Global chi-square = 6.033, df = 3, p=ns

B = beta coefficient; S.E. = standard error of the coefficient; Exp(B) = hazards ratio
CI = confidence intervals

borderline association with increased risk of death in this model. Sex was not associated with increased risk of death.

Model IV

Model IV included the five remaining category scores that are included in the SIP (Sleep and Rest, Home Management, Work, Recreation and Pastime, and Eating). The model was adjusted for age and sex. There were 48 non-censored values and 158 censored values. The significant chi-square indicated that the global model was significant, and the null hypothesis was rejected ($p<0.001$) (Table 4-17). In this model, Home Management and Work categories were statistically significant predictors of increased risk of death. Sleep and Rest and Eating scores had borderline associations. Age and sex were not associated with increased risk of death.

Model V

Model V was made up of the twelve individual categories of the SIP at 6 months, with the scores entered simultaneously and corrected for age and sex (Table 4-18). The significant chi-square indicates that the regression coefficients for this model are not all simultaneously equal to zero and the null hypothesis should be rejected ($p<0.001$). Home Management, Mobility, and Work were statistically significant predictors of death. Sleep and Rest, Social Interaction, and Eating had borderline statistically significant association. The categories of Sleep and Rest, Emotional Behavior, Body Care and Movement, Social Interaction, Ambulation, Alertness Behavior, Communication, Recreation and Pastime, and Eating were not statistically significant predictors of death. Age had a borderline statistically significant association with increased death rate for subjects 62 to 70 years old.

Table 4-17: Estimates of Coefficients, Hazard Ratios, and Confidence Intervals
5 Category Scores at 6 Months

				95% CI	
Model IV Variables	B	S.E.	Exp(B)	Lower	Upper
Sleep and Rest	0.005	0.010	1.005	0.986	1.024
Home Management	0.038	0.013	1.039	1.013	1.066
Work	0.015	0.006	1.015	1.003	1.028
Recreation and Pastime	-0.031	0.014	0.969	0.943	0.996
Eating	0.040	0.028	1.041	0.985	1.100
Age	0.513	0.301	1.670	0.926	3.010
Sex	0.733	0.493	2.082	0.792	5.472

Note: 48 non-censored values, 158 censored values.
Global chi-square = 27.717, df = 7, p<0.0005

Table 4-18: Estimates of Coefficients, Hazard Ratios, and Confidence Intervals
12 Category Scores at 6 Months

				95% CI	
Model V Variables	B	S.E.	Exp(B)	Lower	Upper
Sleep and Rest	0.013	0.015	1.013	0.984	1.042
Emotional Behavior	-0.008	0.023	0.992	0.948	1.039
Body Care & Movement	-0.110	0.092	0.896	0.748	1.074
Home Management	0.044	0.018	1.045	1.01	1.081
Mobility	0.110	0.046	1.117	1.021	1.221
Social Interaction	0.038	0.023	1.039	0.992	1.087
Ambulation	0.019	0.033	1.019	0.0955	1.088
Alertness Behavior	-0.062	0.028	0.940	0.890	0.992
Communication	0.03	0.044	1.03	0.945	1.123
Work	0.015	0.007	1.015	1.002	1.029
Recreation and Pastime	-0.036	0.016	0.964	0.935	0.994
Eating	0.032	0.029	1.032	0.975	1.093
Age	0.61	0.316	1.841	0.991	3.421
Sex	0.409	0.517	1.505	0.546	4.148

Note: 48 non-censored values, 158 censored values.
Global chi-square = 40.656, df = 14, p<0.0005

B = beta coefficient; S.E. = standard error of the coefficient; Exp(B) = hazards ratio
CI = confidence intervals

Model VI: Clinical variables and SIP

Model VI included four clinical variables (digoxin, previous AMI, hypertension, and angina), and the total SIP score at 6 months, corrected for age and sex (Table 4-19). The significant chi-square indicates that the global model was significant and the null hypothesis should be rejected ($p<0.001$). Examination of individual statistics demonstrates that digoxin, previous AMI, and angina had statistically significant associations with higher death, with

previousAMI being the best predictor. The total SIP score at 6 months was not significant. In this model, higher age upon entry to CSECR had a borderline statistically significant association with increased risk of death.

Model VII: Combined Clinical and Exercise Variables and SIP

The last model of this survival analysis included a combination of four clinical variables (digoxin, previous AMI, hypertension, and angina), three exercise variables (systolic blood pressure, ST-segment depression, and ST-segment elevation), and the total SIP score at 6 months. In addition, age and sex were controlled.

The significant chi-square indicates that the global model was significant and the null hypothesis should be rejected ($p<0.001$) (Table 4-20). The variables of previous AMI, angina, systolic blood pressure, and ST-segment depression were statistically significant predictors of increased death rates. Previous AMI was the best predictor, followed by systolic blood pressure, ST-segment depression, and angina, respectively. Digoxin, hypertension, ST-segment elevation, and the total 6 month scores of the SIP did not have statistically significant associations with increased death rates. Age and sex were not significant.

TABLE 4-19: Estimates of Coefficients and Hazards Ratio for Clinical Variables and SIP at 6 Months

Model VI Variables	B	S.E.	Exp(B)	95% CI Lower	Upper
Digoxin	0.831	0.417	2.294	1.014	5.192
Previous MI	1.603	0.334	4.969	2.580	9.570
Hypertension	0.373	0.311	1.453	0.789	2.673
Angina	1.079	0.317	2.940	1.578	5.477
SIP, total, 6 months	0.193	0.614	1.213	0.365	4.038
Age	0.634	0.333	1.884	0.982	3.617
Sex	-0.219	0.502	0.804	0.301	2.149

44 non censored values, 150 censored values
Global chi-square = 56.27, df = 7, p < 0.000

TABLE 4-20: Estimates of Coefficients and Hazards Ratio for Exercise Variables, Clinical Variables, and SIP at 6 Months

Model VII Variables	B	S.E.	Exp(B)	95% CI Lower	Upper
Digoxin	0.785	0.450	2.193	0.908	5.296
Previous MI	1.596	0.351	4.934	2.480	9.817
Hypertension	0.493	0.336	1.637	0.848	3.162
Angina	1.011	0.326	2.749	1.452	5.203
Systolic blood pressure	1.251	0.491	3.492	1.335	9.138
ST-segment depression	1.122	0.344	3.070	1.564	6.026
ST-segment elevation	0.716	0.516	2.046	0.744	5.627
SIP, total, 6 months	0.028	0.618	1.028	0.306	3.454
Age	0.414	0.358	1.512	0.750	3.051
Sex	-0.074	0.536	0.929	0.325	2.656

44 non censored values, 150 censored values
Global chi-square = 73.76, df = 10, p < 0.000

B = beta coefficient; S.E. = standard error of the coefficient; Exp(B) = hazards ratio
CI = confidence intervals

Summary of Results

Multiple analyses of 258 subjects from the original data set of the CSECR were performed on various subsets of the subjects. The distribution of all SIP scores (total, dimensions, categories) were positively skewed towards zero. The means were higher than the medians. The 6 months mean and median scores were frequently lower than at baseline, 3 months, and 10 years.

Comparison of the SIP data between the treatment groups subjects were randomized to at entry to the original study (A, B1, and B2) showed there were no statistically significant differences between the groups. Therefore, the subjects of the treatment groups were pooled for subsequent data analyses.

Comparisons of various pairings of SIP scores from the four data collection periods demonstrated statistically significantly worse overall dysfunction (total SIP score) at 3 months and 10 years than at 6 months. Physical dysfunction was worse at baseline, 3 months, and 10 years than at 6 months. Psychosocial dysfunction was worse at baseline than at 3 and 6 months.

A statistically significant proportion of subjects had worsening in scores rather than improving overall dysfunction at 3 months, 6 months, and 10 years when compared with baseline ($p<0.05$). There was a borderline significant proportion of subjects with improving scores than those with worsening scores at 6 months and 10 years when compared with 3 months ($p=0.055$). At 6 months, more subjects had scores indicating less physical dysfunction than at 3 months and 10 years ($p<0.005$). More subjects had greater psychosocial dysfunction at 10 years than at 6 months ($p<0.005$). There was a borderline significant proportion of subjects with improved psychosocial dysfunction at 6 months when compared to 3 months ($p=0.055$).

There was a borderline significant proportion of subjects with worsened psychosocial dysfunction at 10 years when compared to 3 months (p=0.06).

Analysis was attempted to determine whether clinical and exercise test variables had an association with the 10 year SIP scores. However, there were insufficient data to complete the analysis, and the analysis was abandoned.

Comparisons of baseline, 3 month, and 6 month SIP scores between subjects survivors and non survivors were made. The total SIP and Physical Dimension scores at 3 and 6 months were significantly different between the survivors and non survivors. Analysis with odds ratio demonstrated an increased relative risk of dying with a Physical Dimension score greater than zero at three months.

The results of survival analyses showed that the total SIP and Physical dimension scores at 6 months were predictive of increased death rate when corrected for age and sex. Age also had an association with increased death rate in those models. The Psychosocial Dimension had a borderline association with increased risk of death. When the model included the five remaining category scores which comprise the SIP, Home Management and Work categories were statistically significant predictors of increased death rate. Sleep and Rest and Eating scores had a borderline association.

The twelve individual categories were placed in a model with age and sex resulting in Home Management, Mobility, and Work statistically significantly predictive of increased death rate. Borderline associations were seen with Sleep and Rest, Social Interaction, Eating, and Age. In the model including the clinical and exercise test variables and the SIP score at 6 months, previous AMI, angina, systolic blood pressure and ST-segment depression were statistically significant predictors of increased death rate, but the 6 month total SIP score was not.

CHAPTER 5: DISCUSSION AND CONCLUSIONS

The major purposes of the study were to describe health-related quality of life over ten years after AMI and to determine whether HRQOL of life was predictive of mortality. The study was a secondary analysis of data from the CSECR, a randomized controlled study designed to determine the effects of early exercise and teaching and counseling after AMI (Sivarajan et al, 1981, Sivarajan et al, 1982, Sivarajan et al, 1983). A ten year follow-up study was conducted to determine predictors of mortality for the subjects. Health-related quality of life data were collected at all four data collection points during the original and ten year follow-up study.

The sample of subjects enrolled into the CSECR represents a group of patients who had a confirmed AMI without complications early after AMI and did not have physical limitations prior to the AMI. The age of the study subjects at follow-up must be 66±7.9 years (range 43-80) since their mean age at entry to the original study was 56 ± 7.9 years (range 33-70). The age at entry to CSECR was lower than the mean age of patients at the time of the first AMI that is reported in the literature. In a cohort of 5209 men and women followed in the Framingham Study since 1948, investigators found that the mean age at the time of the first AMI was 63.8± 10.1 years in men and 69.5± 10 years in women (Cupples, Gagnon, Wong, Ostfeld, and Kannel, 1993). The difference is possibly due to the criteria for entry into CSECR. Because the ability to return to work was one of the outcomes of CSECR, the investigators excluded subjects who were over 70 years and may not be eligible for returning to work. In addition, subjects could not have complications after the AMI nor physical limitations which may have excluded other older subjects. The study had a significantly higher percentage of men (84.9%) than the typical population of patients with AMI. This was not unusual for the early studies in terms of male to female ratio of AMI patients. This also may be explained by the exclusion of subjects over 70 years, a subset of patients that contain more women than in earlier years. The small number of women precluded seperate comparisons of men versus women. To control for any potential differences by age and gender, the variables were included as covariates in multivariate analyses. In addition, the sample was predominantly Caucasian (88%) due to the population of eligible patients where the original study was conducted. The ethnic distribution was, however, representative of the Seattle area demographics at that time. Thus, the results of the study need to be interpreted cautiously when attempting to generalize to populations other than Caucasian men.

The primary salient feature of this study which distinguish it from previous studies is that it is one of the first prospective longitudinal studies to follow HRQOL over a period greater than one year in a population of AMI patients. Health-related quality of life after AMI previously has not been described over the course as long as ten years. In addition, the association of HRQOL with long-term survival after AMI is a new finding. A particularly distinguishing feature of the study is the knowledge of the vital statistic (survival versus death) over ten years for each of the original 258 subjects.

Changes in Health-Related Quality of Life over Ten Years After AMI

The purpose of the original study was to determine if there were differences between the three treatment groups who were assigned to control, exercise only, or exercise and education and counseling after AMI. The results of the current study did not find any differences between the groups when the SIP scores at 10 years were compared allowing pooling of data across the three groups. The current study analyzed the differences between the category scores using a nonparametric analysis of variance test (Kruskal Wallis test), rather than evaluating the proportion of subjects with changes in their category scores, as was done in the previous study (Ott et al., 1983). While the previous analysis found statistically significant improvements in one group's scores in two categories (Eating and Social Interaction), the current study did not find significant differences between the three groups in any of the twelve categories. An explanation for the lack of previously reported difference is that the early effect of an education-counseling intervention is diluted by changes in subjects over a period of ten years. In addition, the increased practice and public awareness of the benefits of dietary discretion for all individuals may affect the scores in the Eating category.

This study provides the first view of HRQOL after AMI over the course of the illness. In the recovery period after AMI, subjects report the lowest amount of overall and physical dysfunction at 6 months after an AMI compared to the other data collection points. This difference may be due to several factors. It is possible that the change in scores were due to the selection of subjects who were very ill or who had died. However, the statistical analysis was conducted on matched pairs of scores, thus avoiding unequal comparisons. More likely it represents the gradual resumption of physical activities which may be initially restricted by an individual's physician, family, or by the hesitation of the patient after the life threatening illness. Subjects gradually returned to previous levels of activity with most returning to work, sexual activity, driving, and activities outside the home by 6 months (Froelicher et al., 1994). Seventy-four percent had returned to their previous maximum activity level by 6 months. Gulanick, Kim, and Holm (1991) documented that patients resume home activities at different paces after AMI and coronary artery bypass surgery, making substantial progress by four weeks and further recovery by nine weeks.

The results also identified higher levels of psychosocial dysfunction at baseline than 3 and 6 months. The original study required the subject to complete the baseline SIP within one week after entering into the study, with instructions to answer the items in relation to the week prior to admission. Since many patients often have premordial symptoms that result in patients being anxious and upset immediately after an AMI, it is difficult to determine whether the higher psychosocial dysfunction found at baseline was reflective of dysfunction prior to the AMI or whether it was contaminated by the psychological stress during the initial hospitalization. It is well documented that after having a life threatening illness such as an AMI, many patients experience many extremes in mood and behavior (Byrne & Whyte, 1978; Fraser-Smith, Lesperance, & Talajic, 1993, 1995; Froese et al., 1974; Stern et al., 1977). The current emotional state of an individual can influence the report of HRQOL particularly when recall is required.

The HRQOL issues of concern change as the patient moves from the acute stage of an AMI through recovery. The focus shifts from issues of emotional behaviors, sleep and rest, and physical discomfort during the acute stages of AMI to mobility, physical and social functioning during the later recovery stages. The findings that higher levels of dysfunction are reported earlier than 6 months identify greater needs for patients in the early recovery period after AMI, between discharge and 3 months, and have implications for cardiac rehabilitation programs and case management.

When the proportions of subjects that report changes in scores are examined, the results are not unexpected. A larger proportion of subjects report worsened overall HRQOL at all data points after the AMI than at baseline. This finding is consistent with the substantial changes in health and lifestyle that occur after having an AMI. A larger proportion of subjects report improved physical and psychosocial functioning at 6 months when compared with 3 months. A possible explanation for this finding is that most individuals experience a gradual physical and psychosocial recovery process that continues over the first year after AMI.

In this study, the level of dysfunction measured with the SIP increased over 10 years since it was last measured at 6 months after AMI. The SIP scores at 10 years were higher and a larger proportion of subjects reported worsening physical dysfunction at that time period. The findings are not surprising given length of time that had passed. The findings may reflect the changes that occur with the normal progression of CAD over ten years. Another possible explanation may be that greater dysfunction was reported at ten years due to recurrence of symptoms to subjects who had undergone revascularization procedures. Results of previous studies showed that HRQOL and symptoms of CAD were not significantly different in patients with different treatments for CAD (CABG, PTCA, or medical treatment) after five to ten years (BARI Investigators, 1997; Rogers et al, 1990).

Age is a likely influencing factor in the changes in HRQOL reported by the subjects ten years after AMI. This study found age to be predictive of mortality over ten years, a finding similar to other studies (Adams & Marano, 1995; Herlitz, Bang, Sjolin, Karlson, 1996). While older populations include individuals with wider variations of health and quality of life than younger populations, aging itself does not imply lower quality of life (Mulrow, Gerety, Cornell, Lawrence, & Kanten, 1994). However, it is known that with increasing age, disability and mortality from CAD as well as other medical ailments rises (Adams and Marano, 1995). It is possible that the differences in the ten year SIP scores are related to the increasing disability and worsening health of the aging of the study population.

While the findings that HRQOL changes over time after AMI may not be unexpected, longitudinal studies following HRQOL after AMI over an extended period of time have not previously reported this information. Literature on narrower focused aspects of HRQOL such as physical or psychosocial recovery from AMI is available. It is reported that most subjects returned to their normal activities by six months (Dennis et al, 1988; Froelicher et al., 1994). However, measures of resumption of activities alone without assessment of the HRQOL that the patient is experiencing gives a limited view of recovery and health.

There have been changes in treatment of patients with AMI since the mid-1970's when the patients were enrolled into the study. Different medications and more aggressive interventions, such as PTCA and CABG, in the acute phase after AMI, are more available for treatment and the recommended treatment of choice (Ryan et al., 1996). However, the trajectory of HRQOL would probably have a similar pattern albeit with a shortened recovery time. It is possible that the early benefits of PTCA on HRQOL reported in the literature could have an earlier impact on the SIP scores that were obtained in this study. Nevertheless, patients still undergo dramatic changes in their physical and psychosocial health that will affect their HRQOL after an AMI. Long term HRQOL outcomes have been shown to not be significantly different over five to ten years after the various interventions (BARI Investigators, 1997; Rogers et al, 1990). The extent to which these trends in aggressive medical and surgical interventions would influence 10 year prognosis and follow-up of HRQOL remains an urgent research agenda in this era of outcomes research and heightened consciousness of patient quality of life.

HRQOL as a Predictor for Increased Risk of Mortality

This study identified HRQOL as a predictor for increased risk of mortality over ten years after AMI. Many studies have evaluated clinical cardiovascular conditions as predictors of mortality in patients with AMI (Cupples, Gaggnon, Wong, Ostfeld, & Kannel, 1993; GISSI-3 APPI Study Group, 1996; Herlitz, Bang, Sjolin, & Karlson, 1996). However, few studies systematically examine the relationship between HRQOL and mortality.

Three statistical analyses were conducted comparing differences between subjects who survived ten years and completed SIP at the data collection point under examination (survivors) and those who died (non survivors). Each analyses identified differences between the survivors and non survivors. Overall SIP and Physical Dimensions scores of non survivors were found to be statistically significantly higher at 3 and 6 months than the survivors. In addition, the relative risk of dying over 10 years after AMI was statistically significant if a subject had any physical dysfunction at 3 months. Multivariate survival analyses determined that dysfunction as measured by the 6 month scores of the SIP, Physical dimension, and the SIP categories of Home Management, Mobility, and Work were predictive of the outcome of death over 10 years, when adjusted for age and sex. The items for the three categories reflect activity limitations and endurance and appear to be primarily functional in nature, corresponding to the significance of the Physical Dimension. However, it is possible that there is also a psychosocial component influencing an individual's functional status. Psychosocial Dimension had a borderline association with increased risk of death. There were also borderline associations in Sleep and Rest, Social Interaction, and Eating.

The SIP was not predictive when entered into model with clinical variables for a total of ten covariates. The significance of age also changed when placed in a model with the model with twelve covariates. This may be due to the inadequate sample size for the number of covariates in the model. However, despite the large number of covariates in the model for the sample size, ST-elevation and previous AMI were predictive of increased risk for death.

It can be argued that the results correspond with the well documented increased risk of death in patients with low ejection fraction. While researchers have shown that reduced ejection fraction and heart failure have been shown to be related to increased risk of death (Cupples, Gaggnon, Wong, Ostfeld, & Kannel, 1993; Herlitz, Bang, Sjolin, & Karlson, 1996), it also has been documented that psychosocial factors, such as depression or social isolation, are predictors of death after AMI (Ruberman, Weinblatt, Goldberg, & Chaudhary, 1984; Frasure-Smith, Lesperance, & Talajic, 1993; Frasure-Smith, Lesperance, & Talajic, 1995). Researchers studying a population of patients with low ejection fractions (<35%) found an association of HRQOL with increased risk of mortality in the subjects (Konstam et al, 1996). In univariate analysis, they found that activities of daily living, general health, and social functioning were predictors of relative risk of mortality ($p<0.05$). In multivariate analysis, they found that congestive heart failure symptoms and the domains of "activities of daily living" and "general health" predicted increased risk of mortality in the patient population, with no difference between the groups randomized to medication or placebo. In addition, other researchers have found no relationship between ejection fraction and measures of HRQOL in heart failure patients (Dracup, Walden, Stevenson, & Brecht, 1992). This supports the use of HRQOL instruments to identify factors that cannot be accounted for by clinical measures.

The population of patients with congestive heart failure are potentially subsets of the current study sample. While the findings of Konstam et al (1996) and the current study are difficult to compare due to the different instruments used to measure HRQOL and the patient populations, there are similarities in the nature of the domains found to be predictive of relative risk for mortality.

Other studies identified additional factors, such as socioeconomic factors and social isolation, which affect mortality (Mark et al, 1992; Jenkinson, Madeley, & Turner, 1993). While it is possible to measure various HRQOL domains separately, it is difficult to determine where the relationships between the domains overlap. With the complexity of human nature and behavior, instruments that only measure individual domains of HRQOL cannot replace comprehensive measurement of HRQOL.

Sensitivity of the Sickness Impact Profile to Change

As a result of this study, the sensitivity of the SIP to change was examined. This was the first study which used the SIP over a ten year period. Critics have questioned the ability of the SIP to detect changes (MacKenzie, Charlson, DiGioia & Kelley, 1986). In this study, the SIP detected consistent changes in the subject population over three months and ten years time. deBruin, deWitte, Stevens & Diederiks (1992) suggested that the instrument may not be sensitive to small daily changes, but is better at reflecting changes occurring over longer periods of time. The sensitivity of the SIP to changes over shorter periods of time was not tested in this study. Given the tendency of the scores to be skewed, changes can be detected with the SIP provided the appropriate nonparametric statistical procedure is utilized.

Conclusions

The findings of this study support the conclusion that:

1. Most subjects report worsening HRQOL after AMI.
2. HRQOL at 6 months is better, with less dysfunction, than at 3 months and 10 years after AMI.
3. Physical dysfunction is better at 6 months than at baseline, 3 months, and 10 years after AMI.
4. Psychosocial dysfunction was worse at baseline than at 3 and 6 months.
5. More subjects report worsening psychosocial dysfunction at 10 years.
6. HRQOL at 6 months after AMI, as measured by the SIP, is predictive of increased risk of death. Specifically, the total SIP, Physical Dimension, Home Management, and Work scores and age are strong predictors, when controlling for the effects of age and sex.
7. The Sickness Impact Profile questionnaire is sensitive to change over time.

Clinical and Policy Implications

The findings of this study have clinical implications in the care of patients with AMI. This study identified lower HRQOL during early recovery from AMI and ten years later. These findings suggest that HRQOL early in recovery after AMI can provide information on the overall course and prognosis of patients.

Increased understanding of the course of recovery after AMI provides clinicians with knowledge to utilize resources at times most beneficial to patients. More psychosocial support, financial resources for rehabilitation, and interventions that could have a positive influence on the ratings of HRQOL. In addition, the study identified an increased risk of death with lower HRQOL ratings. The increased risk of death over ten years with lower HRQOL points to the need for clinicians to provide interventions at appropriate times that could potentially improve the HRQOL and survival. Further research is needed to identify the interventions that can have an impact on HRQOL and, thus, survival.

The findings of this study can be used in the decision making process for utilization of health care resources. Policy makers can use the results to identifying the optimal time to provide financial, personnel, and educational resources to the AMI population. The results of the survival analyses supply evidence for targeting populations with high mortality with resources.

Another major implication of this study is that it provides clinicians and researchers with evidence that HRQOL is useful in assessing course outcome. Many have debated the utility of HRQOL in patient outcomes, however, the results of this carefully designed longitudinal study justify the belief that patient reports of HRQOL provide meaningful information that can be used towards determining patient outcome. In addition, the significance of HRQOL as measurement of patient outcome will be recognized.

Strengths and Limitations

The present study was a secondary analysis of an existing data set. The advantage of using an available data set was to answer research questions pertaining to HRQOL over ten years without the cost and time normally required. However, inherent limitations are also posed with its use.

Randomization in CSECR was conducted to minimize the possibility of selection bias. Survival bias due to loss to follow-up was a concern due to the length of follow-up. The 10 year follow-up study was not in the CSECR plans. However, in the follow-up study, the status (alive versus dead) of every subject who had entered the CSECR in 1977 was identified 10 years later. Every subject who was alive at ten years was asked to participate in the follow-up study involving an interview and completion of the SIP. While some subjects refused to participate or did not return the SIP, 74% of the subjects alive at 10 years completed and returned the SIP. It is of note that 100% follow-up was available for vital status.

Recall bias was an issue during the collection of the baseline SIP data. Subjects were asked to answer the SIP at baseline pertaining to the week before hospital admission. Although recall may be influenced by the stress of the illness and hospitalization, it was considered necessary to obtain a measure to determine the patient's function before admission as a baseline and to allow evaluation of patients' during subsequent assessments. Recall bias can be assumed to be equal across all three group assignments, thus allowing a fair comparison. Administration of the SIP was done as soon after enrollment as possible to ensure the best recall.

Using an existing data set limits the data to those collected for the primary purpose of the original study. In the CSECR, HRQOL was one of the primary interests of the investigators as evidenced by the quality of the data collection techniques and the quantity of data available. The decision to use the SIP demonstrates thorough investigation by the principal investigators of the original study into HRQOL. The SIP is presently one of the few instruments to have undergone years of extensive and successful testing for reliability, validity, and clinical validity.

The fixed data set did not account for changes in technology and treatment that have become available over the ten years. Data on diagnostic procedures and technological and therapeutic interventions were collected by patient report, rather than from medical records. The association of various treatments on HRQOL would be of great interest in this study population. In addition, it would be of interest to determine the changes in dysfunction that occur after 6 months and before 10 years in patient after AMI. However, the original study was not designed to obtain that information.

Future Research

The data from the secondary data set served to answer the primary study questions. However, future studies that include a more representative sample of patients with AMI with more women and other ethnic groups are needed.

This study address changes in HRQOL between 6 months and 10 years after AMI. Systematic measures of HRQOL at yearly intervals may be very informative in any future planned study of this kind. In this study, HRQOL was found to be predictive of mortality. Future research is needed to identify and develop interventions to affect HRQOL in the AMI population and subsequently affect mortality.

REFERENCES

Abbott J. & Berry N. (1991). Return to work during the year following first myocardial infarction. British Journal of Clinical Psychiatry, 30:268-270.

Adams, P. F. & Marano, M.A. (1995). Current Estimates From the National Health Interview Survey, 1994. National Center for Health Statistics. Vital and Health Statistics, 10(193).

Ahlmen, E. M., Bengtsson, C. B., Sullivan, B. M., & Bjelle, A. (1990). A comparison of overall health between patients with rheumatoid arthritis and a population with and without rheumatoid arthritis. Scandinavian Journal of Rheumatology, 19(6), 413-21.

Arfvidsson, B, Karlsson, J., Dahllof, A. G., Lundholm, K., & Sullivan, M. (1993). The impact of intermittent claudication on quality of life evaluated by the Sickness Impact Profile technique. European Journal of Clinical Investigation, 23(11), 741-745.

Bergner, L., Bergner, M., Hallstrom, A. P., Eisenberg, M., & Cobb, L. A. (1984). Health status of survivors of out-of-hospital cardiac arrest six months later. American Journal of Public Health, 74(5), 508-10.

Bergner, L., Hallstrom, A. P., Bergner, M., Eisenberg, M. S., & Cobb, L. A. (1985). Health status of survivors of cardiac arrest and of myocardial infarction controls. American Journal of Public Health, 75(11), 1321-3.

Bergner, M. (1985). Measurement of health status. Medical Care. 23(5), 696-704.

Bergner, M. (1989). Quality of life, health status, and clinical research. Medical Care, 27(3 supplement), S148-S156.

Bergner, M., Bobbitt, R. A., Carter, W. B., & Gilson, B. S. (1981). The Sickness Impact Profile: Development and final revision of a health status measure. Medical Care, 19(8), 787-805.

Bergner, M., Bobbitt, R. A., Kressel, S., Pollard, W. E., Gilson, B. S., & Morris, J. R. (1976). The Sickness Impact Profile: Conceptual formulation and methodology for the development of a health status measure. International Journal of Health Services, 6(3), 393-415.

Bergner, M., Bobbitt, R. A., Pollard, W. E., Martin, D. P., & Gilson, B. S. (1976). The sickness impact profile: validation of a health status measure. Medical Care, 14(1), 57-67.

Bergner, M. & Rothman, M. L. (1987). Health status measures: An overview and guide for selection. Annual Review of Public Health, 8:191-210.

Bertie J., King A., Reed N., Marshall A. J., & Ricketts C. (1992). Benefits and weaknesses of a cardiac rehabilitation programme. Journal of the Royal College of Physicians of London, 26:147-151.

Berzon, R., Hays, R. D., & Shumaker, S. A. (1993). International use, application, and performance of health-related quality of life instruments. Quality of Life Research, 2, 367-368.

Bliley, A. V. & Ferrans, C. E. (1993). Psychologic aspects of cardiovascular care: Quality of life after coronary angioplasty. Heart and Lung, 22(3), 193-199.

Booth, D. C., Deupree, R. H., Hultgren, H. N., DeMaria, A. N., Scott, S. M., & Luchi, R. J. (1991). Quality of life after bypass surgery for unstable angina. 5-year follow-up results of a Veterans Affairs Cooperative Study [see comments]. Circulation, 83(1), 87-95.

Burgess, A. W., Lerner, D. J., D'Agostino, R. B., Vokonas, P. S., Hartman, C. R., & Gaccione, P. (1987). A randomized control trial of cardiac rehabilitation. Social Science and Medicine, 24, 359-370.

Bypass Angioplasty Revascularization Investigation (BARI). (1997). Five-year clinical and functional outcome comparing bypass surgery and angioplasty in patients with multivessel coronary disease. Journal of the American Medical Association, 277(9), 715-721.

Byrne, D. G. (1982). Psychological responses to illness and outcome after survived myocardial infarction: A long term follow-up. Journal of Psychosomatic Research, 26, 105-112.

Byrne, D. G. & Whyte, H. M. (1978). Dimensions of illness behavior in survivors of myocardial infarction. Journal of Psychosomatic Research, 22, 485-491.

CASS Principal Investigators and their Associates. (1983). Coronary Artery Surgery Study (CASS): A randomized trial of coronary artery bypass surgery. Quality of life in patients randomly assigned to treatment groups. Circulation, 68(5), 951-960.

Cassem N. & Hackett T. (1973). Psychological rehabilitation of myocardial infaction patients in the acute phase. Heart and Lung, 2: 383-388.

Clark, N. M., Janz, N. K., Becker, M. H., Schork, M. A., Wheeler, J., Liang, J., Dodge, J. A., Keteyian, S., Rhoads, K. L., & Santinga, J. T. (1992). Impact of self-management education on the functional health status of older adults with heart disease. Gerontologist, 32(4), 438-43.

Conn, V. S., Taylor, S. G., & Wiman, P. (1991). Anxiety, depression, quality of life, and self-care among survivors of myocardial infarction. Issues in Mental Health Nursing, 12(4), 321-331.

Cowan, M. J., Young Graham, K., & Cochrane, B. L. (1992). Comparison of a theory of quality of life between myocardial infarction and malignant melanoma: A pilot study. Progress in Cardiovascular Nursing, 7(1),18-28.

Croog, S. H. (1983). Recovery and rehabilitation of heart patients: Psychsocial aspects. In D. S. Krantz, A. Baum, & J. E. Singer (Eds.), Handbook of Psychology and Health, Volume III (pp.295-334).

Croog, S. H., Levine, S., Testa, M. A., Brown, B., Bulpitt, C. J., Jenkins, C. D., Klerman, G. L., & Williams, G. H. (1986). The effects of antihypertensive therapy on the quality of life. New England Journal of Medicine, 314(26), 1657-1664.

Cunny, K. A. & Perri, M. (1991). Single-item vs multiple-item measures of health-related quality of life. Psychological Reports, 69(1), 127-130.

Cupples, L. A., Gagnon, D. R., Wong, N. D., Ostfeld, A. M., & Kannel, W. B. (1993). Preexisting cardiovascular conditions and long-term prognosis after initial myocardial infarction: The Framingham Study. American Heart Journal, 125(3), 863-872.

Damiano, A. M. (1996). The Sickness Impact Profile: User's Manual and Interpretation Guide. Baltimore: John Hopkins University, Department of Health Policy and Management.

Dennis C., Houston-Miller N., Schwartz R. G., Ahn D. K., Kraemer H. C., Gossard D., Juneau M., Taylor B., DeBusk R. F. (1988). Early return to work after uncomplicated myocardial infarction. Journal of American Medical Association, 260: 214-220.

Deyo, R. A. & Diehl, A. K. (1983). Measuring physical and psychosocial function in patients with low-back pain. Spine, 8(6), 635-642.

Deyo, R. A., Inui, T. S., Leininger, J., & Overman, S. (1982). Physical and psychosocial function in rheumatoid arthritis. Clinical use of a self-administered health status instrument. Archives in Internal Medicine, 142(5), 879-82.

Deyo, R. A., Inui, T. S., Leininger, J. D., & Overman, S. S. (1983). Measuring functional outcomes in chronic disease: A comparison of traditional scales and a self-administered health status questionnaire in patients with rheumatoid arthritis. Medical Care, 21(2), 180-192.

Dracup, K., Walden, J. A., Stevenson, L. W., & Brecht, M. (1992). Quality of life in patients with advanced heart failure. Journal of Heart and Lung Transplantation, 11(2 Part1), 273-279.

Drossman, D. A., Patrick, D. L., Mitchell, C. M., Zagami, E. A., & Appelbaum, M. I. (1989). Health-related quality of life in inflammatory bowel disease. Functional status and patient worries and concerns. Digestive Disease and Science, 34(9), 1379-86.

Engle, G. L. (1977). The need for a new medical model: A challenge for biomedicine. Science, 196(4286), 129-136.

Faller, H. (1990). Coping with myocardial infarction: A cognitive-emotional perspective. Psychotherapy and Psychosomatics, 54(1), 8-17.

Faris, J. A. & Stotts, N. A. (1990). The effect of percutaneous transluminal coronary angioplasty on quality of life. Progress in Cardiovascular Nursing, 5(4), 132-140.

Fleiss, J. L. (1981). Statistical Methods for Rates and Proportions. 2nd Edition. New York: Wiley.

Fletcher, A. E., Hunt, B. M., & Bulpitt, C. J. (1987). Evaluation of quality of life in clinical trials of cardiovascular disease. Journal of Chronic Diseases, 40(6), 557-566.

Frasure-Smith, N., Lesperance, F., & Talajic, M. (1993). Depression following myocardial infarction. Impact on 6-month survival. Journal of American Medical Association, 270(15), 1819-1825.

Frasure-Smith, N., Lesperance, F., & Talajic, M. (1995). Depression and 18-month prognosis after myocardial infarction. Circulation, 91(4), 999-1005.

Froelicher, E. S. (1994). Usefulness of exercise testing shortly after acute myocardial infarction for predicting 10-year mortality. American Journal of Cardiology, 74(4), 318-323.

Froelicher, E. S. (1996). Tracing patients with myocardial infarction for a 10-year follow-up study. Nursing Research, 45(6), 341-344.

Froelicher, E. S., Kee, L. L., Newton, K. M., Lindskog, B., & Livingston, M. (1994). Return to work, sexual activity, and other activities after acute myocardial infarction. Heart and Lung, 23(5),423-435.

Froese, A., Hackett, T. P., Cassem, N. H., & Silverberg, A. (1974). Trajectories of anxiety and depression in denying and nondenying acute myocardial infarction patients during hospitalization. Journal of Psychosomatic Research, 18(6), 113-120.

Gilson, B. S., Gilson, J. S., Bergner, M., Bobbitt, R. A., Kressel, S., Pollard, W. E., & Vesselago, M. (1975). The Sickness Impact Profile: Development of an outcome measure of health care. American Journal of Public Health, 65(12), 1304-1310.

GISSI-3 APPI Study Group. (1996). Early and six-month outcome in patients with angina pectoris early after acute myocardial infarction (the GISSI-3 APPI [angina precoce post-infarcto] study). American Journal of Cardiology, 78(11), 1191-1197.

Gorkin L., Norvell, N. K., Rosen, R. C., Charles, E., Shumaker, S. A., McIntyre, K. M., Capone, R. J., Kostis, J., Niaura, R., Woods, P., Hosking, J., Garces, C., Handberg, E., Ahern, D. K., & Follick, M. J. (1993). Assessment of quality of life as observed from the baseline data of the studies of left ventriuclar dysfunction (SOLVD) trial quality-of-life substudy. American Journal of Cardiology, 71(12), 1069-1073.

Grady, K. L., Jalowiec, A., Grusk, B. B., White-Williams, C., & Robinson, J. A. (1992). Symptom distress in cardiac transplant candidates. Heart and Lung, 21(5), 434-439.

Greenfield, S. & Nelson, E. C. (1992). Recent developments and future issues in the use of health status assessment measures in clinical settings. Medical Care, 30(5 Supplement), MS23-MS41.

Gruentzig, A. R., King, S. B. III, Schlumpf, M., & Siegenthaler, W. (1987). Long-term follow-up after percutaneous transluminal coronary angioplasty. New England Journal of Medicine, 316(18), 1127-1132.

Gulanick, M., Kim, M., & Holm, K. (1991). Resumption of home activities following cardiac events. Progress in Cardiovascular Nursing, 6, 1-8.

Guyatt, G. H., Feeny, D. H., & Patrick, D. L. (1991). Issues in quality-of-life measurement in clinical trials. Controlled Clinical Trials, 12(4 Supplement), 81S-90S.

Guyatt, G. H., Van Zantan, S. J. O. V., Feeny, D. H., & Patrick, D. L. (1989). Measuring quality of life in clinical trials: A taxonomy and review. CMAJ, 140, 1441-1448.

Guyatt, G., Walter, S., & Norman, G. (1987). Measuring change over time: Assessing the usefulness of evaluative instruments. Journal of Chronic Diseases, 40(2), 171-178.

Hackett, T. P., Cassem, N. H., & Wishnie, H. A. (1968). The coronary care unit: An appraisal of its psychological hazards. New England Journal of Medicine. 279, 1365-1370.

Hasley, P. B., Brancati, F. L., Rogers, J., Hanusa, B. H., & Kapoor, W. N. (1993). Measuring functional change in community-acquired pneumonia. Medical Care, 31(7), 649-657.

Hellerstein H. K., Friedman E. H. (1970). Sexual activity and the postcoronary patient. Archives of Internal Medicine, 125(6), 987-999.

Herlitz, J., Bang, A., Sjolin, M., Karlson, B. W. (1996). Five-year mortality after acute myocardial infarction in relation to previous history, level of initial care, complications in hospital, and medication at discharge. Cardiovascular Drugs and Therapy, 10(4), 485-490.

Herzog, A. R. & Rodgers, W. L. (1986). Satisfaction among older adults. In F. M. Andrews (Ed.) Research on the Quality of Life (pp. 235-251). Ann Arbor: University of Michigan.

Hoffman, D., Rice, D., & Sung, H. Y. (1996). Persons with chronic conditions. Journal of the American Medical Association, 276(18), 1473-1479.

Holmes, D. R., Van Raden, M. J., Reeder, G. S., Vlietstra, R. E., Geun, C. J., Kent, K. M., Vetrovec, G. W., Cowley, M. J., Dorros, G., Kelsey, S. F., Detre, K. M., & Mock, M. B. (1984). Return to work after coronary angioplasty: A report from the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. American Journal of Cardiology, 53(12), 48C-51C.

Jenkins, C. D., Stanton, B., Savageau, J. A., Denlinger, P., & Klein, M. D. (1983). Coronary artery bypass surgery. Physical, psychological, social, and economic outcomes six months later. Journal of the American Medical Association, 250(6), 782-788.

Jenkinson, C. M., Madeley, R. J., Mitchell, J. R. A., & Turner, I. D. (1993). The influence of psychosocial factors on survival after myocardial infarction. Public Health, 107(5), 305-317.

Kannel, W. B. & Belanger, A. J. (1991). Epidemiology of heart failure. American Heart Journal, 121(3 Part 1), 951-957.

Kannel, W. B. & Thom, T. J. Incidence, prevalence, and mortality of cardiovascular disease. In Schlant, R. C. & Alexander, R. W. (Eds.), The Heart (pp. 185--197). New York: McGraw Hill..

Kaplan, R. M. & Anderson, J. P. (1987). In S. R. Walker & R. Rosser (Eds.), Quality of Life: Asssessment and Application (pp. 51-77). Boston: MTP Press Ltd.

Karnofsky, D. A., Abelmann, W. H., Craver, L. F., and Burchenal, J. H. (1948). The use of the nitrogen mustards in the palliative treatment of cardinoma. Cancer, 1:634-655.

Katz, S., Ford, A. B., Moskowitz, R. W., Jackson, B. A., & Jaffe, M. (1963). Studies of illness in the aged. Journal of the American Medical Association, 185(12), 914-919.

King, K. B., Porter, L. A., Norsen, L. H., & Reis, H. T. (1992). Patient perceptions of quality of life after coronary artery surgery: Was it worth it? Research in Nursing and Health, 15(5), 327-334.

Kinney, M. R., Burfitt, S. N., Stullenbarger, E., Rees, B., DeBolt, M. R. (1996). Quality of life in cardiac patient research: A meta-analysis. Nursing Research, 45(3), 173-180.

Kirshner, B. & Guyatt, G. (1985). A methodological framework for assessing health indices. Journal of Chronic Diseases, 38(1), 27-36.

Konstam, V., Salem, D., Pouler, H., Kostis, J., Gorkin, L., Shumaker, S., Mottard, I., Woods, P. Konstam, M. A., Yusuf, S. (1996). Baseline quality of life as a predictor of mortality and hospitalization in 5,025 patients with congestive heart failure. American Journal of Cardiology, 78(8), 890-895.

Kornfield, D. S., Heller, S. S., Frank, K. A., wilson, S. M., & Malm, J. R. (1982). Psychological and behavioral responses after coronary artery bypass surgery. Circulation, 66, 24-28.

Lee, E. T. (1992). Statistical Methods for Survival Data Analysis. 2nd Edition. John Wiley & sons, Inc: New York.

Levin, L. A. & Jonsson, B. Cost-effectiveness of thrombolysis - a randomized study of intravenous rt-PA in suspected myocardial infarction. European Heart Journal, 13(1), 2-8.

Levine, S., & Croog, S. H. (1984). What constitutes quality of life? A conceptualization of the dimensions of life quality in healthy populations and patients with cardiovascular disease. In N. K. Wenger, M. E. Mattson, C. D. Furberg, J. Elison (Eds.), Assessment of Quality of Life in Clinical Trials of Cardiovascular Therapies (pp. 46-58). LeJacq Publishers.

Lichter, I. Richardson, P. J., Wyke, M. A. (1984). Differential effects of atenolol and enalapril on tests of memory during treatment for essential hypertension. Journal of Hypertension, 2, 560.

Lown, B. & DeSilva, R. A. (1978). Rates of physiologic stress and autonomic nervous system changes in provocation of ventricular premature complexes. American Journal of Cardiology, 41(6), 979-985.

MacKenzie,C. R., Charlson, M. E., DiGioia, D., and Kelly, K. (1986). Can the Sickness Impact Profile measure change? An example of scale assessment. Journal of Chronic Diseases, 39(6), 429-438.

Mann S., Yates J. E., & Raftery E. B. (1981). The effects of myocardial infarction on sexual activity. Journal of Cardiac Rehabilitation, 1:187-192.

Mark, D. B., Lam, L. C., Lee, K. L., Clapp-Channing, N. E., Williams, R. B., Pryor, D. B., Califf, R. M., & Hlatky, M. A. (1992). Identification of patients with coronary disease at high risk for loss of employment. Circulation, 86(5), 1485-1494.

Mayou, R. Foster, A., & Williamson, B. (1978). Psychosocial adjustment in patients one year after myocardial infarction. Journal of Psychosomatic Research, 22(5), 447-453.

McDowell, I. & Newell, C. (1987). Measuring Health: A Guide to Rating Scales and Questionnaires. New York: Oxford University Press.

McKenna, K. T., McEniery, P. T., Maas, F., Aroney, C. N., Bett, J. H. N., Cameron, J., Holt, G. & Hossack, K. F. (1994). Percutaneous transluminal coronary angioplasty: Clinical and quality of life outcomes one year later. Australian and New Zealand Journal of Medicine, 24(1), 15-21.

Meenan, R. F., Gertman, P. M., & Mason, J. H. (1980). Measuring health status in arthritis. Arthritis and Rheumatism, 23(2), 146-152.

Mulrow, C. D., Gerety, M. B., Cornell, J. E., Lawrence, V., A., & Kanten, D. N. (1994). The relationship between disease and function and perceived health in very frail elders. Journal of American Geriatric Society, 42(4), 374-380.

Najman, J. M. & Levine, S. (1981). Evaluating the impact of medical care and technologies on the quality of life: A review and critique. Social Science and Medicine, 15F(2/3), 107-115.

New York Heart Association Criteria Committee. (1979). Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. Boston: Little & Brown.

O'Rourke, R. A. (1994). Chest pain. In Schlant, R. C. & Alexander, R. W. (Eds.) The Heart (pp. 459-467). New York: McGraw Hill.

Ott, C. R., Sivarajan, E. S., Newton, K. M., Almes, M. J., Bruce, R. A., Bergner, M., & Gilson, B. S. (1983). A controlled randomized study of early cardiac rehabilitation: the Sickness Impact Profile as an assessment tool. Heart and Lung, 12(2), 162-70.

Papadantonaki, A., Stotts, N. A., & Paul, S. M. (1994). Comparison of quality of life before and after coronary artery bypass surgery and percutaneous transluminal angioplasty. Heart and Lung, 23(1), 45-52.

Papadopoulos C. (1978). A survey of sexual activity after myocardial infarction. Cardiovascular Medicine, 3:821-826.

Papadopoulos C. Sexual Aspects of Cardiovascular Disease. New York: Praeger Publishers. 1989.

Parisi, A. F., Folland, E. D., & Hartigan, P. (1992). A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. New England Journal of Medicine, 326(1), 10-16.

Patrick, D. L. & Erickson, P. (1987). Assessing health-related quality of life for clinical decision making. In S. R. Walker & R. Rosser (Eds.) Quality of Life: Asssessment and Application (pp. 9-49). Boston: MTP Press Ltd.

Peduzzi, P., Hultgren, H., Thomsen, J., & Detre, K. (1987). Ten-year effect of medical and surgical therapy on quality of life: Veterans Administration Cooperative Study of Coronary Artery Surgery. American Journal of Cardiology, 59(12), 1017-1023.

Philip, A. E., Cay, E. L., Vetter, N. J., & Stuckey, N. A. (1979). Short-term fluctuations in anxiety in patients with myocardial infarction. Journal of Psychosomatic Research, 23(4), 277-280.

Pollard, W. E., Bobbitt, R. A., Bergner, M., Martin, D. P., & Gilson, B. S. (1976). The Sickness Impact Profile: Reliability of a health status measure. Medical Care, 15(2), 146-155.

Read, J. L. (1987). The new era of quality of life assessment. In S. R. Walker & R. Rosser (Eds.) Quality of Life: Asssessment and Application (pp. 1-8). Boston: MTP Press Ltd.

Rector, T. S. & Cohn, J. N. (1992). Assessment of patient outcome with the Minnesota Living with Heart Failure questionnaire: Reliability and validity during a randomized, double-blind, placebo-controlled trail of pimobendan. American Heart Journal, 124(4), 1017-1025.

Rice, S. & Miller, M. D. (1990). Developing a model for the study of quality of life in elderly patients with chronic disease: Use of hypertension as an example. Southern Medical Journal, 83(8), 941-946.

Rizzuto, C. (1983). Psychosocial problems in congestive heart failure: Health care implications. In C. R. Michaelson, Ed. Congestive Heart Failure. St. Louis: Mosby. pp. 378-399.

Rockey, P. H. & Griep, R. J. (1980). Behavioral dysfunction in hyperthyroidism. Archives in Internal Medicine, 140(9), 1194-1197.

Rogers, W. J., Coggin, J., Gersh, B. J., Fisher, L. D., Myers, W. O., Oberman, A., & Sheffield, L. T. (1990). Ten-year follow-up of quality of life in patients randomized to receive medical therapy or coronary artery bypass graft surgery. Circulation, 82(5), 1647-1658.

Rogers, W. J., Johnstone, D. E., Yusuf, S., Weiner, D. H., Gallagher, P., Bittner, V. A., Ahn, S., Schron, E., Shumaker, S. A., & Sheffield, L. T. (1994). Quality of life among 5,025 patients with left ventricular dysfunction randomized between placebo and enalapril: The Studies of Left Ventricular Dysfunction. Journal of American College of Cardiology, 23(2), 393-400.

Rosenblum, D. S., Rosen, M. L., Pine, Z. M., Rosen, S. H., & Borg, S. J. (1993). Health status and quality of life following cardiac transplantation [published erratum appears in Arch Phys Med Rehabil 1993 Jul;74(7):701]. Archives of Physical Medicine and Rehabilitation, 74(5), 490-3.

Ruberman, W., Weinblatt, E., Goldberg, J. D., & Chaudhary, B. S. (1984). Psychosocial influences on mortality after myocardial infarction. New England Journal of Medicine, 311(9), 552-9.

Saeterhaug A. & Nygaard, P. (1989). Early discharge and early rehabilitation and return to work after acute myocardial infarction. Journal of Cardiopulmonary Rehabilitation, 7:268-272.

Scalzi, C. C. & Burke, L. E. (1989). Sexual counseling. In S. L. Underhill, S. L. Woods, E. S. Froelicher, C. J. Halpenny (Eds.). Cardiac Nursing. 2nd edition. Philadelphia: Lippincott.

Schrier, A. C., Dekker, F. W., Kaptein, A. A., & Dijkman, J. H. (1990). Quality of life in elderly patients with chronic nonspecific lung disease seen in family practice. Chest, 98(4), 894-899.

Schulman, S. P. & Weisfeldt, M. L. (1994). Cardiovascular aging and adapation to disease. In Schlant, R. C. & Alexander, R. W. (Eds.) The Heart (pp. 2067-2076). New York: McGraw Hill.

Seidl, A., Bullough, B., Haughey, B., Scherer, Y., Rhodes, M., & Brown, G. (1991). Understanding the effects of a myocardial infarction on sexual functioning: A basis for sexual counseling. Rehabilitation Nursing, 16, 255-264.

Sherbourne, C. D. (1992). Social functioning: Social activity limitations measure. In A. L. Stewart & J. ZE. Ware (Eds.), Measuring Functioning and Well-Being (pp. 182-193). Durham: Duke University Press.

Sherbourne, C. D. & Kamberg, C. J. (1992). Social functioning: Sexual problems measures. In A. L. Stewart & J. ZE. Ware (Eds.), Measuring Functioning and Well-Being (pp. 182-193). Durham: Duke University Press.

Sherbourne, C. D., Stewart, A. L., & Wells, K. B. (1992). Role functioning measures. In A. L. Stewart & J. ZE. Ware (Eds.), Measuring Functioning and Well-Being (pp. 205-234). Durham: Duke University Press.

Shipper, H., Clinch, J. J., Olweny, C. L. M. (1996). Quality of life studies: Definitions and conceptual issues. In B. Spilker (Ed.) Quality of Life and Pharmacoeconomics in Clinical Trials. Philadelphia: Lippincott-Raven.

Shock, N. W., Greulich, R. C., Andres, R., Arenberg, D., Costa, P. T., Lakatta, E. G., & Tobin, J. D. (1984). Normal Human Aging: The Baltimore Longitudinal Study of Aging. Washington D. C.: U. S. Department of Health and Human Services.

Simoons, M. L., Vos, J., Martens, L. L. (1991). Cost-utility analysis of thrombolytic therapy. European Heart Journal, 12(6), 694-699.

Sivarajan, E. S., & Bruce, R. A. (1981). Early exercise testing after myocardial infarction. Cardiovascular Nursing, 17(1), 1-5.

Sivarajan, E. S., Bruce, R. A., Almes, M. J., Green, B., Belanger, L., Lindskog, B. D., Newton, K. M., & Mansfield, L. W. (1981). In-hospital exercise after myocardial infarction does not improve treadmill performance. New England Journal of Medicine, 305(7), 357-62.

Sivarajan, E. S., Bruce, R. A., Lindskog, B. D., Almes, M. J., Belanger, L., & Green, B. (1982). Treadmill test responses to an early exercise program after myocardial infarction: a randomized study. Circulation, 65(7), 1420-1428.

Sivarajan, E. S., & Newton, K. M. (1984). Exercise, education, and counseling for patients with coronary artery disease. Clinical Sports and Medicine, 3(2), 349-369.

Sivarajan, E. S., Newton, K. M., Almes, M. J., Kempf, T. M., Mansfield, L. W., & Bruce, R. A. (1983). Limited effects of outpatient teaching and counseling after myocardial infarction: a controlled study. Heart and Lung, 12(1), 65-73.

Sivarajan Froelicher, E. S. (1989). Ten-year prognostic value of clinical and exercise test variables in patients after myocardial infarction. Unpublished PhD Dissertation, University of California, Los Angeles, Los Angeles.

Smith G. R. & O'Rourke D. F. (1988). Return to work after a first myocardial infarction. Journal of American Medical Association, 259:1673-1677.

Solomon, S., Hotchkiss, E., Saravay, S. M., Bayer, C., Ramsey, P., & Blum, R. S. (1983). Impairment of memory function by antihypertensive medication. Archives of General Psychiatry, 40,1109-1112.

Spitzer, W. O. (1987). State of Science 1986: Quality of life and functional status as target variables for research. Journal of Chronic Diseases, 40(6), 465-471.

Spitzer, W. O., Dobson, A. J., Hall, J., Chesterman, E., Levi, J., Shepherd, R., Battista, R. N., & Catchlove, B. R. (1981). Measuring quality of life of cancer patients. Journal of Chronic Diseases, 34, 585-597.

SPSS. 1994. SPSS 6.1 [Computer Program]. Chicago, IL.

Stern, M. J., Pascale, L., Ackerman, A. (1977). Life adjustment postmyocardial infarction. Archives of Internal Medicine, 137(12), 1680-1685.

Streufert, S., DePadova, A., McGlynn, T. et al. (1988). Impact of B-blockade on complex cognitive functioning. American Heart Journal, 116,311-315.

Stewart, A. L. (1992). The MOS framework. In A. L. Stewart & J. E. Ware, Jr. (Eds.) Measuring Functioning and Well-Being. (pp. 12-24). Durham: Duke University Press.

Stewart, A. & Kamberg, C. J. (1992). Physical functioning measures. In A. L. Stewart & J. ZE. Ware (Eds.), Measuring Functioning and Well-Being. (pp. 86-142). Durham: Duke University Press.

Stewart, A., Ware, J. E. Jr., Sherbourne, C. D., & Wells, K. B. (1992). Psychological functioning. In A. L. Stewart & J. E. Ware Jr. (Eds.), Measuring Functioning and Well-Being (pp. 143-162). Durham: Duke University Press.

Strauss, A. (1984). Chronic Illness and Quality of Life. St Louis: Mosby.

Sugarbaker, P. H., Barofsky, I., Rosenberg, S. A., & Gianola, F. J. (1982). Quality of life assessment of patients in extremity sarcoma clinical trials. Surgery, 91(1), 17-23.

Sullivan, M., Ahlmen, M., & Bjelle, A. (1990). Health status assessment in rheumatoid arthritis. I. Further work on the validity of the Sickness Impact Profile. Journal of Rheumatology, 17(4), 439-47.

Tandon, P. K., Stander, H., & Schwarz, R. P. (1989). Analysis of quality of life data from a randomized, placebo-controlled heart-failure trial. Journal of Clinical Epidemiology, 42(10), 955-962.

Tardiff, G. S. (1989). Sexual activity after a myocardial infarction. Archives of Physical Medicine and Rehabilitation, 70, 763-766.

Tobin, J. D. (1975). Normal aging - The inevitable syndrome. In L. E. Brown & E. O. Ellis, Eds. Quality of Life: The Later Years. Acton, Mass: Publishing Sciences Group.

Townend, J. N. & Littler, W. A. (192). Angiotensin converting enzyme inhibitors in heart failure: How good are they? British Heart Journal, 69; 373-375.

van Dam, F. S. A. M., Somers, R., & van Beek-Couzijn, A. L. (1981). Quality of life: Some theoretical issues. Journal of Clinical Pharmacology, 21(8/9 supplement), 166S-168S.

VandenBurg, M. J. (1988). Measuring quality of life of patients with angina. In S. R. Walker & R. M. Rosser (Eds.) Quality of Life: Assessment and Application. Boston: MTP Press Limited. pp. 267-277.

Veterans Adminstration Coronary Artery Bypass Surgery Cooperative Study Group. (1984). Eleven-year survival in the Veterans Adminstration randomized trial of coronary bypass surgery for stable angina. New England Journal of Medicine, 311(21), 1333-1339.

Visser, M. C., Fletcher, A. E., Parr, G., Simpson, A., & Bulpitt, C. J. (1994). A comparison of three quality of life instruments in subjects with angina pectoris: The Sickness Impact Profile, the Nottingham Health Profile, and the Quality of Well Being Scale. Journal of Clinical Epidemiology, 47(2), 157-163.

Ware, J. E., Jr. (1984). Conceptualizing disease impact and treatment outcomes. Cancer, 53(10 supplement), 2316-2323.

Ware, J. E. Jr. (1987). Standards for validating health measures: Definition and content. Journal of Chronic Diseases, 40(6), 473-480.

Ware, J. E. Jr. (1991). Measuring functioning, well-being, and other generic health concepts. In D. Osaba (Ed.), Effect of Cancer on Quality of Life. (pp.7-23). Boston: CRC Press.

Webster's Third New International Dictionary. (1996). Springfield: Merriam-Webster, Inc.

Wenger, N. K., Mattson, M. E., Furberg, & C. D., Elinson, J. (1984). Assessment of quality of life in clinical trials of cardiovascular therapies. American Journal of Cardiology, 54(7), 908-913.

Wiklund, I., Comerford, M. B., & Dimenas, E. (1991). The relationship between exercise tolerance and quality of life in angina pectoris. Clinical Cardiology, 14(3), 204-208.

Wiklund, I., Herlitz, J., & Hjalmarson, A. (1989). Quality of life five years after myocardial infarction. European Heart Journal, 10(5), 464-472.

Wiklund, I., Sanne, H., Vedin, A., & Wilhelmsson, C. (1984). Psychosocial outcome one year after a first myocardial infarction. Journal of Psychosomatic Research, 28(4), 309-321.

Wilson, A., Wiklund, I., Lahti, T., & Wahl, M. (1991). A summary index for the assessment of quality of life in angina pectoris. Journal of Clinical Epidemiology, 44(9), 981-988.

Winefield, H. R. & Martin, C. J. (1981). Measurement and prediction of recovery after myocardial infarction. International Journal of Psychiatry in Medicine, 11(2), 1981-1982.

World Health Organization. (1947). Chronicle of the World Health Organization. Volume 1.

APPENDIX A

COMMITTEE ON HUMAN RESEARCH
EXEMPT CERTIFICATION FORM

RECEIVED
FEB 24 1997

PRINCIPAL INVESTIGATOR (UCSF Faculty)
(Name & Degree) Erika S. Froelicher, RN, PhD
University Title Professor
Dept. Physiol. Nursin
Mailing Address (Campus) Box 0610
Phone Number 476-4833
Is P.I. Sponsor/Advisor Only? Yes

CO-P.I.
(Name & Degree) Laura-Ann L. Kee, RN, MS
University Title CNIII/Student
Dept. School of Nurs
Mailing Address (Campus) Box 0326, Cardiology
Phone Number 476-8715
SUBMISSION DATE 2/24/97

PROJECT TITLE
(Up to 150 Spaces) Quality of Life in Patients with Acute Myocardial Infarction Over Ten Years

NAMES/DEGREES OF ALL OTHER INVESTIGATORS:

SITE:
☒ Parnassus ☐ VAMC ☐ SFGH ☐ MtZION
☐ Other UCSF site ☐ Foreign
If "other" or "foreign," identify site(s):

BIOSAFETY COMMITTEE (BSC) APPROVAL: Any Human Subject protocols which involve the incidental use of human tissue, blood or body fluids should follow Universal Precautions and other laboratory safety guidelines. BSC approval is not required *unless* there is a deliberate attempt to isolate, concentrate or otherwise manipulate a specific biohazardous agent from the human specimen. Is the latter the case for this study?

☐ Yes ☒ No

If "yes," an application must also be submitted to the BSC for review and approval, if not already done. For information concerning the BSC application process, please contact the BSC at 476-2198 or your EH&S Departmental Safety Advisor.

BSC approval number, if available:

FUNDING:
Will this study be funded?
☐ Yes ☒ Pending ☐ No*
By whom? (Even if pending)
☐ Federal Gov. ☐ Other Gov. (i.e., State, City, WHO)
☐ Pharmaceutical/Device Co. ☐ Other Private
☐ Campus & University-wide Programs
☒ Departmental
Agency/Sponsor Name (and Grant/Contract #, if known):
Century Club - School of Nursing

* If no funding, please explain briefly how study costs will be managed:

Principal Investigator's Signature

2-19-97
Date

CERTIFICATION OF EXEMPT STATUS

On the basis of the information presented here, this research activity qualifies as exempt from review by the Committee on Human Research.

Committee Analyst, Committee on Human Research

2/24/97
Date