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1. CHAPTER 1: INTRODUCTION

Cardiovascular diseases remain the leading cause of death and a major cause of morbidity and disability among both men and women in the United States, with an estimated 13 million people reported as having symptomatic coronary heart disease (CHD). Approximately 1.5 million myocardial infarctions (MI) occur each year, with over 1/2 million deaths from MI (AHA, 1992). In 1993, an estimated 745,000 persons were hospitalized for MI alone. The direct and indirect costs of heart disease in the United States exceed \$100 billion per year.

Recent data show that psychosocial factors, such as lack of social support and depression, are important predictors of morbidity and mortality in CHD patients (Ahern et al., 1990; Berkman et al., 1992; Carney et al., 1988; Williams et al., 1992). These studies suggest that interventions which provide support and/or alleviate depression in MI patients may enhance their psychosocial recovery and decrease morbidity and mortality. To the extent that psychosocial intervention can be shown to impact favorably on survival and recovery in MI patients, the human and financial burden associated with heart disease can be reduced.

The purpose of the Enhancing Recovery in Coronary Heart Disease (ENRICHD) Patients Study is to conduct a multi-center clinical trial to determine the effects of a psychosocial intervention, designed to increase social support and alleviate depression, on the combined endpoint of all cause mortality and nonfatal infarction in patients with recently diagnosed acute MI who are at high psychosocial risk, that is, who are depressed and/or have low perceived social support. Secondary medical endpoints include all cause mortality; cardiovascular mortality; recurrent nonfatal MI; revascularization procedures; cardiovascular hospitalizations; and changes in risk factor profiles. Secondary psychosocial endpoints include severity of depression; adequacy of social support; and health-related quality of life. A pilot phase involved assessment of the feasibility of recruiting and retaining post-MI patients for the trial. On the basis of the pilot phase, the trial continues to accrue sufficient numbers of patients to evaluate the effects of the intervention on mortality and reinfarction.

1.1 BACKGROUND

A growing literature has documented associations between a variety of psychosocial factors and clinical outcomes in CHD patients. In MI and coronary artery disease (CAD) patients, the psychosocial factors most clearly linked to morbidity and mortality are depression and low perceived social support.

1.1.1 Depression

Recent research indicates that depression is common among persons with heart disease. Among studies examining major depression in patients with MI or coronary heart disease, prevalence is reported at nearly 20% (Carney et al., 1987; Schleifer et al., 1989; Forrester et al., 1992). An additional 27% of patients report minor symptoms of depression (Schleifer et al., 1989). Other studies have found that nearly two-thirds of patients with MI have some mental disorder, primarily depression and anxiety (Cassem et al., 1971; Hackett et al., 1985; Schleifer et al., 1989). In contrast, the prevalence of major depression in community samples of individuals of comparable age and gender is only 3% (Myers et al., 1984). Among post-MI patients with major depression, those with a prior history of major depression range from 44 to 56%. (Freedland et al., 1992).

Depression has been found to be a key factor preventing effective and full recovery from MI. Depression following an MI is associated with poor long-term psychosocial prognosis and with a reduced likelihood of returning to normal occupational and social activity levels (Schleifer et al., 1989; Levenson et al., 1985; Fielding, 1991). In a recent study in which 522 male survivors of acute MI were categorized as mildly, moderately or severely depressed, severity of depression was found to be significantly related to occurrence of angina and emotional stability at six months post-MI (Ladwig et al., 1994). The authors conclude that severe depression immediately following an MI is associated with decrements in quality of life, including reduced vigor, lack of initiative and disengagement from normal daily activities, up to six months following the event.

Depression in post-MI patients has also been associated with increased risk for future cardiac events, such as reinfarction, cardiac arrest and cardiac death, independent of disease severity (Ahern et al., 1990; Silverstone, 1987; Carney et al., 1988; Falgar and Appels, 1982; Follick et al., 1988). Frasure-Smith et al. (1993) found that major depression was a significant predictor of cardiac mortality in post-MI patients, even after controlling for left ventricular dysfunction and previous MI (adjusted hazard ratio, 4.29; $p = .013$). A potential mechanism for the effects of depression on post-MI prognosis involves altered autonomic function, which may lead to increased incidence of myocardial ischemia and ventricular arrhythmias (Carney et al., 1989; Carney et al., 1995; Hjemdahl et al., 1991; Podrid et al., 1990). Alternatively, depression may affect clinical outcomes in MI patients through its effects on behavioral risk factors (e.g., smoking, hypertension) and adherence to medication (Guiry et al., 1987; Blumenthal et al., 1982; Carney et al., 1995).

1.1.2 Low Perceived Social Support

Social support has been linked to survival and physical recovery in CAD and MI patients. Studies have shown that heart disease patients who have low perceived social support have an increased risk of future cardiac events as well as cardiac mortality. Ruberman et al. (1984) reported a greater than four-fold increase in post-MI mortality for men who have low perceived social support and high life stress. Gorkin et al. (1993) reported that, for patients randomized to placebo in the Cardiac Arrhythmia Suppression Trial-1 (CAST-1), level of perceived social support was a significant multivariate predictor of mortality after adjusting for measures of disease severity. Orth-Gomer et al. (1988) found that men with CAD who have low perceived social support had three times the rate of total mortality as non-isolated men. Chandra et al. (1983) and Ell et al. (1992) reported that patients who were married at the time of a MI were significantly less likely to die during hospitalization and during follow-up than unmarried patients.

Williams et al. (1992) found that CAD patients who were unmarried or reported having no one in whom they could confide had an unadjusted five-year survival rate of .50, compared with .82 in patients who were married, had a confidant, or both (adjusted hazard ratio: 3.34, $p < .0001$). This difference in survival was independent of all underlying cardiac anatomic and functional factors documented at baseline. In another study, living alone was found to be an independent risk factor (hazard ratio of 1.54, $p < .03$) for a major cardiac event following MI (Case et al., 1992).

Finally, in a study of 194 elderly men and women hospitalized with MI, presence of emotional support prior to the MI was found to be the most powerful and consistent predictor of survival after MI, with lack of sufficient emotional support related to early, in-hospital mortality as well as later mortality over a six month period (Berkman et al., 1992). At the end of 12 months, 55% of those with no sources of emotional support had died in contrast to only 27% with two or more sources of support.

Social support is hypothesized to affect physical recovery in MI patients through two potential mechanisms. The first involves increases in patient adherence to healthier lifestyles and to medical therapy (Berkman and Breslow, 1983; Hanson et al., 1990). The second implicates the role of supportive interactions in lessening the potentially damaging effects of negative emotional states on neuroendocrine and physiological regulatory mechanisms (Cohen, 1988). In this regard, social support has been found to be associated with attenuated blood pressure response to acute laboratory challenge (Kamarck et al., 1995; Gerin et al., 1995) and with neuroendocrine function (Seeman et al., 1994).

1.1.3 Psychosocial Intervention

A number of intervention studies have demonstrated positive effects for interventions designed to enhance psychosocial function in post-MI patients. Interventions that provide psychosocial support, usually in the form of individual counseling or group therapy, have in some cases been associated with decreased coronary events and mortality. A recent review of the literature undertaken by the AHCPR Cardiac Rehabilitation Guideline Panel (AHCPR, 1995) led that Panel to conclude that "intensive education, counseling, and behavioral interventions as components of multifactorial cardiac rehabilitation have been associated with reduction recurrent coronary event rates as well as regression of atherosclerosis."

In an early study, patients were provided with either group counseling, involving provision of information and discussions of psychological problems and concerns, or with usual care (Rahe et al., 1975). Significantly fewer cardiac events were found during a four year follow-up period in the psychosocial treatment group, relative to those receiving usual care (Rahe et al., 1979).

In a study utilizing a behavioral intervention aimed at lessening Type A behavior in 1035 post-MI patients identified as Type A, there was a significant decrease in symptoms of anxiety and depression, as well as fewer cardiac fatalities and a lower reinfarction rate in the behavioral intervention group relative to a control group which received cardiac counseling only (Friedman et al., 1982; Powell et al., 1984). Although the behavioral intervention was designed to target Type A behaviors, it was delivered in a group counseling situation and thus presumably involved provision of social support as well.

Kallio et al. (1979) reported significantly fewer coronary deaths at three years in a post-MI treatment group relative to patients assigned to usual care. The intervention encompassed anti-smoking education and dietary advice, as well as discussions of psychosocial problems. In a more recent study, male MI patients who were contacted by nurses and provided with interventions designed to lower stress were about half as likely to die from ischemic heart disease during the year following their MI as were patients who received standard medical care (Frasure-Smith and Prince, 1985; 1989).

Although these and other studies report favorable outcomes for psychosocial treatments relative to usual care in post-MI and CAD patients (see Linden et al., in press, for a meta-analysis of this literature), some studies have found no effect for psychosocial intervention (Horlick et al., 1984; Ibrahim et al., 1974; Stern et al., 1983). The lack of consistency in findings in this area may be partly attributable to methodological weaknesses that limit the ability of many of these studies to adequately test the effects of psychosocial intervention in the treatment of post-MI patients. Many studies have used very small sample sizes, resulting in a lack of power to detect differences between treatment and control groups. In other cases, flawed randomization procedures, inadequate or unreliable ascertainment of clinical endpoints, differential loss to follow-up between treatment and control groups, and lack of "intent to treat" analyses make interpretation of the existing findings difficult. For example, the study by Frasure-Smith and

Prince (1985) was not a true randomized trial, since patients were randomized prior to, rather than following, informed consent and enrollment, leading to biased assignment to condition and lack of initial comparability between the treatment and control groups. In the studies conducted by Rahe et al. (1975; 1979), Frasure-Smith and Prince (1985), and Friedman et al. (1986), patients who dropped out of either treatment or follow-up were not accounted for in the analyses, posing problems in interpretation of the results.

These methodological limitations preclude drawing firm conclusions regarding the value of psychosocial intervention in preventing death and recurrent cardiac events in post-MI patients. Yet, the epidemiologic literature in post-MI patients, especially in the areas of depression and social support, suggests that treatments that reduce depression and/or increase social support may have beneficial effects on survival and recovery following an MI. Before recommendations can be made regarding the utility of psychosocial intervention in the clinical care of MI patients, a randomized, controlled trial is needed with a sample size sufficient to determine whether interventions that target the psychosocial risk factors of depression and low perceived social support are efficacious in decreasing morbidity and mortality following an MI, relative to usual medical care.

1.2 OBJECTIVES FOR ENRICHD

1.2.1 Primary Objective

The primary objective of the ENRICHD Patients Study is to evaluate the effect of an intervention designed to increase social support and decrease depression in post-MI patients, relative to usual care, on a combined endpoint of all cause mortality and nonfatal infarction.

1.2.2 Secondary Objectives

Additional objectives are to:

- (1) document the effects of the intervention relative to usual care on a variety of secondary outcomes of interest, including all cause mortality; cardiovascular mortality; recurrent nonfatal MI; revascularization procedures; cardiovascular hospitalizations; and changes in selected risk factor profiles; presence and severity of depression; degree and type of social support; and health-related quality of life.
- (2) evaluate (to the extent possible, given limited statistical power) the effect of the intervention in subgroups defined by gender, minority status, and etiology of psychosocial risk.
- (3) conduct exploratory studies where feasible of psychosocial, behavioral and physiologic mechanisms through which the psychosocial intervention used exerts effects on the clinical outcomes of interest.

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2. CHAPTER 2: OVERVIEW OF STUDY DESIGN

ENRICHD will be a multi-center, randomized, controlled clinical trial. The study population will consist of 3,000 patients recently hospitalized with acute MI, who are at high psychosocial risk for mortality or re-infarction due to low perceived social support or depression. The trial will evaluate the effect of a psychosocial intervention, in comparison to usual medical care, on the rates of mortality and re-infarction.

2.1 PROJECT SCHEDULE

The research plan involves a phased approach: During the first year of the trial (Phase I), an initial group of 400 patients were recruited, randomized and evaluated after six months of intervention. The objectives of Phase I were: (1) to determine the feasibility of recruiting adequate numbers of MI patients at high psychosocial risk to the trial; (2) to assess patient acceptance of and adherence to the intervention being studied; and, (3) to determine whether the intervention can be successfully delivered to the study population. Primary endpoints for Phase I were measures of: patient recruitment, to include recruitment of women and minorities; patient adherence to protocol; and delivery of the psychosocial intervention and usual care procedures, according to protocol, Phase II will involve enrolling 2,600 additional patients to allow a comparison of the effects of the psychosocial intervention with those of the usual care conditions on the endpoint of total mortality plus reinfarction.

2.2 PARTICIPANT ELIGIBILITY

All study participants will be recruited during a hospitalization for a verified acute MI. Potential participants will be assessed for psychosocial risk and must meet standardized criteria for depression and/or low perceived social support to be eligible. Every effort will be made to enroll patients as soon after the event as possible; in all cases patients must be randomized within 28 days of onset to be eligible. In order to qualify on the basis of depression, patients must meet modified DSM-IV criteria for major or minor depression or dysthymia. In order to qualify on the basis of low perceived social support patients must have a score on the ENRICHD Social Support Instrument (ESSI) of 2 or less on at least two items, excluding item #4 (help with chores) ; or a score of 3 or less on two items, excluding items #4 and 7 before help with chores and marital status) and a total score of 18 or less on items 1, 2, 3, 5, and 6. Details of the medical and psychological inclusion and exclusion criteria are described in Chapter 3.

2.3 INTERVENTION

Patients in the psychosocial intervention group will receive interventions tailored to their individual deficits in psychosocial functioning. Treatment will begin with individual counseling,

followed by group sessions, both based on cognitive-behavioral therapy. Severely depressed patients will receive standardized pharmacotherapy as indicated.

Patients in both groups will receive health education, to standardize knowledge of cardiovascular disease and its management. Both groups will receive standard medical treatment, as practiced in that institution.

2.4 STUDY SIZE AND DURATION

Three thousand patients will be recruited over a 36 month period. Follow-up of all patients will continue until the last patient randomized has completed 18 months of follow-up. Thus follow-up time will range from a minimum of 1 1/2 to a maximum of 4 1/2 years; assuming uniform recruitment the average follow-up time will be three years. Each patient will have follow-up examinations at 6 and 18 months, and annually thereafter. In addition, patients will be contacted by telephone at several timepoints from date of randomization (three month, nine months, 12 months and annually thereafter.)

3. CHAPTER 3: ELIGIBILITY

The overall approach to recruitment, eligibility determination and randomization is one of attempting to enroll eligible participants who are at increased psychosocial risk for morbidity and mortality as quickly and efficiently as possible after an acute MI. This approach is based on data suggesting that the risks associated with both depression and low perceived social support are especially high during the immediate post-MI period (Frasure-Smith et al., 1993; Berkman et al., 1992). An accelerated approach to recruitment ensures that treatment can begin as quickly as possible in those participants assigned to the intervention, thus maximizing the benefits of treatment. There is evidence that about half of the improvement in depressive symptoms seen during treatment of depression with CBT occurs within the first few weeks of therapy (Ilardi & Craighead, 1994). Furthermore, every effort will be made to overcome barriers to enrollment and participation so that seriously ill patients will be included to the greatest possible extent.

Inclusion and exclusion criteria are summarized in Table 3-1. The sequence of screening, eligibility determination, and randomization are summarized in Figure 4-1. An overview and rationale for each of the inclusion and exclusion criteria are summarized in section 4.3 of Chapter 4.

3.1 INCLUSION CRITERIA

Patients will be enrolled who meet the following criteria.

3.1.1 Hospitalized For MI

Only patients who are hospitalized for an acute MI at initial screening (SV1) will be eligible for enrollment in ENRICHD. An acute MI will be defined by having characteristic increases in biomarkers of myocardial injury twice the upper limit established within the institution from which the patient is being recruited and at least one of the following: (a) symptoms compatible with acute MI; and/or (b) characteristic evolutionary electrocardiographic ST-T changes or new Q waves. Patients with marker values who may still qualify under special circumstances include:

1. Enzyme criteria for MI: If CKMB is the marker used locally and if (a) values are increased above the upper bound of the reference range as assessed by the site cardiologist and are characteristic of MI that manifest a rising and falling pattern, and (b) acute myocardial infarction has been diagnosed locally, and (c) if symptoms are compatible with acute MI and/or characteristic ECG findings are present as defined in the ENRICHD eligibility criteria.

2. Patients who undergo acute angioplasty: Patients who present with ST segment elevation and classic signs and symptoms of MI and meet ENRICHD criteria for marker protein elevations after acute angioplasty are eligible so long as the diagnosis of acute infarction is confirmed by the site cardiologist.

Patients who present with chest pain, ST segment depression, a local diagnosis of acute myocardial infarction, and a three-fold increase in any of the biomarkers of myocardial injury are eligible if the site cardiologist concurs with the diagnosis of acute infarction.

3.1.2 Depressed And/Or Low In Social Support

To be eligible for inclusion, patients must meet the criteria for depression, low perceived social support, or both, within 28 days of the onset of acute MI. Specifics concerning the criteria for depression and low perceived social support are summarized below.

3.1.3 Depression

To meet criteria for depression in ENRICHD, a patient must first meet the modified DSM-IV criteria for a current major or minor depressive disorder or dysthymia (American Psychiatric Association, 1994) (see ENRICHD modified criteria summarized in Table 3-2). The specific modified DSM-IV criteria are:

- Minor depression symptom criteria, 1 \geq duration week; prior HX Major depression.
- Major depression symptom criteria, 1 \geq duration week; prior HX Major depression.
- Major depression symptom criteria, and duration \geq 2 weeks (regardless of prior history).
- Dysthymia symptom criteria and duration \geq 2 years.

The first seven items on the Depression Interview and Structured Hamilton (DISH) assess the cardinal symptoms of depression (dysphoria and anhedonia). If neither is present, the patient cannot meet the DSM-IV criteria for depression.

3.1.4 Low Perceived Social Support

To meet criteria for low perceived social support in ENRICHD, a patient must score 2 or lower on at least two items of the ENRICHD Social Support Instrument (ESSI), excluding item 4 (availability of someone to help you with daily chores) or (b) score 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) with a total score of 18 or less on items 1, 2, 3, 5 and 6.

3.2 SELECTION/DEVELOPMENT OF SCREENING INSTRUMENTS AND CUT-POINTS

3.2.1 Modified DSM-IV Diagnosis Of Major Or Minor Depression from Psychodiagnostic Interview)

Background. In order to determine whether a patient meets the modified DSM-IV criteria for major or minor depression (see Table 3-2), it will be necessary to conduct an interview. Since the inter-rater reliability of depression and other psychiatric diagnoses tends to be relatively low when they are based on nonstandardized interviews, a variety of structured and semi-structured psychodiagnostic interview schedules have been developed.

Several of these interview schedules were considered for use in ENRICHD. The depression section of the National Institute of Mental Health Diagnostic Interview Schedule (DIS; Robins, Hetzer, Croughan, & Ratcliff, 1981) was modified by Carney and Freedland (1988) for use in studies of depression in cardiac patients. Frasure-Smith and her colleagues have also used a modified DIS interview in a series of studies of post-MI patients, in which DSM-III and DSM-III-R depressive disorders have been shown to increase subsequent morbidity and mortality. The modified DIS is relatively brief and can be administered by trained lay interviewers.

Unfortunately, its false positive rate is unacceptably high unless it is overread by experienced diagnosticians, and it does not provide some of the more detailed information that is required by DSM-IV. These drawbacks would limit the utility of the modified DIS in a treatment trial such as ENRICHD.

Other widely-used standardized psychodiagnostic interviews include: the Composite International Diagnostic Interview (CIDI; Robins et al., 1988), which is the successor to the DIS; the Schedules for Clinical Assessment in Neuropsychiatry (SCAN 2.0; World Health Organization, 1992); and the Structured Clinical Interview for DSM-III-R (Spitzer, Williams, Gibbon, & First, 1990). Each of these interviews has its own strengths and weaknesses, and each was considered for use in ENRICHD.

One of the biggest disadvantages all of these standardized interviews share is that their items overlap to a greater or lesser extent with those of the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960; Williams, 1988, 1992). In ENRICHD, HAM-D scores will be obtained at the same times as DSM-IV depression diagnoses (**i.e., at baseline, post-treatment, and 6-month follow-up periods**). Administering a standardized psychodiagnostic interview and a structured HAM-D interview in the same session would consume a great deal of time needlessly and necessitate redundant questioning.

Another problem with most of the existing schedules is that they are not adequately designed to evaluate the longitudinal course of the depressive disorder or to study change over time or treatment phase. They would only provide a cross-sectional “snapshot” of the current situation

when patients are re-interviewed after treatment and at other planned follow-ups, such that important information about chronicity, remission, relapse, and recurrence would be lost.

Finally, some of the interviews, such as the DIS, examine only symptoms which have had a duration of at least two weeks. While this approach enables the diagnosis of major and minor depression at the time of administration, it does not allow for an efficient re-screening of patients who do not initially meet DSM-IV duration criteria for depression. The ideal approach would involve a brief phone follow-up for patients meeting all criteria except duration of depression symptoms, in which patients are queried whether or not symptoms had continued to meet a two-week duration criterion, eliminating the need for readministration of the entire interview.

Consequently, a new interview schedule, the Depression Interview and Structured Hamilton (DISH; Freedland, 1996) was developed specifically to meet the requirements of ENRICHD. It was designed to obtain an accurate DSM-IV diagnosis, an assessment of the longitudinal course of the disorder, and a reliable Hamilton score, in an efficient, integrated interview format that would allow easy telephone follow-up. It was also designed to be suitable for use by diverse personnel and to eliminate most of the need for diagnostic overreading.

3.2.2 Depression Interview And Structured Hamilton (DISH)

The DISH (see Appendix B) integrates material from several different sources, including the Hamilton Rating Scale for Depression (Hamilton, 1960); the standardized version of the Hamilton scale developed by NIMH for use in the Early Clinical Drug Evaluation (ECDEU) program and the Treatment of Depression Collaborative Research Program (William, 1976); the Structured Interview Guide for the Hamilton Depression Rating Scale (Williams, 1988, 1992); the National Institute of Mental Health Diagnostic Interview Schedule (Robins, Hezeer Croghan, & Ratcliff, 1981); the modified version of the NIMH Diagnostic Interview Schedule (Carney & Freedland, 1988) that has been used primarily in research on depression in patients with coronary heart disease; and the DSM-IV manual itself.

The DISH consists of several sections. The Current Depression Symptoms section determines the severity, frequency, and chronicity of all of the DSM-IV criterion symptoms of major and minor depression and dysthymia. It also elicits the information needed to derive the standard (17-item) Hamilton depression severity score for the past week.

The Psychiatric History section provides a brief assessment of the patient's lifetime history of depression, other psychiatric disorders (including disorders that, if present, exclude the patient from participation in the trial), and psychiatric and psychological treatment. It also probes to identify impairment in social, occupational, or other areas of psychosocial functioning. Most of this section will only be administered at baseline.

The Longitudinal Course Chart is administered only at the six-and 12 month follow-up to characterize the longitudinal course of the patient's depressive disorder. It is designed to fill in

the gaps between the “snapshot” views of the patient’s condition that are obtained at each interview.

Finally, the Diagnostic Summary Forms provide a standardized format for coding the current diagnosis and the Hamilton depression score. The versions of this form are designed to increase the reliability of the diagnostic judgments that are formed on the basis of the interview.

3.2.3 ENRICHD Social Support Instrument (ESSI)

The ENRICHD social support instrument is a seven-item scale comprised of items found to be individually predictive of mortality in cardiac patients and items from other well-validated social support scales. The development of a new instrument for social support screening is based on the fact that the lengthier, psychometrically-validated scales available have not been used to predict mortality in MI patients and thus lack predictive validity. The strategy used in selection of the social support screening instrument is therefore one of developing an instrument with items of known predictive value. One of the primary goals of the Pilot Study was to validate this measure by comparing it with other social support instruments with known psychometric properties.

As described above, the ENRICHD Social Support Instrument (ESSI) was developed based on a review of previous scales and items which have predictive validity. This review suggests that the critical element of most items predictive of poor outcomes in MI and CAD patients is perception of low perceived social support, and in particular, emotional support, rather than deficiencies in network structure (e.g., network size, geographical proximity or living arrangements) or subjective feelings of loneliness. The ESSI was created by identifying items from the studies by Williams et al. (1992), Gorkin et al. (1993), and Berkman et al. (1992). Since the item from CAST (Gorkin et al., 1993) was actually an integration of two items from the MOS Social Support Survey (Stewart and Hays, 19--?), these two items have been disaggregated, and two other items from the MOS Social Support instrument that tap a similar construct have been added to produce a 7-item scale. In addition, the response categories have been modified so that they follow a consistent format based on the MOS scale (with the exception of the items about marital status). The items comprising the ENRICHD ESSI appear in Appendix A.

Since most other studies have identified between 18-27% of post-MI and CAD patients as being "high risk" on any single item, it is assumed that about 25% of the population screened for ENRICHD will be defined as "high risk" on the new scale and as therefore meeting criteria for low perceived social support. Based on information gained from the pilot study, a score of 2 or less on two or more items (excluding item 4) was chosen as the criterion. The criteria has been broadened to include (b) a score of 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) and a total score of 18 or less on items 1, 2, 3, 5 and 6.

3.3 EXCLUSION CRITERIA

Patients who meet any of the following 10 criteria will be excluded from participation.

3.3.1 Post-Procedure MI

Patients who have had an MI as a complication of a procedure, such as CABG or other surgery or PTCA except when done for probable acute infarction, will be excluded from ENRICHD (see section 3.1.1).

3.3.2 Presence of Non-Cardiovascular Conditions Likely To Be Fatal Within One Year

Patients with non-cardiac conditions likely to be fatal within one year will be excluded from ENRICHD. Such events represent “competing risks” that are not the focus of ENRICHD, nor are they likely to be influenced by the ENRICHD intervention. In addition, such conditions are likely to compromise patients’ ability to participate actively in the intervention and increase dramatically the difficulty in presenting a standardized psychosocial intervention.

3.3.3 Conditions Likely to Limit the Physical Capacity To Participate Despite Efforts to Overcome Barriers To Participation

Every effort will be made by ENRICHD staff to overcome barriers to participation (e.g., assisting with transportation). Nonetheless, even when co-morbid conditions do not pose an important threat to life, they may impair functional capacity to an extent that clinical units will not be able to overcome them and they will limit participation in the study. In these cases where limitations cannot be overcome, patients will be excluded from participation.

3.3.4 Participation In Concurrent Research Protocols Likely To Conflict With ENRICHD

In general, patients participating in other research protocols will only be excluded from ENRICHD if participation in the concurrent research protocol poses a significant logistical burden or if the concurrent research protocol provides a treatment which might confound evaluation of the ENRICHD intervention. This is not expected to pose a major problem for the trial, since most current research protocols are short-term and focused on treatment with (non-psychopharmacologic) drugs.

3.3.5 Major Psychiatric Co-morbidity

Patients who have major psychiatric co-morbidity which would compromise their participation in ENRICHD, would result in them being inappropriate for the ENRICHD treatment, would be likely to require alternative psychosocial treatment during the ENRICHD study period, or would affect the interpretation of ENRICHD results will be excluded from participation in ENRICHD. These psychiatric conditions include any of the following:

- schizophrenia, bipolar disorder, or other psychotic disorder evidenced by chart review or psychodiagnostic interview;
- dementia evidenced from chart review, psychodiagnostic interview, or by administration of the Short Blessed Dementia Screening Test given at the discretion of the interviewer at any point pre-randomization (patients who score above the standard cutoff score of 10 will be excluded);
- severe, active substance abuse evidenced by chart review or clinical interview;
- other major psychological conditions precluding participation in the trial.

3.3.6 Imminent Suicide Risk

Suicidal ideation is a common symptom of depression, so it is likely to be a common finding among patients screened for eligibility to participate in ENRICHD. Although interviewers should always be duly concerned about suicidal ideation, they should not assume that it always portends suicidal behavior. Indeed, relatively few cases of attempted or completed suicide have been reported in the literature on depression in medically ill patients. However, major depression has been implicated as a contributing factor in between 40 and 60% of all suicides (Claton, 1985; Murphy, 1986). Furthermore, the incidence of completed suicide is especially high among elderly individuals (National Center for Health Statistics, 1992), and the prevalence of attempted suicide is particularly high among individuals who are separated or divorced (Moscicki et al., 1988). Since ENRICHD participants will be depressed and/or have low perceived social support and most will be middle aged or older, a small number of the patients screened for participation will inevitably be at risk for suicide.

Within the context of eligibility screening, the objective of suicide risk assessment is to identify imminent or emergent suicide risk (Clark and Fawcett, 1992). Patients need not be excluded from participation simply because of a possible long-term risk of suicide or because of transient or passive suicidal ideation. In contrast, patients who are identified as possibly or definitely being at imminent risk of attempting suicide or otherwise harming themselves must be excluded from participation and referred immediately for appropriate treatment.

Suicidal ideation will be routinely assessed as part of the standardized psychodiagnostic interview. If a patient reports having had any suicidal ideation during the past week, the interviewer will probe to determine frequency, chronicity, and content of the ideation. Following guidelines delineated by Clark and Fawcett (1992), the identification of active thoughts of suicide will be followed up by determining whether: 1) the patient has considered any specific method(s) of suicide; 2) the patient wants to, intends to, or is planning to attempt suicide in the near future and if so, why; 3) the patient has rehearsed or made preparations to carry out the plan; and 4) the patient has a past history of suicide attempt(s). Patients who report these features will be considered to be at imminent risk for suicide will be excluded from ENRICHD. In such cases, the notification procedures outlined in the Manual of Operations will be implemented to ensure that these patients receive appropriate treatment and follow-up.

3.3.7 Unwillingness To Provide Informed Consent

Patients who unwilling or unable to provide informed consent will not be randomized in ENRICHD.

3.3.8 Inability To Complete Screening Visits

Patients who are not able to complete ENRICHD screening visits within 28 days post-MI and to provide complete baseline data will not be randomized in ENRICHD. (e.g., extreme deafness, persistent delirium).

3.3.9 Inaccessibility For Intervention And/Or Follow-up

Despite active efforts to accommodate patients' special needs, those who are inaccessible and therefore unlikely to be adherent with treatment and follow-up during ENRICHD will be excluded from participation in ENRICHD. Factors associated with inaccessibility may include distance the patient lives from an intervention or assessment site; the time it takes to travel such distances; frequency of business travel; plans to move from the area during the period of the study; and not having access to a telephone for contact and follow-up. Because individual differences exist between sites in terms of urban vs. rural setting, availability of public transportation, and other factors and resources that can be used to overcome accessibility barriers, each site will define specific guidelines for determining accessibility, and patients who are judged to have accessibility barriers which are likely to compromise their active participation in ENRICHD will be excluded.

3.3.10 Use of Antidepressant Medication / Current Psychotherapy

Patients taking antidepressant medication for less than 14 days or in active psychotherapy are excluded from ENRICHD. Patients who have been taking antidepressant medication for 14 days or more can be included provided they still meet the criteria for depression or low social support.

3.4 ETHNICITY AND GENDER COMPOSITION OF ENRICHHD

ENRICHHD has as its overall study goal the recruitment of 50% women and 50% minorities. Recruitment of women and individuals from minority groups will be monitored by the Steering Committee throughout the study to assure that study goals are met. If the overall proportion of women and of minorities falls significantly short of 50% for each at any time during the trial (including during the initial months of the trial), options and approaches to increasing the recruitment of women and minorities at some or all existing clinical sites will be implemented.

Specific methods to increase participation of women and minorities in ENRICHHD are discussed in detail in Chapter 4. In addition, two approaches will be used to determine barriers to recruitment among women and minority patients and to explore methods for overcoming these barriers to ensure adequate enrollment of these patient groups. First, participants in pilot study were queried regarding their perceptions of possible barriers to participating in a study such as ENRICHHD, and these responses will be used to better structure the screening and recruitment procedures. Second, several focus groups have been conducted which targeted patient groups often underrepresented in clinical trials, e.g., women, minorities, lower SES, older individuals. These focus groups explored in depth patients' perceptions of barriers to participation and their suggestions regarding additional methods and study features that would overcome these barriers and encourage their participation in ENRICHHD. The responses will be used by ENRICHHD investigators to structure screening, enrollment, intervention, follow-up and other study procedures to address patient concerns and encourage participation by these patient groups.

3.5 CHAPTER REFERENCES

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TABLE 3-1: ELIGIBILITY CRITERIA FOR ENRICHD**Inclusion Criteria**

1. Hospitalized for MI: defined by having characteristic marker proteins to twice the upper limit established within the institution from which the patient is being recruited and at least one of the following:

(a) symptoms compatible with acute MI; and/or

(b) characteristic evolutionary electrocardiographic ST-T changes or new Q waves.

1. Enzyme criteria for MI: If CKMB is the marker used locally and if (a) values are increased above the upper bound of the reference range as assessed by the site cardiologist and are characteristic of MI that manifest a rising and falling pattern, and (b) acute myocardial infarction has been diagnosed locally, and (c) if symptoms are compatible with acute MI and/or characteristic ECG findings are present as defined in the ENRICHD eligibility criteria.

2. Patients who undergo acute angioplasty: Patients who present with ST segment elevation and classic signs and symptoms of MI and meet ENRICHD criteria for marker protein elevations after acute angioplasty are eligible so long as the diagnosis of acute infarction is confirmed by the site cardiologist.

Patients who present with chest pain, ST segment depression, a local diagnosis of acute myocardial infarction, and a three-fold increase in any of the biomarkers of myocardial injury are eligible if the site cardiologist concurs with the diagnosis of acute infarction

2. Depressed: Depression and Structured Hamilton (DISH-Part A) The patient must meet the ENRICHD modified DSM-IV criteria for major or minor depression or dysthymia based on modified DSM-IV criteria (exclusive of requirement concerning depression being reactive to a physical condition; see Table 3-2 for modified DSM-IV criteria) during SV2.

AND/OR

Low perceived social support: The patient must score 2 or lower on at least two items of the ENRICHD Social Support Instrument (excluding item 4) or (b) a score of 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) and a total score of 18 or less on items 1, 2, 3, 5 and 6 within 14 days of the onset of acute myocardial infarction either while hospitalized or during a rescreening.

Exclusion Criteria

1. Post-procedure MI
2. Presence of Conditions Likely to Terminate Fatally Within One Year
3. Conditions Likely to Limit the Physical Capacity to Participate Despite Efforts to Overcome Barriers to Participation
4. Participation in Concurrent Research Protocols Likely to Conflict with ENRICHD
5. Major Psychological Co-morbidity: defined by any of the following:
 - schizophrenia, bipolar disorder, or psychotic disorder evidenced by chart review or clinical interview
 - dementia evidenced from chart review, clinical interview, or by a Short BLESSED score >10
 - current substance abuse evidenced by chart review or clinical interview
 - other major psychological conditions precluding participation in trial
6. Imminent Suicide Risk
7. Unwillingness to Provide Informed Consent
8. Inability to Complete Screening Visits
9. Inaccessibility for Intervention and/or Follow-up
10. Currently in Active Psychotherapy or Taking Antidepressant Medication for less than 14 days (for any indication)

TABLE 3-2: DSM-IV CRITERIA FOR MAJOR AND MINOR UNIPOLAR DEPRESSIVE DISORDERS

Major Depressive Episode

The diagnosis of a current major depressive episode requires that all criteria (“a” through “e”) be met.

a. Five or more of the following symptoms have been present during the same two-week period and represent a change from previous functioning or they have been present for one week and the patient has a history of major depression. At least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

- (1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
- (2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
- (3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day
- (4) insomnia or hypersomnia nearly every day
- (5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
- (6) fatigue or loss of energy nearly every day
- (7) feelings of worthlessness or excessive or inappropriate guilt nearly every day (not merely self-reproach or guilt about being depressed)
- (8) diminished ability to think or concentrate or indecisiveness, nearly every day (either by subjective account or as observed by others)
- (9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

b. No evidence of concurrent manic episode is present.

c. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

d. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse or a prescribed medication) or a general medical condition (e.g., hypothyroidism).

The symptoms are not better accounted for by acute bereavement. When grief and other depression-like features occur after the loss of a loved one, the diagnosis of major or minor depression is deferred until the symptoms have persisted for longer than 2 months OR until marked morbid preoccupation with worthlessness, suicidal ideation, or severe psychomotor retardation are present for two weeks or longer.

Minor Depressive Episode

- a. Principal Criteria: The DSM-IV criteria for a current minor depressive episode are essentially identical to those for major depression, except that **at least two but less than five** of the depressive symptoms listed above must have been present during the same two-week period or during one week for a patient who has a history of major depression. As in major depression, at least one of the symptoms must be either depressed mood or loss of interest or pleasure.
- b. Exceptional Criteria
 - (1) Dysthymia: As defined by DSM-IV, dysthymia is a form of chronic, mild depression. Its features are similar to those of minor depressive disorder, but the depressive symptoms must have persisted for at least two years to warrant a diagnosis of dysthymia. Because of its chronicity, dysthymia may be more difficult to treat than an acute minor depressive episode, and underlying dysthymia is known to complicate the course and treatment of major depressive episodes (a condition that has been labeled as “double depression”). However, little if anything is known about whether dysthymia and minor depression differ with respect to their prognostic implications in cardiac patients. For the purpose of determining eligibility to participate in the trial, no distinction will be made between minor depression and dysthymia.
 - (2) Major Depression in Partial Remission: Unless the interviewer is very familiar with the patient’s recent psychiatric history, it can be difficult to differentially diagnose minor depression and major depression in partial remission. Virtually nothing is known about whether these two conditions have different prognostic implications for post-MI patients. For the purpose of determining eligibility to participate in the trial, no distinction will be made between minor depression and major depression in partial remission.

4. CHAPTER 4: RECRUITMENT AND SCREENING

4.1 ISSUES RELATED TO RECRUITMENT AND SCREENING

The following considerations underlie the approach to screening and recruitment used in ENRICHD:

- facilitating expeditious enrollment, especially for patients at highest risk

Patients who survive a myocardial infarction will suffer their highest risk for mortality within a relatively brief period (3-6 months) after the infarct. Further, the patients who are at the highest risk for mortality within three to six months after a myocardial infarction are those with major depression (Frasure-Smith, 1993). Since the benefits realized from cognitive-behavioral therapies require some period of treatment, it is essential to enroll patients as soon as possible after the event, so that those randomized to the psychosocial intervention might have sufficient exposure to the intervention to alter their depression/low perceived social support during the time of greatest risk. This is particularly important among those patients at highest risk, i.e., those with major depression.

- the advantages of enrolling participants while they are still in the hospital

Quick, inpatient enrollment allows the opportunity for substantial contact between study personnel and participants and may actually promote adherence and retention by fostering patient feelings of connection to and involvement in the study. This may be particularly important for minorities, low-SES populations, and possibly even women.

- the use of a "behavioral run-in" to ensure high protocol adherence and retention

Social pressure to consent to randomization may be strong during hospitalization. Following discharge, patients who are depressed or have low perceived social support may be particularly likely to change their minds about trial participation. To ensure potential participants are adequately motivated to participate in follow-up visits and adhere to study interventions, it is desirable for participants to have a "behavioral run-in" prior to randomization, to demonstrate that those enrolled will return for study visits. Patients who, in the Investigator's judgment, may not have had adequate time in-hospital to make a solid commitment to participation, may be scheduled for a post-discharge follow-up visit to test compliance prior to randomization.

- additional post-discharge screening for patients likely to meet eligibility criteria, but who do not meet criteria in-hospital

Some patients may have been depressed prior to their MI, while others may become depressed in a reactive manner after their MI has occurred. Hence, while some patients might meet duration criteria for major and minor depression while in the hospital for an acute MI, others may not

meet criteria for up to two weeks after their hospitalization. Similarly, since it is common for patients to experience increased social support from family and friends during a hospitalization only to experience a loss of support upon discharge, some patients will not meet criteria for low perceived social support until after discharge. To avoid excluding these patients, those who do not quite meet criteria in-hospital will be re-evaluated for participation during the immediate post-discharge period.

- early exclusion of patients unlikely to meet eligibility criteria for ENRICHD

To minimize staff time and expense, as well as patient burden, it is desirable that the screening algorithm be designed to expend resources only on those patients who meet, or are likely to meet, study eligibility criteria. Thus, screening and recruitment will be restricted to patients with no known exclusion criteria who meet criteria for depression or low perceived social support in-hospital or are likely to within two weeks of discharge. Specifically, patients with major depression diagnosis and less than 14 day duration, or patients with minor depression less than 14 days and a history of depression, or who score 26-30 on the ESSI while in-hospital, will be re-screened a few days post-discharge to see if they then meet eligibility criteria.

- incorporation of methods to ensure that ENRICHD meets its overall recruitment goals of 50% women and 50% minority representation

Some of the potential barriers of participation in ENRICHD to women and minorities have been identified (see section 4.4.3 below), based on review of the literature (e.g., Becker et al., 1992). As discussed earlier, additional information concerning barriers and methods for overcoming barriers to participation for women and minorities will be gathered during the planned pilot study and focus groups. Based on this information, ENRICHD will employ a number of strategies to facilitate and support women and minorities in overcoming barriers to participation. Central to the methods adopted in ENRICHD is the role of the Case Coordinator (CC) who will facilitate developing an adequate “infrastructure” for the patient and who will be trained to maintain personalized contact with participants and address logistical, belief and attitudinal issues that are likely to emerge among these individuals.

4.2 GENERAL APPROACH TO SCREENING AND RECRUITMENT

Key to addressing the above issues in the approach to screening and recruitment for ENRICHD is ensuring an adequate “infrastructure” to facilitate the recruitment, screening, and later active participation of all participants based on their individual needs. Given the demands of ENRICHD -- in particular, the need for recruitment of high numbers of women and minority patients, the level of psychosocial dysfunction of participants, and the complex array of medical tests and treatments to which these patients will be exposed -- it will be important to identify a cadre of health professionals who can assume responsibility for working with hospital staff, the patient’s physician(s), and study staff to enroll and retain patients. The Case Coordinator, a

nurse with a coronary care or acute medical care background, is best situated by training, experience and location to perform these activities.

Since patients will be enrolled soon after acute myocardial infarction from coronary care units or medical intensive care units, an effective liaison between the staffs of these units and the Case Coordinators will be essential. The Case Coordinators will be responsible for identifying potentially eligible patients, describing the study to them, gaining their informed consent to obtain information from the medical record, querying the primary physician to obtain critical information known only to the physician. The Case Coordinator will ensure that a “relationship” is established with participants to address their individual needs, including issues and problems often encountered by minorities and women, as described more fully in Section 4.4.3 below.

Figure 4-1. Psychosocial Screening and Eligibility Decision Rules

Psychosocial Measure Eligibility Criteria

	+	?	-
ESSI	2 or more items scored ≤ 2	1 item scored ≤ 2 or 1 items scored ≤ 3	0 items scored ≤ 2 and 1 or fewer items scored ≤ 3
DISH	<ol style="list-style-type: none"> 1. Major depression, ≥ 14 days (if no history of major depression) 2. Major depression, ≥ 7 days (if history of major depression) 3. Minor depression, ≥ 14 days (only if history of major depression) 4. Minor depression, ≥ 7 days (only if history of major depression) 5. Dysthymia, ≥ 2 years 	<ol style="list-style-type: none"> 1. Minor depression, any duration, no history of major depression 2. Major depression, < 14 days, no history of major depression 3. Major depression, < 7 days, with history of major derpession. 	Not DISH

Screening Visit 1 (SV1) Outcomes

DISH

ESSI	+	?	-
+	Eligible Complete SV2, SV3 Randomize	Eligible Complete SV2, SV3 Randomize	Eligible Complete SV2, SV3 Randomize
?	Complete SV2 Optional ESSI rescreen*	Optional ESSI rescreen	Optional ESSI rescreen
-	Complete SV2	Optional DISH	Ineligible

*Patients with borderline (“?”) scores on either scale can be re-evaluated up to 21 days post-MI. Patients with positive (“+”) scores at any rescreen can proceed to Screening Visit 2; others are ineligible.

Screening Visit 2 Outcomes

DISH

ESSI	+	?	-
+	Eligible Complete SV3 Randomize	Eligible Complete SV3 Randomize	Eligible Complete SV3 Randomize
-	Eligible Complete SV3 Randomize	Optional DISH rescreen*	Ineligible

*Patients with borderline (“?”) scores on the DISH can be re-evaluated (SV2A) up to 21 days post-MI. Patients with positive (“+”) scores at any rescreen can proceed to Screening Visit 3; others are ineligible.

4.3 OVERVIEW OF SCREENING VISITS AND STUDY ELIGIBILITY

The following sections describe the sequence of screening, recruitment and baseline data collection by visit.

4.3.1 Pre-Screening (PS)

Each center will document the eligibility status of each patient admitted for a possible myocardial infarction by completing a Medical Eligibility (MEA) form. The Case Coordinator and individual hospital screening contacts will be responsible for approaching potentially eligible post-MI patients in participating hospitals for whom the patient's physician has provided consent.

4.3.2 Screening Visit 1 (SV1)

In cases in which patient consent is not required prior to chart review, informed consent will be obtained after chart review for eligible participants so that all patients will have provided informed consent prior to SV1. SV1 will consist of administration of the DISH (Part A) and the ESSI. For both the DISH and ESSI, patients' progression through screening will be determined by their classification according to these two instruments. For the ESSI, eligibility for social support/isolation will be determined totally by classification on the ESSI. . Those who score 2 or less on two items (excluding item 4) or (b) a score of 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) and a total score of 18 or less on items 1, 2, 3, 5 and 6. will be classified as meeting eligibility for social support/isolation and will progress to SV2 for further screening with the DISH. Those who score 2 or less on one item, or 3 or less on two items, will be eligible for re-screening (at SV1a) upon discharge from the hospital.

4.3.3 Screening Visit 1a (SV1a)

Follow-up screening once discharged from the hospital (within 28 days after patients' events) will be administered who score 2 or less on one item or three or less on two items on ESSI at initial screening (SV1). SV1a can be administered either over the phone or in person at the discretion of the local clinic. Patients who fall into the re-screening range on one psychosocial factor, but meet eligibility criteria for the other factor (i.e., eligible on the ESSI, or eligible on the DISH (Part A) but have one item below 2 on the ESSI) will immediately proceed with screening at SV2 and not be re-screened with a SV1a.

4.3.4 Screening Visit 2 (SV2)

Once a patient meets screening criteria either at initial screening (SV1) or re-screening (SV1a), they will be evaluated for depression using the DISH (Part B) at SV2. SV2 can, at the discretion of the local site, occur immediately after eligibility determination at SV1 or SV1a or at a later visit but must occur within 21 days of patients' myocardial infarctions. Screening at SV2 will include administration of the BLESSED if determined to be warranted to gain further information concerning patients' cognitive functioning. The DISH will be administered in this

manner to all patients who qualify at SV1 or SV1a, even those who meet eligibility based on ESSI score. Patients eligible on the basis of low social support then proceed to baseline data collection at SV3, regardless of their score on the DISH. Patients not suffering from low social support, who fail to meet criteria for major or minor depression will be eligible for re-screening (SV2a) during a follow-up to SV2. Those patients who meet depression criteria (i.e., have either major or minor depression according to modified DSM-IV criteria) and/or meet social support criteria (i.e., score 2 or less on two items on the ESSI or (b) a score of 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) and a total score of 18 or less on items 1, 2, 3, 5 and 6.) and who meet all other eligibility criteria will proceed to baseline data collection at SV3.

4.3.5 Follow-up Screening Visit 2 (SV2a)

Those patients screening at SV2, who do not meet criteria for low social support and who have not been found to meet criteria for major or minor depression can be re-screened at SV2a. SV2a will be scheduled on a date that might be expected to allow patients to have had symptoms previously endorsed during DISH administration at SV2 for a period of two weeks (but it must be scheduled within 28 days after patients' myocardial infarctions). Determination of major or minor depression during SV2a will be conducted by querying patients about the duration of symptoms endorsed during the previous DISH administration as a follow-up to the DISH. SV2a may be conducted either via phone or in-person visit at the discretion of the local clinic. Patients who do not have either major or minor depression according to DSM-IV criteria at SV2a will be ineligible to participate further. Patients who meet criteria for major or minor depression and all other eligibility criteria will proceed to SV3.

4.3.6 Screening Visit 3 (SV3)

Patients who meet eligibility criteria at SV2 will then be scheduled for a visit (SV3) during which additional baseline data will be collected. The measures to be collected at this visit are described in the baseline determination section of the Manual of Operations. SV3 can, at the discretion of the local site, occur immediately after eligibility determination at SV2 or at a later visit but must occur within 21 days of patients' myocardial infarctions. However, every effort should be made to enroll patients as quickly as possible.

4.4 SPECIFIC RECRUITMENT APPROACHES AND METHODS

Specific recruitment approaches and methods to be used in ENRICHD to ensure active participation of physicians/hospitals, to promote receptivity of potential patients for ENRICHD, and to address particular logistical, belief and attitudinal issues common among minorities that may affect participation, are summarized below.

4.4.1 Promoting Active Participation Of Physicians/Hospitals

Strategies will be adopted to ensure that providers and hospitals will be likely to support recruitment, adherence and active participation of patients. As discussed in Section 4.2, the Case Coordinator plays a critical role by developing personal relationships with the providers in the study hospitals, ensuring that the providers are appropriately engaged in recruitment generally and particularly in decisions that are being made concerning individual patients.

Additional approaches to promote the active participation of providers and hospitals are:

- promoting articles, flyers and community talks to disseminate information to the broader community about the risks associated with depression and low social support and awareness of the project

General awareness of the project within the broader community was thought to be important to generate support both from the professional community as well as from potential patients and their families.

- support for the project from relevant professional groups

We will endeavor to gain support not only from cardiologists who may be treating patients at the time of enrollment but also from other professionals who may influence the cardiologists and the patients, including primary care physicians affiliated with referring hospitals who may have great influence over their patients; cardiac rehabilitation staff who may have substantial contact and influence with patients during their rehabilitation; and inpatient and outpatient nursing staffs who also may influence both patients as well as physicians. Support from these professional groups will be promoted by: personal contacts with the Case Coordinator and/or local hospital nurse responsible for recruitment; professional talks; mailings (such as a letter, announcing the project and asking for their support from the Director of NHLBI). While the active support of the professional community is seen as very important for ENRICHD, a balance must be struck between fostering the interest and support of these professionals while avoiding promotion of efforts to identify and manage depression and/or low perceived social support to the extent that management of patients assigned to the usual care group is affected.

- involvement of HMOs as appropriate

For some sites, we recognize that the active support of HMOs will be important in efforts to recruit participants. In other sites, given the rapid changes in managed care, the active support of newly-emerging HMOs may become more important over the proposed three years of recruitment for ENRICHD. All of the sites are aware of these issues and either already have solicited the support of HMOs or are prepared to do so when appropriate.

- educating the professional community through a HomePage WWW (www.bios-sph.unc.edu/cscc)

Many members of the professional community have become avid purveyors of the WWW. A HomePage on the WWW will further educate providers about ENRICHD and promote their support of recruitment and retention efforts.

4.4.2 Promoting Receptivity of Potential Patients and Families

- community education to promote receptivity by potential participants and their families

As mentioned in section 4.4.1., we anticipate active efforts to promote community education through multiple channels, using the media as well as talks within the community. Educating potential patients and families about the risks associated with depression and/or low perceived social support may be important in promoting their receptivity to enrollment in ENRICHD. However, as with efforts within the professional community, care will need to be taken to ensure that concerns are not raised to the point that patients and families do not significantly alter their approach to seek care or self-manage depression and low perceived social support for those patients assigned to usual care.

- developing tools and methods to ensure that potentially eligible post-MI patients and their families can be educated quickly and efficiently

Much of the orientation and education of post-MI patients and their families concerning ENRICHD will need to occur while the patients are hospitalized since few will have been exposed to such education prior to the MI. While patients and their families will need to be fully informed, constraints imposed by the nature of the post-MI period necessitate creative strategies for informing patients and families about the study. Since little time may be available during the day to meet with patients and their families to inform them as well as to screen them, ENRICHD will develop brochures and a videotape in an effort to facilitate efficient education and orientation of patients and their families. Videotapes have been successfully used in other studies, and should prove useful for ENRICHD since most hospital rooms are now equipped with VCRs. In addition, staffing patterns will be structured to accommodate patients' needs for recruitment and screening to take place primarily during evening hours.

- incorporating motivational interviewing methods to promote patients to identify and clarify their own, personal reasons for participating in ENRICHD

Within the past few years, several of the ENRICHD investigators have had particular success in teaching recruitment staff to incorporate motivational interviewing methods into their discussions with patients. Motivational interviewing was originally developed by Miller (1991), and colleagues as a method of systematically identifying personal reasons for reducing alcohol consumption among problem drinkers but has more recently been applied in efforts to promote recruitment, adherence and retention within clinical trials. Thus, training of the Case

Coordinators and local hospital recruitment nurses will incorporate the use of motivational interviewing methods in an effort to promote recruitment and active participation.

4.4.3 Addressing Barriers To Recruitment For Minorities And Women

ENRICHD has a goal of enrolling 50% women and 50% minorities in the total sample (Appendix D provides the NIH definition of minority group membership). Several clinical centers will be recruiting from hospitals that serve neighborhoods with high proportions of minority residents. In addition, ENRICHD staff will implement a number of recruitment strategies specifically designed to assist women and minority patients in participating in the study. Since both of these patient groups have often been underrepresented in previous clinical trials concerning the management of MI, a set of standardized recruitment strategies will be adopted which are aimed at facilitating participation by both patient groups. The issues that have been identified and will be addressed that are of particular importance for women, minority and low-SES participants can be categorized into logistical, belief and attitudinal issues, and are further considered below.

- logistical issues such as transportation, dependent care, timing of visits, etc.

When necessary, we will provide transportation, meals, care of dependents and other family obligations, tailored timing of counseling sessions etc. In some cases, this will require liaison with social workers and other health professionals. In other cases, it will involve the Case Coordinator serving as an advocate for participants within the site activities to ensure that methods for overcoming dependent care and session timing concerns are addressed at the local level.

- cultural diversity and sensitivity of staff

Recruitment efforts often suffer from a lack in diversity and sensitivity in study personnel, leading to poor recruitment results in certain subsets of patients. Obviously, this issue is not limited to female and minority patients, and may apply generally to the heterogeneous mix of patients that will be targeted for this trial. We will, therefore, endeavor to hire appropriate personnel aimed at maximizing the diversity of the staff. This will enable us, in most cases, to match staff to patients in terms of gender and ethnicity. In addition, we will have bilingual staff at the sites that plan to recruit Spanish-speaking patients.

In addition, training will be designed to ensure cultural sensitivity. Sensitivity on the part of the staff is not only important regarding the mixed gender and ethnic composition of the study sample, but also regarding the age and specific psychosocial characteristics of the patients targeted in this trial. For example, given the recruitment objective of 50% women, we will likely enroll a substantial number of older and potentially quite frail patients, who might need special assistance during recruitment. Equally important is the fact that the ENRICHD trial is aimed at patients who are depressed and have low perceived social support, and therefore requires that

recruitment staff be educated regarding the nature of these conditions, and trained in how to deal sensitively with these patients during the recruitment process. Severely depressed patients may form a particular challenge during recruitment, and recruitment staff will undergo special training to help them develop the skills to enroll these patients in adequate numbers.

- literacy and language issues

In a study which attempts to enroll bilingual people, mono-lingual non-English speaking people, and low-SES persons, literacy and language issues are extremely important. Populations for ENRICHD in which language is a concern are largely limited to Hispanic populations. While there is clearly variation in language across different segments of the Hispanic population, diversity in our target recruitment population is sufficiently limited to make it possible to use a single translation of text material. Those centers recruiting non-English speaking participants will have sufficient recruitment, screening, clinical and intervention staff who are fluent in Spanish to address communication concerns. We will also ensure that appropriate text materials are used. Many of the instruments to be used in ENRICHD already have been translated into Spanish. For those instruments that have not been translated and for intervention materials, we will translate, using independent back translation with adjudication to ensure accuracy of the translation.

Patients with low literacy levels will likely be encountered by all of the ENRICHD centers. To address this issue, all written materials to be provided to participants will be developed at an 8th-grade level. However, we have also found that it is essential that appropriate options be available to participants for assistance in reading and completing assessment and intervention materials. For assessment materials, all of the ENRICHD centers will use procedures to ensure that clinic staff are available to help patients, and that they ascertain, in sensitive ways, whether participants need questionnaires and materials to be read to them.

Many participants will have family members or friends who can assist in reading materials that are sent home. Particularly for a study such as ENRICHD, which focuses on the treatment of persons who are depressed and/or have low perceived social support, efforts to involve significant others in this manner might be seen as having therapeutic benefit in addition to ensuring that the content of materials can be conveyed. Any record keeping by participants assigned to the intervention can also adequately be accomplished by having significant others record the information, or by providing tape recorders for the recording of information. The Case Coordinator and therapists will work individually with patients to ensure that appropriate measures are being used to address literacy issues.

- complex belief and attitudinal issues

Low-SES and minority participants often report beliefs and attitudes that serve as barriers to participation in trials such as ENRICHD. Common among these belief and attitudinal barriers are: fear of large institutional settings; fear/distrust of "research" and/or academic institutions; concern/unfamiliarity with randomization methods; and concerns about continuity of care and primary care. Training of therapists, Case Coordinators and other staff will ensure that ENRICHD project staff are aware of and sensitive to these issues and prepared to openly discuss these matters with participants. Within the overall context of a supportive environment, acknowledging these common beliefs and attitudes from the outset can allow for open discussion between staff members and participants, and is often sufficient to address these concerns.

Belief and attitudinal barriers to participation will also be addressed through soliciting the support and endorsement of community leaders who are women and who are minorities. Comments by these individuals will be incorporated into video and print materials to be used in ENRICHD.

4.5 TRACKING SYSTEMS/SCREENING DATA TO MONITOR RECRUITMENT

We have found accrual tracking systems to be essential to efficient recruitment, and for examining comparability of enrolled versus not enrolled patients. These data can be used to facilitate recruitment by allowing quick determinations to be made not only of recruitment progress but also to characterize rates at which participants are attending visits, reasons for ineligibility, and recruitment methods that prompted participants to volunteer. These data can then be used to refine recruitment methods and procedures for more efficient recruitment over time. In a study (such as ENRICHD) which seeks to recruit specific proportions of particular groups, these data are also useful for tailoring recruitment methods over time in an attempt to meet goals for these groups. Additionally, these data will allow us to describe individuals who were not eligible for randomization, characterizing their demographic characteristics and specific reasons for ineligibility, as well as individuals who choose not to participate.

Hence, the Coordinating Center will develop an accrual tracking system, incorporating variables seen as useful by the Clinical Units. Variables that will be included are:

- overall yields by screening visits (consent, show and eligibility determination rates)
- responses and yields by recruitment method/hospitals
- key baseline sociodemographic and medical variables from those not randomized.

5. CHAPTER 5: INTERVENTION

5.1 INTRODUCTION

5.1.1 Goals

The overall goal of the psychosocial intervention is to reduce mortality and morbidity following an acute MI, through reduction of high psychosocial risk. Primary treatment aims are to reduce depression in depressed patients and increase social support in those who have low perceived social support. Secondary aims are to further reduce depression and low perceived emotional support by increasing self-efficacy at coping and life satisfaction. Reduction of psychosocial risk involves a combination of individual and group counseling that uses cognitive behavior therapy (CBT) as its foundation, and in cases of severe depression, adjunctive pharmacotherapy. The goal of the usual care control group is to provide a comparison with the psychosocial group in participants who receive usual care from their own providers.

Psychosocial Intervention: Based on the eligibility screening, patients will be classified into one of three groups--depressed only, low perceived social support only, or both depressed and low perceived social support. Treatment begins with individual counseling for all participants, and progresses to 12, two-hour sessions of group counseling. Participants can be seen in both individual and group counseling concurrently. The total length of the Psychosocial Intervention is up to six months from the time of randomization. Participants who receive supplemental psychopharmacology receive such treatment for 12 months. Individual counseling allows treatment to begin immediately after randomization. Group counseling makes it possible to apply skills learned in individual counseling to real life interactions with peers in a supportive setting, and to gain insights not only from the counselor but also from other group members. To increase relevance for post-MI patients, group counseling will be tailored to concerns surrounding the heart attack.

5.1.2 Overview

For depressed participants, treatment sessions will follow CBT for depression, based upon Cognitive Therapy of Depression (Beck, 1979) and Cognitive Therapy: Basics and Beyond (J.S. Beck, 1995). Individual counseling will continue until a significant reduction in depression occurs. In cases of severe depression or depression that is unresponsive to counseling, adjunctive psychopharmacology with sertraline will be used, or if the participant is taking anti-depressants at entry, the medication will be reviewed for safety and efficacy.

For participants who have low perceived social support, individual counseling will utilize a broad range of behavioral, cognitive, and social techniques. Treatment focuses on the development of a supportive therapeutic alliance to address the participant's sense of being unsupported, and the mobilization of potential sources of social support from the

participant's social network which will endure after treatment has ended. It is tailored to match a particular participant's needs, whether it be improving communication skills, changing maladaptive cognitions, and or true social isolation. Treatment can include a spouse, family member or friend, especially for the purpose of mobilization of potential sources of support from the participant's network.

For participants who are both depressed and have low perceived social support, individual treatment will be combined. The therapist has the flexibility to increase the length and/or frequency of the sessions as long as they do not extend beyond 6 months from the time of randomization.

Treatment will be deemed successful if: (1) a minimum of six treatment contacts were achieved. A treatment contact is defined as a contact that is ≥ 20 minutes in duration where, in the judgment of the counselor, the protocol is being followed; (2) a reducing in the psychosocial risk factor(s) has occurred over two serial assessments. It is desirable to conduct weekly assessments, but the counselor has flexibility to make them less frequent if needed; (3) the participant can independently conduct Beck self-therapy; and (4) the participant is engaged in at least one satisfying, supportive relationship (for participants with low social support only).

Treatment will continue only as long as it takes to meet these criteria. They can be met either through individual or group counseling. There is only one exception in which counseling can be terminated before all these criteria are met. This is the case where the participant cannot conduct Beck self-therapy independently (i.e., achieve a score of 12 on the CBT Performance Criteria Scale), but can achieve a score of 5. In this case, counseling can be terminated if the counselor believes that he/she cannot attain a higher score, there is mutual agreement between the participant and the counselor, mutual agreement between the counselor and the supervisor, no remission of the depression and/or low social support; and no important clinical issue anticipated in the future.

Treatment of protocol-compatible problems (e.g., adjustment problems, stress, anxiety, anger, conflict) may and should be treated if they are a route to alleviation of depression or low social support. Protocol incompatible problems which interfere with participant's ENRICHD treatment (e.g., severe panic, alcohol/drug abuse, obsessive-compulsive disorder, borderline personality) should be referred to health professionals in the participant's community. If interest in joining support groups is expressed by the participant, counselors may encourage participation if it is judged to help, rather than hinder, ENRICHD treatment.

Participants will be referred to group counseling when a group becomes available. Groups will be made up of a minimum of three participants and will feature cognitive-behavioral techniques offered in a blend of didactic-instructional and supportive-expressive counseling. Group counseling will be aimed at continuing reductions in depression and low perceived social support achieved during the individual intervention. It will foster further reductions in

these psychosocial factors, prevent relapse, and promote maintenance of treatment effects. It also will be aimed at increasing self-efficacy in cognitive, behavioral, and emotional coping, and at increasing overall life satisfaction.

Usual Care Group: Participants will receive the care usually provided by their own physicians.

Health Education: All participants in ENRICHD (i.e., both psychosocial intervention and usual care groups) will receive basic information on risk factors while they are in the hospital, but will receive no further information after discharge.

5.2 DEPRESSION INTERVENTION

5.2.1 Scientific Rationale

Cognitive behavior therapy (CBT) will be used to treat major and minor depression. Of all existing psychotherapies for unipolar depression, CBT (Beck, 1979) and interpersonal therapy (Klerman, 1984) are best supported by outcomes research. Both were significantly more effective than a placebo plus clinical management, and nearly as effective as imipramine, in the NIMH Treatment of Depression Collaborative Research Program (Elkin, 1989), but a much more extensive database supports the efficacy of CBT for depression (AHCPR, 1993; Dobson, 1989; Hollon, 1991; Robinson, 1990). CBT has been shown to be an effective treatment for depression when used with older adults (Thompson, 1987; Depression Panel, 1993), those with severe depression (Elkin, 1989; Thase, 1991), and minorities, as long as the therapist has cultural sensitivity (Hays, 1995). For the subgroup of patients who are both depressed and socially withdrawn or have poor social skills, CBT has been shown to be superior to interpersonal psychotherapy (Rude, 1991; Sotsky, 1991).

As a relatively brief, goal-oriented, collaborative, and emotionally supportive form of treatment, CBT is generally well accepted by cardiac patients. It can be easily adapted to the typical psychosocial problems and to the mild-to-moderate depressions, commonly observed in cardiac populations (Carney, 1987). In the early phases of therapy with post-MI patients, typical themes are behavioral activation and desensitization of health-related anxieties (e.g., overcoming unwarranted fears about, and avoidance of, returning to work, leisure activities, sexual intercourse, etc.). During the course of treatment, themes turn to cognitive distortions common among post-MI patients, such as "catastrophizing" in response to mild exertional fatigue, "fortune-telling" in response to fears of abandonment, and "black-and-white thinking" in response to shifting from medically risky leisure activities to safer alternatives.

5.2.2 Goals and Performance Criteria

The primary goal of the depression intervention is to significantly reduce depressive symptoms in as short a time as possible. To monitor progress in meeting this goal, the Beck Depression Inventory (BDI) will be administered every other week during the course of counseling. The CBT intervention helps participants to achieve the following performance criteria: (1) an ability to identify problem situations, and the associated cognitions, that promote depressed mood; (2) an ability to apply CBT skills in a review of experiences over the past week; (3) an ability to appraise one's own thinking about current problematic situations or issues; and (4) an ability and willingness to apply CBT skills appropriately to new situations.

5.2.3 Structure and Setting

Counseling will take place in weekly 50-minute sessions. Patients will be seen in the counselor's offices on most occasions, but home sessions may be scheduled, if needed. At the discretion of the counselor, participants may be scheduled for twice weekly sessions. This is encouraged, especially in the first several weeks of treatment.

5.2.4 Typical Session

A typical 50-minute session begins with the establishment of rapport between counselor and participant, often within the context of the participant's reaction to the prior session. Next, homework from the prior session is reviewed with an emphasis on problems and accomplishments over the past week. During this discussion, the counselor will use the participant's experiences to reinforce previously learned concepts or introduce new ones. The session will end with an assignment of new homework and an elicitation of the participant's reaction to that session.

Early sessions of CBT focus on explanations of cognitive-behavioral strategies. They emphasize the rationale for identifying and changing inappropriate automatic thoughts and for behavioral assignments and homework. Participants receive instruction in identifying negative automatic thoughts, using such techniques as "induced fantasy" or role-playing, as needed. They also learn how automatic thoughts represent distortions of reality and trigger symptoms of depression. Counselors directly elicit automatic thoughts relating to homework assignments to help achieve this goal. As the sessions progress, there is increasing delegation of responsibility to the participant for setting the agenda. Participants are expected to identify needed skills, and to focus on these in each session. Toward the end of treatment, participants are expected to be able to apply all CBT skills, as needed.

5.2.5 Criteria for Successful Completion of Treatment

Treatment will continue until the participant has (1) completed at least six sessions, (2) can conduct the Beck self-therapy in the judgment of the counselor, by virtue of scoring 12 on the CBT Performance Criteria Scale (see goals and performance criteria, above), and (3) scores below seven on the BDI for two consecutive assessments. As needed counseling will be extended for participants who do not meet these criteria after six sessions.

Either individual or group counseling can be used to achieve performance criteria. A participant can be terminated without meeting criteria if plans are to begin a group. If the group cannot achieve performance criteria, individual counseling may be begun again. If performance criteria have been met before the group has finished, the participant should still be encouraged to complete all the 12 sessions of the group.

Among the reasons for not referring a participant to group counseling are: (1) presence of psychotic features, including hallucinations or delusions; (2) severe, nonremitting psychomotor retardation; (3) Axis II disorders which, in the therapist's judgment, would be disruptive to the group process, or would affect the patient's ability to derive benefit from the group (e.g., borderline personality disorder); and (4) severe social anxiety. If such a reason is absent, the participant will generally be referred to group counseling.

For participants who meet criteria for successful completion of counseling, but who later develop scores ≥ 7 on the BDI for two consecutive assessments, referral back to individual counseling will be made. Participants with major depression who have not decreased their BDI scores at least 50% by the fifth week of treatment, will be evaluated for antidepressants (see below). How does the inclusion of folks on anti-depressants change this line if any?

5.2.6 Psychopharmacological Intervention

5.2.6.1 Goals

The goal of psychopharmacology is to ensure that participants with more severe forms of depression, and those who fail to benefit adequately from the ENRICHD individual CBT/Group intervention, are provided the full range of therapeutic options for depression.

5.2.6.2 Eligibility

Candidates for antidepressant treatment will:

1. Fulfill DSM-IV criteria for major depression at baseline or during therapy

and

- 2a. Score ≥ 24 on the 17-item Hamilton Depression Scale rating at the baseline evaluation.

or

2b. Have an inadequate response to individual CBT (i.e., <50% reduction in BDI score after five weeks of therapy; be judged to have an inadequate response to CBT during “refresher” sessions following depression relapse)

or

2c. Score > 20 on the Hamilton Depression Scale during the 12 month period after randomization.

5.2.6.3 Exclusion Criteria

Candidates for antidepressant counseling will be referred to primary care providers for depression management, rather than receive treatment by the ENRICHD psychiatrist, if they fulfill any of the following criteria:

1. DSM-IV Major Depression with Psychosis;
2. Judged to be a serious suicide risk (see MOO Depression Intervention);
3. Severe major depression requiring electroconvulsive therapy;
4. Active alcohol or substance abuse;
5. Patient or primary physician/cardiologist unwillingness to accept pharmacological treatment.

5.2.6.4 Evaluation Of Participants Who Are Taking Psychopharmacological Medications At The Time Of Enrollment

The ENRICHD psychiatrist at each site needs to review the safety and apparent efficacy of any antidepressants used by patients on antidepressants at the time of enrollment. The review will occur through discussion of the case with the case coordinator (or other individuals involved in the patient’s assessment) and should occur within three weeks of enrollment.

1. Safety: The safety of the medication will be considered from a statement of potential harmful effects of the medication as used in patients with cardiovascular disease and interactions with other medications the patient may be taking. A decision to intervene with the treating physician will be based on the discretion of the local ENRICHD psychiatrist.
2. Efficacy: The efficacy of the antidepressants the patient may be taking at the time of enrollment will be considered in terms of medication type, dose, length, and the patient’s response. The decision to intervene (e.g., to call the local psychiatrist or the physician treating the patient) will be left with the local ENRICHD psychiatrist.

The ENRICHD psychiatrist should review the status of patients on medications at entry, 3 months and 6 months, and more often as indicated.

5.2.6.5 Management Protocol

- Assessment for possible pharmacological treatment will be performed by ENRICHD psychiatrists.
- Pharmacologic treatment will be given in conjunction with individual CBT/Group interventions.
- Pharmacologic treatment interventions will adhere to Agency for Health Care Policy and Research (AHCPR) Clinical Practice Guidelines.
- Concurrence for initiating pharmacological treatment will be obtained from patients' primary medical providers/cardiologists.
- Pre-treatment assessment will include:
 - appropriate laboratory assessment to identify medical, metabolic, or medication-induced depression
 - baseline electrocardiogram
 - review of medications to identify possible drug incompatibilities, e.g., coumadin, terfenadine
- Treatment will be initiated with sertraline 50 mg/daily, unless contraindicated by medical status or history of non-response to sertraline. Patients will be evaluated weekly for the first three to five weeks of treatment. Dosage adjustments to a maximum of 200 mg/day will be determined by clinical judgment. Thereafter, patients will be assessed at two to four week intervals as needed.
- Benzodiazepine hypnotics or anxiolytics will be permitted for short term use (3 - 14 days) when sleep or anxiety cause significant distress or interference with function.
- Participants unable to tolerate sertraline or those judged to have an inadequate response to treatment after 4-5 weeks will be considered for alternative pharmacotherapy using another SSRI or nortriptyline. Cardiac conduction disturbances or hypotension may limit nortriptyline use. Patients who are unresponsive to the alternative agent or who require more complex pharmacologic interventions will be referred to community providers for pharmacologic management.

- Participants who achieve a therapeutic response to pharmacologic treatment will be maintained on antidepressants for up to 12 months from the time of randomization. The frequency of periodic follow-up assessments and eventual termination of pharmacotherapy will be determined by the treating psychiatrist.

5.2.6.6 Role Of Psychiatrist

Participants considered to be candidates for pharmacotherapy, according to the criteria above, will be referred for assessment by a psychiatrist who is identified as a member of the ENRICHD project. The ENRICHD psychiatrist (s) will assume primary responsibility for implementing the pharmacologic management protocol during the 12- month intervention period. Thereafter, participants will be referred to providers in the community for treatment.

5.2.6.7 Criteria For Termination

Pharmacological treatment will be provided in conjunction with individual CBT and group counseling. Thus, the decision algorithms governing the matriculation through the individual and group CBT will apply to patients receiving concurrent pharmacotherapy. Efforts should be made to coordinate pharmacotherapy visits with the routine ENRICHD protocol in order to reduce the burden of participation in the project. As noted above, patients who achieve a therapeutic response to pharmacotherapy will be treated for a twelve-month duration. In rare cases, participants might develop psychosis, be judged at risk for suicide, require hospitalization, or otherwise require more intensive intervention than can be safely provided by ENRICHD providers. Such participants will be referred for appropriate ongoing care in the local community.

5.3 SOCIAL SUPPORT INTERVENTION

5.3.1 Scientific Rationale

A number of interventions targeting perceptions of low perceived social support have been described (Andersson). These multi-modal interventions take the form of clinical treatment, family enhancement, neighborhood helping, and case management (Biegel, 1985). They target such components as social interaction and communication skills, cognitive and affective aspects of isolation, self-efficacy and empowerment, and access to public and private services. The social support intervention targets three interacting mechanisms--behavioral, psychological, and physiological--which may provide links between low perceived emotional support and cardiac outcomes (Amick, 1994). In the behavioral domain, supportive interactions may encourage risk reduction efforts, adherence to medical regimens, and timely seeking of medical attention should clinical symptoms occur. In the psychological domain, supportive interactions can serve to buffer the impact of stressful encounters, help participants redefine stressors as benign, provide encouragement, particularly with regard to recovery from MI, and enhance self-esteem and self-efficacy (Ockene, 1981). Such support can then have an impact on the physiological realm by reducing the degree of physiological activation that occurs during stressful encounters (Uden, 1989; Kamarck, 1990; Fleming, 1982).

5.3.2 Goals

The primary goal of the social support intervention is to alleviate the participant's perception of low perceived emotional support. To accomplish this goal, the social support intervention will have four targets: (1) the immediate establishment of a supportive alliance between the therapist and the participant; (2) the development of a social skills repertoire that will facilitate the development of supportive social ties; (3) the mobilization and utilization of social resources that naturally exist in the participant's network; and (4) the alteration of automatic thoughts that interfere with establishing supportive relationships.

Specific interventions will be determined by a multi-modal assessment that will guide the counselor to match the treatment to the participant's support deficits (Biegel, 1985; Smith, 1994). This assessment is aimed at determining the nature of the participant's perceived lack of support, the social, behavioral, and cognitive factors that contribute to the sense of low emotional support, and the potential natural sources of support that exist in the larger community. Assessment will feature both qualitative and quantitative strategies, including the concentric circle method of determining social networks (Kahn, 1980). Specific targets of the assessment can include:

- instrumental needs;
- emotional needs;
- communication skill repertoire;

- cognitions, attitudes, and beliefs relating to social ties and network availability;
- social anxiety or phobia;
- degree of social integration;
- satisfaction with sources of support;
- preference for, and importance of, types of support;
- problem-solving and planning skill repertoire.

Treatment is individually tailored according to this dynamic, multi-modal assessment. The social support intervention initiates a change process, and the group treatment serves to reinforce and expand upon it. In the delivery of treatment, the MI serves as the context for an examination and alteration of social interchange. The early focus of the social support intervention is on establishing a therapeutic alliance and a relationship of trust and support with the counselor. Next, the focus is on altering any behavioral and/or cognitive schema that lead to the perception of low emotional support (Biegel, 1985; Rook, 1984; Baucom, 1990). At the same time, the counselor examines the social network (i.e., family, spouse, neighbors, and friends) with the aim of identifying likely potential sources of satisfying support and involving them in the treatment effort. Specific skills that may be taught include problem solving, communication skills, cognitive restructuring, support mobilization, and network restructuring. In the delivery of these components, the counselor relies upon proven treatment techniques, including modeling, prompting and shaping.

5.3.3 Performance Criteria

The social support intervention helps participants to achieve the following performance criteria: (1) an ability to identify situations and relationships that contribute to dissatisfaction and low perceived emotional support; (2) an ability to apply communications skills to modify conflictual or demanding relationships; (3) an ability to identify and utilize new sources of emotional, informational, and instrumental support; (4) an ability to identify and modify cognitive and affective experiences that contribute to dissatisfaction and low perceived social support; and (5) a willingness to participate in the group treatment.

5.3.4 Typical Session

A typical session begins with the establishment of rapport, instilling in the participant a sense of belonging and connectedness to a supportive other (i.e., the therapist). Focusing on the past week and associated homework assignments, the participant and therapist discuss supportive and unsupportive experiences, identifying what contributed to these experiences and why. The counselor reinforces positive efforts and successes, probes to examine the actions, attitudes, and beliefs associated with failed attempts, continued problematic interactions, or continued low perceived social support. When an attitude/belief or a preferred method of coping has been identified as ineffective, the therapist engages the participant in a problem solving process

designed to identify other actions or attitudes that could have produced more desirable results. Family or significant others can be included in all or part of a session to facilitate the learning of support-related behaviors, the modification of unsupportive or conflictual behaviors, and/or the mobilization of specific types of support.

5.3.5 Evolution Of Tasks Over Sessions

In the initial sessions, the counselor insures that the participants' feelings of low support are alleviated by establishing a supportive relationship with the participant. The dynamic assessment attempts to identify the factors associated with the participant's sense of low perceived emotional support.

When the task is to improve social and interpersonal skills, early sessions focus on identifying the participant's habitual behaviors and exploring new alternatives. Behavioral strategies, including social and communication skills training, are utilized to teach the participant and, where applicable, significant network members, more supportive ways of interacting.

When the task is to mobilize support for a participant who is truly isolated, early sessions focus on the identification of unsupportive or conflictual relationships, the formal community-based resources (e.g., social rehabilitation, and recreational groups) and central figures (e.g., spouse, child, neighbor, friends) that potentially exist in the network. As treatment progresses, the goal is to modify or remove unsupportive or conflictual relationships, and initiate new supportive ties through involvement in activities and provision of opportunities for socializing. Modifying unsupportive relationships may entail discussions with significant others about what constitutes supportive interactions and can include a process of modeling, prompting, and shaping of communication and behavior to provide desired support.

When the task is to modify automatic thoughts that lead to social withdrawal, the technique associated with CBT (Section 5.3) are used.

5.3.6 Structure And Setting

The social support intervention can take place in the home or the clinic. There will be no specific order to the topics covered but all sessions should target support deficits that have been identified in the multi-modal assessment.

5.3.6.1 Criteria for Movement To Group Counseling

The transition to group counseling is based upon the existence of: (1) a group to enter; (2) the judgment of the counselor; and (3) the absence of contraindications, including character pathology that will cause disruption in a group setting, continued significant levels of social phobia or severe shyness, or other factors that the counselor judges will result in the participant being lost to treatment. Transition to group may be gradual, with the participant undergoing both individual and group counseling at the same time. It is especially important that the

counselor refer the participant with low social support to a group as soon as possible, because the group offers a powerful context for improving feelings of low emotional support.

5.3.7 Criteria For Successful Treatment

Criteria for successful treatment for low perceived social support can be met with either individual or group counseling. They include: 1) the presence of at least one satisfying and supportive social relationship (other than the counselor), 2) the ability to do "self therapy" (e.g., perform, unassisted, the cognitive and behavioral operations that support the development and maintenance of supportive social ties), defined as a score of 12 on the CBT Performance Scale; 3) achievement of an improvement in perceived emotional support defined as a score of 4 or more on at least 2 items of the Modified Duke Social Support Scale; and 4) completion of a minimum of 6 sessions of either individual or group counseling.

5.3.8 Intervention For Participants Who Are Both Depressed and Have Low Perceived Social Support

The intervention for participants who have both of these presentations requires neither a change of focus nor the addition of treatment strategies or techniques. When both depression and low perceived social support are part of the clinical presentation, they are likely to be highly related, interacting synergistically to maintain each other. Moreover, there is a high degree of overlap between the two individual interventions (e.g., behavioral activation, effective problem solving). The participant continues to play a central role, the content of each session is determined by the past week's experiences, and goals and performance criteria become additive. The counselor is given increased flexibility regarding the length and/or frequency of sessions so that the depression and social support content can be addressed as needed, however all treatment is still discontinued after 6 months from the time of randomization.

5.4 GROUP COUNSELING INTERVENTION

5.4.1 Scientific Rationale

Group-based interventions are widely used in the treatment of chronically ill medical patients (Antoni, 1991; Ceccoli, 1992; Compton, 1992; Jakes, 1992; James, 1993; Spiegel, 1994; Lorig). Cognitive-behavioral procedures have been widely implemented in groups and have been effective in the treatment of major depression (Beck, 1995; Stravynski, 1994), minor depression (Antoni, 1991; Beck, 1995; Trzcieniecka-Green, 1992), anxiety disorders (Stern, 1983; Telch, 1993; Trzcieniecka-Green, 1992), and distress (Antoni, 1991; Fawzy, 1990). Coping skills have been shown to be mediators of the connection between low perceived social support and depressive symptoms (Holahan, 1995; Holahan, 1991).

Group-based interventions are well suited to coronary heart disease (CHD) patients (Thoresen & Bracke, 1996). The CHD patient groups become cohesive and patients benefit in learning from each other's experiences (Shuster, 1992). The groups also provide a "laboratory" to rehearse

skills and promote social support. The results of controlled group-based interventions show considerable promise with respect to favorably influencing primary CHD endpoints in post-MI, post CABG, and coronary artery disease patients (Burell, 1995; Friedman, 1986; Powell, 1988; Ornish, 1990; Rahe, 1979; Ibriham, 1974; Thoresen & Powell, 1992).

The small group intervention seeks to achieve the following primary objectives: (1) to further reduce, maintain and generalize progress in reduction of depression-related experience as well as increase pleasant activities; and (2) to further reduce, maintain, and generalize reductions in low perceived social support and increase perceptions of high social support. Secondary goals, accomplished in the service of furthering a reduction in depression and improvement in social support, are to enhance self-efficacy at coping, increase perceived self-esteem and increase overall life satisfaction.

5.4.2 Goals

The goals of the small group intervention have been guided by several assumptions. First, treating participants in a group setting will provide an opportunity to practice, generalize and maintain skills learned to reduce depression and increase social support. Second, promotion and maintenance of behavior change can be maximized when conducted in a supportive and caring learning environment. Third, an ability to learn and use effective self-management skills is essential for maintenance of behavior change.

5.4.3 Structure And Setting

The small cognitive-behavioral group intervention will feature a modified open group format three reliable members are identified and participate regularly, and other participants can enter and exit at any time. Within a group, members may include those who were initially depressed, had low perceived social support or both. If no group is available, a participant will continue in individual counseling until performance criteria are met or a group becomes available.

The small group intervention will be comprised of a minimum of three participants and will meet for 12 consecutive sessions of two hours each. Following the last group session, each participant will be followed by the counselor by telephone once a month, from for up to the six month total intervention period (from the point of initiating individual intervention). Participants who are treated for the entire six-month period will receive the telephone call at the seven-month mark and subsequent telephone calls, as needed. A participant can enter a group up until their 6-month anniversary from the time of randomization. Thus for those entering a group the day before their anniversary, their treatment will end nine months from the time of randomization.

5.4.4 Transitioning Patients From Individual Counseling

The group leader is to meet with participants prior to the onset of the group. This meeting can be accomplished as part of individual counseling when the group leader is also the individual counselor. The leader will provide the rationale for group treatment, orient the participant on

how groups function, and address any participant concerns. There are no specific criteria to enter groups although contraindications should be observed (see Section 5.2.5 and 5.3.7). Entry into groups is largely based on the counselor's judgment. If a group is available, participants should be referred to the group intervention. In some cases, participants will receive individual and group counseling concurrently.

5.4.5 Typical Session

Each two-hour session will be approximately standardized so that group members develop an understanding of what to expect from the leader, the group, and themselves. The generic flow typically will be as follows:

- Setting the agenda;
- Initial relaxation/meditation practice (15 min.);
- Announcements (5 min.);
- Focused discussion of script review/homework and sharing of experiences for past week (30-35 min.);
- Planned topic(s) of session. (55 min.);
- Brief group recap of session's main point(s) and clarification of tasks to be completed before next meeting (3-4 min.);
- member feedback, preview of next session (10 min.)

5.4.6 Evolution Of Tasks Over Sessions

The sessions are intended to build upon work done in individual counseling. The leader has latitude to address members' issues as they arise, even though no specific curriculum exists. Initial sessions will primarily provide targeted information, promote understanding, and encourage completion of outside group tasks via behavioral contracting (Lorig, 1993). Emphasis will also be on encouraging group members to share experiences, raise concerns, and listen to each other. The session length of 2 hours is needed to provide sufficient time to cover a variety of activities and to ensure that each group member has the opportunity to participate actively, receive constructive feedback, and develop skills.

5.4.7 Procedures If A Group Is Unavailable

In cases where group treatment is not possible because of geographical or recruiting constraints, the content of the group curriculum will be offered as a continuation of the individual counseling.

5.4.8 Group Counselors

The selection, orientation, supervision, and support of group counselors is crucial. In representing the ENRICHD program, these professionals will play the key role in success of this trial. In a recent meta-analysis, Crits-Christoph et al. (1991) examined factors that accounted for therapist efficacy differences in psychotherapy outcome studies and found that the use of treatment manuals and more experienced counselors were associated with smaller differences between therapists.

To promote continuity between the individual and group treatments, when possible, the same counselors will conduct both. However, sites will have the flexibility to identify different people for these treatments. In cases where the therapists are different, communication among them will be essential, and will take place during regularly scheduled (e.g., weekly) local case conferences.

Educational criteria include substantial advanced graduate training in clinical/ counseling psychology (PhD), clinical social work (MSW), clinical psychiatry (MD), or psychiatric nursing (MS or greater). Seasoned counselors with experience are optimal. Desirable experience includes treatment of depression, work with couples, families, and/or groups, work with patients with chronic disease or, more specifically, coronary disease, and competency in CBT. Information on counselor training, certification and the monitoring of counselor performance is provided in Chapter 13.

5.5 USUAL CARE

5.5.1 Goals

(1) To minimize the extent to which interactions with study personnel could alter the participants psychosocial status, or alter aspects of their medical care; (2) to increase motivation for participation in the study, and (3) to offer a basic standardized health education component.

5.5.2 Overview

After determination of eligibility, contacts with participants randomized to the Usual Care group will occur for two reasons. (1) Education: This will be the same written material provided to participants randomized to the psychosocial intervention. (2) Follow-up Assessments: Usual care participants will receive follow-up assessments that are identical to those received by participants randomized to the psychosocial intervention, by assessors not involved in the intervention.

5.5.3 Scientific Rationale

A control group (not receiving the experimental intervention) is a necessary part of a controlled scientific trial.

5.6 HEALTH EDUCATION

5.6.1 Overview

After determination of eligibility, participants will receive, from the Case Coordinator, some written materials providing education on standard CHD risk factors (American Heart Active Partnership For The Health Of Your Heart). The Case Coordinator will provide a short overview of the material and the participant will use it on his/her own.

5.6.2 Scientific Rationale

To provide information that is consistent with the recently released Agency for Health Care Policy and Research/American Association of Cardiac Pulmonary Research (AHCPR/AACVPR) Guidelines, a uniform message about the importance of exercise and cardiovascular risk reduction will be provided. However, no more extensive education will be provided, to guard against the possibility that the education contact or information will alter the participant's psychosocial status or in other ways compete with the psychosocial intervention. There are a number of programs available for risk factor education. In choosing the information for health education, the following guidelines were followed: (1) the information should be appropriate for the AHCPR guidelines; (2) the education materials should be appropriate for a wide range of reading skills and socioeconomic groups; and (3) the educational materials should require no contact with the participant beyond the initial hospital visit.

Education will be provided in written materials. These written materials will be the American Heart Association's Active Partnership. The Case Coordinator will introduce the materials following a written script, and will show the participant that the manual contains sections on understanding coronary heart disease, food, exercise, stress, and smoking (as appropriate for the subject). The total time to review this information should be less than 15 minutes.

5.7 SPECIAL POPULATIONS

5.7.1 Evidence That CBT Is Effective With Older Adults

Several studies have addressed the efficacy of CBT in older adult patients. The findings of these studies have been fairly consistent. First, elderly depressed patients respond as well to CBT as to most recognized forms of psychotherapy for depression. For example, Thompson and colleagues (1987) randomly assigned 90 elderly depressed patients to receive either individual CBT, behavior therapy, or brief psychodynamic psychotherapy. After 16-20 weeks of treatment, 52% of patients in all 3 treatments remitted, 18% were significantly improved, and 30% were unimproved.

Second, older adults generally respond to CBT as well as their younger, depressed counterparts. In a quantitative review of all available randomized clinical trials, using the intent-to-treat

principle, it was found that the overall efficacy of cognitive therapy was 51.3% in geriatric patients, compared to 46.9% for adult outpatients of all ages (Depression Guideline Panel, 1993).

5.7.2 Evidence That CBT Is Effective With Depressed Minority Patients

Although there are few studies that specifically address the efficacy of CBT for the treatment of depression in minority patients, the opinion of most authors who have published papers in this area is that CBT works well with minority patients, **if** the therapist is sensitive to the cultural needs of each patient (Hays, 1995; Organista, 1994). Several of the sites report having had good success in using CBT with minority populations. The University of Miami, for example, has begun to use CBT to treat African-American and Hispanic women in groups. The therapists report overall success with slight modification of the standard CBT protocol used by their project. Most difficulty has been with persons in the lowest SES level. This experience is consistent with that reported in a survey of clinicians at the University of Alabama at Birmingham. Overall, these clinicians report success in using CBT in treating depression, anxiety, chronic pain, and eating disorders in African-Americans. However, some modification of the protocol is often needed for those persons in the lowest SES. In summary, therapists experienced in working with various minority groups have generally found ways to adapt the treatment protocol to the cultural and educational differences of their patients and clients.

5.8 CHAPTER REFERENCES

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6. CHAPTER 6: MEDICAL ENDPOINTS AND MEASUREMENTS

The primary objective of the ENRICHD Patients Study is to evaluate the effects of psychosocial intervention, relative to usual care, on the combined endpoint of all-cause mortality and reinfarction in recently diagnosed acute MI patients who are depressed and/or have low perceived social support. Secondary objectives include evaluation of the effects of the intervention on a number of medical and psychosocial endpoints of interest. This chapter describes the medical measurements to be collected in ENRICHD; Chapter 7 will describe the psychosocial measures to be included in the study.

6.1 PRIMARY ENDPOINT

The primary endpoint of this study is the first occurrence of a nonfatal myocardial infarction or all-cause mortality. This endpoint is clinically relevant, regardless of the outcome of the study. If the study finds that psychosocial intervention improves clinical outcome, it will strongly support an aggressive strategy of secondary prevention involving these psychosocial techniques in acute MI patients. However, if there is no difference between the groups, then the strategy, which has been a component of many cardiac rehabilitation programs, will have to be re-evaluated.

All-cause mortality as a component of the primary endpoint is preferred to cardiovascular mortality because it eliminates the possible ambiguity of a differential result between cardiovascular death and non-cardiovascular death. It is possible that, in a trial involving a population at risk for other comorbidities and for suicidal deaths, an unanticipated excess of non-cardiovascular mortality could be seen. Furthermore, although it is important to understand the mechanism of death, the cause of death can often be difficult to classify.

The addition of nonfatal MI to the primary endpoint is appropriate, since the natural history of patients with acute MI places them at risk for a recurrent nonfatal MI which is related to the underlying pathophysiology and disease process. A nonfatal MI has been utilized as a component of the primary endpoint in many major secondary prevention trials (e.g., CARE, GUSTO II). The recurrence of a nonfatal MI increases the risk of subsequent death and, thus serves as an adequate surrogate endpoint for mortality. In addition, combining all-cause mortality and recurrent MI allows for an increased event rate and therefore a reduced sample size.

6.2 SECONDARY MEDICAL ENDPOINTS

The secondary medical endpoints in this study are:

1. All cause mortality
2. Cardiovascular mortality (due to sudden death, fatal MI, or intractable heart failure death)
3. Recurrent nonfatal myocardial infarction
4. Revascularization procedures (PTCA, CABG, cardiac transplantation)
5. Cardiovascular hospitalizations
6. HCFA quality of care process indicators
7. Risk factor profile change

Appendix F contains specific definitions for the primary and secondary medical endpoints outlined above.

6.2.1 Justification of Secondary Medical Endpoints

6.2.1.1 All-cause Mortality

All-cause mortality is indisputable and has the advantage over cardiovascular death of taking into account for any unanticipated non-cardiovascular death rates that may occur. This is particularly important in this population of depressed and/or socially isolated post-MI patients, in whom suicides, homicide rates, and accidental deaths may be important.

6.2.1.2 Cardiovascular Mortality

The psychosocial intervention used in ENRICHD is expected to affect cardiovascular mortality specifically. Therefore, cardiovascular mortality should be a more sensitive measure of treatment efficacy than all-cause mortality. An Events Classification Committee will classify the mode of death using death certificates and appropriate clinical summary information to categorize cardiovascular death into one of three major types of cardiovascular mortality (sudden cardiac death, death due to fatal myocardial infarction and death due to intractable heart failure). Other cardiovascular causes of death will also be classified, but these three are expected to account for 90% of the cardiovascular deaths.

6.2.1.3 Recurrent Nonfatal MI

Recurrent nonfatal myocardial infarctions will be ascertained in two ways. At each follow-up visit and phone call, patients will be asked about any hospitalizations, emergency room visits, or other events that may indicate the occurrence of an event. All

such reports will be investigated, using hospital records, interviews with attending physicians, etc. In addition, at each annual follow-up visit, a standard 12-lead resting ECG will be performed, using a standard protocol. These ECGs will be transferred to St Louis University Core ECG reading center, which will evaluate them for evidence of unrecognized MIs. We anticipate that 10% of the nonfatal MIs will be unrecognized. All suspected recurrent nonfatal myocardial infarctions will be reviewed and classified by the Events Classification Committee. The diagnoses of acute myocardial infarction during follow-up will utilize the same criteria as that used for eligibility purposes.

6.2.1.4 Revascularization Procedures

Revascularization procedures (PTCA, CABG, and cardiac transplantation) will be recorded. All percutaneous procedures including angioplasty, stent deployment, atherectomy, and other percutaneous procedures will be included as well as coronary artery bypass grafting. We expect the cardiac transplantation rate to be low, but it will also be included for completeness. A reduction in the combined revascularization rates was seen in the 4S Lipid Lowering trial, the Pravastatin Post Myocardial Infarction Trial, and the Cholesterol and Recurrent Events (CARE) Trial, and interpreted as an important benefit of the therapeutic intervention.

6.2.1.5 Cardiovascular Hospitalization

Hospitalization for cardiac reasons incur significant morbidity and healthcare costs. We will define a hospitalization having a discharge ICD-9 code of 401, 402, 404, 411-414, 428 or 429 as a cardiovascular hospitalization.

6.2.1.6 The HCFA Quality Of Care Process Indicators

The HCFA quality of care process indicators (see Appendix G) are minimum standards that are felt to be an important component of the management of acute MI patients, such as the use of aspirin or thrombolytic therapy in appropriate patients. These indicators will be ascertained at baseline and at six month follow-up.

6.2.1.7 Risk Factor Profile Changes

Risk factor profile changes will be ascertained at the 6 and 18 month visits and yearly thereafter. Ascertainment of risk factor changes will include blood pressure measurement, self-report of compliance with medical regimens, and ascertainment of smoking status.

6.3 ENDPOINT CLASSIFICATION COMMITTEE

Standardized, treatment-masked classification of all-cause mortality and nonfatal MI as the primary endpoint and the individual components of the endpoint including cardiovascular mortality, non-cardiovascular mortality, fatal and nonfatal MI, and mode of death will be

performed by an Endpoint Classification Committee. For each suspect event, the Coordinating Center will compile the relevant documentation from medical records submitted by the clinical centers and reports from the ECG core lab. All information concerning treatment assignment will be masked by the Coordinating Center before the packets are distributed for review and classification. The committee will be chaired by a cardiologist and consist of eight cardiologists as members. The committee will meet on a six month basis to adjudicate all deaths and potential MIs.

6.4 COLLECTION OF MEDICAL MEASUREMENTS

Medical evaluation in this trial will be conducted at baseline, six months, 18 months, and then annually for the remainder of each individual's participation in the study.

6.4.1 Medical History And Physical Exam

At baseline, a number of important prognostic indicators will be collected, including demographic information, a standardized medical history, a physical exam, and documentation of the index MI. In addition to the qualifying diagnostic information (enzymes, ECG abnormalities, etc.), the locus of the infarction (q-wave or non-q-wave, as well as the location) will be documented. We will make efforts to maximize the proportion of patients for whom a baseline estimate of ejection fraction made since this measurement is a key prognostic covariate (DeBusk et al., 1989; Killip, 1967). We estimate, based on the pilot study, that 75% of patients will have an ejection fraction study as part of their clinical care; when necessary, ENRICHD cardiologists will be responsible for reading any studies for which a quantitative estimate of ejection fraction was not recorded in the chart. To the extent possible, the study will provide funding to obtain those that are not available. This approach will result in data that is measured with a variety of techniques (radionuclide approaches, echocardiography, etc) but has been used in studies of congestive heart failure and been shown to provide sufficient accuracy for clinical correlation (Kirlin, et al., 1994, Benedict et al., 1993).

At the six month, eighteen month, and annual follow-up visits, historical, and physical exam information will be obtained, most typically, by the Case Coordinator. Historical information will involve the patient's clinical course, including endpoint ascertainment and utilization of healthcare resources. Medical compliance, risk profile, and lifestyle behaviors will be ascertained by interview. At the Investigator's discretion, a simplified physical examination will be conducted. This will include the measurement of blood pressure and vital signs only. Finally, a standard 12-lead resting electrocardiogram will be obtained at 6, and 18 months and yearly thereafter, for ascertainment of unrecognized MI. The ECGs will be sent to the St. Louis ECG Core Laboratory central Reading Center for quantitative analysis.

6.4.2 Follow-up Visit Schedule

Follow-up assessments are designed to coincide with the natural history of the disease state post-MI. Since 75% of cardiovascular events occur in the first six months post-MI, and the event rate then flattens out to an annual rate of approximately 6% per year (Multi-center Post-Infarction Research Group, 1983), it is appropriate after the first six months to conduct follow-up on an annual basis. All patients will be asked to return to the Outpatient Clinic at 6 and 18 months after enrollment and annually thereafter for a medical evaluation.

In the event a patient misses a medical follow-up visit, telephone contact will occur. Through patient education at the time of enrollment we anticipate that at least 90% of the patients will comply with the medical follow-up. However, the 10% who do not comply will be contacted by the study coordinator via telephone. During the call, medical information will be reviewed. Additionally, the patient will be encouraged to come to the clinic for evaluation. In the event they are unable or unwilling to return to the clinic, as much information will be ascertained over the telephone as possible.

6.5 EVENT REPORTING AND SUBMISSION OF EVENTS

The potential endpoint events that will be collected will be the occurrence of death, suspected MI, other cardiovascular events, and revascularization. The Coordinating Center will be notified about these events in two ways. During the follow-up visits and phone calls, the patients will be asked if any of these events have occurred since they were last contacted. The information will be recorded on a follow-up form along with the date, name of the hospital, and care physician. A wallet card will also be given to each patient and will constitute a back-up method of notification, in which patients will be advised to notify the Clinical Center about any event.

6.6 CHAPTER REFERENCES

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7. CHAPTER 7: PSYCHOSOCIAL MEASUREMENTS

Because the psychosocial intervention to be used in ENRICHD has as its goal amelioration of depression and/or increasing social support, an important secondary objective is evaluation of the effects of the intervention on the presence and severity of depression, and degree and type of social support. Additional objectives include evaluation of the effects of the intervention on health-related quality of life (HQL) and on psychosocial factors such as perceived stress and self-efficacy. This chapter describes the measures proposed for assessment of psychosocial outcomes in ENRICHD; Table 7-1 provides an overview of the instruments, their content, the schedule of assessment and additional comments and length for each instrument.

7.1 PSYCHOSOCIAL ENDPOINTS

The following psychosocial endpoints will be measured in ENRICHD:

1. Presence of clinical depression and severity of depression
2. Social support
3. Health-related quality of life
4. Perceived stress
5. Self-efficacy

7.2 MEASUREMENT OF PSYCHOSOCIAL ENDPOINTS

7.2.1 Presence And Severity Of Depression

Assessment of depression in ENRICHD is intended to provide a diagnosis of major or minor depression, and to assess severity of depression at baseline and during treatment and follow-up. Two measures will be used to assess depression:

7.2.1.1 Beck Depression Inventory

The 21-item BDI is used to evaluate baseline status, to assess progress during treatment, and to monitor patients for relapse. The BDI will be administered to all randomized participants at baseline, 6 months, 12 months and 18 months, and annually thereafter. Each item in the BDI is rated on a 0-3 scale, with a total score ranging from 0 to 63. In patients with diagnosed depression, scores of 10-15 reflect mild depression; 16-23 reflect moderate depression; and 24-63 reflect severe depression.

7.2.1.2 The Depression Interview And Structured Hamilton (DISH)

The DISH (Part A and B) is a structured psychodiagnostic interview, developed specifically for ENRICHD and described in detail in Chapter 3, will be used to screen patients for eligibility (DISH Part A). Part B of the DISH will be administered to eligible participants during screening and at the six month follow-up visit in order to classify the patient according to DSM-IV criteria for major and minor depressive disorders and dysthymia and to allow evaluation of the severity of depression using the HAM-D.

7.2.2 Social Support

The measures of social support used in ENRICHD reflect the multidimensional nature of social relationships and the related concepts of social networks and support. The proposed instruments are designed to measure the effects of the intervention on the following major dimensions of social relationships: (1) the structure of networks (e.g., size, composition, density of networks); (2) content and function of different types of support (e.g., availability, amount and source of support, as well as type of support--emotional, tangible, informational); and (3) subjectively perceived adequacy of support or, conversely, amount of conflict and strain produced by members of the individual's network.

7.2.2.1 ENRICHD Social Support Instrument (ESSI)

The weight of the empirical evidence linking social support to survival in post-MI patients suggests that functional aspects of support, especially emotional support, are most important in the immediate post-MI period. As described in Chapter 3, development of the 7-item ESSI was based on the known predictive validity of the individual items used in several studies of post-MI and CAD patients (Berkman et al., 1992; Williams et al., 1992; Gorkin et al., 1993). The ESSI includes items which primarily measure functional support, and in particular, emotional support. The ESSI is used both as a screening tool to determine patients' eligibility for ENRICHD based on low perceived social support, and to assess changes in patients' social support during treatment (at six, and 12 month follow-ups) and following the intervention (at the 18-month follow-up visit and annually thereafter).

7.2.2.2 The Interpersonal Support Evaluation List (ISEL)

The 10-item tangible support subscale of the ISEL is used to assess the extent to which the patient has someone in his or her life to call on for help with practical, financial and other tangible assistance, when needed. The ISEL subscale will be collected in a subset of patients (the first 400 randomized) at baseline and at the six-month follow-up visit.

7.2.2.3 The Perceived Social Support Scale (PSSS)

Developed by Blumenthal et al. (1982), this measure is a 12-item scale incorporating subscales which address perceived support from family, friends and significant others. The PSSS has established reliability and has been shown to be inversely related to CAD (Blumenthal et al., 1982). It is administered to all patients at baseline, and at the six-month follow-up.

7.2.2.4 The New Haven EPESE Social Network Questionnaire (SNQ)

The EPESE SNQ will be used to measure the structure of participants' social networks. The 19-item questionnaire covers size, frequency of visual and non-visual contact, geographic proximity of close relatives and friends, marital status, and religious and group membership. A summary scale, the Social Network Index (SNI), can be created from selected items. The SNI has its origins in the Alameda County Study and has been shown to predict CHD mortality in the Alameda County Study (Berkman et al., 1979), the New Haven EPESE (Seeman et al., 1992) and the North Karelia Studies (Kaplan et al., 1988). The EPESE SNQ will be administered to a subset of patients (the first 800 randomized) participants at baseline and at six month follow-up.

7.2.3 Health-Related Quality Of Life

Health-related quality of life (HQL) has become a standard concept in the evaluation of medical treatment and patient care. In general, HQL provides an overall measure of the impact of disease and medical treatment on patients' overall functioning and well-being (Guyatt et al., 1993 Ware, 1995). HQL is thought to be a multidimensional concept, including the domains of physical, social, and sexual functioning, well-being, negative affect, the experience of fatigue, pain, and other physical symptoms, and overall perceived health ratings.

In addition to the more traditional measures of treatment efficacy such as survival and recurrent clinical disease, measures of HQL are increasingly used to determine the efficacy of various treatment modalities in terms of their effects on patients' lives. HQL assessments have now also been included in major clinical trials for cardiovascular disease. For example, HQL effects have been examined in a clinical trial testing the use of a new antiplatelet agent in patients undergoing PTCA (Cleary et al., 1991) and in the ACME trial which compared PTCA to optimized medical therapy in patients with one-vessel coronary artery disease (Strauss et al., 1995).

Decreases in depression and increased social support have been associated with improvements in HQL (Follick et al., 1988; Mayou et al., 1981; Dracupe et al., 1991). Because the emphasis of the psychosocial intervention to be used in ENRICHD is on reducing depression and increasing social support, it is expected that patients randomized to the psychosocial intervention will show significantly greater improvements in HQL compared to patients assigned to usual care. The HQL measures described below will be administered to a subset of patients (the first 800 randomized) participants at the six month follow-up to determine whether the psychosocial treatment affects HQL relative to usual care.

7.2.3.1 Specific Items And Subscales From The Medical Outcomes Study Short Form-36

The MOS SF-36 is a generic, standardized survey instrument for the assessment of HQL which is comprehensive, easy to administer, and has been found to provide a reliable and valid assessment of the HQL domains it was designed to measure (Ware & Sherbourne, 1992). The scale assesses eight health concepts: 1) physical functioning 2) role limitations because of physical health problems 3) bodily pain 4) social functioning 5) general mental health 6) role limitations because of emotional problems 7) vitality (energy/fatigue) and 8) general health perceptions. The SF-36 has been used in a wide spectrum of patient populations, including numerous clinical trials of cardiovascular disease, as well as disease-free populations. Selected subscales from the SF-36 to be used in ENRICHD include physical functioning, role limitations and social functioning. Individual items from the SF-36 that assess health perceptions, pain, and aspects of emotional functioning not captured in the depression measures, such as vitality, will also be used. Embedded within the SF-36 scales chosen are 12 items which comprise the MOS-12 item Short Form Health Survey, a brief version of the SF-36 that has been devised by Ware and colleagues to provide a shorter but still reliable and valid assessment of HQL (McHorney et al., 1992). The selected subscales will be administered to a subsample (first 800 randomized) participants at the six - month follow-up visit.

7.2.3.2 Life Satisfaction

Two measures of life satisfaction will be used: first, an eight-item scale measuring satisfaction with life and meaning in life which was derived from studies of long-term survivors of AIDS (Ironson et al., 1995) and includes items from Ironson's Purpose in Life scale (Ironson et al., 1995) and Neugarten's Life Satisfaction measure (Neugarten, et al., 1961) and secondly, the Ladder of Life, an item developed by Cantril (1965) which uses a 1-10 scale ladder technique to assess patients' overall satisfaction with their lives now, their satisfaction with their lives in the past, and their perceptions of how satisfied they will be in the future. This technique allows for an assessment of the individual's overall well-being, and has been used in a variety of studies of HQL in patient and normal populations. These

will be administered to a subset of patients (the first 400 randomized) participants at the six-month follow-up visit.

7.2.4 Other Psychosocial Measures

7.2.4.1 Perceived Stress Scale (PSS)

The Perceived Stress Scale (Cohen, et al., 1983) is a 10-item scale that measures the degree to which situations in patients' lives are perceived as stressful (unpredictable, uncontrollable, overwhelming). Because this scale is expected to predict outcomes as well as function as a secondary outcome measure, it will be administered to the first 400 randomized patients at baseline and at six month follow-up.

7.2.4.2 Self-Efficacy Scale

Self-efficacy refers to the confidence in one's ability to behave in such a way as to produce a desirable outcome (Bandura, 1977). In the cardiovascular area, self-efficacy has been related to heart rate, blood pressure and serum catecholamines in threatening situations (Bandura et al., 1982, 1985). The self-efficacy scale to be used in ENRICHD was developed to reflect the intervention's expected effects on patients self-efficacy related to the targets of depression and social support. Ten items cover depressive thoughts and behavior and social support (getting social support and having social skills). The self-efficacy items will be administered a subset of patients (the first 400 randomized) participants at baseline and at six month follow-up.

7.3 CHAPTER REFERENCES

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Table 7-1: Content And Schedule Of Psychosocial Instruments

Instrument	Content	Schedule	Comments/Length
Modified DIS + Hamilton (DISH)	Depression	Screen, Baseline & 6 mos.; 12 mos. (longitudinal course chart only)	Given by interview Hamilton has 17 items
Beck Depression Inventory (BDI)	Depression	Baseline, 6, 12 & 18 mos.	21 items
Social Support Instrument (ESSI)	Social Support	Screen, Baseline, 6, 12 & 18 mos.	7 items
Interpersonal Support Evaluation List (ISEL) subscale	Tangible Support	Baseline & 6 mos.; (Subsample of first 400 patients)	10 items
Perceived Social Support Scale (PSSS)	Social Support	Baseline & 6 mos.	12 items
EPESE Social Network Questionnaire (SNQ)	Social Network	Baseline & 6 mos.; (subsample first 400)	19 items
Items and subscale from MOS SF-36	Health Quality of Life	6 mos.; 18 mos. (subsample first 800)	Assesses 6 HQL domains using 3 intact subscales (19 items) and 8 additional items (total 27 items)
Life Satisfaction (LSS & LOL)	Life Satisfaction & meaning	6 mos. (subsample first 400)	Ladder of Life item, plus 8 items from Neugarten, Ironson
Perceived Stress Scale (PSS)	Perceived Stress	Baseline & 6 mos. (subsample first 400)	10 items
Self-Efficacy	ENRICHD Intervention	Baseline & 6 mos.(subsample first 400)	10 items

8. CHAPTER 8: DATA COLLECTION CONTENT AND SCHEDULE

8.1 INTRODUCTION

The accurate collection and recording of information throughout the entire course of the study will be crucial to the unbiased evaluation of the primary and secondary endpoints. The data collected will be kept to the minimum necessary to achieve the main goals of the study. This section details briefly the schedule of data collection to be used during the study. Additional data may be collected for substudies, ancillary studies, or local patient management, and will not be discussed in this chapter (see Table 8-1 for data collection schedule).

8.1.1 Method Of Data Collection

Collection of medical data will be conducted in most cases by the Case Coordinator (CC) or another interviewer/data collector who is supervised by the Case Coordinator. In addition, the Case Coordinator or interviewer will be expected to fill out summary forms for potential events, i.e. death, nonfatal myocardial infarction, revascularization procedure, or hospitalization for cardiovascular reasons. In some cases, the Case Coordinator will also administer the psychosocial assessments to be used in ENRICHD; however, it is expected that psychosocial eligibility, baseline and follow-up assessments may be administered by a research assistant (e.g., graduate student) or other individual whose sole responsibility is outcome assessment. Each site will determine the extent to which these functions will be performed by Case Coordinators, or by other personnel.

8.1.2 Recruitment, Screening, And Pre-Randomization Visits

A Medical Eligibility form will be completed for each acute MI patient seen in the participating hospital CCUs to document the pool of prospective participants. Limited information will be recorded. The focus will be on assessment of the nature and severity of the MI and whether each patient meets the major medical entry criteria detailed in Chapter 3. This information will be used to evaluate the screening yield for patients randomized, and the race and gender composition of the population seen at the center.

The psychosocial assessments involved in the screening, recruitment and pre-randomization visits include Social Support Instrument and administration of the DISH to obtain depression diagnosis, and administration of the Short Blessed to ascertain cognitive functioning, where warranted. A detailed description of the instruments to be used in determining psychosocial eligibility, and the methods for determining eligibility by psychosocial criteria, is provided in Chapters 3 and 4.

8.1.3 Baseline Visit

For each patient suitable for randomization into the study, documentation about the index MI and the individual medical history and risk factor profile will be recorded. The Medical History form, administered as a patient interview, will collect the basic demographic information and background cardiovascular health history of the patient. Risk factor data and current medications are also collected as part of the history interview. The Baseline Examination form, to be completed prior to randomization, contains the detailed medical record documentation of the patients qualifying MI and the course of treatment for that event. The last section of the Baseline Visit form will be used to record data from the brief examination by the study physician (or their designate) for vital signs and symptoms of heart disease. Psychosocial assessments at baseline include the instruments detailed in 7-1, and described in detail in Chapter 7.

8.1.4 Randomization

Each qualifying patient who provides informed consent, meets all inclusion criteria, and does not violate the exclusion criteria will be randomized into the trial after collection of the baseline medical and psycho-social measurements. Patient randomization will occur via a phone call to an automated randomization system at the ENRICHD Coordinating Center. The automated system will be online for study use 24 hours a day throughout the week so that weekend and evening recruitment of patients into the study is facilitated. Whenever the system is down for maintenance, calls will be forwarded to staff at the Coordinating Center so that a manual backup for randomization is always provided. Field center personnel using the randomization system will follow a series of spoken menu prompts entering the individual center and patient ID information and asked to verify basic eligibility criteria. In addition to the immediate spoken assignment of the patient to the intervention or usual care group, the automated system will fax confirmation information about randomization to the center. Randomization reports will be provided weekly to the Executive Committee, and Steering Committee and semi-annually to the DSMB to track recruitment by centers. Randomization assignment will be stratified by field center in a permuted blocks design with sequencing of treatment assignment kept confidential by the Coordinating Center.

8.1.5 Follow-up Visits

At six and 18 months post-randomization, and annually thereafter, patients will be seen in-clinic for ascertainment of intervening events, and assessment of current health status. The medical information collected at these regular visits parallels the content of data acquired at baseline (vital signs, current risk factors, and medication use). Each patient will be probed for details concerning any illnesses since the last visit, and in particular hospitalizations that occurred for any reason. Psychosocial assessments at the six month and 18 month visit are provided in Table 7-1 in Chapter 7. A standard 12-lead resting electrocardiogram will be obtained at 6 and 18 months and yearly thereafter, for ascertainment of unrecognized MI.

8.1.6 Special Follow-up Visit Data

The Hospitalization form should be completed for each admission since the last patient visit. They will be completed retrospectively from medical records by study center personnel, and reviewed by the study physician. Hospitalization information will be collected for each patient admission, regardless of outcome. Mortality information will be collected on the Death form based on the patient's death certificate, autopsy report, and hospital record. On the basis of all available clinical information presented to the study physician, each death should be classified as cardiovascular or non-cardiovascular. If the data is present in the record, each Death form should also provide the more detailed category of cardiac death. The vital status of all participants who fail to make a scheduled clinic appointment should be verified as soon as possible.

8.1.7 Monitoring Data Quality

Since the integrity and credibility of the study results depend on data quality, data collection will be monitored on a regular basis during the study. The data management system provided by the Coordinating Center will perform the majority of edit checks on the data as they are entered. Reports will be generated for the Executive Committee and Steering Committee that tabulate by clinical center, the timeliness of receipt of data, consistency of data over forms, error rates, screening and randomization rates, and participant follow-up.

Quality assurance measures for data collection will be initiated before the start of the study with training and certification of clinic staff in operational procedures. Periodically through the study, the Coordinating Center staff will provide retraining and recertification. Staff from the Coordinating Center will provide assistance to the clinical centers in answering questions about the protocol and helping to solve operational problems. During visits to the clinical centers, Coordinating Center staff will compare data from randomly selected patient files with against data values from central files. The Coordinating Center staff will also coordinate data collection activities with the other study agencies.

It is the responsibility of the Principal Investigator at each site to insure that all data for ENRICHD from their center are representative and accurate. Since the entry criteria and possible endpoints are crucial to the study, the Principal Investigator will meet with the staffs of the participating hospitals on a regular basis to review the entry criteria documenting the index qualifying MI (enzymes, ECGs, MI signs and symptoms) for consistent application to the patients screened and recruited into the study.

TABLE 8-1: ENRICHD Medical Measurements Data Collection Schedule

Instrument	Content	Schedule/Number of Participants	Comments/Length
Screening Log	Screen results	Screen; All	7 items
Medical Eligibility	Eligibility	Screen; All	9 items
Medical History	History	Baseline; All	Only eligibility, 54 items
Baseline Exam	Physical exam/labs	Baseline; All	Only eligibility, 62 items
Randomization	Administrative	Baseline; All	Only eligibility, 7 items
ECG	Medical ECGs	Baseline, Annually; All + Per Event	End points, 56 items
Follow-up Exam	Medical	6 mo + annual Follow-up	46 items
Hospitalization	Chart abstraction	Per event	As needed, 54 items
Death certificate	Record abstraction	Per event	As needed, 24 items
End point classification	End point review	Per event	As needed, 12 items

9. CHAPTER 9: ADHERENCE, RETENTION AND DROP-OUT RECOVERY

9.1 INTRODUCTION

ENRICHD will adopt a variety of approaches to promote adherence and retention during the study, and to aid in drop-out recovery. The first set of strategies consists of commonly used methods of assisting participants in adhering to the study protocol, and will be described as general adherence strategies in Section 1. that follows. In addition, we will use motivational interview methods from the moment of recruitment in order to reinforce adherence during the study as previously described in Chapter 4 and further discussed below. Finally, we will describe strategies aimed specifically at recovering drop-outs, either due to a failure to return to follow-up assessments or failure to return to intervention sessions (see Section 9.4 below).

9.2 APPROACHES TO ADHERENCE

Four general strategies will be incorporated to facilitate adherence to the intervention follow-up assessments, and to retain study subjects throughout follow-up. These strategies include logistical assistance, interim phone calls, reminders, and involvement by family and/or friends and are discussed further below.

9.2.1 Logistical Assistance/Support

As discussed in Chapter 4, the Case Coordinator (CC) will ensure that participants have sufficient logistical assistance to attend first screening visits and then intervention and assessment sessions once they are randomized. Issues that we anticipate commonly being addressed with patients include providing assistance with transportation, offering meals during return visits to the hospital, and arranging for dependent care and other family obligations. The Case Coordinator will also try to schedule visits at times least likely to interfere with other social or work activities.

9.2.1.1 Interim Telephone Contacts

Each participant will be contacted by phone mid-way between annual study visits. While the primary goal of these calls is ascertainment of potential endpoints, they will also be used as an opportunity to reinforce continued participation in the study. This will also allow earlier identification of participants who may have moved without providing the clinical center with updated address information.

9.2.1.2 Reminders

We will provide all study participants with calendars indicating intervention and/or assessment sessions, and to send them reminders in advance of follow-up assessments. A newsletter will also be developed and sent to both intervention and usual care participants in order to encourage continued involvement in the study. Appropriate care will be taken to ensure, however, that the newsletter content does not address issues related to either depression or low perceived social support.

9.2.1.3 Eliciting Support From Family/Friends

Lack of support is a common barrier to participation for all participants, but may be a particularly common issue among low-SES participants, minorities and women. This may be especially the case with a study which focuses on psychosocial issues where there may be less cultural acceptance of these factors than among more affluent or non-minority groups. We will thus plan to inform family and/or friends of participants during the recruitment phase and to solicit their support and involvement (see Chapter 4, Section 4.3.2). Fortunately, a focus of intervention will be on developing skills to increase social support which should be sufficient for those participants assigned to the active intervention to deal with these issues that may affect participation. For those participants assigned to usual care, however, it will be essential for the Case Coordinator to facilitate participants addressing barriers to participation without actually providing them with much support. For these usual care participants, issues concerning social support barriers to participation will be addressed through developed text materials to be sent to participants and newsletter articles.

9.3 MOTIVATIONAL INTERVIEWING METHODS

Motivational interviewing methods will be incorporated in the earliest stages of recruitment as previously described in Chapter 4. However, these methods will be extended throughout activities of ENRICHD to encompass interactions of participants with Case Coordinators, interviewers and clinic follow-up staff. Our experience has been that these methods, when used consistently across contacts, are extremely effective in promoting active participation.

9.4 DROP-OUT RECOVERY

Drop-out recovery methods have been demonstrated in clinical trials to re-engage participants who have become inactive when applied systematically (Probstfield, Russell, Insull, & Yusuf, 1990). While not originally conceptualized in this manner, this approach incorporates the use of good reflective-listening and directive skills to elicit barriers to participation from subjects. This information is then used to problem-solve with participants for methods to overcome the identified participation barriers. Finally, an essential component of drop-out recovery is the application of motivational interviewing

methods in an attempt to further elicit and clarify participants' personal reason for continued participation.

The general approach to drop-out recovery will involve contact by the Case Coordinator in an attempt to: 1) identify barriers to participation; 2) problem-solve for solutions to overcome identified barriers; and 3) apply motivational interviewing methods. These efforts will be discussed and reviewed during Case Management Review sessions by the Case Coordinators, therapists, and behavioral investigators. If the Case Coordinator is not successful in re-engaging the participant, then contact will be initiated by a therapist or other team member at the discretion of the Case Management Team. Often, contact by a new member of the staff results in new perspectives and is to be encouraged in drop-out recovery.

In general, drop-out may be seen from clinic follow-up visits for all enrolled participants. It is common, though, for participants assigned to active intervention to drop out selectively from either clinic follow-up or intervention sessions. Some intervention participants will, of course, drop out from both intervention and clinic follow-up. Drop-out recovery of intervention participants thus requires close coordination and sharing of information between intervention and clinic staffs.

9.5 CHAPTER REFERENCES

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10. CHAPTER 10: PARTICIPANT SAFETY AND CONFIDENTIALITY

10.1 INTRODUCTION

The psychosocial intervention consists of individual and group cognitive-behavioral therapy for all participants, supplemented by antidepressant therapy, as needed. The active treatment phase will last approximately one year with follow-up for two to five years. The experimental treatments for the ENRICHD study are not expected to pose any particular risk. Each participating investigator has primary responsibility for the individual participants under his/her care.

10.2 PROTOCOL REVIEW AND STUDY MONITORING

An independent Data and Safety Monitoring Board (DSMB) appointed by NHLBI is charged with monitoring the progress of the study. The DSMB reviews and approves the protocol prior to study initiation. During the study the DSMB meets periodically to review study progress. These reviews include evaluation of interim data as well as the monitoring of participant safety and the quality of all aspects of study operations.

Prior to study initiation, the study protocol will be reviewed and approved by each center's Institutional Review Board (IRB).

After enrollment, each individual Principal Investigator monitors safety issues at his/her site continuously and reports any problems to the Coordinating Center, which informs the NHLBI Project Officer. A procedure is developed for reporting deaths to the Coordinating Center and the Program Office.

10.3 EXCLUSIONS

Persons with medical or psychological contraindications to the experimental treatment will not be eligible to be enrolled. Exclusions are detailed in Chapter 3.

10.4 INFORMED CONSENT

Informed consent is obtained from each participant before they are enrolled in the study. The consent form describes the potential risks and benefits of study participation as well as the responsibilities of the participants and the investigators. Appendix H provides the informed consent form to be used.

10.5 ADVERSE EVENT REPORTING AND DISCONTINUATION OF STUDY TREATMENT

As treatment progresses and at all follow-up visits, possible adverse effects of the experimental treatment will be assessed. If participant assessment indicates an adverse reaction, the study investigator may, at his/her discretion and according to the psychosocial intervention design described in Chapter 5, refer the participant for additional medical follow-up, additional individual therapy sessions, and/or assessment for psychopharmacological intervention. Depending on the situation, the change may be temporary or continue throughout the study term. In rare cases the experimental treatment may need to be discontinued, however the participant would continue to be followed.

10.6 PROTECTION OF PARTICIPANT PRIVACY

Privacy in the context of this study includes confidentiality of data and personal information at the Clinical Center and in the handling and reporting of data by the Coordinating Center. It also includes discretion on the part of the clinical center staff and arrangements for physical privacy during interviews and examinations. Each Clinical Center is responsible for ensuring physical privacy of participants and ensuring that data are stored in a secured area accessible only to ENRICHD staff. These provisions will be monitored during periodic site visits from the Coordinating Center.

10.7 DATA SECURITY AND CONFIDENTIALITY

The original paper data collection forms are retained at the clinical centers. They should be stored using the confidentiality procedures provided for other medical records at the institution.

All data transferred to the Coordinating Center are stored, processed, and analyzed within the Coordinating Center office suite. At the Coordinating Center, all access to office space containing data is controlled through manned reception areas. Visitors are screened by the receptionists and cannot move about without an escort. All office space is locked after working hours. Access to computer data files is controlled by passwords released only to those Coordinating Center personnel who use the files. In addition, critical data files are encrypted.

A backup of the database is made daily to a second disk drive on the Coordinating Center local area network. Automatic magnetic tape backups of the database are also made daily. Once a month, the current backup tape is removed from the cycle and permanently archived at the Coordinating Center's off-site data storage facility.

Output mailed to clinical center staff will identify participants only by ID number. No individually identifiable information will be distributed to clinical centers. When printed material containing confidential information is to be discarded, it is loaded, transported, and

stored under supervision (using a chain of custody control process) until the material can be recycled into paper pulp.

All Coordinating Center staff are required to complete a confidentiality certification procedure upon employment. Policies regarding the confidential nature of the data collected, processed, and stored at the Coordinating Center, are explained to all personnel, who must then sign a "confidentiality certification," before being allowed access to confidential information. In addition to this initial training, the Coordinating Center reinforces the need for careful and confidential handling of data at staff meetings.

11. CHAPTER 11: CLOSE-OUT PROCEDURES

11.1 OBJECTIVES

The ENRICHD trial may terminate on schedule, or at an earlier date if circumstances warrant. Regardless of the circumstances, the objectives of study close-out are:

- To complete data collection and processing quickly, while maximizing data quality and completeness.
- To fulfill our ethical obligations to trial participants.
- To ensure the maximum possible analysis and dissemination of the information from the trial.

11.2 ENDPOINT ASCERTAINMENT

The primary and secondary endpoints of the trial are based on death or hospitalization. On a routine basis, potential events will be ascertained by participant interview at scheduled follow-up visits and phone calls, from follow-up contacts for missed visits, or by participant (or next of kin) telephone report between scheduled contacts. As the trial progresses, a few participants will be lost to follow-up. Thus at any point during follow-up, several months will have elapsed since most participants were last screened for potential endpoints. As the end of the follow-up period approaches, it is essential to make special efforts to identify all potential events in all patients as close as possible to the agreed-upon date of termination of follow-up. Clinical centers will be given a short window (e.g., two weeks) just before the follow-up termination date, within which to contact each of their participants to screen for any potential endpoints since the last contact. A number of weeks earlier, the Coordinating Center will communicate frequently with the clinical centers regarding attempts to recover all patients lost to follow-up. Verification of final vital status for all participants is critical for the validity of the statistical analysis of the primary endpoints. Therefore, for those participants the clinical centers were unable to locate, the Coordinating Center will use a contract with a commercial credit agency to locate or determine vital status in the few problem cases of drop-outs.

Given the unmasked nature of the intervention, and the use of a cause-specific component in the primary endpoint (recurrent MI), independent verification and classification of potential events by a treatment-blinded committee is essential to the scientific credibility of the trial. Such clinical events processing systems typically operate with a several month lag between event detection and final classification. As the end of the follow-up period approaches, it is essential to speed up all the steps in this process (medical record abstraction and transfer, blinding, committee review and adjudication, etc.) to minimize the

time lag between the end of scheduled follow-up and the availability of a closed endpoints file that can be used for the primary results manuscript.

11.3 DATA CLEAN-UP AND CLOSURE

The routine data processing and data closure activities described in Chapter 12 will also be accelerated as the end of follow-up approaches. Data closure checks will be generated more frequently, with tighter windows between scheduled collection and query for missing forms. In extreme cases, Coordinating Center staff may need to schedule site visits of clinical centers to help address significant data management backlogs or volumes of outstanding data closure problems.

11.4 UNMASK THE INVESTIGATORS TO THE STUDY RESULTS

As the end of follow-up approaches, a small writing committee will be formed to draft the primary results manuscript, before follow-up is complete. This will include the Chair and Co-Chair of the Steering Committee, the Principal Investigator of the Coordinating Center, the Project Officer, and a small number of other Investigators. Of necessity, this group is unblinded to the preliminary trial results several months prior to the meeting at which the results will be presented to the Steering Committee. Once data collection is complete, a closed Steering Committee meeting will be held to present the results to the Investigators and to provide them with an opportunity to review the draft manuscript and provide comments to shape the revision for final submission.

11.5 COMPLETE THE PRIMARY RESULTS MANUSCRIPT

As soon as those components of the database necessary for the primary manuscript have been closed, the statistical analyses will be re-run on the finalized database, and the manuscript submitted to the journal for publication.

11.6 INFORM PARTICIPANTS OF THE STUDY RESULTS

In the interval after the Investigators have been notified, but before the primary paper appears, each participant will be scheduled for a close-out visit. At this visit some final on-study data will be collected (e.g., consent and updated contact information to permit long-term follow-up through the national death index). Each participant will be informed of the major results of the study, and counseled concerning the implications of the trial for their future care. Participants will be encouraged to schedule an appointment with their primary care physicians to discuss their post-trial management.

11.7 CLOSE-OUT CLINICAL CENTER ACTIVITIES

The Coordinating Center will work with each clinical center to finalize all data transfer and clean-up. Clinical centers will arrange for archival storage of patient data and other study materials in line with their institutional requirements for retention of research data.

12. CHAPTER 12: DATA MANAGEMENT

ENRICHD involves a variety of data sources, including abstracting from medical records, participant interviews by case managers and therapists, and self-administered questionnaires. The data management system must be flexible enough to mesh with the variety of institutional facilities, and operational procedures likely to be in use at the participating centers, while still providing the necessary standardization and quality assurance in data collection and processing.

12.1 DATA COLLECTION

A number of different data collection methodologies used for ENRICHD are:

- Recording of data on paper forms by clinic staff during medical exams / interviews and when administering psychosocial instruments by interview (by handprinting or optical mark recording).
- Recording of data on electronic forms by clinic staff, by keying on PCs/laptops during medical exams / interviews and medical record abstraction.
- Participant self-completion of psychosocial instruments (again, by handprinting or optical mark recording.)

Printing on paper forms requires the least training and equipment. Optical mark forms can be a cost-effective alternative to handprinting for multiple choice items. Recording extensive numeric responses or text on OMR forms is generally not efficient. Accurate completion of OMR forms is somewhat slower and requires more training than completing forms for key entry, but can reduce overall data processing costs (particularly if participants self-administer the questionnaires).

Collecting data on electronic forms requires the most training and the highest equipment cost, but will reduce overall personnel cost. In addition, the software can assist the data collection process, preventing items from being left blank, automating skip rules, providing integrated coding lists, etc. It can provide the highest data quality by validating responses during collection, while the source records (or even the participants) are at hand to confirm or correct suspicious responses. Another major advantage to this approach is the availability of a local database at each clinical center. A variety of scheduling and quality control reports will be provided to allow each clinical center to monitor and manage their screening, recruitment and follow-up activities.

Medical data will be recorded by the case coordinator or other project staff. When practical, these data will be collected electronically, using laptop-based software provided

by the coordinating center. The remainder of the medical data will be collected on paper forms and later keyed by clinical center staff using the same laptop systems. When possible, psychosocial instruments will be self-administered by the participants, using forms designed for optical mark reading. When necessary, clinical center staff will administer the psychosocial instruments by interview, recording the data on OMR forms.

12.2 DATA ENTRY

Optical mark forms used, are scanned at the Coordinating Center, producing an electronic record from each form. This simply replaces key entry. Re-scanning could be implemented, but is probably not necessary. The reproducibility of scanners is very high. That is, feeding a particular sheet through a scanner multiple times will produce the same electronic record in a very high fraction of cases. However, the accuracy of the scanning is highly dependent on the quality of forms completion. Thus if circles are not filled darkly and neatly, or stray marks are made on the form, the error rate in reading can be equal to (or even higher than) that with key entry. Clinical center staff will be instructed to carefully review the completeness and quality of self-administered forms before the participant leaves the center.

If the data are collected by printing on paper forms, key entry will be required. This can be done centrally, at the Coordinating Center, or remotely, at the Clinical Centers. The data entry system displays data entry screens which closely resemble the paper data collection forms. The system is menu driven, with context-sensitive help available at any time. Each data value is validated (edited) during entry, as described below.

Decisions will have to be made of whether to require verification (re-keying) of either selected fields or all data keyed. In our experience, complete double entry is not necessary in distributed systems, provided that the data is keyed by protocol-knowledgeable individuals (e.g., data collectors or study coordinators). Entry by such staff provides a level of human review during entry that reduces errors to an acceptable level (Neaton 1990, Mullooly 1990). Instead, we will implement a data entry quality control system, with a sample of forms re-keyed at the Coordinating Center to monitor and control data entry error rates at the Clinical Centers. However, should data entry be done centrally at the Coordinating Center, or should the Clinical Centers opt to have data entered by clerical data entry staff, complete re-key verification is desirable (Blumenstein 1993, Reynolds-Haertle 1992).

12.3 DATA TRANSFER

Completed data forms are transferred from the Clinical Centers to the Coordinating Center in batches. A batch consists of all the forms collected by a single center during a pre-specified time period (e.g., a week). A fixed schedule is established for shipping batches to the Coordinating Center. The forms comprising a batch will be accompanied by a batch

inventory sheet, tabulating the contents of the batch. Each batch will be assigned a unique sequence number for tracking purposes. On the day of receipt, the Coordinating Center will fax an acknowledgment of the receipt of the batch to the Clinical Center. The receipt of each batch will be logged. Within one working day of receipt, the Coordinating Center will reconcile the contents of the batch against the inventory sheet, notifying the Clinical Center of any discrepancy. Within two working days, the receipt of each data form will be keyed into a computerized inventory system which will track the status of each form through the subsequent processing steps.

Most clinical centers are recruiting from multiple hospitals, and require more than one laptop system for collection of medical data. The data collected on these systems will first be consolidated into an integrated clinical center database on a designated "local database" system. This system is used to generate the scheduling, tracking, and monitoring reports for the clinical center. It is also used to produce data transfer files for shipment to the coordinating center. Given the relatively large data volume expected per center, data will be transferred to the coordinating center weekly.

An additional type of data transfer that will likely be needed is the shipment of samples (e.g., ECG tracings or tapes, plasma samples from substudies) to central labs and reading centers and the transfer of results from those agencies to the Coordinating Center. Specific procedures for labeling, packing, and shipping samples will be part of the manual of operations). These procedures will be pilot tested in each Clinical Center before the initiation of the first protocol.

The data management system provides for inventorying samples as they are collected, and generate packaging lists for inclusion in each shipment (as an electronic file or on paper if the laboratory / reading center prefers). This information will be transferred to the Coordinating Center along with other study data, allowing the completeness and timeliness of sample collection, and shipping to be monitored. Procedures are also developed for transfer of data from central agencies to the Coordinating Center. If desirable, the Coordinating Center may provide the central agencies with a version of the study data management system with screens to allow their determinations to be entered. If their equipment is capable of recording results electronically, we will develop procedures for transferring those files to the Coordinating Center.

12.4 DATA VALIDATION

Each data field will be edited during collection / entry (or immediately after scanning). The data management system will flag each data value with a "status character" documenting the current validation status of the item (empty, skipped, questionable, clean, confirmed, etc.). When electronic collection or distributed entry are being used, values which fail a validation routine will cause a message to be displayed. The person entering data will then have 3 options:

- to correct the value, in which case the new value will be validated as was the previous entry.
- to flag the value as questionable, in which case the system will generate a printed form to document the question, and for use in recording a resolution.
- to confirm the value as known to be correct, overriding the validation routine.

For data keyed / scanned at the coordinating center, values which fail a validation routine will cause a data query form to be generated. The generation of each data query form will automatically be logged in the inventory system. Generated queries are reviewed in-house to identify and correct any which may be due to errors in data entry or processing. The remaining queries will be printed and mailed to the Clinical Centers in batches, using the same data transfer procedures described above. After investigation and resolution by Clinical Center staff, completed query forms will be returned to the Coordinating Center as part of the regular data transfer batches. Returned queries will be processed at the Coordinating Center like original data forms. Updated values will be entered, verified, and edited in the same manner as the original data values.

12.5 DATABASE CLOSURE

Before each major analysis, the database will go through a series of closure checks to insure the completeness and correctness of data collection and processing. These checks will be performed on a "frozen" version of the database defined by a specific time cut point. The classes of checks done at closure include:

- Determining the status (excluded, ongoing, completed, withdrawn, etc.) of each patient entered.
- Assuring all expected forms have been received.
- Assuring all received forms have been processed.
- Assuring all queries generated have been resolved.

12.6 DATA RETRIEVAL AND STATISTICAL COMPUTING

Data will be retrieved from the study database and converted into SAS files on a monthly schedule tied to the production of the study status report and data closure checks. Additional retrievals will be done as needed for the production of other reports. These retrieval files will be stored as SAS datasets within a SAS data library. The SAS database created for each report will be permanently archived on magnetic tape cartridge or CD-ROM.

All statistical computing performed is done using the SAS system or BMDP. All computing is documented using the Coordinating Center's statistical computing request

system. This system requires the responsible Coordinating Center statistician to produce a written specification of each analysis to be done. The specification, the resulting analysis program, and the output produced are all catalogued and archived (in both paper and electronic format) to provide complete documentation of each computing task. All computing requests whose output is distributed outside the Coordinating Center (e.g., to the study investigators or Project Officer) are independently reviewed by a second programmer for accuracy.

12.7 DATA SECURITY AND CONFIDENTIALITY

The original paper data collection forms will be retained at the Clinical Centers. They should be stored using the same confidentiality procedures provided for other medical records at the institution.

Each user of the data collection / management systems at the Clinical Centers will need an individual user ID and password to access the local database. Individually identifying fields within the database is encrypted, and decrypted only for display on-screen. Only electronic records of study data will be transferred to the Coordinating Center as described above. These transfer files will be encrypted when created by the Clinical Center data management system. All data transferred to the Coordinating Center will be stored, processed, and analyzed within the Coordinating Center office suite. At the Coordinating Center, all access to office space containing data is controlled through manned reception areas. Visitors are screened by the receptionists and cannot move about without a Coordinating Center escort. All office space is locked after working hours. Access to computer data files is controlled by passwords released only to those Coordinating Center personnel who use the files. In addition, critical data files are encrypted.

Paper data forms transferred to the Coordinating Center will be filed in the Coordinating Center secure forms room. This is an interior room within the Coordinating Center office suite which remains locked at all times. Only selected project staff with a demonstrated need for access (e.g., data processors) have access to this room. Should another member of the project staff (e.g., a statistician) have a legitimate need to examine a data form, data processing personnel will provide them with photocopies, which are logged out and disposed of securely upon return.

A backup of the database is made daily to a second disk drive on the Coordinating Center local area network. Automated magnetic tape backups of the database are also made daily. Once a month, the current backup tape will be removed from the cycle and permanently archived at the Coordinating Center's off-site data storage facility. Output mailed to Clinical Center staff will identify participants only by ID number. No individually identifiable information will be distributed to Clinical Centers. When printed material containing confidential information is to be discarded, it is loaded, transported, and stored under

supervision (using a chain of custody control process) until the material can be recycled into paper pulp.

All Coordinating Center staff are required to complete a confidentiality certification procedure upon employment. Policies regarding the confidential nature of the data collected, processed, and stored at the Coordinating Center, are explained to all personnel, who must then sign a "confidentiality certification," before being allowed access to confidential information. In addition to this initial training, the Coordinating Center reinforces the need for careful and confidential handling of data at staff meetings.

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13. CHAPTER 13: QUALITY CONTROL

13.1 OVERALL PLAN

The overall functions of quality assurance are: training; supervision and monitoring of the intervention; standardization of the measurements; and supervision and monitoring of eligibility and enrollment criteria.

Training Plan

The overall training plan involves:

- Training of the Intervention counselors
- Training of the interviewers (i.e., training in all data collection/data management protocols
- Training of the Case Coordinators

13.2 SUPERVISION AND MONITORING OF INTERVENTION

The overall plan for supervision and monitoring of the intervention involves:

- Adherence to treatment protocol; treatment manual; written checklist of clinician adherence to protocol
- Monitoring of performance: weekly site supervision; across-site supervision; audiotapes
- Process variables to assess if mediating effects of the intervention are working

13.2.1 Standardization Of Measurements

The overall plan for standardization of the measurements involves:

- A three month pilot study on all measurements for feasibility and respondent burden purposes
- Computer checklist of interviewers'/data collectors' adherence to data collection protocol
- Computer checklist of interviewers'/data collectors' adherence to data collection of eligibility criteria protocol
- Endpoint Classification Committee to review adherence to measurement of primary medical endpoints
- Case Coordinator monitoring data collection at each site and serving as a liaison to the Coordinating Center for the editing, updating, and transmission of study data.
- Monthly conference calls of Case Coordinators across sites

13.2.2 Monitoring Eligibility And Enrollment Criteria

The overall plan for monitoring eligibility and enrollment criteria is:

- Computer checklist of interviewers' adherence to eligibility criteria
- Quality control data collected by the Coordinating Center to monitor and correct operational data collection
- Case Coordinator monitoring data collection at each site and serving as a liaison to the Coordinating Center for the editing, updating, and transmission of study data.
- Monthly conference calls of Case Coordinators across sites

13.3 TRAINING: SPECIFIC STAFF RESPONSIBILITIES

The following clinic functions/responsibilities are identified in relation to training in the study protocol: counselors, case managers, and interviewers. Each is described below:

13.3.1 Training Of The Intervention Counselors

The overall goal of training the counselors is to assure equal implementation of the therapy across sites. The psychosocial intervention is composed of a depression component and a social support component (refer to Chapter 5). Cognitive behavioral therapy (CBT) is used to treat major and minor depression. Treatment for low perceived social support is informed by multi-modal strategies that may include problem solving, communication skills, cognitive restructuring, network restructuring, and assertiveness training. The intervention consists of individual and group sessions. Thus the training of the counselors is aimed at CBT as well as the repertoire of strategies to enhance social skills and training in individual as well as group sessions. Most important is that all the training is in the context of psychological and physiological adaptation after acute myocardial infarction.

13.3.2 Qualifications Of Counselors

The 'gold standard' for delivery of the intervention is assured through the identification, training, and maintenance of qualified counselors. Educational criteria for counselors are discussed in Chapter 5. Counselors may have either a doctoral or a master's degree in a suitable discipline, and clinical experience in cognitive-behavioral therapy, counseling, group therapy, and therapeutic strategies to enhance social support.

13.3.3 Training Of Counselors For Both Depression And Low Perceived Social Support Aspects Of The Intervention

Training, certification, and monitoring of the intervention across sites is performed by the Beck Institute. Dr. Aaron Beck and Dr. Judith Beck have the experience and the supervisors within the Beck Institute to train the counselors in cognitive-behavioral therapy as well as various skills training that may be used in the treatment of low perceived social support and group therapy for patients adapting to myocardial infarction. The approach is flexible with the primary aim of helping the cardiac person 'get back on their feet'. The use of these therapeutic strategies in minority and low SES populations is included in the

training. The Beck Institute has supervisors who speak Spanish and has had experience in working with Hispanic, African-American, and Asian-American (mostly Vietnamese and Korean) populations. The Beck Institute also works with experts from among the ENRICHD investigators who have experience in working with MI patients whose presentation of depression is closely linked with their cardiac disease; Dr. Christine J. Reilly, a Beck supervisor works with depression in post MI patients.

The entire group of 22 counselors from all sites and the investigators supervision (i.e. supervising investigators) convened at the Beck Institute in Philadelphia for a five-day workshop in August 1996. The counselors were trained in the therapy; the supervising investigators were trained in the supervision of counselors.

In October 1996 with the beginning of ENRICHD recruitment, each counselor is required to complete 12 weeks of supervised therapy with a patient randomized to treatment. Weekly tapes are sent to the Beck Institute by each counselor and hourly supervision for each counselor is performed via telephone weekly by the Beck Institute. Certification of the counselors by the Beck Institute occurs at the end of 12 weeks, at which point Beck Institute staff will have listened to the weekly tapes and evaluated these tapes using pre-established criteria.

13.3.4 Training Of The Interviewers/Data Collectors

Initial training is conducted in for eight persons (one from each site) who will be responsible for training the rest of the interviewers/data collectors at each site. Training includes the following activities: overview of the study and study protocol; review of the eligibility criteria; specific instructions on interviewing for the DISH and the BLESSED; review of the Screening/Recruitment Visits; specific instructions on ascertaining the medical eligibility criteria from the charts; and randomization procedures. review data collection on all the psychological measurements; introduction to the laptop computer-based system with screen data entry and editing, edits, and data transmission; and review of word processing and other file management software which may be available and useful in the sites. Training is also done in interviewing techniques: how to elicit responses, how to get consent, etc. Role playing is used. Videotapes are also taken of the training and one is sent to each site for training of interviewers/data collectors, which might have to be done if attrition of data collectors occurs during the study.

13.3.5 Qualifications Of Interviewers/Data Collectors

The primary qualification of the interviewers is for them to be comfortable in accessing patients in the Coronary Care Units of hospitals for screening and enrollment into the study and familiarity with medical research data acquisition from charts. Most sites hire interviewers who are registered nurses. Emphasis is placed upon the interviewers/data collectors' ability to serve as an effective liaison among the various clinic personnel, ENRICHD staff and the Coordinating Center.

13.3.6 Certification Of Interviewers/Data Collectors

Upon successful completion of training, the data collectors/interviewers are certified as Clinical Data Coordinators. The quality of their data forms, timeliness, and completeness of work is routinely assessed. Quality control forms is gathered from the sites for regular quality control checks. The ongoing certification of interviewers/data collectors is subject to continued completion of their duties.

13.3.7 Training The Case Coordinators

The Case Coordinator is responsible for initial contacts and minimal education regarding risk factors of cardiovascular disease and recovery after myocardial infarction before randomization and for insuring attendance at follow-up exams for both the usual care and intervention participants (see Chapter 4). For the intervention participants only, the case coordinator is responsible for assistance in their care and treatment during the course of treatment. The Case Coordinator facilitates attendance at sessions, gives limited instrumental social support, facilitate medical treatment, and coordinate psychopharmacology (refer to Chapter 5). In addition, depending upon the clinical site's specification, the Case Coordinator in some cases conducts medical/psychosocial screening, and collects medical baseline medical and psychosocial data via interview or administration of self-report instruments, or supervise other interviewers/data collectors' in the performance of these activities. Duties and responsibilities of Case Coordinators are discussed more fully in Chapters 4, 5 and 8.

13.3.7.1 Qualifications of Case Coordinators

The Case Coordinator should be familiar with medical chart review, medical nomenclature, interpreting medical data and working with physicians and cardiac patients in a medical setting. The case manager should be familiar with medical issues related to heart disease, including risk factors, and should have experience working with heart disease patients. The Case Coordinator should be familiar with criteria for depression and low perceived social support and be familiar with drugs prescribed for cardiac disease and their interactions. Therefore, a registered nurse with a graduate education and experience working in a coronary care unit and/or cardiac rehabilitation would be optimal.

13.3.7.2 Training of Case Coordinators

Case Coordinators are centrally trained. Training includes review of the study purpose, protocol, study forms, Manual of Operations, all of the training listed above for the interviewers/data collectors, material to be included in the education of patients about cardiovascular disease and risk factors, common cardiovascular drugs and their interactions, psychopharmacology drug interaction, sources of institutional support to be located at the clinical sites, basic review of case management techniques and cognitive-therapy techniques.

13.4 SUPERVISION AND MONITORING OF THE INTERVENTION

13.4.1 Adherence To Treatment Protocol

Adherence to treatment protocol is accomplished by the development of a Manual of Operations describing the goals of each session and a written checklist of clinician adherence to treatment protocol.

13.4.2 Manual Of Operations

The Manual of Operations Volume 2 (Intervention) contains a chapter describing the psychosocial intervention procedures in detail. A brief description of these procedures is provided in Chapter 5.

13.4.3 Written Checklist of Clinician Adherence To Treatment Protocol

Clinicians can monitor the integrity of their own performance daily within general prescribed techniques and check-off on a computer form. The two forms that clinicians use are the Treatment Process Data Log (TPD) and the Delivery of Intervention Checklist (DIC). These forms ensure adherence to the protocol and standardization across sites. Protocol adherence is developed for each session using the Operational Manual as the reference. The protocol is monitored frequently by supervisory staff on an individual basis and the supervisory staff provides feedback to the clinicians.

13.4.4 Monitoring of Performance Of Intervention

Audiotapes. All treatment sessions are audiotaped. Audiotapes help to ensure specificity of the treatment (i.e., treatment of depression versus social support) and that treatment protocols are adhered to in a consistent, reliable fashion across counselors and sites (treatment integrity).

Monitoring at each site. Each site performs monitoring and supervision of the counselors in weekly clinical meetings by a supervising investigator who is part of the site research team.

Monitoring by the Beck Institute. The Beck Institute will monitor integrity of all site intervention counselors by randomly selecting one session tape for each patient within the initial six sessions and one tape for any patient requiring an additional six sessions. The Beck Institute develop a set of guidelines for undertaking remedial work with errant counselors, if required. Beck Institute establishes a time limit for remedying cognitive therapy practice. Counselors who are unable to improve by deadline will be discussed as possibly needing replacement. This monitoring is conducted for the full three years of the intervention.

The Beck Institute monitors the supervisory investigators (i.e. those investigators at each site who are supervising the counselors) through 90 minute telephone conference calls among all sites to discuss supervision issues. The conference calls across sites continue for the duration of the study but the frequency will decrease with time: weekly for the first six months; then biweekly; then monthly.

13.5 PROCESS VARIABLES

Definition of process variable.

Process measures refer to psychosocial measures that are required for one or more of the following purposes: (1) clinical evaluation, (2) monitoring administration of the intervention, (3) monitoring the subject's progress in, and successful completion of, treatment, (4) testing hypotheses about the mechanisms of action of the various components of the intervention, and (5) testing hypotheses about individual differences in response to treatment.

Process variables. Process variables are categorized as either nonspecific or condition-specific. Nonspecific measures are used to document the administration of the intervention. Specific measures are used to assess various aspects of depression, social support, and/or the intervention components that target these risk factors.

In an effort to streamline the protocol the number of process variables was reduced from 38 to 9.

13.5.1 Mandatory Treatment Process Measures

The following nine process measures are mandatory

1. DSM-IV Axis I Diagnosis
2. 17 - Item Hamilton Depression Scale
3. Social Network in Adult Life (SNAL)
4. CBT Performance Criteria
5. Social Performance Criterion Scale
6. Beck Depression Inventory (BDI)
7. Non Study Treatment Form (NST)
8. Modified Duke Social Support Scale (MDuke)
9. Delivery of Intervention Check (DIC)

Mandatory Treatment Process Variables
(As Approved by the ENRICHD Steering Committee, February 1998)

Data Form	Measure	Condition	Data Yield
CED	DSM-IV Axis I diagnosis	Depression intervention Social support intervention	Presence of depressive disorders, disorders affecting social functioning, and other current psychopathology
	17-Item Hamilton Depression scale	Depression intervention	Severity of depression
TPD	Date of contact	Nonspecific	Frequency of contacts; time from randomization to clinical eval. & treatment
	Staff ID#	Nonspecific	Between-therapist variability in treatment outcomes
	Individual mode	Nonspecific	Delivery of intervention
	Individuals present	Nonspecific	Delivery of intervention
	Group #	Group intervention	Delivery of intervention
	Session Duration / Reason for non-contact	Nonspecific	Delivery of intervention
	Session count	Nonspecific	Delivery of intervention
	Homework completion	Depression, social support, and group intervention	Participant adherence to prescribed treatment
	CBT Performance Criteria Scale	Depression, social support, and group intervention	Acquisition of CBT skills (one of the criteria for successful completion)
	Social Relationship Criterion Scale	Social support intervention	Development of socially supportive relationships (one of the criteria for successful completion)
	Beck Depression Inventory	Depression, social support, and group intervention	Number and severity of depressive symptoms (one of the criteria for successful completion)
	Modified Duke Perceived Social Support Scale	Social support intervention	Perceived social support (one of the criteria for successful completion)
	Group size	Group intervention	Delivery of intervention
Group participation	Group intervention	Participant adherence to group treatment	
DIC	Delivery of Intervention Checklist	Depression, social support, and group intervention	Delivery of intervention
NST	Non-Study Treatment Form	Depression, social support, and group intervention	Participation in non-ENRICHD psychological or psychiatric treatment or support groups during the participant's ENRICHD intervention phase.
CTS	Cognitive Therapy Scale	Depression, social support, and group intervention	Beck Institute's ratings of the quality of randomly-sampled CBT sessions.

13.5.2 Optional Treatment Process Variables:

The following 28 process measures are optional clinical tools.

1. DSM-IV Axis II Diagnosis
2. DSM-IV Axis V
3. Case Summary Worksheet
4. Progress Notes
5. Termination Summary
6. Brief Cope Scale
7. McLeod Conflict Scale
8. Group Session Mastery Form
9. Activity Chart
10. Clients Session Feedback Form
11. Dysfunctional Thought Record (DTR)
12. Testing Your Thoughts
13. LOG Version of DTR
14. Automatic Thoughts Worksheet
15. Belief Barriers to Social Support
16. Beliefs Worksheet
17. Coping Cards
18. Emotion Chart
19. Emotional Intensity Scale
20. Guide to Booster Sessions
21. Guide to Self-Therapy Sessions
22. Group Homework Assignment Record
23. Homework Schedule Cards
24. Nonverbal Communication Form
25. Problem Solving CBT Homework Sheet
26. Problem Solving Homework Sheet
27. Session Bridging Worksheet
28. Functions of a Social Network

The following two process measures were discontinued :

- 1) Treatment Expectation Scale (TES),
- 2) the 17-Item Self Efficacy Scale.

13.6 STANDARDIZATION OF MEASUREMENTS

13.6.1 Monitoring Of The Interviewers/Data Collectors

The work of the interviewers/data collectors is monitored through the completeness and timeliness of data transmissions to the Coordinating Center. Depending on the volume of activity of a clinical site, forms of adherence to data collection protocol and adherence to data collection of eligibility protocol are checked by the interviewers/data collectors, computerized, verified, and transmitted weekly or every two weeks on a regular schedule. The responsibilities of the interviewers/data collectors include:

- 1) Collecting data on all the primary endpoint measurements
- 2) Monitoring data quality control by submitting computer checklist of adherence to data collection protocol and eligibility protocol
- 3) Serving as a liaison to the Data Coordinating Center for the editing, updating, and transmission of study data
- 4) Running computerized patient and study status reports

13.6.2 Endpoint Classification Committee

The responsibility of this committee is to validate the evidence of the primary endpoints of mortality and recurrent myocardial infarction and other medical endpoints according to criteria (refer to Chapter 6). The committee is composed of cardiologists, one member from each site.

14. CHAPTER 14: STATISTICAL ANALYSIS

14.1 PRIMARY ENDPOINT

The primary study endpoint is mortality from any cause, or re-infarction. The primary analysis will test the null hypothesis of no difference in the event-free survival curves between the two treatment groups, using a two-sided test at a significance level of .05 (with adjustment for multiple looks, as described in chapter 15). All analyses will be based on the principal of intention to treat (i.e., by the treatment assignment of patients at randomization, regardless of subsequent compliance to the assigned treatment). As described in chapter 11, at the end of the trial, we will aggressively pursue data on mortality and re-infarction for any patients lost to follow-up; using these approaches has resulted in much less than 1% loss to follow-up for those event-types in previous multi-center trials we have coordinated (e.g., LRC, 1984; SOLVD, 1992). Thus we expect the impact of missing data on the primary analysis to be negligible, and for the primary analysis we will simply censor any patients lost to follow-up at the last point at which their event status was ascertained. We will also perform “sensitivity analyses” making assumptions about patients lost to follow-up that are biased towards the null hypothesis (e.g., assuming the event rate for incomplete patients in each group is equal to that of observed patients in the opposite treatment).

For unrecognized MIs, the date of event will be approximated by the midpoint of the dates of the two ECGs between which diagnostic changes occurred. Simulation studies conducted at the coordinating center demonstrate that substituting the midpoint for the (unknown) exact date of unrecognized MIs does not adversely affect the type I error rate of the logrank test. We expect the power of the logrank test with the substituted midpoint to differ little from that of a logrank test computed with the actual time of the MI's since we expect unrecognized MIs to comprise only 5-10% of all events, and the midpoint can differ from the actual date by at most a few months. However, statistical methods for interval censored data are an area of active research, and we will use an alternative imputation method for the time of silent MI's if a broad consensus and appropriate software are available to support the use of a more powerful statistic when final reporting is performed.

Supplemental analyses will use survival-time regression techniques (Cox, 1972; Kalbfleish and Prentice, 1980) to adjust the estimated treatment effects for baseline covariates measuring severity of the coronary heart disease, depression, low perceived social support, and other prognostic variables.

14.2 OTHER ENDPOINTS

The relationship between treatment and the secondary endpoints listed in Section 6.2 will be explored using a variety of methods. Many of the endpoints are time to event variables and will be analyzed using the same types of methods described above for the primary endpoint. Other secondary endpoints are continuous (or approximately so); these will be analyzed using conventional linear models and rank statistics.

14.3 SUB-POPULATION COMPARISONS

Treatment effects for the primary endpoint will be estimated and compared for subpopulations defined by gender, race/ethnicity, and etiology of psychosocial risk (depression vs. low perceived social support) using Cox regression models. Models will be fit including treatment by sub-population interactions. Sub-population differences in treatment effects will only be reported if the interactions are significant (at the .05 level). An analogous approach will be used for the various secondary endpoints.

The power of these comparisons is low for the primary endpoint, and other time-to-event endpoints; the study is only likely to detect marked differences in treatment efficacy for these outcomes. The trial will have much better power to detect differences among sub-populations for continuous outcome variable, such as severity of depression.

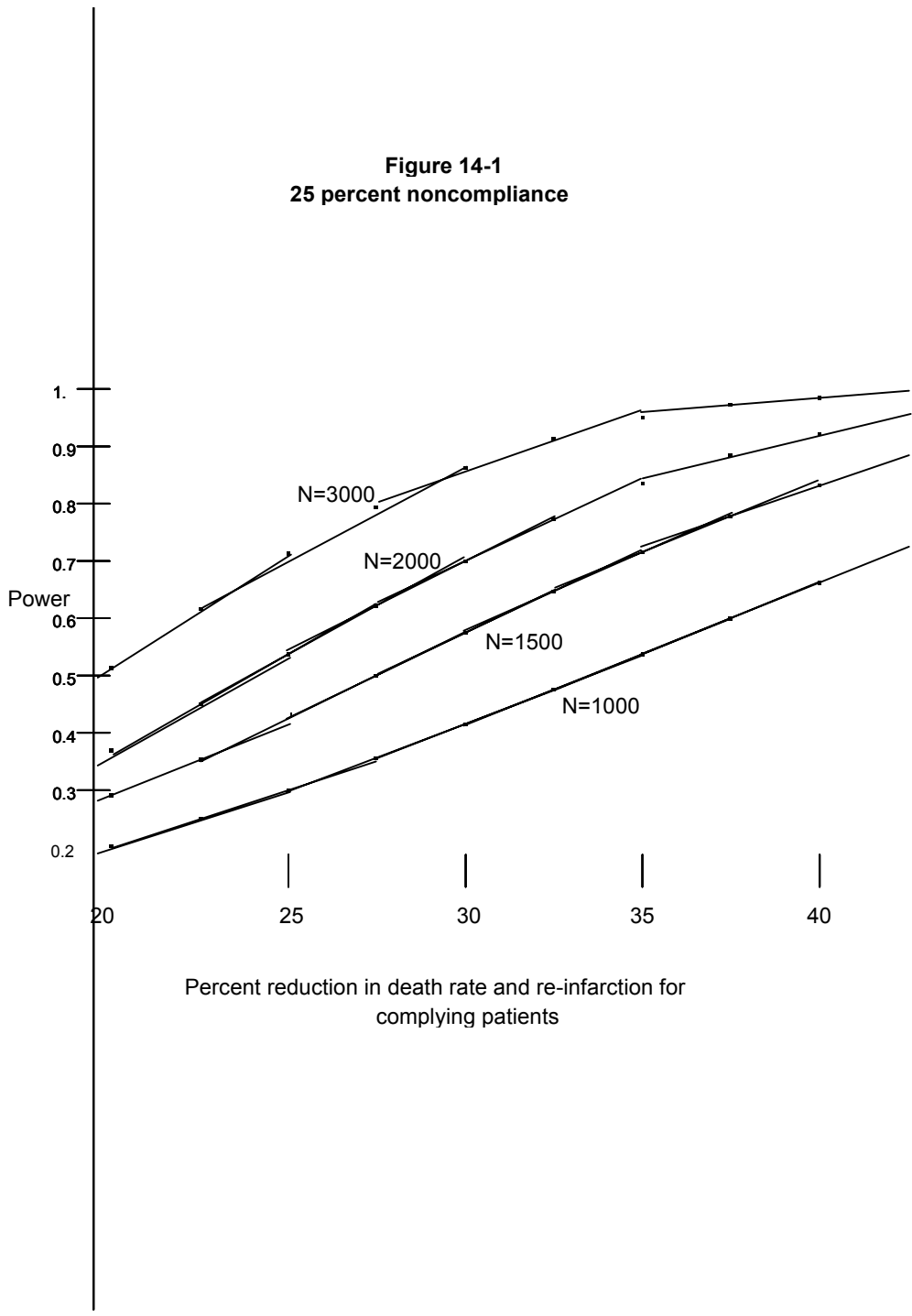
14.4 STUDY POWER

Power calculations were based on a simple comparison of the difference in proportion of events between treatment groups; the power for this statistic will be a conservative estimate of the power for the logrank statistic. Based on previous studies (Jenkinson, 1993; Frasier-Smith, 1991) we assumed a cumulative event rate of 23% in the usual care group ($P_E = P(\text{EVENT}) = 0.23$). We assumed that two thirds of the first events post-MI would be deaths ($P_{DGE} = P(\text{DEATH}|\text{EVENT}) = 0.667$), that 80% of deaths would be cardiovascular ($P_{MID} = P(\text{CARDIAC SPECIFIC DEATH}|\text{DEATH}) = 0.8$) (Kannel, 1990), and that the treatment would have no effect on non-cardiovascular deaths.

We also assumed a non-compliance rate of $P_N = 0.25$, along with the assumption that the non-compliers have events at the same rate as the usual care group. The event rate with cognitive therapy assuming a 100δ reduction in cardiac-specific death and re-infarction is calculated as

$P_\delta = \left[\left\{ P_{MID} P_{DGE} P_E + (1 - P_{DGE}) P_E \right\} (1 - \delta) + (1 - P_{MID}) P_{DGE} P_E \right] (1 - P_N) + P_N P_E$. The results of the power calculations for a two-sided 0.05 level test for several sample sizes, and 100δ values from 20 to 40 are displayed in Figure 14.1. For example, the study has a power of .88 to detect a treatment effect of 30% in complying patients.

Figure 14-1
25 percent noncompliance



14.5 CHAPTER REFERENCES

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15. CHAPTER 15: INTERIM DATA MONITORING

15.1 STEERING COMMITTEE REPORTS

To assist in the operation of the study, the Coordinating Center prepares routine reports for the Steering Committee. These reports cover 1) recruitment, 2) patient adherence, 3) clinician adherence to the intervention protocol, and 4) quality control. Special attention is given to minority and female recruitment, and recruitment by the depression and the low perceived social support criteria. Data on screening and recruitment is forwarded to the Coordinating Center at least weekly, and a weekly recruiting report is produced. Reports will include summaries for each clinical center. No endpoints or safety data will be included in the Steering Committee reports.

15.2 DATA AND SAFETY MONITORING BOARD (DSMB) REPORTS

The Data Safety Monitoring Board Reports will be prepared two times a year (or as specified by the DSMB). Although the DSMB determines the format of the report, each report consists of (seven) sections: 1) recruitment, 2) treatment efficacy, 3) adverse effects of the psychosocial and supplemental drug therapies, 4) patient adherence, 5) clinician adherence to protocols, 6) data quality, and 7) ancillary sub-studies. The recruitment section compares overall recruitment, and recruitment for women and minorities, with the pre-specified targets. The treatment efficacy section contains a comparison of all cause mortality and re-infarction in the psychosocial intervention group and the usual care group. The section on adverse effects of the treatments reports any adverse outcomes associated with the psychosocial intervention, and it will summarize the use of drugs to treat depression among patients receiving the psychosocial intervention and the usual care control group. Patient adherence data will compare the distribution of the number of therapy sessions attended by each patient with the targeted number of sessions. The section on clinician adherence to the protocol will describe the efforts at each clinical site to ensure that the designed intervention is administered. The quality control sections will include summaries of the quality control data collected by the Coordinating Center to monitor and correct operational data collection. Sub-studies will be monitored to ensure that they do not adversely effect recruitment or adherence.

Approximately six weeks prior to the scheduled meeting of the DSMB, an edited data file is created by the Coordinating Center. A random sample of the records on the file are compared to the original data sources to check that patient records have not been altered or processing errors have occurred. Key data fields are checked to ensure that invalid values have not been entered. A report based on the data file are sent to members of the DSMB two weeks prior to the meeting. Steps taken to insure security and confidentiality include distribution by certified mail and enactment of a return policy of all reports.

Tables comparing the primary endpoint and other major outcomes are updated the week before the DSMB meeting to provide the committee with the most up-to-date data.

The Coordinating Center will provide analyses to assist judgments about whether the study should be terminated early because of proven efficacy or unanticipated harmful effects of the treatment. The primary measure of efficacy is mortality from any cause or re-infarction. A number of methods for the repeated analysis of accumulating data have been proposed (O'Brien and Fleming, 1979; Lan and DeMets, 1983). When considering the stopping of a trial in which efficacy of the experimental treatment is claimed, the method used for monitoring the trial should be conservative in the sense that the trial should be stopped before its planned end only if the treatment is clearly superior. The methods referenced here provide such a conservative approach. The Logrank statistic will be the primary statistic evaluated by the interim stopping methods. We propose to use the Lan-Demets boundaries based on nine evaluations of the Logrank statistic beginning at the end of the first year and proceeding each six months until the end of the study after the fifth year. Stopping boundaries for the tests using the end-loaded quadratic alpha spending function are given in Table 15-1. The calculations are based on "information time" at each look, based on the expected number of events in the control group at the time of each look. They were computed using a program supplied by Demets and his colleagues.

Table 15-1

Year	Bounds	Cumulative alpha
1	±3.55	0.0004
1.5	±3.33	0.0012
2	±3.08	0.0029
2.5	±2.86	0.0061
3	±2.66	0.0114
3.5	±2.51	0.0185
4	±2.38	0.0273
4.5	±2.26	0.0378
5	±2.15	0.0500

The method proposed by Halperin, et al., 1982, will also be reported to guide judgments by the DSMB about whether interim data is sufficient to determine that the treatment

effect is likely to be 1) too small to be of practical importance or 2) so small that it cannot be demonstrated with a trial of the currently planned size.

Although we have proposed methods for monitoring the progress of the trial and we will provide data management and statistical computing to support the monitoring, the actual recommendation concerning the cessation or continuation of the trial will be made by the DSMB to the NHLBI.

15.3 CHAPTER REFERENCES

Halperin, M., Lan, K.K.G., & Ware, J.H. (1982). An aid to data monitoring in long-term clinical trials. Controlled Clinical Trials 3, 311-323.

Lan, K.K.G., & DeMets, D.L. (1983). Discrete sequential boundaries for clinical trials. Biometrika, 70, 659-663.

O'Brien, P.C. & Fleming, T.R. (1979). A multiple testing procedure for clinical trials. Biometrics, 35, 549-556.

16. CHAPTER 16: STUDY ORGANIZATION

16.1 STEERING COMMITTEE

The Steering Committee is composed of the Principal Investigator of each of the Clinical Centers, the Principal Investigator of the Coordinating Center, the Steering Committee Chair and Co-Chair and the NHLBI Project Officer. The Chair and Co-Chair are appointed by the Director of NHLBI. Other members may be appointed by the Project Office on the basis of special expertise. The Steering Committee oversees all aspects of the design, execution, and publication of the study. The Steering Committee meets monthly via telephone conference call and semi-annually to monitor the progress of the study and review non-endpoints data and Endpoints data will be provided only to the DSMB until the trial is completed. The Steering Committee will establish subcommittees to develop and monitor aspects of the study, reporting recommendations to the full committee for approval. The subcommittee Chairs are appointed by NHLBI.

16.2 EXECUTIVE COMMITTEE

The Executive Committee manages the day-to-day operations of the study between Steering Committee meetings. It develops the agendas for and prepare recommendations for the Steering Committee meetings. Membership consists of the NHLBI Project Officer (Susan Czajkowski, Ph.D.), Steering Committee Chair (Lisa Berkman, Ph.D.) and Co-Chair (Allan Jaffe, M.D.), Coordinating Center Principal Investigator (James Hosking, Ph.D.), and a Clinical Center Principal Investigator (Robert Carney, Ph.D.). Ex-officio members may be appointed from the Project Office and the Coordinating Center. The Executive Committee meets weekly by conference call.

16.3 SUBCOMMITTEES

The Steering Committee establishes subcommittees to develop and monitor various aspects of the study. Subcommittee members can include Investigators and staff of the Clinical Centers, Coordinating Center, and Project Office, as appropriate. Subcommittees develop recommendations and proposals for Steering Committee review and decision., the following subcommittees are established:

- Eligibility, Recruitment, Adherence and Retention (James Raczynski, Ph.D., Chair; Robert DeBusk, M.D., Co-Chair)
- Intervention (Lynda Powell, Ph.D.Chair)
- Measurement and Endpoints (Gail Ironson, M.D., and Ken Freedland, Ph.D., Co-chairs, Chair - Psychosocial; Christopher O'Connor, M.D., Chair - Medical)

- Quality Control (Marie Cowan, Ph.D., Chair; Matthew Burg, Ph.D.Co-Chair)
- Substudies and Ancillary studies (Neil Schneiderman, Ph.D., Chair; Redford Williams, M.D., Co-Chair)
- Publications (James Blumenthal, Ph.D., Chair)

16.4 DATA AND SAFETY MONITORING BOARD

The Data and Safety Monitoring Board (DSMB) is an independent group of experts in the relevant biomedical and behavior fields, biostatistics, and bioethics, appointed by NHLBI. The primary role of the DSMB is to advise the NHLBI on scientific, safety, ethical, and other policy issues relating to the study. The DSMB meets twice a year. The NHLBI, Steering Committee Chair and Co-Chair, and Coordinating Center Principal Investigator participate in DSMB meetings as non-voting members. The DSMB reviews the protocol prior to study initiation. During the execution of the study, the DSMB will monitor study progress and review interim analyses of outcome and safety data. As appropriate, it will make recommendations to the Institute and Steering Committee concerning changes in study conduct.

16.5 CLINICAL STUDY CENTERS

The Principal Investigator and location of each ENRICHD study center is provided below.

Clinical Centers:	James A. Blumenthal, Ph.D. Duke University Durham, NC
	Matthew M. Burg, Ph.D. Yale University New Haven, CT
	Robert M. Carney, Ph.D. Washington University St. Louis, MO
	Pamela Mitchell, Ph.D. University of Washington Seattle, WA
	Robert F. DeBusk, M.D. Stanford University Palo Alto, CA

Clinical Centers

Lynda H. Powell, Ph.D.
Rush-Presbyterian-St. Lukes Medical Center
Chicago, IL

James M. Raczynski, Ph.D.
University of Alabama at Birmingham
Birmingham, AL

Neil Schneiderman, Ph.D.
University of Miami
Coral Gables, FL

Coordinating Center:

James D. Hosking, Ph. D.
University of North Carolina at Chapel Hill
Chapel Hill, NC

Project Office:

Susan Czajkowski, Ph. D.
National Heart Lung and Blood Institute
Bethesda, MD

17. CHAPTER 17: PUBLICATION POLICY

17.1 GENERAL STATEMENT OF EDITORIAL POLICY AND PURPOSE OF PROCEDURAL GUIDELINES

This document concerns procedures and guidelines for organizing and managing the presentation and manuscript generation for ENRICHD. The procedures recognize that ENRICHD is a long-term, multi-site project that has the obligation to produce numerous publications and presentations.

The purpose of these guidelines is to facilitate generating a large number of high quality publications and presentations that address important issues in a timely manner. Further, the procedures adopted by the ENRICHD investigators for utilization of ENRICHD data are intended to protect the interests of all participants in the study, to assure that study data conform to the requirements of study design and are accurately presented, that authorship is appropriately acknowledged, that the text of each publication is well-written, to ensure that all investigators are aware of ongoing analysis projects, to avoid duplication of analysis projects and to ensure that publication or presentation of ENRICHD data does not occur without the knowledge and approval of the Steering Committee.

The guidelines reflect the creation of writing groups and an orderly system for the ENRICHD Steering Committee to approve and set priorities for each approved manuscript or abstract. The guidelines are intended to facilitate adherence to the publication procedures mandated by the ENRICHD protocol. If there should be any apparent conflict, the protocol takes precedent over these guidelines.

Several assumptions underlie these guidelines:

1. In general, abstract or manuscript generation begins with the preparation of a brief proposal, one copy of which is sent to the Publications Subcommittee Chair, and one copy submitted to the ENRICHD Coordinating Center at UNC for distribution to the ENRICHD Publications Committee. Data-based proposals should contain a brief description of the objectives, methods, analysis plan, significance of paper, and proposed collaborators; non-data based proposals (e.g., presentation of the ENRICHD protocol) should contain a brief statement of objectives, outline of the content of presentation and proposed collaborators. The Publications Committee will review the proposal and forward it either to the ENRICHD Steering Committee for action, or return it to the originator for further development.
2. There is to be a separate proposal for each separate manuscript or abstract, even if a series of related manuscripts or abstracts are proposed.

3. Authorship will be proposed by the writing group or writing group chair (originator of the proposal) and approved by the Publications Committee. Additional authors may be suggested by the Publications Subcommittee to ensure fairness and balance, among other reasons. For example, preference may be given to those individuals who contributed most to the enrollment, retention and treatment of study participants, and not just to the contribution to the conceptualization and writing of the manuscript.
4. The Publications Subcommittee will set priorities for publication and presentation. A summary table of all ongoing and completed manuscripts and abstracts will be circulated periodically by the Coordinating Center. Conflicts regarding priorities will be resolved by the ENRICHD Steering Committee.
5. Once a proposal has been approved by the Publications Subcommittee and Steering Committee, the writing group will work with the Coordinating Center to request analyses, and develop the manuscript or presentation. After the manuscript or presentation has been completed and is ready for submission for publication or for presentation, it will be forwarded to the Publications Subcommittee for final review and approval.

It is anticipated that ENRICHD will generate considerable new data relative to post-MI patients undergoing psychosocial interventions. The ENRICHD Steering Committee will foster and guide development of scientific reports originating from data obtained in the ENRICHD project. Safeguarding scientific integrity of the project requires that all data from all ENRICHD sites be analyzed study wide and reported as such. Thus, an individual site is not expected either to report or publish data collected from its site alone under the byline of the ENRICHD project. All presentations and publications of any type (ENRICHD or related studies) are expected to protect the integrity of the main objectives of the overall project. Major findings will not be presented prior to release of “mainline” results of the study by agreement of the entire study group of Principal Investigators. The Steering Committee will determine the timing of presentation of main results publications (including papers on design and methods) and designation of the meetings at which they might be presented.

Publications will be grouped into five general types of papers (see Section 16.1.2). Proposals may be either submitted by investigators or topics of consideration to be developed into publications can be generated from questions or hypotheses that are submitted to the Publications Committee by principal and co-investigators, study coordinators and other ENRICHD staff. In the latter case, a writing group with a Chair will be designated for each topic.

The Steering Committee has primary responsibility for final review of all proposed publications and presentations evolving from ENRICHD. The Publications Committee is responsible for reviewing and approving all abstracts submitted to scientific meetings and all manuscripts submitted for publication from ENRICHD major findings, substudies, or ancillary studies and making recommendations regarding the disposition of these to the Steering Committee. The

Publications Committee determines priorities for analysis among proposals which have been approved, and communicates any recommendations regarding changes or revisions to the proposals or final publications to the investigators involved. The members of the Publications Committee are appointed by the Study Chairperson and NHLBI program staff.

Investigators at all ENRICHD sites, including the Core Laboratories, the Coordinating Center and NHLBI Program Office have equal status with regard to the development and publication of research papers based on ENRICHD data. With the approval of the Principal Investigator at each respective site, study coordinators and other ENRICHD staff at the various sites are encouraged to participate in this process. The Publications Committee will develop standards for regular evaluation of the submission and completion of proposals.

THE COORDINATING CENTER INVESTIGATORS MUST BE CONSULTED IN THE DEVELOPMENT OF PROPOSALS THAT REQUIRE REVIEW OF ACCUMULATED DATA FROM THE CLINICAL SITES OR ANALYSIS OF DATA ON FILE AT THE COORDINATING CENTER. The members of the Coordinating Center and NHLBI Program Office are available to collaborate in designing and carrying out all ENRICHD research.

17.1.1 Types Of ENRICHD Research

ENRICHD research and the resulting presentations and publications may be grouped into the following categories:

1. Design and Methodology
2. Major Findings
3. Substudies
4. Ancillary Studies
5. Data Bank Studies
6. Independent Studies.

Distinctions among these types of studies are given in Section 17.2 and in Chapter 18. Research other than analyses of end point data may be conducted prior to the end of the ENRICHD investigation and is strongly encouraged, so that the maximum information can be obtained from this study and that the methods for evaluating and analyzing study data may be refined in preparation for later analyses.

17.1.2 Authorship

17.1.2.1 Primary Outcome

Design papers, reports on study methodology, and major findings (see section 17.1.2) are considered to be Primary Outcome Papers.

The primary publication(s) pertaining to the fundamental goals of ENRICHD that present outcome data on the ENRICHD patient group may not have individual authors but may be published under the byline of “the ENRICHD Study Group.” There will be an appendix at the end of the manuscript listing all Principal and Co-Investigators for each of the sites in ENRICHD. Sites will include the Clinical Centers, the Coordinating Center, and the Program office at NHLBI. The Data and Safety Monitoring Board and the Writing Group of the manuscript also will be listed under those designations in an appendix.

17.1.2.2 Other Study Papers, Abstracts And Presentations

All studies other than those designated as “Primary Outcome” fall within this category. Papers or abstracts resulting from these studies will have named authorship of individuals involved, ending with the phrase “for the ENRICHD Investigators.” In addition, papers will have an appendix containing the names of the sites, their Principal Investigators and Co-Investigators and other individuals participating in the study. Sites will include the Clinical Centers, the Coordinating Center, Central Laboratory and the NHLBI Project Office. All papers and abstracts must be approved by the Publications Committee before they are submitted. All abstracts prepared for presentation must be submitted to the Publications Committee and to the Coordinating Center at least 1 month prior to the deadline. In addition, all abstracts must receive separate approval for any meeting or presentation. An approved abstract or symposium for one meeting must obtain independent approval for submission to a separate meeting

17.1.2.3 Invited Papers

In certain instances, ENRICHD investigators may be asked to contribute papers to workshops, symposia, volumes, etc. The individuals to work on such requests should be appointed by the Publications Committee, but, a proposal will be circulated soliciting other participants as in the case of other study papers as described in the application Review Process.

17.1.2.4 Co-authors

Co-authorship invitation for out of the ordinary scientific input into a manuscript: Prior to submitting a manuscript proposal, lead authors should be instructed to invite to participate in their writing groups a representative from any unit of the study (clinical site, Coordinating Center or NHLBI) making an inordinate contribution to a given paper, i.e., data or services specific to the manuscript and exceeding the scope of ordinary activities. The Publications Committee will be alert to inadvertent oversights in this regard and, when observed, will ask the lead author to offer such inclusion to the indicated unit of the study.

Required of co-authors on all ENRICHD manuscripts: To be listed as a co-author on a published ENRICHD work, each co-author must, as a minimum requirement, read, critique and reply to the drafts provided by the lead author. If the co-author sees nothing in need of changing or adding, he (she) must reply to this effect to the lead author as evidence of having reviewed the document critically. Failure to meet the minimum standard will result in being dropped as a co-author. If the lead author feels a writing group member should be dropped, he should bring this to the attention of the Publications Committee for its determination of action.

All lead authors are required to circulate drafts of their manuscripts for co-author review, comments and suggestions. They will be reminded of this obligation through the letter sent by the Publications Committee notifying them when their manuscript proposal receives approval from the Steering Committee.

17.1.2.5 Number Of Authors

Generally, ENRICHD writing groups will contain no more than 11 authors; however, on a case-by-case basis authority to expand writing groups when deemed appropriate will be extended to the ENRICHD Publications Committee.

Principal Investigators may advocate for additional writing group members. Authority is delegated to the ENRICHD Publications Committee to decide when extension of the co-author group beyond 11 members is appropriate.

At the point of ENRICHD Steering Committee review of manuscript proposals, principal investigators are encouraged to identify investigators whom they judge may make a significant contribution to specific proposals.

17.1.3 Restrictions On Release Of Data

Findings which might jeopardize successful continuation of the ENRICHD project will not be released to ENRICHD Investigators or the public until a time deemed appropriate by the ENRICHD Data and Safety Monitoring Board, the NHLBI Project Office, and the Study Chair.

17.2 DESIGN AND METHODS REPORTS AND MAJOR FINDINGS PAPERS/INDEPENDENT STUDIES

17.2.1 Design Paper And Reports On Methodology

Manuscripts concerning the ENRICHD Study's overall design, protocol, procedures, or organizational structure which do not involve major findings or data collected on ENRICHD patients may be published prior to the end of the study. Such publications will be developed and reviewed according to the same guidelines used for reports of major findings.

Many public presentations or publications about ENRICHD which do not involve protocol data, substudies or ancillary study data (e.g., grand rounds talks concerning the study's general design and objectives) will not require formal preliminary review and approval by the Steering Committee. However, if there is any doubt, investigators are expected to consult with the ENRICHD Publications Committee indicating their intention to publish or present the material, in order to avoid the premature release of ENRICHD data or the inappropriate publication of confidential information.

17.2.2 Reports Of Major Findings

Major findings address the fundamental goals of ENRICHD or involve protocol data (such as morbidity data related to the psychosocial interventions) which cannot be released prior to the end of the study. These studies will summarize the findings based on the entire study population and will be written at the conclusion of the project.

17.3 MANUSCRIPT AND ABSTRACT (PRESENTATION) APPROVAL PROCESS

Figure 17-1 summarizes the process to be used for submission, review and approval of manuscripts and abstracts or presentations concerning ENRICHD. One copy of each proposal for a manuscript or presentation should be submitted to the Chair of the ENRICHD Publications Committee, and a separate copy submitted to the Coordinating Center Principal Investigator.

17.3.1 Proposal Submission

Each proposal for a data based publication or presentation should contain a brief description of the objectives, methods, analysis plans, significance of the publication or presentation and proposed collaborators. Non-data based proposals (e.g., presentations of the ENRICHD protocol or other information about ENRICHD at a conference) should include a description of the objectives, outline of the content of the presentation or publication and proposed collaborators. Abstract proposals must be submitted at least one month prior to expected submission of the abstract for presentation.

17.3.2 Writing Group Analysis Process

The Coordinating Center is responsible for review and approval of all proposed analyses, and for conducting all data analyses performed using ENRICHD data. Writing groups will receive support during the analysis process from the Coordinating Center. Documentation and updated analysis files of the ENRICHD database will be distributed by the Coordinating Center. Statistical computing support for analysis will be provided by the Coordinating Center. The routing process for computing requests is displayed in Figure 17-2. The Coordinating Center will coordinate the efforts of writing groups to identify and correct suspicious data values and to arrive at and disseminate official derived variables. Finally, the Coordinating Center will verify results reported in the final manuscript as a means to assure high quality. The Coordinating Center will prepare a list of publications and presentations and their status and distribute this to the Steering Committee periodically.

17.3.3 Final Review And Approval Of Manuscripts And Abstracts

Every study manuscript considered suitable for publication and papers to be presented will be submitted by the Chair of the Writing Subcommittee to the ENRICHD Coordinating Center for distribution to the ENRICHD Publications Committee. The Chair of the Publications Committee will be responsible for arranging and implementing review by study participants and NHLBI according to the procedures (applicable to both manuscripts and abstracts).

17.3.4 Priorities For Performing Work

Because of the routine work load at the Coordinating Center, it will be necessary to establish priorities for data processing and analysis. Therefore, the Coordinating Center will, as necessary, conduct analyses on substudies in the order in which they have been approved or seek guidance from the Steering Committee for determining priorities for analysis.

17.4 CONFLICT OF INTEREST

17.4.1 Introduction

The ENRICHD Study is a multicenter clinical trial that compares two strategies of treatment for post-MI patients who are depressed and/or socially isolated. Because the findings of this investigation may have implications for future clinical practice, potential conflict of interest policies have been formulated by the ENRICHD Investigators and adopted by the ENRICHD Investigators.

To address actual or perceived conflict of interest in the ENRICHD Study, the participating investigators voluntarily agree to abide by the guidelines reflected in the copy of the Financial Disclosure Statement (Exhibit 17.1).

17.4.2 Individuals To Be Governed by These Guidelines

Members of the ENRICHD Study Group who will be governed by these guidelines include the Study Chair, the Study Co-Chair, the Principal Investigator at each Clinical Unit, the principal personnel in the Coordinating Center, and the Principal Investigators of the Core Laboratories. Co-Investigators and other staff who have major responsibility for enrollment, recruitment, follow-up or collection of data for ENRICHD at Clinical Units, affiliated hospitals or Core Laboratories will also be governed by these guidelines. The Principal Investigator for each ENRICHD Unit will submit a list of individuals who will be governed by these guidelines at the beginning of the study. The Principal Investigator of each participating unit will review the guidelines with all appropriate staff prior to the start of patient recruitment and at least annually thereafter.

17.4.3 Time Period Of The Policy

The guidelines set forth in this policy will commence at the start of patient recruitment and will terminate at the time of initial public presentation or publication of the principal results. Investigators not privy to end point data who discontinue participation in the trial during recruitment will be subject to these guidelines until their departure from the study.

17.4.4 Financial Guidelines

1. The investigators agree not to own, buy or sell stock or stock options during the aforementioned time period in any of the pharmaceutical companies or related medical equipment companies whose products are used in this trial, or who have provided financial support for the study. In addition, the investigators agree not to have retainer-type consultant positions with these companies for the time period defined above.
2. The Coordinating Center will maintain conflict of interest statements updated annually from each investigator.

Activities not explicitly prohibited, but to be reported annually to the Study Chairperson, and information to be maintained on file by the Coordinating Center include:

- I. Ad hoc consultant relationships to companies providing drugs or financial support to the trial.
- II. Participation of investigators in any educational activities that are supported by such companies.
- III. Participation of investigators in other research projects supported by such companies.
- IV. Financial interests in these companies, over which the investigators have no control, such as mutual funds or blind trusts.

17.4.5 Reporting Of Financial Disclosures And Other Activities

The investigators agree to update their financial disclosure statements (Exhibit 16.1) and related activities as described above on an annual basis and submit these data to the Coordinating Center for storage. The Coordinating Center will maintain the confidentiality of these records and present them to a review committee, to be constituted by the Study Chair. In the case of actual or perceived conflict of interest, the Study Chair will bring it to the attention of the Executive Committee, NHLBI Program Office and the Data and Safety Monitoring Board.

17.4.6 Review Of The Policy Statement

The investigators agree to review these guidelines on an annual basis and take any additional steps to ensure that the scientific integrity of the trial remains intact.

17.4.7 Relationship To Institutional Policies On Conflict Of Interest

Since existing policies on conflict of interest may differ among participating institutions, in addition to the above policy, it is expected that investigators will comply with the policies on conflict of interest which exist within their individual participating institutions (medical schools and hospitals). This is the responsibility of each individual investigator.

17.5 ACKNOWLEDGMENT OF NON-NHLBI FUNDING

In the reports on major findings, substudies and ancillary studies, the financial support of all non-federal groups will be acknowledged at the end of each manuscript.

ENRICHD FINANCIAL DISCLOSURE STATEMENT

I, the undersigned certify that:

1. As of _____, neither I, nor my spouse or dependent children own or will buy or trade stock or stock options in any of the companies² providing medication, equipment or financial support in the trial. In addition, I don't have a retainer-type consultant position with any of these other companies.*
2. I agree to disclose financial interests as outlined in the ENRICHD Policy on Conflict of Interest during my participation in the ENRICHD Study.

If Investigator disagrees with question 1 or 2, an explanatory letter is required.

Investigator (type name)

Signature

Date

Table 17-1: ENRICHD Policy Regarding Approval Of Manuscripts And Abstracts

The following procedures should be followed before a paper is submitted or accepted for publication:

1. Prior to submitting a paper to a journal, it should be reviewed and approved by the ENRICHD Publications Committee (see Figure 17-1 for sequence of review and approval process). Any disputes will be resolved by the ENRICHD Steering Committee.
2. Before submitting the paper for publication, and before the paper is submitted for Steering Committee review, official data analysis should be completed by the Coordinating Center.
3. The paper should be submitted to the Coordinating Center for data verification prior to submission to a journal. If the Coordinating Center does not provide data verification within two weeks of receipt of the paper, the author(s) may submit the paper to a journal. Data verification must be completed and corrections made before the paper is in press.
4. NIH approval is needed before submitting the paper for publication. NIH approval is conveyed by means of a memo/letter from the Project Office to the lead author.

Once a manuscript proposal has been approved by the Steering Committee, and the Chair of the Publications Committee sends the lead author a letter of confirmation, a request must be received by the Coordinating Center for analysis within two months, or the manuscript will be placed on a delinquent paper list for further discussion.

The official Analysis Log is a key component of this request. It associates data presented in the text, tables, and figures of the manuscript with the unique identification number on each printout from the official analyses.

Figure 17-1: ENRICHD Flow of Manuscript Proposals

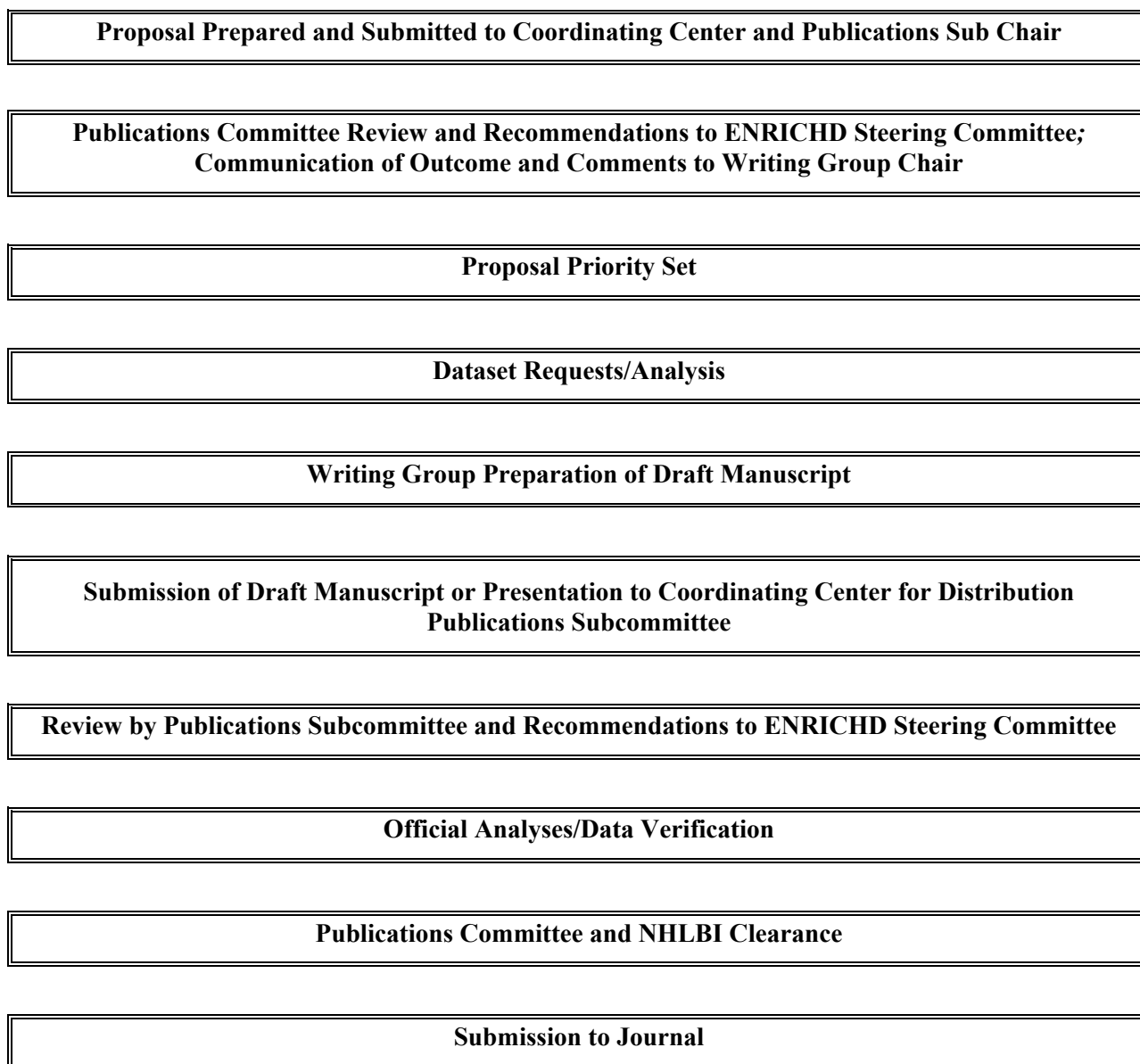


Table 17-2: STATISTICAL COMPUTING REQUEST

Send copies to : Request Number

2. _____ 3. _____

Priority Initials

Coordinating Center ADMINISTRATION

4. Statistical Computing Title (Length 40)

5. Manuscript or Project Number

6. Manuscript or Project Short Title (Length 26)

7. Brief Description _____

8. Requested By _____ 9. Submitted By _____

10. Date Submitted _____

11. Requested Priority _____ 12. Special Deadline _____

13. Reason for Priority/Deadline _____

17. CPR Lead _____ 14. Date Received ____/____/____

R

E 18. Statistical Reviewer _____ 15. Review Completed ____/____/____

V

I 19. Initials ____ 20. Action ____ 16. Priority Assigned ____/____/____

E

W 21. Date Reviewed ____/____/____ CPR ADMINISTRATION

E

R 22. Comments

,

S

T 23. Date Received _ / _ / _ 24. Programmer

C 25. Date Assigned _ / _ / _ 26. Program Completed _ / _ / _

O

M 27. Approved By _____ 28. Date Approved _ / _ / _

P

STATISTICAL COMPUTING REQUEST

Coordinating Center ADMINISTRATION

TRACKING DATA

2. Is this directly related to a previous request?

Yes

3. _____

Related Request Number

Related Request Number

Related Request Number

4. Is this related to a working group?

No Yes

5. _____

Working Group Number

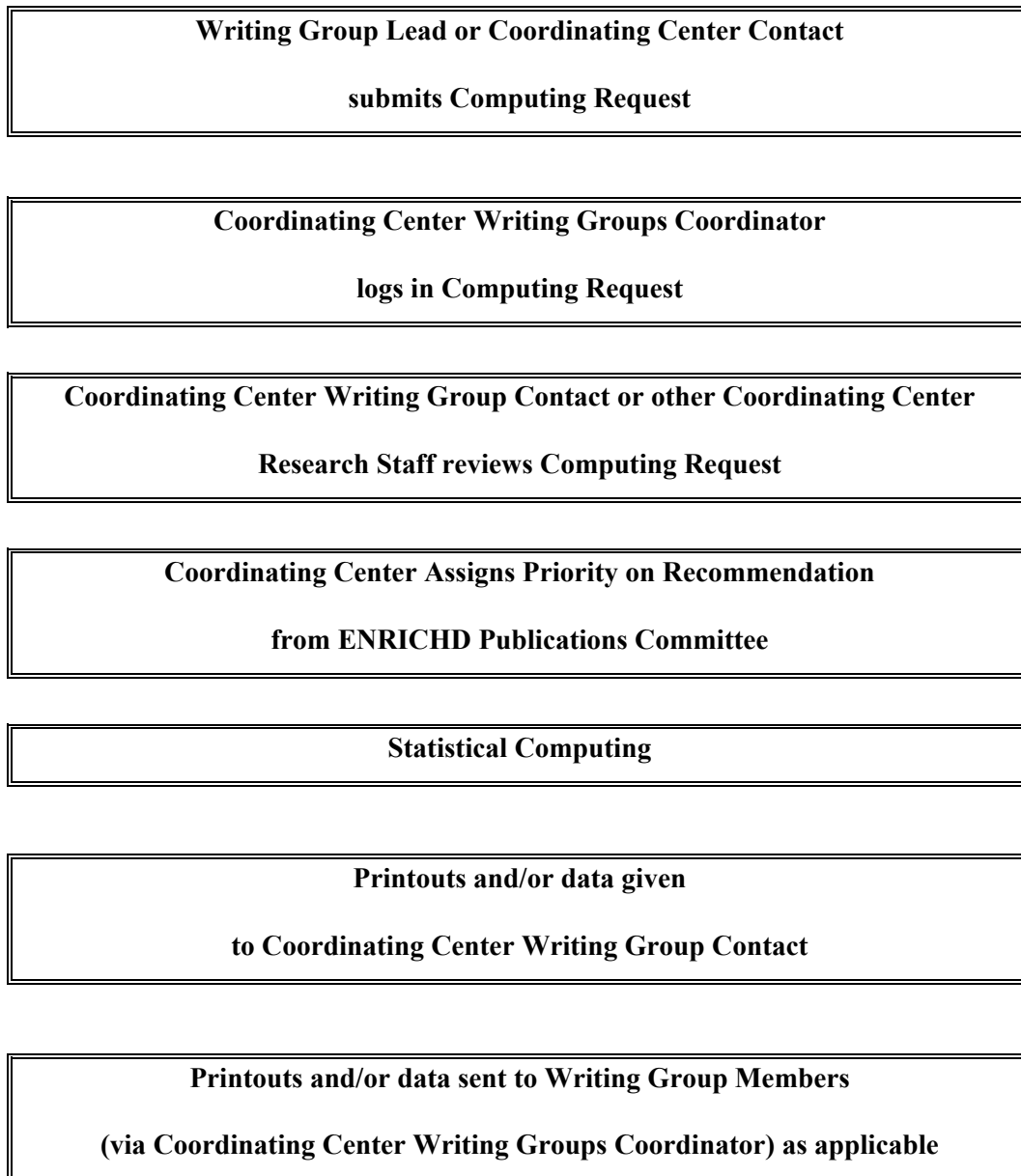
PROGRAM SPECIFICATIONS

6. Describe data files to be used:

7. Exclusions/Inclusions

8. Detailed description of analysis to be done:

Figure 17-2: Routing Process For Computing Requests



18. CHAPTER 18: SUBSTUDIES AND ANCILLARY STUDIES

18.1 SUBSTUDIES

A Substudy uses data collected on a portion of patients who are screened for entry into, or enrolled in ENRICHD, over and above the data collection required by the overall ENRICHD protocol. The data may be collected either on a fraction of subjects seen at each Clinical Center or may consist of subjects seen at selected Clinical Centers. Funding for a Substudy is derived from the overall ENRICHD budget. Substudies must be reviewed and approved by the ENRICHD Substudies and Ancillary Studies (SAS) committee and ratified by the Steering Committee. Review by the SAS Committee is required for presentation or publication of a Substudy.

18.2 ANCILLARY STUDIES

An Ancillary Study uses supplementary data that are collected on patients who are screened for entry into, or enrolled in ENRICHD, over and above the data collection required by the ENRICHD protocol. Such studies are restricted to consideration of a specific test technique or involve only supplemental data collected on ENRICHD patients. Ancillary studies must be reviewed and approved by the ENRICHD SAS Committee and ratified by the Steering Committee prior to initiation to ensure that they do not conflict with the main protocol. Ancillary Studies may be funded either through the overall ENRICHD budget or through separate funding sources. Review by the ENRICHD SAS Committee is required for presentation or publication of an ancillary study.

18.3 DATA BANK STUDIES

A Data Bank Study uses data, specimens, or recordings, which are routinely collected on patients who are screened for entry into, or enrolled in ENRICHD. Analysis of these data is used to answer a specific scientific question. Data used in this research are not directly related to the fundamental goals of the study. Data bank studies must be approved by the SAS Committee and ratified by the Steering Committee. All presentations or publications are to be reviewed by the SAS Committee.

18.4 INDEPENDENT STUDIES

Independent studies of concern to the ENRICHD Study are studies conducted in patients with recent myocardial infarction who enter the ENRICHD Study Clinical Unit but are not enrolled in the ENRICHD Study.

It is understood that each Clinical Unit has the right to conduct studies which are independent of the ENRICHD Study in post-myocardial infarction patients, who do not meet criteria for enrollment into the ENRICHD Study. Independent studies of patients

who meet any of the ENRICHD eligibility criteria must be reviewed by the ENRICHD SAS Committee. ENRICHD Study investigators agree not to conduct independent studies which would compete with or have a detrimental effect on the conduct of the ENRICHD Study during the period of recruitment and follow-up of patients by the ENRICHD Study.

18.5 PREPARATION OF PROPOSAL FOR SUBSTUDY, DATA BANK OR ANCILLARY STUDIES

Each proposal for a Substudy, Ancillary Study or Data Bank Study should contain a brief description of the objectives, methods, analysis plans, significance of the study, and proposed collaborators. Full details should be given concerning any procedures to be carried out on a study patient such as psychiatric interviews, psychological testing, biochemical assay procedures, etc. Any substances to be injected or otherwise administered to the patients should be described. Any observations to be made or procedures to be carried out on a patient outside of the Clinical Unit should be described. Mention should be made of the extent to which the Substudy, Data Bank Study or Ancillary Study will require extra clinic visits by the patient or will prolong the patient's usual clinic visits. Information should be given concerning the extent to which the study will require fluid or biopsy specimens in addition to those already required for ENRICHD. If blood specimens are to be obtained from the patients, all procedures to be carried out on these specimens should be described.

18.6 SUBMISSION OF PROPOSALS

Two copies of each proposal should be submitted to the Coordinating Center for inventory and transmission to the SAS Committee. The Coordinating Center will notify the Investigator when the project is approved, disapproved or additional information is needed before a decision can be made.

18.7 CONDUCT OF RESEARCH

After approval of a proposed Substudy, Data Bank Study or Ancillary Study, members will be invited to serve on an ad hoc Writing Subcommittee and a Chair will be chosen. These investigators will work with the Coordinating Center and NHLBI staff to conduct the data analysis needed to investigate the question at hand and prepare a manuscript based on these findings. Every effort will be made by the Subcommittee to consider and incorporate comments and suggestions from the SAS Committee and the Publications Committee in this manuscript. Subcommittee members may meet with staff from the Coordinating Center or other ENRICHD Clinical Units for development of these papers. Final versions of the manuscript must be approved by the Steering Committee.

18.8 PUBLICATIONS AND PRESENTATIONS

Policies regarding publications and presentations based on Substudies, Data Base Studies and Ancillary Studies will follow the procedures described in Chapter 17.

18.9 INDEPENDENT STUDIES

Results of independent studies which are approved as acceptable within ENRICHD may be published or presented at the discretion of investigators initiating the independent study.

18.10 INDIVIDUALS TO BE GOVERNED BY THESE GUIDELINES

Members of the ENRICHD Study Group who will be governed by these guidelines include the Study Chair, the Principal Investigator at each Clinical Unit, the principal personnel at the Coordinating Center and the Principal Investigators of the Core Laboratories. Co-Investigators and other staff who have major responsibility for enrollment, recruitment, follow-up or collection of data for ENRICHD at Clinical Units, affiliated hospitals or Core Laboratories will also be governed by these guidelines. The Principal Investigator for each ENRICHD Unit will submit a list of individuals who will be governed by these guidelines at the beginning of the study. The Principal Investigator of each participating unit will review the guidelines with all appropriate staff prior to the start of patient recruitment and at least annually thereafter.

19. APPENDICES

Appendix A: ENRICHD SOCIAL SUPPORT INSTRUMENT (ESSI)

Administrative Use Only

Center:

Patient ID #:

Patient Initials:

Visit:

Date: ___ / ___ / 19___
mo. da. yr.

Staff ID#:

INSTRUCTIONS

Please read the following questions and circle the response that most closely describes your current situation.

1. Is there someone available to you whom you can count on to listen to you when you need to talk?

None of
the time
1

A little
of the time
2

Some of
the time
3

Most of
the time
4

All of
the time
5

2. Is there someone available to give you good advice about a problem?

None of
the time
1

A little
of the time
2

Some of
the time
3

Most of
the time
4

All of
the time
5

3. Is there someone available to you who shows you love and affection?

None of
the time
1

A little
of the time
2

Some of
the time
3

Most of
the time
4

All of
the time
5

Please read the following questions and circle the response that most closely describes your current situation.

4. Is there someone available to help you with daily chores?

None of <u>the time</u> 1	A little <u>of the time</u> 2	Some of <u>the time</u> 3	Most of <u>the time</u> 4	All of <u>the time</u> 5
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5. Can you count on anyone to provide you with emotional support (talking over problems or helping you make a difficult decision)?

None of <u>the time</u> 1	A little <u>of the time</u> 2	Some of <u>the time</u> 3	Most of <u>the time</u> 4	All of <u>the time</u> 5
---------------------------------	-------------------------------------	---------------------------------	---------------------------------	--------------------------------

6. Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide?

None of <u>the time</u> 1	A little <u>of the time</u> 2	Some of <u>the time</u> 3	Most of <u>the time</u> 4	All of <u>the time</u> 5
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7. Are you currently married or living with a partner?

Yes No

Appendix B: DSM-IV Depression Interview and Structured Hamilton

PARTS A and B

ENRICH D Study DSM-IV DEPRESSION INTERVIEW AND STRUCTURED HAMILTON (DISH, Version 2d, Revised 3/31/98)

Center: ~ ~ Patient ID: ~ ~ ~ ~ ~ ~ ~ ~ Pt. Initials: ~ ~ ~
 Interview Started: __ / __ / 19 __ Completed: __ / __ / 19 __ Staff ID#: ~ ~ ~
 mo da yr mo da yr

INTERVIEW LOCATION: if interview was initiated while the patient was still hospitalized but completed after discharge, circle both "inpatient" and the location at completion.	INPATIENT (I)	OUTPATIENT (O)	PATIENT'S RESIDENCE (R)	TELEPHONE (T)
ASSESSMENT PHASE [THERAPISTS ONLY]: Circle the applicable box if you use this form as a clinical evaluation tool.	INITIAL EVALUATION (SESSION 0)	INDIVIDUAL Tx TERMINATION	FOLLOW-UP	OTHER
RELIABILITY CHECK: If you are secondary interviewer conducting a reliability check on the "real" interview, circle the method you're using to watch and/or listen to the interview.	IN PERSON (I)	AUDIOTAPE (A)	VIDEOTAPE (V)	TELEPHONE (T)

#	VIDEOTAPED INTERVIEWS: Complete this section if you are coding a videotaped interview, and staple the DSF or DFU to the DISH.									
1	PURPOSE	1=Training 2=Certification 3=Coding Test	4=Clinical judge 5=Clinical consensus 6=Primary interviewer	7=Other						
2	SUBJECT'S INITIALS:	AGE:	GENDER:	INTERVIEWER:						
3	TAPED INTERVIEW NUMBER	Center--Vignette #					--			
4	DATE OF INTERVIEW	(mmddyy)								
5	Dx FORM TO ATTACH	1=DSF	2=DFU							

ACKNOWLEDGEMENTS: This interview was designed for use in the National Heart, Lung, and Blood Institute's Enhancing Recovery in Coronary Heart Disease (ENRICH D) Project and related studies. Its purpose is to obtain the information needed to (1) diagnose current major and minor depressive episodes and dysthymia according to the DSM-IV criteria (American Psychiatric Association, 1994); (2) assess the past history and longitudinal course of depressive disorders, including partial and full remissions, relapses, and recurrences; (3) determine the 17-item Hamilton Rating Scale for Depression severity score for the past week; and (4) perform preliminary screening for other neuropsychiatric disorders. The form integrates material from several different sources, including the Hamilton Rating Scale for Depression (Hamilton, 1960); the standardized version of the Hamilton scale developed by NIMH for use in the Early Clinical Drug Evaluation (ECDEU) program (Guy, 1976) and the Treatment of Depression Collaborative Research Program (Elkin et al. 1985, 1989); the Structured Interview Guide for the Hamilton Depression Rating Scale (Williams, 1988, 1992); the National Institute of Mental Health Diagnostic Interview Schedule (Robins, Helzer, Croughan, and Ratcliff, 1981; Robins, Cottler, Bucholz, and Compton, 1995); a modified version of the NIMH Diagnostic Interview Schedule (Carney and Freedland, 1988) that has been used primarily in research on depression in patients with coronary heart disease; and the DSM-IV manual. Most of the Hamilton items were adapted from, or taken verbatim from, the SIGH-D (Williams, 1988, 1992). Finally, numerous ENRICH D investigators, staff, and consultants contributed to this version of the DISH.

#	DISH PART "A" SCREENING OUTCOME	U
1	SCREENED OUT (Re-screening not indicated)	
2	RESCREEN AFTER (Date):	[Use a new Part A form for re-screening]
3	RESCREEN BY (Date):	[Use a new Part A form for re-screening]

OPTIONAL OPENING QUESTIONS

#	
1	<p>[OPT] I'D LIKE TO START BY ASKING YOU ABOUT YOUR FAMILY. {ARE YOU MARRIED? CHILDREN? GRANDCHILDREN? HOW OLD? ETC.}</p> <p>[OPT] WOULD YOU MIND TELLING ME ABOUT YOUR HEART ATTACK? WAS IT PAINFUL? FRIGHTENING? DID ANYONE HELP YOU GET TO THE HOSPITAL, OR WERE YOU ALL ALONE?</p> <p>[OPT] BEFORE THIS HAPPENED, DID YOU ALREADY KNOW THAT YOU HAD HEART DISEASE, OR DID THE HEART ATTACK COME AS A COMPLETE SURPRISE?</p> <p>[OPT] WHAT'S IT BEEN LIKE FOR YOU HERE IN THE HOSPITAL? HAS IT BEEN HARD TO COPE WITH ALL OF THIS? HAS IT BEEN HARD FOR YOUR {SPOUSE, FAMILY}?</p> <p>[OPT] HAVE YOU HAD MANY VISITORS? WHO'S BEEN ABLE TO COME AND VISIT? IS THERE ANYONE WHO'S TOO FAR AWAY OR WHO CAN'T BE HERE FOR SOME REASON? HOW DO YOU FEEL ABOUT THAT?</p> <p>[OPT] ARE YOU WORRIED ABOUT HOW LIFE IS GOING TO BE FOR YOU {AND YOUR SPOUSE, FAMILY} AFTER YOU GET OUT OF THE HOSPITAL? WHAT KINDS OF PROBLEMS DO YOU THINK YOU MIGHT HAVE TO FACE?</p> <p>[OPT] WHAT KIND OF WORK {DO, DID} YOU DO? ARE YOU RETIRED OR ON LEAVE?</p> <p>[OPT] [IF NOT WORKING]: HOW LONG HAVE YOU BEEN {RETIRED, ON LEAVE, etc.}? DID YOU {RETIRE, STOP WORKING, etc.} BECAUSE OF YOUR AGE, YOUR HEALTH, OR SOME OTHER REASON?</p>

CURRENT DEPRESSION SYMPTOMS					
#	ANHEDONIA AND INACTIVITY	CODE	HRSD	DSM-IV	DURATION
2	[REQ] [IF INPATIENT OR <1 WEEK POST-DISCHARGE]: WHAT HAVE YOU BEEN DOING TO PASS THE TIME OVER THE PAST FEW DAYS?				
	[REQ] [IF >1 WEEK POST-DISCHARGE]: HAVE YOU BEEN WORKING THIS WEEK?				
	[OPT] [IF YES]: HAVE YOU BEEN WORKING AS MANY HOURS AS USUAL? HAVE YOU BEEN ABLE TO GET AS MUCH DONE AS YOU USUALLY DO {WHEN YOU'RE FEELING OKAY}?				
	[OPT] [IF NO]: WHAT ARE THE REASONS WHY YOU AREN'T WORKING?				
	[REQ] [IF >1 WEEK POST-DISCHARGE]: HOW HAVE YOU BEEN SPENDING YOUR FREE TIME THIS PAST WEEK {WHEN YOU'RE NOT AT WORK}?				
	[OPT] HAVE YOU BEEN DOING ANYTHING FOR FUN OR RECREATION?				
	[OPT] HAVE YOU REALLY FELT INTERESTED IN DOING {THOSE THINGS}, OR HAVE YOU HAD TO PUSH YOURSELF TO DO THEM?				
	[OPT] HAVE YOU STOPPED DOING ANYTHING YOU USED TO ENJOY DOING? [IF YES]: WHY?				
	[OPT] IF/WHEN YOU ARE ABLE TO RESUME {YOUR FAVORITE ACTIVITIES}, DO YOU THINK THAT YOU WOULD YOU STILL ENJOY THEM, OR HAVE YOU LOST INTEREST IN {THESE ACTIVITIES}?				
	[REQ] HAVE YOU BEEN FEELING LIKE YOU'VE LOST INTEREST IN MOST THINGS, OR LIKE YOU'RE NOT GETTING MUCH PLEASURE FROM THINGS YOU USED TO ENJOY? [IF YES]: HAVE YOU BEEN FEELING LIKE THAT MOST OF THE TIME? HOW LONG HAVE YOU YOU BEEN FEELING THAT WAY?				
[OPT] IS THERE ANYTHING YOU ARE LOOKING FORWARD TO DOING?					
[REQ] [RATE WORK & ACTIVITIES THIS WEEK.] 0---- NO DIFFICULTY 1---- THOUGHTS & FEELINGS OF INCAPACITY, FATIGUE, OR WEAKNESS RELATED TO ACTIVITIES, WORK, OR HOBBIES 2---- LOSS OF INTEREST IN ACTIVITIES, HOBBIES, OR WORK, OR PT.			HRSD		

CURRENT DEPRESSION SYMPTOMS						
#	ANHEDONIA AND INACTIVITY	CODE	HRSD	DSM-IV	DURATION	
3	<p>[REQ] LATELY, HAVE YOU LOST INTEREST IN SPENDING TIME WITH OTHER PEOPLE, OR HAVE YOU FELT LIKE AVOIDING PEOPLE YOU USUALLY LIKE TO VISIT? [IF YES, PROBE FOR FREQUENCY]: HAVE YOU BEEN FEELING LIKE THAT MOST OF THE TIME?</p>					
	<p>[REQ] [RATE SOCIAL WITHDRAWAL]</p> <p>0---- NO LOSS OF INTEREST IN OR AVOIDANCE OF SOCIAL CONTACT</p> <p>1---- SOCIALLY WITHDRAWN SOME DAYS</p> <p>2---- SOCIALLY WITHDRAWN MOST DAYS</p> <p>M-- MEDICAL Sx</p> <p>R-- REFUSED</p> <p>U-- UNABLE TO ASSESS</p>	CODE				
4	<p>[REQ] [RATE ANHEDONIA BASED ON ITEMS 1-3.]</p> <p>0---- NO SIGNIFICANT LOSS OF INTEREST OR PLEASURE IN ACTIVITIES (Duration=N)</p> <p>1---- LOSS OF INTEREST OR PLEASURE IN MOST ACTIVITIES IS PRESENT SOME DAYS (Duration=Weeks)</p> <p>2---- LOSS OF INTEREST OR PLEASURE IN MOST ACTIVITIES IS PRESENT MOST DAYS (Duration=Weeks)</p> <p>M-- MEDICAL Sx (Duration=Weeks)</p> <p>R-- REFUSED (Duration=R)</p> <p>U-- UNABLE TO ASSESS (Duration=U)</p> <p style="text-align: right;">DURATION IN DAYS IF <2 WEEKS: _____</p>			<p>DSM-IV MINOR: 2 MAJOR: 2</p>		

CURRENT DEPRESSION SYMPTOMS						
#	DYSPHORIC MOOD	CODE	HRSD	DSM-IV	DURATION	
5	<p>[REQ] WHAT'S YOUR MOOD BEEN LIKE THIS WEEK?</p> <p>[OPT] HAVE YOU BEEN FEELING {SAD, DOWN, DEPRESSED, UNHAPPY, etc.}?</p> <p>[OPT] HAVE YOU FELT LIKE CRYING, OR HAVE YOU ACTUALLY BEEN CRYING OR HAD CRYING SPELLS SOMETIME IN THE LAST WEEK ?</p>					
	<p>[REQ] [RATE MOOD THIS WEEK, BASED ON PATIENT'S ANSWERS TO THIS ITEM AND YOUR OBSERVATIONS.]</p> <p>0---- MOOD IS NOT DYSPHORIC</p> <p>1---- MOOD IS DYSPHORIC, BUT THIS IS APPARENT ONLY IN PT.'s ANSWERS TO QUESTIONS</p> <p>2---- MOOD IS DYSPHORIC, AND IS SEVERE ENOUGH THAT THE PT. TALKS SPONTANEOUSLY (WITHOUT BEING ASKED) ABOUT IT.</p> <p>3---- MOOD IS DYSPHORIC, AND IS SEVERE ENOUGH THAT YOU CAN TELL NOT ONLY FROM THE PT.'s ANSWERS BUT ALSO FROM HIS/HER FACIAL EXPRESSION, VOICE, POSTURE, CRYING, ETC.</p> <p>4---- MOOD IS DYSPHORIC, AND IS SO SEVERE THAT IT IS OBVIOUS IN VIRTUALLY EVERYTHING THE PT. SAYS AND DOES; PT. LOOKS AND SOUNDS VERY DEPRESSED</p>		HRSD			
6	<p>[REQ] [RATE CURRENT MOOD, BASED ON ITEM #5, PROBES FOR FREQUENCY & DURATION, AND YOUR OBSERVATIONS. IF MOOD IS DYSPHORIC, ASK]: HAVE YOU BEEN FEELING {SAD, DEPRESSED, EMPTY, etc.} MOST OF THE TIME? HOW LONG HAVE YOU BEEN FEELING LIKE THAT?</p> <p>0---- NOT DYSPHORIC (Duration=N)</p> <p>1---- DYSPHORIC SOME DAYS (Duration=weeks)</p> <p>2---- DYSPHORIC MOST DAYS (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks)</p> <p>R--- REFUSED (Duration=R)</p> <p>U--- UNABLE TO ASSESS (Duration=U)</p>			<p>DSM-IV MAJOR: 2 MINOR: 2 DYSTH: 2</p>		

CURRENT DEPRESSION SYMPTOMS					
#	DYSPHORIC MOOD	CODE	HRSD	DSM-IV	DURATION
7	<p>[SCREENING INTERVIEWS ONLY]</p> <p>[REQ] [IF THE PATIENT SCREENED POSITIVE ON THE ESSI, COMPLETE BOTH PARTS "A" AND "B" OF THE DISH (i.e., the Current Depression Symptoms and Psychiatric History Sections), EVEN IF THE PATIENT IS NOT DEPRESSED.]</p> <hr/> <p>[REQ] [A POSITIVE SCREEN ON DISH PART "A" REQUIRES EITHER: A RATING OF "2" ON ITEM #4 WITH A DURATION \$7 DAYS, OR A RATING OF "2" ON ITEM #6 WITH A DURATION \$7 DAYS.]</p> <p>[IF THE PATIENT SCREENED POSITIVE FOR DEPRESSION ON DISH PART "A" (OR ON THE BDI) BUT NEGATIVE ON THE ESSI, CONTINUE THE INTERVIEW AND COMPLETE DISH PART "B".]</p> <p>[OPT] [YOU MAY TERMINATE THE INTERVIEW IF THESE MINIMUM CRITERIA FOR DYSPHORIA AND/OR ANHEDONIA ARE NOT MET AND THE PATIENT IS ALSO ESSI-NEGATIVE, SINCE THE PATIENT IS NOT CURRENTLY ELIGIBLE FOR ENROLLMENT.</p> <p>[HOWEVER, IF YOU BELIEVE THAT THE PATIENT MAY ACTUALLY BE DEPRESSED DESPITE HIS/HER ANSWERS TO THE CONTRARY, TRY ASKING SOME (OR SOME MORE OF) THE OPTIONAL QUESTIONS FROM ITEM #1, AND/OR OTHER ITEMS FROM OTHER PARTS OF THE DISH, TO ENCOURAGE THE PATIENT TO OPEN UP TO YOU ABOUT HIS/HER PROBLEMS AND FEELINGS. THEN, RE-ADMINISTER THE ANHEDONIA AND DYSPHORIA ITEMS. IF THE PATIENT NOW ADMITS TO THESE SYMPTOMS, REVISE THE CODES ON ITEMS 1-6 ACCORDINGLY, AND THEN CONTINUE THE INTERVIEW.]</p>				
8	<p>[REQ] [IF MOOD IS DYSPHORIC, BASED ON ITEMS 5 & 6 , ASK ONE OR BOTH OF THE FOLLOWING QUESTIONS.]</p> <p>A. DID SOMETHING HAPPEN THAT MADE YOU START TO FEEL {SAD, DEPRESSED, etc.}? WHAT SEEMS TO BE GETTING YOU DOWN?</p> <p>B. IS THERE ANYTHING ELSE BESIDES {e.g., YOUR HEART ATTACK} THAT'S {GETTING YOU DOWN, MAKING YOU SAD, etc.}?</p> <p>[DESCRIBE THE EVENT(S), IF ANY ARE IDENTIFIED, THAT MAY HAVE PRECIPITATED OR WORSENERD THE PT's DEPRESSED MOOD, ALONG WITH APPROXIMATE DATE(S) OR DURATION(S). DOCUMENT BEREAVEMENT IF THE PT. HAS SUFFERED A SIGNIFICANT LOSS.]</p>				
9	<p>[REQ] THIS PAST WEEK, HAVE YOU FELT IRRITABLE OR ANGRY AT TIMES? [IF YES]: HAVE YOU BEEN FEELING THAT WAY MOST OF THE TIME?</p> <p>[OPT] [IF YES]: HAVE YOU BEEN {IRRITABLE, ANGRY} ABOUT ANYTHING IN PARTICULAR? WHAT'S BEEN MAKING YOU {e.g., MAD}?</p>				

CURRENT DEPRESSION SYMPTOMS						
#	APPETITE AND WEIGHT	CODE	HRSD	DSM-IV	DURATION	
10	<p>[REQ] HOW HAS YOUR APPETITE BEEN THIS PAST WEEK?</p> <p>[OPT] IS THAT {DIFFERENT, MORE, LESS} THAN YOUR USUAL APPETITE?</p> <p>[OPT] HAVE YOU HAD TO FORCE YOURSELF TO EAT?</p> <p>[OPT] HAVE OTHER PEOPLE HAD TO URGE YOU TO EAT?</p> <p>[OPT] HAVE YOU BEEN SKIPPING MEALS?</p> <p>[OPT] HAVE YOU BEEN HAVING ANY STOMACH OR INTESTINAL PROBLEMS THAT ARE MAKING IT HARD FOR YOU TO EAT? [IF YES]: IS THAT SOMETHING YOUR DOCTOR IS TREATING YOU FOR, OR IS IT JUST THAT YOU DON'T FEEL VERY GOOD?</p>					
	<p>[REQ] [RATE APPETITE THIS WEEK & ANY G.I. SYMPTOMS ASSOCIATED WITH LOSS OF APPETITE.]</p> <p>0---- NO LOSS OF APPETITE</p> <p>1---- LOSS OF APPETITE IS PRESENT BUT PT. IS EATING WITHOUT URGING OR ENCOURAGEMENT FROM OTHER PEOPLE</p> <p>2---- PT. HAS DIFFICULTY EATING WITHOUT BEING URGED TO DO SO, OR APPETITE LOSS IS SO SEVERE THAT PT. REPORTS RELATED G.I. SYMPTOMS SUCH AS NAUSEA</p>		HRSD			
11	<p>[REQ] HAVE YOU LOST OR GAINED ANY WEIGHT LATELY? [IF YES]: HOW MUCH? HOW LONG DID IT TAKE?</p> <p>[OPT] [IF WEIGHT GAIN]: IS THAT ONLY BECAUSE OF SWELLING & WATER RETENTION, OR HAVE YOU ACTUALLY GAINED SOME WEIGHT?</p> <p>[OPT] [IF WEIGHT LOSS]: HAVE YOU BEEN DIETING TO LOSE WEIGHT? HAVE YOU BEEN TAKING DIURETICS (WATER PILLS)?</p> <p>[OPT] __ LOST __ GAINED _____ POUNDS IN _____ WEEKS</p> <p>USUAL WEIGHT: _____ POUNDS WEIGHT NOW: _____</p>					
	<p>[REQ] [RATE WEIGHT LOSS.]</p> <p>0---- NO WEIGHT LOSS (OR LOSS DUE SOLELY TO ILLNESS OR DIET)</p> <p>1---- PROBABLE WEIGHT LOSS DUE TO CURRENT DEPRESSION</p> <p>2---- DEFINITE WEIGHT LOSS DUE TO CURRENT DEPRESSION</p>		HRSD			
12	<p>[REQ] [RATE CHANGE IN APPETITE AND/OR WEIGHT, BASED ON ITEMS 10-11 AND PROBES FOR FREQUENCY & DURATION.] [IF APPETITE HAS CHANGED]: HAS YOUR APPETITE BEEN LIKE THAT MOST OF THE TIME? HOW LONG HAS IT BEEN THAT WAY?</p> <p>0---- NORMAL APPETITE & WEIGHT (Duration=N)</p> <p>1---- APPETITE IS DECREASED OR INCREASED SOME DAYS, OR WEIGHT HAS CHANGED BUT LESS THAN 5% IN THE LAST MONTH (Duration=weeks)</p> <p>2---- APPETITE IS DECREASED OR INCREASED MOST DAYS, OR</p>			DSM-IV MAJOR: 2 MINOR: 2 DYSTH: 2		

CURRENT DEPRESSION SYMPTOMS					
#	SLEEP DISTURBANCE AND FATIGUE	CODE	HRSD	DSM-IV	DURATION
13	[REQ] HOW HAVE YOU BEEN SLEEPING OVER THE PAST WEEK? HAVE YOU BEEN SLEEPING {LESS THAN, MORE THAN, THE SAME AS} USUAL?				
	[OPT] [IF MORE OR LESS]: IS THAT MAKING YOU VERY SLEEPY DURING THE DAY, OR INTERFERING WITH YOUR DAYTIME ACTIVITIES?				
	[OPT] HAVE YOU BEEN TAKING ANY MEDICINE TO HELP YOU SLEEP? [IF YES]: IS IT HELPING? IS IT MAKING YOU SLEEP TOO MUCH?				
14	[REQ] HAVE YOU HAD TROUBLE FALLING ASLEEP AT NIGHT THIS WEEK?				
	[OPT] RIGHT AFTER YOU GO TO BED, HOW LONG HAS IT BEEN TAKING YOU TO FALL ASLEEP?				
	[OPT] HOW MANY NIGHTS THIS WEEK HAVE YOU HAD TROUBLE?				
	[REQ] [RATE SLEEP ONSET INSOMNIA THIS WEEK, BASED ON ITEMS 13-14.] 0---- NO DIFFICULTY FALLING ASLEEP 1---- OCCASIONAL DIFFICULTY FALLING ASLEEP (TAKES > 1/2 HOUR) 2---- NIGHTLY DIFFICULTY FALLING ASLEEP (TAKES > 1/2 HOUR)		HRSD		
15	[REQ] DURING THE PAST WEEK, HAVE YOU BEEN WAKING UP IN THE MIDDLE OF THE NIGHT? [IF YES]: IS THAT USUALLY BECAUSE YOU HAVE TO GO TO THE BATHROOM, OR FOR SOME OTHER REASON?				
	[OPT] DO YOU GET OUT OF BED? WHEN YOU GET BACK INTO BED, ARE YOU ABLE TO FALL RIGHT BACK ASLEEP?				
	[OPT] HAVE YOU BEEN SLEEPING RESTLESSLY? TOSSING & TURNING?				
	[REQ] [RATE MIDDLE INSOMNIA & RESTLESS SLEEP THIS WEEK BASED ON ITEMS 13 & 15.] 0---- NO DIFFICULTY STAYING ASLEEP; SLEEP IS RESTFUL 1---- SLEEP IS RESTLESS OR DISTURBED DURING THE NIGHT 2---- PT. HAS BEEN WAKING UP DURING THE NIGHT AND HAVING DIFFULTY FALLING BACK ASLEEP. (DO NOT COUNT IF PT. IS ONLY WAKING UP TO GO TO THE BATHROOM.)		HRSD		
16	[REQ] WHAT TIME HAVE YOU BEEN WAKING UP IN THE MORNING THIS WEEK? [IF EARLY]: IS THAT EARLIER THAN YOU USUALLY WAKE UP? IS IT <u>TOO</u> EARLY, OR IS THAT THE TIME THAT YOU WANT TO WAKE UP?				

CURRENT DEPRESSION SYMPTOMS							
#	SLEEP DISTURBANCE AND FATIGUE	CODE	HRSD	DSM-IV	DURATION		
17	<p>[REQ] [RATE SLEEP DISTURBANCE, BASED ON ITEMS 13-16, AND PROBES FOR FREQUENCY AND DURATION. IF SLEEP IS DISTURBED, ASK]: HAVE YOU BEEN {e.g., HAVING TROUBLE SLEEPING, SLEEPING TOO MUCH, etc.} ALMOST EVERY DAY? HOW LONG HAS THIS BEEN HAPPENING?</p> <p>0---- NO SIGNIFICANT SLEEP DISTURBANCE (Duration=N)</p> <p>1---- INSOMNIA OR HYPERSOMNIA SOME DAYS, USUALLY NOT BAD ENOUGH TO CAUSE DAYTIME SLEEPINESS OR TO AFFECT DAYTIME FUNCTIONING (Duration=weeks)</p> <p>2---- INSOMNIA OR HYPERSOMNIA MOST DAYS, USUALLY BAD ENOUGH TO CAUSE DAYTIME SLEEPINESS OR TO AFFECT DAYTIME FUNCTIONING (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks) R--- REFUSED (Duration=R) U--- UNABLE TO ASSESS (Duration=U)</p> <p>DURATION IN DAYS IF <2 WEEKS: _____</p>			DSM-IV MAJOR: 2 MINOR: 2 DYSTH: 2			
18	<p>[REQ] HOW HAS YOUR ENERGY LEVEL BEEN THIS PAST WEEK? HAVE YOU BEEN FEELING TIRED OR FATIGUED THIS WEEK? [IF YES]: HOW BAD HAS IT BEEN?</p> <p>[OPT] [IF TIRED, FATIGUED, OR LOW ON ENERGY]: AT THOSE TIMES WHEN YOU ARE FEELING ESPECIALLY {TIRED, FATIGUED, etc.}, HAVE YOU ALSO BEEN GETTING ANY ACHES & PAINS {e.g., BACKACHES, HEADACHES, HEAVINESS IN LIMBS, etc.}</p>						
	<p>[REQ] [RATE THE SEVERITY OF FATIGUE OR LOW ENERGY THIS WEEK]</p> <p>0---- NONE (NORMAL ENERGY, NOT FATIGUED) 1---- PT. REPORTS MILD TO MODERATE LOSS OF ENERGY OR FATIGUE 2---- PT. REPORTS SEVERE LOSS OF ENERGY OR FATIGUE; MAY COMPLAIN OF ASSOCIATED SYMPTOMS (E.G., ACHES & PAINS)</p>		HRSD				
19	<p>[REQ] [RATE FATIGUE OR LOSS OF ENERGY, BASED ON ITEM #18 AND PROBES FOR FREQUENCY & DURATION. IF FATIGUE OR LOSS OF ENERGY IS PRESENT, ASK]: HAVE YOU BEEN FEELING {e.g., FATIGUED, LOW ON ENERGY} MOST OF THE TIME? HOW LONG HAVE YOU BEEN FEELING LIKE THAT?</p> <p>0---- NO SIGNIFICANT FATIGUE OR LOSS OF ENERGY (Duration=N)</p> <p>1---- FATIGUE OR LOW ENERGY SOME DAYS (Duration=weeks)</p> <p>2---- FATIGUE OR LOW ENERGY MOST DAYS (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks) R--- REFUSED (Duration=R) U--- UNABLE TO ASSESS (Duration=U)</p>			DSM-IV MAJOR: 2 MINOR: 2 DYSTH: 2			

CURRENT DEPRESSION SYMPTOMS						
#	GUILT, WORTHLESSNESS, AND LOW SELF-ESTEEM	CODE	HRSD	DSM-IV	DURATION	
20	<p>[REQ] THIS PAST WEEK, HAVE YOU BEEN THINKING THAT YOU'VE DONE SOMETHING BAD OR WRONG, OR THAT YOU'VE LET OTHER PEOPLE DOWN IN SOME WAY?</p> <p>[REQ] HAVE YOU BEEN FEELING GUILTY ABOUT ANYTHING?</p> <p>[OPT] HAVE YOU BEEN THINKING THAT YOU BROUGHT (e.g., YOUR PROBLEMS, ILLNESS, DEPRESSION, etc.) ON YOURSELF? THAT IT'S YOUR FAULT? DOES IT SEEM LIKE YOU'RE BEING PUNISHED?</p>					
	<p>[REQ] [RATE THE SEVERITY OF GUILT THIS WEEK.]</p> <p>0---- ABSENT; PT. DOES NOT FEEL GUILTY</p> <p>1---- PT. FEELS SOMEWHAT GUILTY, EXPRESSES SELF-REPROACH, THINKS S/HE HAS LET OTHER PEOPLE DOWN</p> <p>2---- PT. FEELS VERY GUILTY OR IS RUMINATING ABOUT PAST ERRORS OR SINFUL DEEDS</p> <p>3---- PT. BELIEVES THAT S/HE IS ACTUALLY BEING PUNISHED IN SOME WAY (e.g., AS IF FEELING BAD OR BEING ILL IS HIS/HER PUNISHMENT FOR A SIN, MISTAKE, ETC.); OR DELUSIONAL GUILT (e.g., IRRATIONALLY BLAMES SELF FOR PROBLEMS, REAL OR IMAGINED, THAT PROBABLY AREN'T HIS/HER FAULT.)</p> <p>4---- PT. HAS ACCUSATORY OR DENUNCIATORY HALLUCINATIONS</p>		HRSD			
21	<p>[REQ] OVER THE LAST WEEK, HAVE YOU BEEN: {CRITICIZING, COMING DOWN PRETTY HARD ON} YOURSELF? FEELING WORTHLESS OR INADEQUATE?</p> <p>[OPT] HAVE YOU BEEN PUTTING YOURSELF DOWN? THINKING THAT YOU DON'T LIKE YOURSELF VERY MUCH?</p>					
	<p>[REQ] [RATE PATIENT'S SELF-ESTEEM, BASED ON RESPONSES TO THIS ITEM, PROBES FOR SEVERITY & DURATION, & YOUR OBSERVATIONS THROUGHOUT THE INTERVIEW.]</p> <p>0---- PT. HAS GOOD SELF-ESTEEM; MAY OCCASIONALLY HAVE NEGATIVE THOUGHTS ABOUT SELF, BUT GENERALLY LIKES AND ACCEPTS SELF (Duration=N)</p> <p>1---- PT. HAS FAIR SELF-ESTEEM; SOMETIMES DISLIKES, DISAPPROVES OF, IS DISAPPOINTED IN, OR IS CRITICAL OF SELF (Duration=weeks)</p>			DSM-IV DYSTH: 2		

CURRENT DEPRESSION SYMPTOMS						
#	GUILT, WORTHLESSNESS, AND LOW SELF-ESTEEM	CODE	HRSD	DSM-IV	DURATION	
22	<p>[REQ] [RATE <u>EXCESSIVE</u> OR <u>INAPPROPRIATE</u> GUILT OR FEELINGS OF WORTHLESS, BASED ON ITEMS 20-21 AND PROBES FOR FREQUENCY & DURATION. IF PRESENT, ASK]: HAVE YOU BEEN FEELING {e.g., GUILTY, WORTHLESS, etc.} MOST OF THE TIME? HOW LONG HAVE YOU BEEN FEELING LIKE THAT?</p> <p>0---- DOES NOT FEEL WORTHLESS OR EXCESSIVELY OR INAPPROPRIATELY GUILTY (Duration=N)</p> <p>1---- FEELS WORTHLESS OR EXCESSIVELY OR INAPPROPRIATELY GUILTY SOME DAYS (Duration=weeks)</p> <p>2---- FEELS WORTHLESS OR EXCESSIVELY OR INAPPROPRIATELY GUILTY MOST DAYS (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks) R--- REFUSED (Duration=R) U--- UNABLE TO ASSESS (Duration=U)</p> <p style="text-align: right;">DURATION IN DAYS IF <2 WEEKS: _____</p>			DSM-IV MAJOR: 2 MINOR: 2		

CURRENT DEPRESSION SYMPTOMS					
#	HOPELESSNESS AND SUICIDAL FEATURES	CODE	HRSD	DSM-IV	DURATION
23	<p>[REQ] OVER THE LAST WEEK, HAVE YOU BEEN FEELING DISCOURAGED OR PESSIMISTIC ABOUT THE FUTURE? HAVE YOU FELT HOPELESS?</p> <p>[OPT] [IF YES]: WHAT ARE YOU FEELING {e.g., DISCOURAGED, HOPELESS, etc.} ABOUT? HOW SURE ARE YOU THAT THINGS WON'T GET BETTER?</p>				
	<p>[REQ] [RATE FEELINGS OF HOPELESSNESS BASED ON THIS ITEM AND PROBES FOR FREQUENCY & DURATION. IF FEELING HOPELESS, ASK]: HAVE YOU BEEN FEELING HOPELESS MOST OF THE TIME? HOW LONG HAVE YOU BEEN FEELING THAT WAY?</p> <p>0---- NOT FEELING HOPELESS (Duration=N)</p> <p>1---- FEELS HOPELESS SOME DAYS (Duration=weeks)</p> <p>2---- FEELS HOPELESS MOST DAYS (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks)</p> <p>R--- REFUSED (Duration=R)</p> <p>U--- UNABLE TO ASSESS (Duration=U)</p>			DSM-IV DYSTH: 2	
24	<p>[REQ] THIS PAST WEEK, HAVE YOU BEEN THINKING ABOUT DEATH OR DYING?</p> <p>[OPT] [IF YES]: ARE YOU AFRAID OF THAT? LOOKING FORWARD TO IT?</p>				
	<p>[REQ] HAD ANY THOUGHTS THAT LIFE IS NOT WORTH LIVING ANYMORE?</p>				
	<p>[REQ] ANY THOUGHTS THAT YOU'D BE BETTER OFF DEAD, OR THAT YOUR {SPOUSE, FAMILY} WOULD BE BETTER OFF?</p>				
	<p>[REQ] HAVE YOU HAD ANY THOUGHTS OF HURTING OR KILLING YOURSELF?</p>				
	<p>[REQ] [IF YES]: WHAT HAVE YOU BEEN THINKING ABOUT DOING?</p>				
	<p>[REQ] [IF YES]: DO YOU THINK YOU MIGHT ACTUALLY DO THAT? HAVE YOU MADE ANY PLANS TO DO THIS? HOW SOON? DO YOU ACTUALLY HAVE THE {e.g., PILLS, WEAPON} YOU'D NEED?</p>				
	<p>[REQ] [IF YES]: HAVE YOU ACTUALLY DONE ANYTHING TO HURT YOURSELF {OR TO TRY TO KILL YOURSELF}?</p>				

CURRENT DEPRESSION SYMPTOMS						
#	HOPELESSNESS AND SUICIDAL FEATURES	CODE	HRSD	DSM-IV	DURATION	
24	<p>[REQ] [RATE THE SEVERITY OF CURRENT SUICIDAL FEATURES.]</p> <p>0---- ABSENT</p> <p>1---- PT. FEELS LIFE IS NOT WORTH LIVING OR THAT S/HE (OR FAMILY) WOULD BE BETTER OFF IF S/HE WERE DEAD</p> <p>2---- PT. WISHES S/HE WERE DEAD</p> <p>3---- PT. IS ACTIVELY THINKING ABOUT, PLANNING TO, OR PREPARING TO ATTEMPT SUICIDE, OR HAS MADE A NON-LETHAL SUICIDAL GESTURE (e.g., TAKING A FEW PILLS) WITHIN THE PAST WEEK</p> <p>4---- PT. HAS ACTUALLY ATTEMPTED SUICIDE THIS WEEK</p>		HRSD			
25	<p>[REQ] [RATE CURRENT SUICIDAL FEATURES, BASED ON ITEM #24 AND PROBES FOR FREQUENCY AND DURATION.]</p> <p>0---- NO SUICIDAL IDEATION OR BEHAVIOR. Patient may have occasional, normal (non-morbid) thoughts about death and dying (e.g., is afraid of dying), but does not dwell on the subject. Risk of a suicide attempt appears negligible at this time. (Duration=N)</p> <p>1---- MINIMAL SUICIDAL IDEATION OR BEHAVIOR. Patient may have occasional thoughts about "being better off dead" or passing thoughts about suicide, but denies any desire, intent, plans, or means to attempt suicide, and does not dwell on thoughts of death, dying, or suicide. Risk of a suicide attempt appears minimal. (Duration=weeks)</p> <p>2---- SIGNIFICANT SUICIDAL IDEATION OR BEHAVIOR. Patient has one or more of the following: Recurrent thoughts of death (not just fear of dying), frequent thoughts of "being better off dead", recurrent suicidal ideation, a specific plan for committing suicide, or has recently attempted suicide. Risk of a suicide attempt is significant. (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks) R--- REFUSED (Duration=R) U--- UNABLE TO ASSESS (Duration=U)</p> <p>DURATION IN DAYS IF <2 WEEKS: _____</p>			DSM-IV MAJOR: 2 MINOR: 2		
26	<p>[SUICIDE RISK ASSESSMENT, ACTION PLAN, & DOCUMENTATION]</p> <p>[REQ] [IF PATIENT HAS SIGNIFICANT SUICIDAL IDEATION OR BEHAVIOR (i.e., Item 25 = 2), CIRCLE "A" or "B"]:</p> <p>A. PATIENT IS AT <u>IMMINENT</u> RISK OF ATTEMPTING SUICIDE WITHIN HOURS OR DAYS.</p> <p>B. PATIENT IS AT <u>ELEVATED</u> RISK OF ATTEMPTING SUICIDE AT SOME POINT, BUT PROBABLY NOT IMMEDIATELY.</p> <p>[REQ] IF PT. IS AT <u>IMMINENT RISK</u> OF ATTEMPTING SUICIDE, FOLLOW YOUR SITE'S <u>IMMINENT SUICIDE RISK PLAN</u>, AND DOCUMENT YOUR ACTIONS IN THE PATIENT'S ENRICHD FILE (NOT IN HIS/HER HOSPITAL CHART.)</p> <p>IF PT. IS AT <u>INCREASED RISK</u> OF ATTEMPTING SUICIDE SOMETIME IN THE FUTURE, FOLLOW YOUR SITE'S <u>NOTIFICATION PLAN FOR ACTIVE SUICIDAL IDEATION</u> AND DOCUMENT YOUR ACTIONS IN THE PATIENT'S ENRICHD FILE (NOT IN HIS/HER HOSPITAL CHART.)</p>					

CURRENT DEPRESSION SYMPTOMS					
#	COGNITIVE AND SOMATIC FEATURES	CODE	HRSD	DSM-IV	DURATION
27	<p>[REQ] DURING THE PAST WEEK, HAVE YOU HAD TROUBLE CONCENTRATING?</p> <p>[OPT] HAVE YOU BEEN LOSING YOUR TRAIN OF THOUGHT, LIKE YOUR MIND IS OFF SOMEWHERE ELSE?</p> <p>[OPT] HAVE YOU BEEN HAVING A HARD TIME {KEEPING YOUR MIND ON, PAYING ATTENTION TO} CONVERSATIONS, TV PROGRAMS, THE BOOKS OR MAGAZINES YOU'RE READING, ETC.?</p> <p>[OPT] HAS IT SEEMED AT TIMES LIKE YOUR THOUGHTS ARE MIXED UP OR CONFUSED?</p> <p>[REQ] LATELY, HAS IT BEEN VERY HARD FOR YOU TO MAKE DECISIONS OR CHOICES? EVEN SMALL ONES?</p>				
	<p>[REQ] [RATE IMPAIRED CONCENTRATION AND/OR INDECISIVENESS, BASED ON THIS ITEM, PROBES FOR FREQUENCY & DURATION, AND YOUR OBSERVATIONS DURING THE INTERVIEW. IF PRESENT, ASK]: HAVE YOU BEEN HAVING TROUBLE (e.g., CONCENTRATING, MAKING DECISIONS) MOST OF THE TIME LATELY? HOW LONG HAS THAT BEEN HAPPENING?</p> <p>0--- NO SIGNIFICANT COGNITIVE IMPAIRMENT (Duration=N)</p> <p>1--- DIMINISHED ABILITY TO CONCENTRATE OR MAKE DECISIONS SOME DAYS (Duration=weeks)</p> <p>2--- DIMINISHED ABILITY TO CONCENTRATE OR MAKE DECISIONS MOST DAYS (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks)</p> <p>R--- REFUSED (Duration=R)</p> <p>U--- UNABLE TO ASSESS (Duration=U)</p> <p style="text-align: right;">DURATION IN DAYS IF <2 WEEKS: _____</p>			DSM-IV MAJOR: 2 MINOR: 2 DYSTH: 2	
28	<p>[REQ] THIS PAST WEEK, HAVE YOU BEEN WORRYING A LOT? ABOUT BIG PROBLEMS, OR ABOUT LITTLE THINGS THAT YOU DON'T ORDINARILY WORRY MUCH ABOUT? [IF YES]: LIKE WHAT, FOR EXAMPLE?</p>				
	<p>[REQ] [RATE SEVERITY OF COGNITIVE ANXIETY THIS WEEK.]</p> <p>0--- PT. IS NOT WORRIED OR ANXIOUS</p> <p>1--- PT. IS WORRIED, ANXIOUS, OR APPREHENSIVE, BUT THIS IS APPARENT ONLY IN PT.'s ANSWERS TO THIS ITEM</p> <p>2--- PT. IS WORRIED, ANXIOUS, OR APPREHENSIVE, AND THIS IS APPARENT NOT ONLY IN ANSWERS TO THIS ITEM BUT IN SOME OF</p>		HRSD		

CURRENT DEPRESSION SYMPTOMS					
#	COGNITIVE AND SOMATIC FEATURES	CODE	HRSD	DSM-IV	DURATION
29	<p>[REQ] IN THE PAST WEEK, HAVE YOU BEEN FEELING PHYSICALLY TENSE OR NERVOUS? [IF YES]: HOW {TENSE, NERVOUS} HAVE YOU BEEN?</p> <p>[OPT] DO YOU KNOW WHAT'S BEEN MAKING YOU FEEL THIS WAY?</p> <p>[OPT] WHEN YOU'RE FEELING {TENSE, NERVOUS}, DO YOU GET ANY OTHER SYMPTOMS LIKE DRY MOUTH, INDIGESTION, HEART PALPITATIONS, HYPERVENTILATION, SWEATING, FREQ. URINATION, ETC.?</p>				
	<p>[REQ] [BASED ON THIS ITEM AND ON YOUR OWN OBSERVATIONS, RATE SEVERITY OF SOMATIC ANXIETY THIS WEEK.]</p> <p>0---- ABSENT</p> <p>1---- MILD (ONLY APPARENT IN PT.'s VERBAL ANSWERS TO THIS ITEM.)</p> <p>2---- MODERATE (PT. REPORTS BOTHERSOME SYMPTOMS; MAY LOOK TENSE OR NERVOUS)</p> <p>3---- SEVERE (PT. REPORTS SEVERE SYMPTOMS; LOOKS VERY TENSE OR NERVOUS)</p> <p>4---- INCAPACITATING (PT. IS DEBILITATED BY NERVOUSNESS)</p>		HRSD		
30	<p>[REQ] IN THE LAST WEEK, HOW MUCH HAVE YOUR THOUGHTS BEEN FOCUSED ON YOUR PHYSICAL HEALTH OR HOW YOUR BODY IS WORKING?</p> <p>[OPT] HAVE YOU BEEN WORRYING A LOT ABOUT {BEING, BECOMING} ILL?</p> <p>[OPT] HAVE YOU BEEN COMPLAINING A LOT ABOUT YOUR HEALTH PROBLEMS OR ABOUT HOW YOU FEEL PHYSICALLY?</p> <p>[OPT] HAVE YOU FOUND YOURSELF ASKING FOR HELP WITH THINGS YOU COULD REALLY DO FOR YOURSELF? [IF YES]: LIKE WHAT, FOR EXAMPLE? HOW OFTEN HAS THAT HAPPENED?</p>				
	<p>[REQ] [RATE THE CURRENT SEVERITY OF HYPOCHONDRIACAL CONCERNS & BEHAVIOR. FOR PATIENTS WHO ARE CLEARLY MEDICALLY ILL, A RATING OF 1 OR 2 IS NOT EXCEPTIONAL; A 3 OR 4 WOULD INDICATE HYPOCHONDRIACAL CONCERNS OR BEHAVIORS THAT ARE EXCESSIVE EVEN FOR SOMEONE WHO IS MEDICALLY ILL.]</p> <p>0---- PT. IS NOT WORRIED ABOUT HEALTH</p> <p>1---- PT. IS SOMEWHAT WORRIED OR CONCERNED ABOUT HEALTH</p> <p>2---- PT. IS PREOCCUPIED WITH WORRIES OR CONCERNS ABOUT HEALTH, ILLNESS, OR MEDICAL CARE</p>		HRSD		

CURRENT DEPRESSION SYMPTOMS					
#	COGNITIVE AND SOMATIC FEATURES	CODE	HRSD	DSM-IV	DURATION
31	[REQ] HOW HAS YOUR INTEREST IN SEX BEEN THIS WEEK?				
	[OPT] I'M NOT ASKING ABOUT YOUR ACTUAL SEXUAL ACTIVITY, BUT ABOUT YOUR INTEREST IN SEX -- HOW MUCH YOU THINK ABOUT IT. HAVE YOU HAD LESS INTEREST IN SEX LATELY THAN YOU USUALLY DO?				
	[OPT] [[IF NO PARTNER AT PRESENT, ADD, IF APPROPRIATE]: DO YOU THINK YOU'D BE INTERESTED IN SEX IF YOU MET SOMEONE SPECIAL?				
	[OPT] [[IF FRIGHTENED ABOUT SEX DUE TO PHYSICAL HEALTH]: IF YOU WERE SURE THAT IT WAS SAFE FOR YOU TO HAVE SEX AGAIN, HOW MUCH INTEREST DO YOU THINK WOULD YOU HAVE?				
	[REQ] [RATE SEVERITY OF LOSS OF INTEREST IN SEX.] 0---- NO REAL LOSS OF INTEREST IN SEX COMPARED TO USUAL LEVEL 1---- MILD LOSS OF INTEREST IN SEX 2---- SEVERE LOSS OF INTEREST IN SEX		HRSD		

CURRENT DEPRESSION SYMPTOMS						
#	OBSERVATIONS DURING INTERVIEW	CODE	HRSD	DSM-IV	DURATION	
32	<p>[REQ] [OBSERVE PATIENT'S PSYCHOMOTOR BEHAVIOR.]</p> <p>PSYCHOMOTOR RETARDATION IS PRESENT IF PT. TAKES A LONG TIME TO RESPOND TO QUESTIONS, TALKS SLOWLY WITH NUMEROUS PAUSES OR HESITATIONS, MOVES AS IF IN SLOW MOTION (MORE SLOWLY THAN PHYSICAL CONDITION WARRANTS), ETC.</p> <p>PSYCHOMOTOR AGITATION IS PRESENT IF PT. IS RESTLESS, OVERACTIVE, EDGY, FIDGETY, UNABLE TO SIT STILL.]</p> <p>[REQ] [IF TELEPHONE INTERVIEW] DO YOU FEEL SLUGGISH? DOES IT SEEM LIKE YOU'RE TALKING & MOVING IN SLOW MOTION? LIKE YOUR THOUGHTS ARE VERY SLOW IN COMING TO YOU?</p> <p>ARE YOU FEELING RESTLESS OR HAVING TROUBLE SITTING STILL? FIDGETING?</p>					
33	<p>[REQ] [RATE CURRENT PSYCHOMOTOR RETARDATION]</p> <p>0---- NORMAL SPEECH, THOUGHT, SPEED OF BEHAVIOR, ETC. 1---- SLIGHT RETARDATION AT INTERVIEW 2---- OBVIOUS RETARDATION AT INTERVIEW 3---- RETARDATION SO SEVERE THAT PT IS DIFFICULT TO INTERVIEW 4---- PT. IS STUPOROUS, UNRESPONSIVE TO MOST QUESTIONS</p>		HRSD			
34	<p>[REQ] [RATE CURRENT PSYCHOMOTOR AGITATION]</p> <p>0---- NOT AGITATED 1---- PT. IS EDGY OR MILDLY RESTLESS 2---- PT. IS FIDGETY OR UNCOMFORTABLY RESTLESS 3---- PT. IS OVERACTIVE, UNABLE TO SIT STILL 4---- PT. IS STRIKINGLY AGITATED, E.G., RELENTLESSLY PACING, WRINGING HANDS, BITING NAILS OR LIPS, PULLING HAIR, ETC.</p>		HRSD			
35	<p>[REQ] [RATE PT.'S CURRENT PSYCHOMOTOR BEHAVIOR.]</p> <p>[IF AGITATION OR RETARDATION IS PRESENT, TRY (WITHIN THE LIMITS OF FEASIBILITY), TO USE THE BEST AVAILABLE SOURCES OF INFORMATION (INCLUDING PATIENT, CAREGIVERS, ETC.) TO ASSESS THE FREQUENCY AND DURATION OF THIS FEATURE. IF YOU OBSERVE PSYCHOMOTOR SIGNS BUT ARE UNABLE TO ESTIMATE THE FREQUENCY OR DURATION, ENTER A "1" IN THE DSM-IV COLUMN AND A "U" IN THE DURATION COLUMN.]</p> <p>0---- NO SIGNIFICANT PSYCHOMOTOR SIGNS OBSERVED (Duration=N) 1---- PSYCHOMOTOR RETARDATION OR AGITATION OBSERVED, BUT IT IS MILD AND/OR HAS BEEN PRESENT ONLY SOME DAYS (Duration=weeks) 2---- PSYCHOMOTOR RETARDATION OR AGITATION OBSERVED, AND IT HAS BEEN PRESENT ON MOST OF THE DAYS PRECEDING THE INTERVIEW (Duration=weeks)</p> <p>M--- MEDICAL Sx (Duration=weeks) R--- REFUSED (Duration=R) U--- UNABLE TO ASSESS (Duration=U)</p>			DSM-IV MAJOR: 2 MINOR: 2		

CURRENT DEPRESSION SYMPTOMS					
#	OBSERVATIONS DURING INTERVIEW	CODE	HRSD	DSM-IV	DURATION
36	<p>[REQ] [RATE THE PATIENT'S LEVEL OF INSIGHT (OR LACK OF INSIGHT) INTO HIS/HER DEPRESSION. NOTE THAT THERE ARE TWO DIFFERENT WAYS TO SCORE A ZERO ON THIS ITEM.]</p> <p>0---- PT. IS NOT DEPRESSED (IN THE INTERVIEWER'S JUDGMENT)</p> <p>0---- PT. IS DEPRESSED (IN THE INTERVIEWER'S JUDGMENT), AND IS AWARE OF (AND <u>ACKNOWLEDGES</u>) BEING DEPRESSED</p> <p>1---- PT. IS DEPRESSED (IN THE INTERVIEWER'S JUDGMENT), AND ALTHOUGH THE PT. ADMITS TO HAVING SOME DEPRESSIVE SYMPTOMS, S/HE <u>DENIES</u> BEING DEPRESSED OR BLAMES THE SYMPTOMS ON UNLIKELY CAUSES</p> <p>2---- PT. IS DEPRESSED (IN THE INTERVIEWER'S JUDGMENT), AND IS SO SEVERELY DEPRESSED THAT S/HE BELIEVES HIS/HER CURRENT STATE IS SOMETHING OTHER THAN (AND PERHAPS MUCH WORSE THAN) DEPRESSION (E.G., PT. BELIEVES S/HE IS DOOMED, CURSED, OR NEAR DEATH.)</p>		HRSD		
37	<p>[DSM-IV DISTRESS OR FUNCTIONAL IMPAIRMENT CRITERION]</p> <p>[REQ] [IF YOU BELIEVE THAT THE PATIENT IS CURRENTLY DEPRESSED, DOES THE DEPRESSION APPEAR TO BE CAUSING THE PATIENT ANY EMOTIONAL DISTRESS OR IS IT HAVING ANY ADVERSE EFFECTS ON THE PATIENT'S DAY-TO-DAY SOCIAL OR OCCUPATIONAL FUNCTIONING, ABILITY TO CARE FOR SELF, ABILITY TO COPE WITH PROBLEMS, ETC.?)</p> <p>0--- NO 1--- YES [DESCRIBE] N--- NOT APPLICABLE (PT. IS NOT DEPRESSED) U--- UNABLE TO ASSESS</p>	CODE			
38	<p>[REQ] [NOTE WHETHER DURING THE INTERVIEW, YOU HAVE OBSERVED SIGNS OF ANY MAJOR NEUROPSYCHIATRIC PROBLEMS.]</p> <p>[SCREENING INTERVIEWS: NOTE ANY NEUROPSYCHIATRIC PROBLEMS THAT MIGHT -- OR DEFINITELY WILL -- DISQUALIFY THE PATIENT FROM PARTICIPATION. CHECK WITH THE DESIGNATED CLINICIAN(S) AT YOUR SITE IF YOU ARE UNSURE AS TO WHETHER THESE PROBLEMS ARE LIKELY TO BE SO SEVERE OR PERSISTENT THAT THE PATIENT WILL HAVE TO BE EXCLUDED.</p> <p>NOTE: PATIENTS WITH A HISTORY OF STROKE, BRAIN INJURY, COMA, OR OTHER CNS INSULTS MAY HAVE SUBTLE COGNITIVE DEFICITS. CHECK WITH A DESIGNATED CLINICIAN WHEN RECRUITING PATIENTS WHO MAY HAVE BRAIN DAMAGE.</p> <p>EXAMPLES OF EXCLUSIONARY NEUROPSYCHIATRIC PROBLEMS]:</p> <p>PARANOIA HYPOMANIA OR MANIA DEMENTIA DELUSIONS BIZARRE BEHAVIOR CONFUSION</p>				

PSYCHIATRIC HISTORY [ADMINISTER THIS SECTION AT SCREENING / BASELINE ASSESSMENT ONLY]			
#	ITEM	CODE	
39	<p>[REQ] HAVE YOU EVER BEEN DEPRESSED BEFORE {OTHER THAN THIS TIME}?</p> <p>0--- NO 1--- YES R--- REFUSED U--- UNABLE TO ASSESS</p>		
40	<p>[REQ] [IF YES TO ITEM #39: PROBE TO ESTIMATE PROBABLE NUMBER OF PRIOR MAJOR DEPRESSIVE EPISODES. FOR EACH REPORTED PERIOD OF DEPRESSION, BRIEFLY ASSESS WHETHER IT LASTED AT LEAST TWO WEEKS AND WHETHER IT WAS PROBABLY A MAJOR DEPRESSIVE EPISODE. COUNT IT AS A PROBABLE MAJOR DEPRESSIVE EPISODE IF THE PT. RECALLS NOT ONLY FEELING DEPRESSED BUT ALSO THAT (1) THE DEPRESSION WAS BAD ENOUGH TO AFFECT FUNCTIONING IN SOME WAY (E.G., MAKING IT HARDER TO HANDLE WORK OR INTERPERSONAL RELATIONSHIPS), AND/OR (2) THAT SOME OTHER DEPRESSIVE SYMPTOMS WERE PROBABLY PRESENT AT THE SAME TIME AS WELL, SUCH AS:</p> <p>ANHEDONIA SLEEP DISTURBANCE FEELING WORTHLESS OR GUILTY APPETITE CHANGE AGITATION OR RETARDATION POOR CONCENTRATION OR INDECISION WEIGHT CHANGE FATIGUE OR LOSS OF ENERGY SUICIDAL IDEATION</p> <p>[REQ] [RECORD THE PROBABLE NUMBER OF PRIOR MAJOR DEPRESSIVE EPISODES.]</p> <p>0--- NONE #--- NUMBER OF PROBABLE MAJOR DEPRESSIVE EPISODES R--- REFUSED U--- UNABLE TO ASSESS</p>		
41	<p>[REQ] [IF ANY PRIOR EPISODES]: HOW OLD WERE YOU {THE FIRST TIME}?</p> <p>#--- AGE AT ONSET OF FIRST (PRIOR) EPISODE OF MAJOR DEPRESSION N--- NOT APPLICABLE (NO PRIOR EPISODES) R--- REFUSED U--- UNABLE TO ASSESS</p>		
42	<p>[REQ] [IF MORE THAN ONE PRIOR EPISODE: HOW OLD WERE YOU THE LAST TIME {BEFORE THIS}?</p> <p>#--- AGE AT ONSET OF LAST (PRIOR) EPISODE OF MAJOR DEPRESSION N--- NOT APPLICABLE (<2 PRIOR EPISODES) R--- REFUSED U--- UNABLE TO ASSESS</p>		
43	<p>[REQ] [IF ANY PRIOR EPISODES]: WERE YOU EVER TREATED FOR DEPRESSION DURING ANY OF THESE TIMES? [IF YES, DETERMINE WHICH TREATMENT MODALITIES THE PT. EVER RECEIVED FOR PAST DEPRESSIVE EPISODES. WRITE "1" IN THE CORRESPONDING BOXES TO THE RIGHT (OR CODE ZERO, N, R, OR U).]</p> <p>-----</p> <p>A. PSYCHOTHERAPY or COUNSELING</p> <p>B. ANTIDEPRESSANT MEDICATION</p> <p>C. ECT (ELECTROCONVULSIVE OR SHOCK THERAPY)</p> <p>D. PSYCHIATRIC HOSPITALIZATION</p>		
44	<p>[REQ] ARE YOU CURRENTLY BEING TREATED FOR DEPRESSION {OR TAKING AN ANTIDEPRESSANT}? [IF YES, WRITE "1" IN THE CORRESPONDING BOXES TO THE RIGHT (OR CODE ZERO, N, R, OR U).]</p> <p>-----</p> <p>A. PSYCHOTHERAPY or COUNSELING</p> <p>-----</p> <p>-----</p> <p>-----</p>		

PSYCHIATRIC HISTORY [ADMINISTER THIS SECTION AT SCREENING / BASELINE ASSESSMENT ONLY]		
#	ITEM	CODE
45	<p>[REQ] [IF PT. HAS HAD 2 OR MORE PRIOR DEPRESSIVE EPISODES] HAVE YOU EVER BEEN TOLD BY A PSYCHIATRIST THAT YOU HAVE MANIC DEPRESSION?</p> <p>0---- NO 1---- YES N--- NOT APPLICABLE (<2 PRIOR DEPRESSIVE EPISODES) R--- REFUSED U--- UNABLE TO ASSESS</p>	
46	<p>[REQ] HAS ANYONE IN YOUR IMMEDIATE FAMILY EVER BEEN DEPRESSED FOR TWO WEEKS OR LONGER? [IF YES, PROBE FOR THE NUMBER OF AFFECTED 1st DEGREE BIOLOGICAL RELATIVES (PARENTS, SIBLINGS, CHILDREN). IN THE CODE COLUMN, RECORD THE NUMBER OF THOSE WITH UNIPOLAR DEPRESSION, AND IN THE SPACE BELOW, WRITE A NOTE ABOUT ANY RELATIVE WHO REPORTEDLY HAS/HAD MANIC DEPRESSION (BIPOLAR DISORDER).</p> <p>0---- NONE #---- NUMBER OF AFFECTED 1st DEGREE RELATIVES WITH UNIPOLAR DEPRESSION R--- REFUSED U--- UNABLE TO ASSESS</p>	
47	<p>[REQ] HAVE YOU EVER BEEN TREATED FOR ANY OTHER PSYCHIATRIC DISORDER OR EMOTIONAL PROBLEM?</p> <p>[REQ] HAVE YOU HAD ANY PROBLEMS WITH DRUGS OR ALCOHOL? [IF YES]: WHAT PROBLEMS? WHEN? ARE YOU STILL HAVING {THESE PROBLEMS}? ARE YOU BEING TREATED FOR THEM?</p> <p>[OPT] [IF YOU BELIEVE THAT THE PATIENT MAY HAVE A CURRENT ALCOHOL PROBLEM BUT ARE NOT SURE (OR ARE NOT SURE HOW SERIOUS IT IS), ADMINISTER THE CAGE ALCOHOLISM SCREEN, IF YOU HAVE NOT ALREADY DONE SO.</p>	
	<p>[REQ] [RATE PSYCHIATRIC HISTORY OTHER THAN UNIPOLAR DEPRESSION. IF THE PATIENT HAS MORE THAN ONE PSYCHIATRIC PROBLEM, CHOOSE THE HIGHEST APPLICABLE RATING.]</p> <p>0---- NO OTHER PSYCHIATRIC PROBLEMS REPORTED</p> <p>1---- PT. REPORTS OTHER PSYCHIATRIC PROBLEMS THAT ARE CLEARLY <u>NOT</u> GROUNDS FOR EXCLUSION FROM THE TRIAL (e.g., ANXIETY, ORDINARY ADJUSTMENT PROBLEMS, ETC.)</p> <p>2---- PT. REPORTS OTHER PSYCHIATRY PROBLEMS THAT <u>MIGHT</u> REQUIRE EXCLUSION (e.g., PAST HISTORY OF DRUG ADDICTION, PREVIOUS TREATMENT FOR PSYCHOSIS, etc.)</p>	

LONGITUDINAL COURSE CHART [ADMINISTER THIS SECTION ONLY AT 6-MONTH FOLLOW-UP]			
#	ITEM	CODE	
	NOTE: EACH TIME THE PATIENT IS ASSESSED (AT SCREENING/BASELINE AND FOLLOW-UP), THE INTERVIEW ONLY GIVES US A "SNAPSHOT" VIEW OF THE PATIENT'S CONDITION AT THE TIME. SINCE DEPRESSIVE EPISODES CAN START, GET WORSE, GET BETTER, OR END ENTIRELY IN BETWEEN INTERVIEWS, WE NEED TO EVALUATE WHAT HAS HAPPENED TO THE PATIENT IN THE INTERVAL BETWEEN BASELINE AND FOLLOW-UP. THIS INFORMATION SERVES TWO PURPOSES. FIRST, IT "FILLS IN THE GAPS" BETWEEN THE INTERVIEWS. SECOND, YOU MAY NEED THIS INFORMATION TO MAKE THE CURRENT DIAGNOSIS.		
48	<p>[REQ] [OPEN THE ENVELOPE CONTAINING A COPY OF THE COMPLETED SCREENING / BASELINE DIAGNOSTIC SUMMARY FORM FOR THIS PATIENT. WHAT WAS THE PT.'S DIAGNOSIS?</p> <p>0---- NONDEPRESSED 1---- DYSTHYMIA 2---- MINOR DEPRESSION 3---- MAJOR DEPRESSION 4---- DOUBLE DEPRESSION (BOTH MAJOR DEPRESSION AND DYSTHYMIA)</p>		
49	<p>[REQ] [PROBE AS NEEDED TO DETERMINE WHETHER AND WHEN THERE WERE ANY EXACERBATIONS (i.e., WHEN MINOR DEPRESSION GETS WORSE & TURNS INTO MAJOR DEPRESSION, OR WHEN MILD-MODERATE MAJOR DEPRESSION GETS WORSE & TURNS INTO MORE SEVERE DEPRESSION), REMISSIONS, RELAPSES, RECURRENCES, NEW DEPRESSIVE EPISODES, OR TREATMENT OUTSIDE OF THE STUDY BETWEEN THE SCREENING/BASELINE INTERVIEW AND THIS ONE. THE INTERVAL STARTS AT BASELINE AND ENDS WITH THE ONSET OF THE PATIENT'S CURRENT CONDITION AS ASSESSED ON THIS FOLLOW-UP INTERVIEW. DOCUMENT YOUR FINDINGS BELOW. IF POSSIBLE, LIST APPROXIMATE DATES AND/OR DURATIONS OF EACH PHASE IN THE INTERIM COURSE OF THE DEPRESSIVE DISORDER.]</p>		
	EVENT OR PHASE IN THE COURSE OF DEPRESSION SINCE LAST INTERVIEW	APPROX START DATE	APPROX END DATE OR DURATION
50	<p>[REQ] [DIAGNOSTIC IMPRESSION: Did the patient meet the criteria for major depression, minor depression, or dysthymia for at least 2 continuous weeks at any time between baseline and now? Rate the most severe 2-week period. CODE THE DURATION OF THE MOST SEVERE PERIOD OF DEPRESSION.]</p> <p>0---- NONDEPRESSED (Duration = N)</p>	CODE	DURATION (WEEKS)

Appendix C: Narrative Summary of ENRICHD Pilot Study

Narrative Summary for Clinical Exemption Review Committee (CERC) ENHANCING RECOVERY IN CORONARY HEART DISEASE (ENRICHD) PATIENTS PILOT STUDY

Revised in Response to Clinical Exemption Committee Meeting Comments
6/4/96

1. Precis of Study

Recent data show that psychosocial factors, particularly the presence of low perceived social support and depression, increase the likelihood of morbidity and mortality in CHD patients. These findings emphasize the importance of testing whether interventions which provide social support and alleviate depression will extend life. Methodological limitations of published studies prohibit drawing firm conclusions regarding the efficacy of intervening on depression and low perceived social support in MI patients.

A clinical trial designed to address this question has been funded by the NHLBI and expects to begin recruitment in October, 1996. The trial, entitled "Enhancing Recovery in Coronary Heart Disease (ENRICHD) Patients," is a randomized, controlled clinical trial which will recruit 3,000 MI patients to determine whether psychosocial intervention will reduce mortality and reinfarction. An application for clinical exemption for the ENRICHD Patients Study is currently being developed and will be submitted separately.

The study covered by the current application is a pilot study designed to provide information to guide screening, recruitment and assessment procedures to be used in the main ENRICHD trial. This study, the ENRICHD Patients Pilot Study, will:

- (1) determine the yield of depressed and socially isolated patients based on the screening and recruitment procedures to be used in the main ENRICHD trial;
- (2) refine staff skills and recruitment procedures to minimize patient burden and facilitate recruitment of patients in the main trial;
- (3) allow refinement of study instruments to ensure they are psychometrically valid for the specific population of MI patients to be recruited into the main trial, and to reduce redundancy among instruments; and
- (4) elicit feedback from patients regarding the psychosocial assessment instruments to be used to allow streamlining of these instruments and to minimize patient burden in the main trial.

Overview of the ENRICHD Patients Pilot Study. The proposed preliminary study covered by this application to the CERC will precede the main ENRICHD clinical trial, but will provide

extremely important information for conducting the trial. It is proposed that a total of approximately 250 participants be enrolled with at least 10 participants being enrolled in each of two separate hospitals in each of the eight clinical units involved in ENRICHD (i.e., in at least 16 hospitals). These 16 hospitals will be selected by clinical units to have patient populations representative of the ethnic minorities found in the hospitals from which they will recruit for the main clinical trial for ENRICHD; thus, the patients selected for this preliminary study will represent broad geographic and ethnic groups and should be similar in characteristics to those patients who are approached for recruitment in the main clinical trial. These ethnic minority groups include African Americans, Hispanic Americans, Asian Americans and Native Americans. The recruitment goal is to enroll 50% of the study's participants who are an ethnic minority and 50% who are women.

The screening portion of this preliminary study will provide information key to determining appropriate instruments and methods for use in screening and determining eligibility for the clinical trial, as well as estimating the proportions of MI patients who will be eligible for recruitment in the main ENRICHD study. This screening portion is not meant to provide comparative information on depressed or socially isolated MI patients relative to other patient populations, but rather to provide information only on patients similar to those to be recruited into the main ENRICHD trial, that is, patients hospitalized with acute MI who meet other ENRICHD medical eligibility criteria, in order to refine screening and recruitment procedures to be used in the main study. In addition to the screening portion of this preliminary study, in a subset of the approximately 250 participants (10 per clinical site or a total of 80), we propose to administer the anticipated baseline psychosocial measures to assist us in determining how much time is needed, and whether this battery of measures is acceptable to potential patients.

Specific aims. The overall goal of this pilot study is not to conduct comparisons between different patient groups; rather, the overall goals are to assess what proportion of the population of MI patients to be recruited into the main ENRICHD trial are depressed and/or socially isolated in order to plan recruitment, and to refine staff skills and study procedures. In detail, the specific aims of the pilot study are:

- (1) To determine the proportion of patients who meet eligibility criteria for low perceived social support based on the distribution of scores on the ENRICHD social support instrument (ESSI), which has been developed for use in cardiac patients, and to compare the ESSI with other social support instruments. A two week re-testing will be given to determine if change has occurred from the initial evaluation.
- (2) To determine the percentage of patients who meet criteria for major and minor depression according to clinical criteria summarized in the Diagnostic and Statistical Manual for Mental Disorders, 4th edition (DSM-IV) while in hospital, and determine changes in scores on these depression instruments at two-week follow-up.
- (3) To determine the proportion of MI patients overall and by demographic group who are classified as depressed, socially isolated, or both while in hospital and then at a two-week follow-up.

(4) To determine the numbers of eligible patients who express a willingness to enter into the study, to identify barriers to recruitment, and to determine what additional preparation is needed to meet recruitment goals for the main trial.

(5) To determine the numbers of eligible patients who will need to have the psychosocial instruments read to them in order to plan staffing requirements for the main study, to determine the length of the psychosocial assessment battery, and to elicit feedback from patients regarding any difficulties they may have with the assessment instruments to refine the battery to be given in the main trial.

(6) To establish proficiency of the staff in screening, recruiting and administering psychosocial assessments to medically eligible MI patients similar to those to be recruited into the main ENRICHHD trial.

Design criteria for selecting population. For the preliminary study, we propose to recruit a total of 250 patients who meet medical eligibility criteria for ENRICHHD from at least two, culturally-diverse hospitals participating at each of eight clinical centers involved in ENRICHHD. At least 10 patients will be enrolled from each hospital. The inclusion criteria for those patients who are asked to complete the screening portion of this study will be similar to those that will be employed in the main ENRICHHD clinical trial and include: hospitalized for MI, defined by having characteristic enzyme increases twice the upper normal limit established within the institution from which the patient is being recruited and at least one of the following a) symptoms compatible with acute MI, and/or b) characteristic evolutionary electrocardiographic ST-T changes or new Q waves. The exclusion criteria for the preliminary study include: (1) history of post-procedure MI (e.g., subsequent to CABG surgery or PTCA); (2) presence of conditions likely to terminate fatally within one year; (3) presence of conditions likely to limit the physical capacity to participate in a study such as ENRICHHD; (4) participation in a current research protocol likely to conflict with participation in ENRICHHD; and (5) unwillingness to provide informed consent.

The medical exclusion criteria will be determined from chart review and from patients' physicians so as to avoid upsetting patients by discussing these issues with them or burdening patients who may not be eligible to participate.

A subsample of those patients (10 patients per clinical unit for a total of 80 patients overall) who are asked to complete the screening measures will also be asked to complete the anticipated baseline assessment instruments. This sample will be selected so as to represent the diversity of patients to be recruited into the main ENRICHHD trial (e.g., both genders, all minority groups represented at the eight ENRICHHD clinical sites).

Types of information to be collected. Data to be collected from those participants who are asked to complete the screening measures are of three varieties: hospital chart data, interview data, and self-report questionnaires. Interviewers will be selected based on education at least at the bachelor's level as well as experience in conducting interviews and administering psychosocial instruments to patient populations. They will also be carefully trained in the administration of all measures and carefully trained to note signs of fatigue or other indications that the patient is in

distress. The interview will be discontinued or postponed should it become onerous to the patient.

Data to characterize the medical eligibility criteria will be obtained from medical chart review or from patients' physicians prior to approaching the patients for the initial interview during hospitalization. Interview with patients and self-report questionnaires will be used to collect all other data. Interview and self-report questionnaire data obtained during hospitalization include: informed consent; degree of low perceived social support/social support as determined by the ESSI; related measures of low perceived social support/support as determined from administration of the ISEL scale, the Blumenthal Perceived Social Support Scale, EPSE items; likelihood of depression as determined by the Beck Depression Inventory (BDI); presence of depression according to DSM-IV criteria for major or minor depression and degree of depression as determined from administration of the DISH; willingness to participate in a treatment-outcome study similar to that planned for ENRICHHD, barriers to participation; and self-report of responses to assessment. Generally, these data will be collected at more than one time during hospitalization to minimize patient burden.

Interview data collected by phone at a two-week follow-up after initial interview will include: degree of low perceived social support/social support as determined by the ESSI; likelihood of depression as determined by the Beck Depression Inventory; presence of depression according to DSM-IV criteria for major or minor depression and degree of depression as determined from administration of the DISH; willingness to participate and barriers to participation; and self-report of responses to assessment.

Data to be collected from those participants who are asked to complete the baseline instruments will be collected from either interview or via self-administered questionnaire (depending on participants' preferences) while participants are still hospitalized, but at a separate time from that when they are asked to complete the screening portion of this preliminary study. The baseline instruments will include: a subset of items from the MOS SF-36 Health Status questionnaire; the Ladder of Life; Life Satisfaction scale; the Perceived Stress Scale; Self-Efficacy Scale; and self-report of responses to assessment.

The sources of information and the time required for data collection are summarized below in the following tables:

Table 1: DATA COLLECTED WHILE AN INPATIENT (SCREENING)

SOURCE OF INFORMATION	TIME FOR DATACOLLECTION	PARTICIPANT TIME REQUIRED
Medical Screening Data: Screening Log	12 min.	0 min.
Medical Eligibility	30 min.	0 min.
Medical History	20 min.	5 min.
Baseline Examination	20 min.	10 min.
Informed Consent	10 min	10 min.
ESSI	3 min.	3 min.
BDI	5 min.	5 min.
ISEL Scale	15 min.	15 min.
Blumenthal Perceived Social Support Scale	6 min.	6 min.
EPESE Items	15 min.	15 min.
McLeod Scale	5 min.	5 min.
DISH	40 min.	40 min.
Willingness to Participate/ Barriers to Participation	5 min.	5 min.
Short Blessed (optional at staff discretion)	3 min.	3 min.
Interview Evaluation and Effort (IEE)	8 min.	5 min.
TIME SUBTOTALS	197 minutes	127 minutes

Table 2: INTERVIEW DATA COLLECTED AT 2-WEEK FOLLOW-UP- SCREENING

SOURCE OF INFORMATION	TIME FOR DATA COLLECTION	PARTICIPANT TIME REQUIRED
ESSI	3 min.	3 min.
BDI	5 min.	5 min.
DISH	40 min.	40 min.
Willingness to Participate/ Barriers to Participation	5 min.	5 min.
Interview Evaluation and Effort (IEE)	8 min.	5 min.
TIME SUBTOTALS	61 minutes	58 minutes

Table 3: INTERVIEW/SELF-REPORT BASELINE DATA COLLECTED WHILE AN INPATIENT FOR SUBSET OF PARTICIPANTS

SOURCE OF INFORMATION	TIME FOR DATA COLLECTION	PARTICIPANT TIME REQUIRED
MOS SF-36 items	5 min.	5 min.
Ladder of Life	1 min.	1 min.
Life Satisfaction Scale	2 min.	2 min.
Perceived Stress Scale	5 min.	5 min.
Self-Efficacy Scale	5 min.	5 min.
Interview Evaluation and Effort (IEE)	8 min.	5 min.
TIME SUBTOTALS	26 minutes	23 minutes

Methods of data collection. Data will be collected while patients are still hospitalized, approximately one week after their MI, from chart record, interview, and self-administered questionnaire for participants who participate in the screening portion of this preliminary study, as well as for the subset of participants who are asked to participate in the baseline data collection portion of the preliminary study. The screening data and baseline data will be collected at separate times for those who are asked to participate in both portions of the preliminary study. At the two-week follow-up for all participants, data will be collected from phone interview.

Consultants. Additionally, we are proposing to use a group of consultants who will provide advice to the ENRICHD investigators during the pilot period. The purpose of convening these consultant groups during the pilot study is to determine how cultural and subcultural factors influence willingness to participate in the main trial protocol, and to identify psychosocial needs following the heart attack. This information will be used to modify the main trial protocol, as necessary, to better meet the needs of MI patients in various population subgroups who have been underrepresented in past trials and for whom little information is available concerning methods to promote participation (e.g., minority groups).

Similar types of consultant groups have been used in other NIH trials (e.g., the REACT trial, the Menopause Study) and have been found to provide valuable information concerning barriers to participation and acceptability of various study procedures to traditionally underrepresented demographic groups (e.g., minorities, women), leading to refinement of recruitment and other study procedures to address issues of importance to these groups (J. Raczynski and L. Powell, personal communication). To ensure that these consultant groups are effective in eliciting useful feedback from participants, the standardized procedures and topic areas which have been successfully used for consultant groups in other NIH trials will be closely followed. These procedures are outlined briefly below.

Consultant group procedures. A sufficient number of minority participants in the pilot study or identified from hospital patients who have had a recent MI will be invited to attend a consultant group to constitute 2-3 groups per center of up to 10 patients per group. The groups will be formed to be as homogeneous as possible with regard to gender, race and ethnicity. The emphasis will be on understanding how subcultural influences--not psychosocial status--affect participation and psychosocial needs.

The groups will be led by individuals with special training and expertise in eliciting feedback from such consultant groups. Group sessions will consist of a one-time session of approximately two hours. Incentives for participation will include a monetary reimbursement and refreshments. Discussion will be encouraged in the following categories:

1. Barriers to participation in the main trial protocol: Included will be questions concerning financial constraints, time constraints and other structural problems, and questions concerning willingness to undergo individual and group therapy;
2. Needs: These questions will be aimed at better understanding the concerns and needs of individuals who have had a recent MI, including satisfaction with their medical treatment and other resources that are available;
3. Emotional experience: These questions will be aimed at determining the range of emotions that have been triggered by the MI, and to better understand the cause and consequences of feelings of depression and low perceived social support.

Consultant discussions will be recorded, evaluated and analyzed. The resulting report will be provided to the clinical sites and modifications in the main trial protocol and manual of operations will be proposed to minimize cultural barriers to participation and to maximize representation of all population subgroups.

2. Subject Recruitment and Care

Manner in which the study will be presented to potential participants. Patients recovering from a heart attack often go through a period of feeling down or even somewhat depressed. Patients' reactions to a heart attack has been shown to affect how well patients do after having a heart attack. Similarly, how close patients feel to others after having a heart attack seems to affect how well they do recover. This study is designed to provide preliminary information concerning depression and social support after a heart attack. This information will be used to plan a study to determine the benefit of treating people who are depressed or who feel unsupported after having a heart attack.

Participants will be approached as follows:

If you choose to participate in this study, we will interview you concerning symptoms that may be associated with feeling low or depressed and feeling unsupported as well as your interest in participating in a project that is designed to determine the effects of treating people who feel low, depressed, and/or have few sources of social support. About two weeks later, we will also call you and interview you over the phone, asking you about how close you then feel to others and how low or depressed you feel.

Your doctor will be informed of the results of these interviews. If it is determined that you are feeling sufficiently low that you might benefit from treatment, this information will be provided to your doctor.

Participants asked to complete the baseline instruments will be approached in the following manner:

We would also like to ask your cooperation in answering some additional questions for us. This information will also be used to help us design a project to help people who feel low and unsupported by others after they have had a heart attack. If you choose to participate in completing this information, I will come back to talk with you at a time that is convenient. I'll be able to either leave questionnaires for you to complete or I can ask you the questions, whatever is more acceptable to you.

Relation to optimal treatment. This preliminary study does not include a treatment phase for participants. However, it will facilitate identification of depressed and/or socially isolated post-MI patients who would potentially benefit from treatment for their psychosocial condition. Depression and low perceived social support have been demonstrated to be strong predictors of greater morbidity and mortality and are not currently evaluated in any systematic manner in most clinical settings. If depression and/or low perceived social support is determined for a participant, then this information will be provided to participants' physicians. Additionally, the physician will be informed of the patient's increased risk for increased morbidity and mortality, and treatment referral information will be provided. Thus, this study will result in improved identification of patients who might benefit from psychosocial treatment and potentially increased referral for detected depression and/or low perceived social support.

3. Relevant Documents

The Consent Form and proposed measures are attached.

4. Confidentiality/Human Subjects

(a) The Privacy Act. All data collection forms will only be identified with a participant number. Names associated with participants' numbers will be kept separately under secure conditions. All data will be analyzed and reported only in groups and not by individuals.

(b) Basic HHS Policy for Protection of Human Research Subjects (45 CFR 46). IRB review is currently underway in all clinical centers and all participating hospitals.

Appendix D: NIH Definitions of Minority Group Membership

MINORITY GROUPS

AMERICAN INDIAN OR ALASKAN NATIVE:

A person having origins in any of the original peoples of North America, and who maintains cultural identification through tribal affiliation or community recognition.

- American Indian
- Alaska Eskimo
- Aleut
- Native Hawaiian
- Other

ASIAN OR PACIFIC ISLANDER:

A person having origins in any of the original peoples of the Far East, Southeast Asia, the Indian subcontinent, or the Pacific Islands. This area includes, for example, China, India, Japan, Korea, the Philippine Islands and Samoa.

- Chinese
- Japanese
- Asian Indian
- Korean
- Vietnamese
- Other

BLACK, NOT OF HISPANIC ORIGIN:

A person having origins in any of the black racial groups of Africa.

- Native-born Black American
- Caribbean Black
- African
- Other

HISPANIC:

A person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin, regardless of race.

- Mexican
- Puerto Rican
- Cuban
- Other

Appendix E: Justification for Selection of Sertraline as a Primary Antidepressant for ENRICHHD

ENRICHHD participants will be relatively older with cardiac disease requiring concurrent medication treatment. They will potentially be prone to hypotension, conduction delays, anticholinergic effects, and drug-drug interactions if prescribed anti-depressants. Accordingly, the preferred antidepressant should be short-acting and judged to be the least problematic in producing the adverse effects noted above.

Tricyclic antidepressants delay intracardiac conduction, cause hypertension in therapeutic dose ranges, and are to varying degrees anticholinergic. Their quinidine-like properties produce antiarrhythmic effects but raise the specter of also being proarrhythmic. Therefore, current clinical practice indicates that SSRIs are the preferred antidepressants for mild-to-moderately depressed patients who have medical illness.

Pharmacologic factors considered important in selecting among the SSRI's are duration of action, linearity of pharmacokinetics, age effects of pharmacokinetics, antimuscarinic properties (paroxetine), and effects on hepatic P450 microsomal enzymes. Five SSRIs are presently available. Unlike the tricyclic antidepressants, the SSRIs are generally non-anticholinergic (except paroxetine), tend not to be sedating, and do not delay cardiac conduction or affect blood pressure (except venlafaxine). All cause some GI distress, headaches, and sexual dysfunction. The SSRIs do differ in some properties that are relevant in selecting an agent for patients such as those in ENRICHHD. It is increasingly apparent that these agents have differential effects on the hepatic P-450 isoenzyme system that is important in metabolism of many pharmacologic agents. Of particular concern is the potent effect of several SSRIs on the P-450 3A3/4 isoenzyme pathway that metabolizes several of the longer acting benzodiazepines, terfenadine, several antiarrhythmics, and calcium channel blockers, for example. Based upon the clinical and scientific literature, the following is an overview of the properties considered by the Pharmacological Subcommittee in recommending sertraline as the agent of choice.

Agent	Advantages	Disadvantages
Fluoxetine (Prozac)		Prolonged half-life Non-linear kinetics Age effects on clearance Potent effects on P-450 (3A3/4) hepatic isoenzymes
Sertraline (Zoloft)	Intermediate half-life Linear kinetics No age effects on clearance	Moderate effects on P-450 (2D6) -- less than fluoxetine, paroxetine
Paroxetine (Paxil)	Intermediate half-life	Equal to imipramine in anti-muscarinic effects Non-linear kinetics Age effects on clearances Potent effects on P-450 (2D6)
Venlafaxine (Effexor)	Short-half life (twice-day dosing)	Hypertensive in older patients Prominent nausea
Nefazodone (Serzone)	Short-half-life (twice-day dosing)	Non-linear kinetics Potent effects on P-450 3A3/4 isoenzymes

Appendix F: Medical Endpoint Definitions

1. All cause mortality is defined as death from cardiovascular and non cardiovascular cause confirmed by a death certificate.

(a) Cardiovascular mortality is death due to cardiovascular causes as outlined in the next section: Subclassification for Cardiovascular Death.

2. Nonfatal myocardial infarction is defined as having characteristic enzyme increases twice the upper limit established within the institution from which the patient has been hospitalized and at least one of the following:

(a) symptoms compatible with acute myocardial infarction.

(b) characteristics evolutionary electrocardiographic ST-T wave changes or new Q wave.

Silent myocardial will be defined by the core ECG lab criteria. The ECG criteria for nonfatal MI will be defined by the central ECG lab.

Subclassification for Cardiovascular Death

Sudden Death

Death from cardiac or unknown causes that occur instantaneously or within 60 minutes of the onset of symptoms. The classification of sudden will be made on the basis of time onset of symptoms to death regardless of subsequent pathologic findings. Patients who are resuscitated from cardiac arrest but are pronounced death within 60 minutes from the onset of symptoms will be classified as sudden death. Unobserved death within 60 minutes of symptoms or last contact will be classified as sudden death. Sudden death may occur in the hospital - e.g., and unexpected arrhythmia death.

Post - Resuscitation Death: Patients in whom a cardiac and/or respiratory arrest occurs within 60 minutes of the onset of symptoms but a) are resuscitated and b) do not regain normal vital functions and c) die more than 60 minutes from the onset of symptoms leading to the arrest.

Unobserved Death

Patients last alive more than 60 minutes prior to the discovery of death and the circumstances directly leading to the death are unknown.

Definite Myocardial Infarction: Death which occurs more than 60 minutes from the onset of symptoms occurs during the hospitalization for the MI and is related to a cardiac complication. (e.g., CHF, arrhythmia, shock,) or non-cardiac complications (e.g., pulmonary embolus) of the acute event. MI is documented by clinical, electrocardiographic and enzyme criteria or pathologic findings. If patient has a documented MI then dies “suddenly” while making an otherwise normal recovery the cause of death will be classified “Definite MI.”

Probable Myocardial Infarction

As above but MI is documented by two or three criteria (ECG, enzyme, clinical setting,) or the attending physician states that the patient died from MI but does not provide information.

Possible Myocardial Infarction

Typical clinical setting with chest pain or other findings suggestive of acute MI in the absence of diagnostic enzyme or ECG changes.

Congestive Heart Failure: Death from intractable congestive heart failure not associated with an acute event.

During or Post Cardiac Surgery

Death occurring during or prior to discharge from cardiac surgery. If patient is transferred to another hospital or to a nursing home for continued care as a result of operative or postoperative surgical complications and subsequently dies, the death may be classified as "Cardiac Surgery".

Patients who are taken to surgery as a heroic measure may not be classified as a surgical death according to the opinion of the reviewers.

During Cardiac Catheterization: Death during or following cardiac catheterization when the death is directly attributed to the catheterization.

Other Cardiac

Death in which there is no evidence of a primary etiology which cannot be classified as Definite MI, CHF, Sudden, etc.

Vascular

Death due to stroke, aneurysm rupture, aortic dissection, pulmonary embolus or attributed to the vascular system. (ischemic lower extremity or bowel infarction secondary to vascular disease).

Appendix G: HCFA Quality of Care Process Indicators

1. Confirmation of the diagnosis of acute myocardial infarction.
2. Timing and use of aspirin in the hospital.
3. Prescription of aspirin at discharge.
4. Use of thrombolytics in patients with ST-segment elevation.
5. Timing of thrombolytic administration.
6. Administration of IV nitroglycerin for persistent chest pain.
7. Prescription of beta blockers at discharge.
8. Prescription of ACE inhibitors for patients with low left ventricular ejection fraction (LVEF).
9. Documentation of smoking cessation advice.
10. Administration of low or full dose heparin.
11. Avoidance of calcium channel blockers in patients with low LVEF.
12. Catheterization or transfer of patient for recurrent angina.
13. Performance of exercise stress test in patients not undergoing cardiac catheterization.

Appendix H: ENRICHD Informed Consent Forms

Enhancing Recovery in Coronary Heart Disease (ENRICHD) Patients Study

DRAFT INFORMED CONSENT

After being hospitalized for a heart attack some people are depressed or have feelings of low perceived social support. Symptoms of depression include sadness, tiredness, feeling bad, a loss of interest in usual activities and other symptoms. Low perceived social support is a feeling that you don't have someone you can count on for help doing day-to-day activities such as driving to the doctor or cooking, or just someone to talk with about your feelings.

People who have had a heart attack and who are depressed or have low perceived social support are more likely to have another heart attack than people who are not depressed or who do not have low perceived social support. But doctors do not know whether giving advice (counsel) to a person who has depression or low perceived social support will help them to lessen their chance of another heart attack or of dying from heart disease.

The doctors at this hospital have asked you to take part in a research study that will help them find out the answer to this question. This study is called the Enhancing Recovery in Coronary Heart Disease (ENRICHD) Patients Study.

Before you can decide whether or not you should agree to join this study, you should find out enough about its risks and benefits to make a good judgment. This is called informed consent.

The consent form you are reading describes the research study which the doctor will talk to you about. Once you know what the study is about, you will be asked to sign this form if you want to join. You will have a copy of this form to keep as a record.

PURPOSE OF THE ENRICHD STUDY: We hope to learn whether counseling for a person who is depressed or who has low perceived social support will not only reduce their depression and increase

their social support, but will also lower their risk of a future heart attack or of dying from heart disease. This study will help doctors find the best treatment to use in the future.

DESCRIPTION OF THE STUDY

About 3,000 patients across the country will take part in the ENRICHD study. You were selected to take part in this study because you are being treated in the hospital for a heart attack. If you agree to be in the study, we will look at your hospital records to find out if there are any medical reasons that would not allow you to enter into the study.

We will then ask you questions that will help the doctors decide whether you have depression and/or feelings of low perceived social support, and if so, how much you are having these feelings or symptoms. If you have certain symptoms, such as thoughts of suicide, you would not be eligible to enter the study.

These questions will be asked at least once while you are in the hospital and, in many cases, during an outpatient visit to your doctor or on a telephone call to you within the first three weeks after your heart attack. Once it has been decided that you may take part in the ENRICHD study, you will be chosen by chance, or randomized, to be in one of the two groups. In one group, called a usual care group, you will receive the care you would ordinarily receive from your doctor. In the other group, you will receive usual care and counseling sessions for depression or low perceived social support, or both.

In the usual care group, your primary care doctor will keep taking care of you, and will not withhold any treatment from you. This includes counseling and prescribing and following up on any drugs he or she feels you need. You will also be asked by the ENRICHD study doctors to come to the clinic for follow-up visits, and you will be contacted by telephone, as described in the "FOLLOW-UP" section below.

In the group that receives usual cardiac care and the counseling we are examining in this study, your primary care doctor will also continue to take care of you. You will also be scheduled for

counseling sessions by the ENRICHD study doctors, at no cost to you. These counseling sessions will involve from 16 to 28 individual and/or group sessions with specially trained ENRICHD study doctors or health care personnel. These sessions would start up to three weeks after your heart attack. Four to six individual sessions will first be held between you and your ENRICHD study doctor. Then you will go to the group meetings once a week for about 12 weeks. These group meetings will be with other patients in the ENRICHD study who, like you, have had a heart attack.

FOLLOW-UP

You will be contacted every six months during the ENRICHD study for either a clinic visit or telephone call to answer questions about your health. Each clinic visit will last about an hour. You will be part of the ENRICHD study until _____ (DATE).

If your depression does not improve or if it gets worse, we may talk to your primary care doctor about giving you medication for your depression. We will also talk to your primary care doctor if other symptoms of depression occur, such as thoughts of suicide. If it is thought that you would benefit from medication for depression, an ENRICHD study doctor will work with your primary care doctor to prescribe the best medication for your depression, and will follow you to see how you are doing on these medications. You will be tested for any medical conditions that would affect which medications you should take. If you are in the usual care group and your primary care doctor feels you need counseling or medications for depression, these will not be kept from you. However, they will not be paid for by the ENRICHD study.

RISKS AND DISCOMFORTS

All medical care, including the type given in studies such as this, has some risk of injury, but there are no known risks for the type of counseling involved in the ENRICHHD study. You may feel nervous about sharing your feelings or experiences, but this type of counseling mostly involves problem solving and positive thinking. Patients who have had a heart attack and who were depressed or had low perceived social support have done well with counseling of this type, but the ENRICHHD study does not know or promise that you will receive any benefits from this study.

If any medical conditions or severe depression occur, the ENRICHHD doctors will help you find the correct treatment, but the study will not provide any money for the treatment. You may call Dr. (name of Principal Investigator, address, telephone number) or _____ (alternate) if you have questions at any time or if a problem comes up while you are taking part in the ENRICHHD study.

BENEFITS

The benefits of this study to you include close follow-up of your medical care. Also, by being in this study, you may help doctors find out whether treating people with depression or low perceived social support will lower their risk of another heart attack or death, which might help patients like you in the future. Many patients like to have someone to talk to or to meet other heart patients. If you wish, results of your tests for the ENRICHHD study will be given to your doctor at no cost to you.

ALTERNATIVE TREATMENT

If you choose not to join this study, you may decide to talk to your primary care doctor about the potential benefits of counseling for depression or low perceived social support. Choosing not to join this study will not change or decrease the health care you receive. You may continue with your usual health care whether you join the study or not.

CONFIDENTIALITY

All information on your medical condition and your answers to questions that are asked for the ENRICHHD study will be kept confidential to the extent the law allows. Records about you will be put under a code number. In some cases, personnel from the National Heart, Lung, and Blood Institute or the Food and Drug Administration may need to see your records to verify study information, but they will not be told who you are. The results of the study may be published, but your identity will not be given and the results will be given only for groups of people, not individuals. At the end of the study, all paper forms with your name or other information that could identify you will be kept in a locked room for a period of _____ years (determined by State regulations) and then will be destroyed.

You will be asked to give your Social Security number (under Public Health Service Act 42 USC 285a) so that study staff can locate you in the future if you cannot be located by other means. Giving this information is up to you and you may still take part in the study even if you refuse to give us this information. You will not be denied any federal right, benefit or privilege by refusing to give this information.

Your name, Social Security number, Medicare number and all other publicly identifying information will be kept in computer records separate from the data collected as part of your taking part in this study. Any medical information about you will be kept in computer records for analysis with such information from all other individuals in the study, but these records will not contain your name or Social Security or Medicare number or any other publicly identifying information.

COSTS

There will be no payment to patients who take part in this study. Your ENRICHHD counseling sessions and ENRICHHD clinic visits will be covered by the ENRICHHD study. All other treatments, procedures, and clinic visits for your heart condition are considered usual medical care and their costs are expected to be covered by your insurance carrier or you.

Study Investigator: (Name, Address, Phone)

Alternative Study Staff: (Name, Address, Phone)

Enhancing Recovery in Coronary Heart Disease (ENRICHD) Patients Study
DRAFT INFORMED CONSENT FOR ANTIDEPRESSANT TREATMENT

ENRICHD Study Doctor:

24-Hour Emergency Phone:

You have become a part of the ENRICHD study, which hopes to learn whether counseling that reduces depression and/or increases social support will lower the risk of future heart attack or death from heart disease. The ENRICHD study doctors now believe that your feelings of depression would be lessened if you began taking medication, called antidepressants, for these symptoms.

Procedures

If you agree to begin taking antidepressant medication, you will be asked to come to the medical center for an evaluation (assessment interview) by an ENRICHD study doctor. This interview will take about an hour. After this visit, you will be asked to come back every two to four weeks, as needed, for follow-up visits. These will last about 30 minutes each. These visits will take place for a maximum of one year. Every effort will be made to combine these visits with your other ENRICHD counseling and clinic visits so they will not be inconvenient for you. When you first start taking the medication, you will be evaluated for three to five sessions by an ENRICHD study doctor who will provide support and will decide whether your medication needs to be adjusted. You will continue to take the antidepressant medication for nine months to one year, and then you will be evaluated to find out if the medication should be stopped or continued, depending on your feelings of depression at that time. If the ENRICHD study doctor thinks you would benefit by continuing the antidepressant medication, the ENRICHD doctor will help you find a doctor in the community who will continue to provide you with this medication and who will follow up to see how you do on the medication.

Assessment Interview

An ENRICHHD study doctor will look over your medical and depression symptoms and history to determine whether or not you might benefit from antidepressant medication. You will be asked some questions that you might consider to be personal and sensitive. For example, you will be asked if you have had psychiatric treatment in the past, or if you have ever been suicidal. You will be asked to answer questions indicating how you feel. Sample questions are, "I feel so sad or unhappy that I can't stand it" and "I feel irritated all of the time now." You are free not to answer any of these questions. The total time required for this assessment interview is approximately 1 hour.

Antidepressant Medication

If you agree to begin to take antidepressant medication, you will be prescribed the medicine sertraline (trade name Zoloft), for up to one year. This is a commonly prescribed medication to treat depression. During the first week of antidepressant medication, you will receive either 25 or 50 milligrams of the medication daily, depending on your body weight and medical condition. After that, the ENRICHHD doctor will increase your dose to no more than 200 milligrams daily, as needed. During the time you are taking the medicine you will be evaluated on a regular basis to provide support, to monitor your depression symptoms, to see if there are any medicine side-effects, and maybe to adjust the amount of medication you receive. At the end of this period of up to one year, the ENRICHHD doctor will discuss with you whether or not to continue antidepressant medication. These procedures are the usual way that antidepressant medications are used and are not experimental.

Depending upon the severity of your depression or your previous medical history, the ENRICHHD study doctor may recommend treatment with a different medicine or even a combination of medicines. It is also possible that you might experience side-effects or fail to benefit enough from sertraline to continue its use. These decisions will be made by the ENRICHHD study doctor, who will talk with you about it. Decisions about using other antidepressant medications will be made by the ENRICHHD study doctor in order to provide the best way to lessen your feelings of depression.

Risks, Stress and Discomfort

Sertraline may cause nausea, loose stools, nervousness, headache, and difficulty with sexual function. These side effects are generally minor and can be lessened by adjusting the sertraline dose, stopping the medication, or switching to a different medication. Medicines of this kind (antidepressants) can affect judgment and motor skills, so you should be careful when operating large and dangerous machinery, including automobiles, until you are reasonably certain the medicine does not affect your judgment or motor skills. As with any medicine, other side effects can happen.

Other Information

Your agreement to take antidepressant medicine is entirely voluntary. You are free to refuse to take medicine and to withdraw your consent at any time. No penalty or loss of benefits to which you are entitled will occur if you do not wish to take this medicine.

All information about your medical condition and your answers to questions, will be kept confidential to the extent the law allows. Records about you will be put under a code number. In some cases, personnel from the National Heart, Lung, and Blood Institute or Food and Drug Administration may need to see your records to verify study information, but they will not be told who you are. The results of the study may be published, but your identity will not be given and the results will be given only for groups of people, not individuals. At the end of the study, all paper forms with your name or other information that could identify you will be kept in a locked room for a period of _____ years (determined by State regulations) and then will be destroyed.

Any medical information about you will be kept in computer records for analysis with such information from all other individuals in the study, but these records will not contain your name or Social Security or Medicare number or any other publicly identifying information.

All medical care, including the type given in studies such as this, has some risk of injury. If any complications occur based on your taking part in this study, the ENRICHD doctors will help you find the correct treatment, but the study will not provide any money for the treatment. You do not give up any right for personal injury by signing this form.

Signature of Investigator Date

Patient's Statement

The ENRICHD antidepressant medication care described above has been explained to me, and I voluntarily agree to this care. I have asked any questions I have, and understand that any future questions I may have about this study or my rights will be answered by the ENRICHD study personnel listed above.

Signature of Patient Date

Copies to:

Patient

File

