2. Chapter 2: Eligibility

2.1 Overview of Approach and Goals

The overall approach to recruitment, eligibility determination, baseline assessment and randomization is one of attempting to enroll eligible participants who are at increased risk for morbidity and mortality as quickly and efficiently as possible after an acute MI. This approach was adopted in an effort to begin treatment as quickly as possible in those participants assigned to treatment so that the benefits of treatment might be realized early after the MI, when patients are at the highest risk. It is important that every effort be made to overcome barriers to enrollment and participation of eligible patients so that those who are the most ill or who might face other barriers to participation will not be excluded, except in cases in which barriers to active participation cannot be overcome.

2.2 Inclusion and Exclusion Criteria

Inclusion and exclusion criteria are summarized in Table 1. The sequence of screening, eligibility determination, and randomization are summarized in Figure 1. An overview and rationale for each of the inclusion and exclusion criteria are summarized below.

2.2.1 Inclusion Criteria

Patients will be enrolled who meet the following criteria.

2.2.1.1 Hospitalized for MI

Only patients who have been hospitalized for an acute MI at visit (SV1) will be eligible for enrollment in ENRICHD. For ENRICHD, an acute MI will be determined by:

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 underwent 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.

These determinations will be possible by chart review in most cases. A few cases may require confirmation by patients’ physicians or investigation of results of tests done at referring hospitals. The diagnostic criteria for patients who undergo acute PTCA or have elevations of CK-MB less than twice the upper bound of the reference range used locally should be reviewed by the site cardiologist. Information may be found on:

a) the ambulance run sheet;

b) an ER triage sheet;

c) the emergency room sheet;

d) the admitting history and physical; and

e) the physician’s or nurse’s narrative notes.

Read the chart carefully. Once signs and symptoms of MI are documented in the medical record, similar confirming notes are usually found in other sections of the chart, and may be more extensive. Medical student’s notes are usually a very thorough review of the patient’s condition.

2.2.1.2 Characteristic enzyme increases

Since elevations in enzyme levels may result from conditions other than cardiac injury, patients who meet enzyme criteria are only eligible if the local physician has determined that the cause for the elevations is an acute MI. Elevations in enzyme levels may be seen, in particular, after an acute intervention (PTCA or CABG); these patients will only be included if the indication for the intervention was acute myocardial intervention.

Enzyme increases that qualify patients as eligible include an increase in cardiac enzyme levels (CK, LDH, Troponin T or I ) to twice the upper limit of the normal value for the institution. Only the values of the marker protein used to make the diagnosis has to be reported to the data center.
**CK-MB**

Check first to see if a CK-MB was ordered on each patient. This information should be noted on the ER flow sheet in the MD orders portion, or in the general notes, and specific laboratory values should be available in the laboratory section of the medical record, under the cardiac enzymes section, if it has been ordered and conducted.

To qualify for ENRICHD, the CK-MB must manifest a rising and falling pattern of elevations with at least one value above the upper bound of the reference range. If elevations are more than two-fold the upper bound of the reference range, no consultation is necessary. To ensure accurate diagnosis when values are lower, the case and the values should be discussed with the site cardiologist. In addition, the local physician must have determined that these changes have resulted from an acute myocardial infarction. Normal ranges for institutions are usually found on each lab report for the test being reported. An MB bump (elevation) will appear in patients presenting to the hospital early in the course of an evolving MI.

For patients who present with ST segment depression and undergo acute PTCA, a three-fold elevation of CK-MB is required for diagnosis. For patients who present 24 hours after onset of the MI symptoms, LD or troponins can be used instead of CK-MB to determine an MI has occurred.

**2.2.1.3 LD**

LD (or LDH; Lactic Dehydrogenase) appears in the blood approximately 24 hours after the onset of MI symptoms. In the absence of CK-MB elevation, look for LD elevation.

To qualify for ENRICHD, patients must have an LDH elevation ≥ 1.5 times the upper limits of normal for your institution and LDH1 > LDH2.

For patients who present with ST segment depression and undergo acute PTCA, a three-fold elevation of LD is required for diagnosis.

**2.2.1.4 Cardiac Troponin T or I**

To qualify for ENRICHD, a patients must have Troponin T or I greater than two times the upper limit of normal at the institution in which the patient is being recruited.

For patients who present with ST segment depression and undergo acute PTCA, a three-fold elevation of Troponin is required for diagnosis.

**2.2.1.5 Signs and symptoms of MI.**

Signs and symptoms of MI include:

a) Chest pain/chest pressure
b) Jaw pain
c) Arm or back pain
d) Diaphoresis (sweating)
e) Shortness of breath
f) Nausea/vomiting
g) Abdominal discomfort

Chest pain and/or pressure is the most common symptom found in patients of both genders and all race/ethnic groups and ages. Yet, it is not necessarily the most common complaint, and it does not occur in all patients, particularly older patients. In a patient experiencing an MI and reporting chest pain, the pain may get somewhat better and worse over time. Chest pain may be described as burning, tightness, squeezing or pressure, and the pain may be felt in places other than the chest. Left arm pain that may radiate to the jaw, back pain, and even just jaw pain is common. Patients may complain only of severe chest pressure rather than pain - i.e. - “I feel like an elephant is sitting on my chest”.

### 2.2.1.6 Evolutionary electrocardiographic ST-T changes or new Q waves

ECG changes can be determined in the report of the 12-lead ECG obtained on the patient. These are usually found together in one section of the medical record. Do not confuse rhythm strips with 12-lead ECGs.

Characteristic evolutionary changes include:

a. Evolving ST or T wave elevations (at least 1 mm in two contiguous leads)

b. T wave inversion

c. New Q waves (> 30 msec and 1 mm depth)

Compare several ECGs. If an ECG done prior to this episode is available, compare it with the series from this event. Note the changes. Do not be afraid to ask for assistance with ECG interpretation; this is a skill that comes with time.

### 2.2.2 Depressed and/or socially isolated

To be eligible for inclusion, patients must meet the criteria for depression, social isolation, or both, as discussed below within 28 days of the onset of acute myocardial infarction. Patients are eligible for randomization as soon as they:

1. meet criteria for depression and/or low social support;

2. satisfy the other inclusion and exclusion criteria; and
3. complete baseline data collection.

Every effort should be made to enroll patients while they are still in the hospital. For those patients who are discharged prior to completing baseline data collection and who may be eligible, every effort should be made to complete eligibility determination and baseline data collection as soon after discharge as possible, as described in Chapter 4. Specifics concerning the criteria for depression and social isolation are summarized below.

### 2.2.2.1 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 2). The specific modified DSM-IV criteria are:

- Minor depression symptom criteria, $1 \leq$ duration week; prior HX Major depression.
- Major depression symptom criteria, $1 \leq$ duration week; prior HX Major depression.
- Major depression symptom criteria, and duration $> 2$ weeks (regardless of prior history).

The first 7 items on the DISH (Part A) assess the cardinal symptoms of depression (dysphoria and anhedonia). If neither is present, the patient cannot meet the DSM-IV criteria for depression.

### 2.2.2.2 Psychodiagnostic Interview

The modified DSM-IV criteria for major or minor depression are summarized in Table 2 and will be determined from psychodiagnostic interview. In order to be eligible for inclusion in ENRICHD, patients must meet these criteria for major or minor depression based on a psychodiagnostic interview to be administered (DISH) at the initial visit (SV1 while hospitalized for an MI; see Figure 1) or re-screening visit (to be conducted post-discharge from 0-14 days from the index MI; see Figure 1) and within 21 days of the index MI. Issues concerning differentiating between medical and depressive symptoms and the standardized psychodiagnostic interview are summarized below.

In order to determine whether a patient meets the modified DSM-IV criteria for major or minor depression (see Table 2), it will be necessary to conduct an interview with a new interview schedule, the Depression Interview and Structured Hamilton; Freedland, 1996), 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 phone follow-up. It was also designed to be suitable for use by diverse personnel and to eliminate most of the need for diagnostic overreading.

The DISH (see Appendix A) 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; 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); a 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 (see Appendix A). 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 Recent History of Depressive Disorder section evaluates whether there have been any changes in depressive symptomatology in the interval between the present and the previous interview. This section will not be administered at baseline but at a later follow-up visit.

The Notification section directs the interviewer to take appropriate steps when it is necessary to notify the patient's physician and/or nurse about severe depression or active suicidality, and to document these steps. This section will be used to assist in determining exclusion from ENRICHD prior to randomization (see discussion of suicidality in section on Exclusion Criteria #7 in this chapter) as well as to implement an appropriate action in the case of patients who become suicidal after enrollment in ENRICHD.

The History and Course Chart is used in conjunction with the Psychiatric History and the Recent History of Depressive Disorder sections to characterize the longitudinal course of the patient’s depressive disorder or dysthymia. 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 Form provides a standardized format for coding the current diagnosis and the Hamilton depression score. The form is designed to increase the reliability of the diagnostic judgments that are formed on the basis of the interview, and serves as one basis for randomizing a patient into the study.

### 2.2.2.3 Differentiation Between Medical and Depressive Symptoms.

The threshold is very high in DSM-IV for calling something a “medical symptom” (i.e., a symptom of medical illness, medication, or substance abuse rather than of depression):

> “Some of the criterion items of a Major Depressive Episode are identical to the characteristic signs and symptoms of general medical conditions (e.g., weight loss with untreated diabetes, fatigue with cancer). Such symptoms should count toward a Major Depressive Episode except
when they are clearly and fully accounted for by a general medical condition. For example, weight loss in a person with ulcerative colitis who has many bowel movements and little food intake should not be counted toward a Major Depressive Episode. On the other hand, when sadness, guilt, insomnia, or weight loss are present in a person with a recent myocardial infarction, each symptom would count toward a Major Depressive Episode because these are not clearly and fully accounted for by the physiological effects of a myocardial infarction” (DSM-IV, pp. 322-323).

The burden is on the interviewer to judge whether any individual symptom exceeds this DSM-IV threshold and to document the medical condition or medication that is believed to account for the symptom. It is not possible to devise rules that would be applicable in every case. For example, weight loss in a post-MI patient may not be due to the direct physiological effects of the myocardial infarction, but it is not uncommon for cardiac patients to be given diuretics to control edema. If a patient’s weight loss is due entirely to diuresis rather than to loss of appetite, it should not count as a depressive symptom. The Manual of Operations, therefore, will include guidelines to assist interviewers in making these judgments, and interviewers are expected to consult with the appropriate medical personnel, when necessary, to reach an informed conclusion about a symptom.

It may be difficult or impossible for an interviewer to judge whether a depressive syndrome is due entirely to the direct physiological effects of an underlying medical condition such as hypothyroidism. For this reason, consultation may be needed with appropriate medical personnel when a co-morbid medical conditions may be masquerading as depression in post-MI patients. Interviewers are expected to attempt to diagnose depression in the presence of these medical conditions, and it will be the responsibility of each clinic to establish procedures to review decisions made by interviewers in diagnosing depression in such circumstances.

Beck Depression Inventory:

For those sites in which screening with the DISH is not feasible, the BDI may continue to be used as a screening tool under the original protocol (ver. 5.0 protocol criteria). However, note that for randomization into the study, depressed patients no longer need to have a BDI $\geq 10$ for entry, as long as patients meet one of the qualifying diagnoses from the DISH.

2.2.2.4 Social Isolation

To meet criteria for social isolation 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). The criteria has been broadened to include 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.

The ESSI is a seven-item scale based on items which have been individually predictive of mortality in cardiac patients and/or came from larger well-validated social support scales. It was developed based on a review of previous scales and items which have predictive validity. A summary of this review suggests that the critical element of most items predictive of poor prognosis is related to
perceptions of social support, emotional support in particular, rather than dimensions of either network structure (e.g. network size, geographical proximity or living arrangements) or subjective feelings of loneliness. The scale was created by identifying items from the following three studies by Williams et al, Gorkin et al, and Berkman et al. The item from CAST was actually an integration of two items from the MOS. In an effort to develop a scale with 6-7 items, we disaggregated those two items and added two other items from the MOS which tap a similar construct. The questions about confidant and marital status are directly from the Williams et al study. The question on emotional support is from the New Haven EPESE. The response categories have been modified so that they follow a consistent format based on the MOS (with the exception of the items about marital status).

2.2.3 Exclusion Criteria

As summarized in the Medical Eligibility Form (see forms in Forms Appendix), patients will be excluded from participation who meet any of the following 10 criteria.

2.2.3.1 Post-procedure MI

Patients who have had an MI subsequent to a procedure, such as CABG surgery or PTCA, will be excluded from ENRICHD. These patients can be identified by:

a. admission for a cardiac procedure with MI occurring subsequently; or

b. an elevation on a CK-MB done during or just after a cardiac procedure.

Refer to interventional cardiac catheterization lab procedure notes for determination of whether the MI was procedure related. Often clues may be found there that the MI occurred during or just after the procedure.

However, patients in whom these procedures are done to treat an acute infarction need not be excluded. Even if enzyme criteria are not met prior to the intervention, these patients are eligible provided the intervention was initiated to treat the acute infarction and enzyme criteria are met subsequent to the procedure.

Patients who have undergone noncardiac surgery (orthopedic, abdominal or vascular) and suffer a subsequent myocardial infarction will be candidates for the study. Only those MIs presumably caused by procedures that affect the coronary arteries will be excluded from the study.

2.2.3.2 Presence of Conditions Likely to Terminate Fatally Within One Year

Patients with these conditions will be excluded from ENRICHD since they potentially reduce the number of outcomes attributable to the intervention, are likely to compromise patients’ ability to participate actively in the intervention as they become more ill, and increase dramatically the difficulty in presenting a standardized psychosocial intervention.

Check the history and physical exam sections of the chart for disease process which severely limit life expectancy. These would include advance lung or liver cancer, lymphomas, leukemia, advanced
liver disease, active AIDS, severe CHF or COPD, and advanced rheumatologic disease. Patients on the cardiac transplantation list are also excluded. On the other hand, patients with prostate carcinoma, limited breast cancer, skin malignancy, and endstage renal disease receiving dialysis would be candidates for the study.

In the laboratory section of the chart, look for values that may indicate underlying disease process likely to cause death within the year. These could include elevated creatinine, elevated BUN, very low hemoglobin or hematocrit, or very low platelet or white cell counts. Read all lab reports and note any values markedly outside the normal range. Investigate to determine the meaning of such values.

This determination should be based primarily on the judgment of the patient’s physician(s). However, the PI at each site (or designee) should be consulted before any patient is excluded on this basis.

**2.2.3.3 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 limit participation in the study. In these cases where limitations cannot be overcome, patients will be excluded from participation.

This determination should be made on the basis of the patient’s judgment, after the study activities have been explained to them and in collaboration with the Clinical Center PI. Efforts should be made to find ways to help patients with physical limitations participate if the patient is interested in the study. For instance, patients with severe COPD could come to a group with an oxygen tank. At the same time realistic considerations about the patients potentially dropping out need to be considered.

Note that physicians may express a concern that the patient may not feel well enough to participate. Health status (except as it may be terminal) is not an exclusion criterion.

**2.2.3.4 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 the other protocol provides a treatment similar or (or conflicting with) the ENRICHD intervention.

Patients who are currently in a research protocol investigating depression or social isolation in post MI patients, such as the testing of antidepressant pharmacologic therapies would be excluded from ENRICHD. However, patients involved in investigations of standard or novel pharmacologic therapies for myocardial infarction such as new thrombolytic therapy agents, new lipid lowering
agents, new beta blockers, new ACE inhibitors, new forms of anti-platelet, or anti-thrombin agents are potentially eligible.

2.2.3.5 Major Psychological Co-morbidity

Patients who have major psychological co-morbidity which either 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 psychological conditions include any of the following:

a. schizophrenia or bipolar disorder evidenced by chart review or psychodiagnostic interview;

b. dementia evidenced from chart review, psychodiagnostic interview, or by administration of the Short Blessed Dementia Screening Test given by discretion of the interviewer during the psychodiagnostic interview at SV2 (patients who score above the standard cutoff score of 10 will be excluded; see copy of Short Blessed Test in the Forms Appendix);

c. active substance abuse evidenced by chart review or clinical interview;

d. other major psychological conditions precluding participation in trial.

Note that these are not absolute contraindications. For instance, a patient with schizophrenia in remission, with adequate interpersonal skills to participate in group, should not de facto be excluded from the social isolation intervention (they may be excluded from the depression arm). These exclusions should be relatively rare.

2.2.3.6 Active Suicidal Ideation

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 socially isolated and most will be middle aged or older, a small number of the patients screened for participation will inevitably be at risk for suicide.

In screening a patient for ENRICHD, the objective of suicide risk assessment is to classify him or her as (1) possibly or definitely at imminent risk of attempting suicide or otherwise harming him/herself (a psychiatric emergency); (2) not at imminent risk, but possibly or definitely at elevated risk of attempting suicide within the next few weeks or months (not an emergency, but a serious situation nevertheless); or (3) not at elevated risk of attempting suicide.
The information upon which to base this classification is to be obtained from the BDI, the DISH, and, when applicable, from collateral sources (the patient’s medical chart, caregivers, etc).

**Beck Depression Inventory**: Item #9 on the BDI asks the patient about suicidal ideation. Since the BDI is only a questionnaire rather than a more in-depth psychodiagnostic interview, it does not provide sufficient information to judge whether there is any real risk of suicide. Nevertheless, whenever the BDI is administered at baseline, treatment process, or outcome measure, it is to be reviewed in a timely manner to ascertain whether the patient has reported any suicidal ideation.

A score of 1 on BDI Item #9 indicates that the patient has recently had some thoughts about suicide but that he or she “would not carry them out”. This suggests (but does not guarantee) that the patient is not at imminent risk, and that his or her longer-term risk is only mildly elevated, if at all. If this is an isolated finding (e.g., no other suicidal features are detected), the designated senior project staff member(s) should be informed, but it is not necessary to notify the patient’s physician or to take any other actions unless so directed by the senior project staff.

A score of 2 on BDI Item #9 suggests the presence of suicidal ideation that may be more significant, and a score of 3 is a fairly clear warning sign of suicidal intent. Even if this is an isolated finding (i.e., no other suicidal features are detected), the designated senior project staff member(s) should be informed and the patient’s physician(s) should be notified in a timely manner. See Chapter 8 for details on the physician notification procedure.

**Depression Interview**: Suicidal ideation is assessed as part of the standardized psychodiagnostic interview, but only if the entire interview is administered (i.e., suicidality is not assessed if the screening interview is terminated early due to negative responses to questions about the cardinal symptoms of depression). If the full interview is administered and the patient reports having had any suicidal ideation during the past week, the interviewer is to probe to determine the frequency, chronicity, and content of the ideation.

Following guidelines delineated by Clark and Fawcett (1992), the identification of active thoughts of suicide is to be followed up by determining whether (1) the patient has considered and/or has access to any specific method(s) of suicide; (2) the patient wants to or 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; (4) the patient has a past history of suicide attempt(s); and (5) there are any additional circumstances that may add to the risk of attempting or completing suicide (e.g., current alcohol abuse, social isolation, hopelessness, or crisis such as job loss).

If one or more of these features are detected, the interviewer must attempt to determine whether the patient is at imminent risk (i.e., in immediate danger of attempting suicide or otherwise harming him/herself). If the interviewer believes that the risk may be or definitely is imminent, the situation is to be treated as a psychiatric emergency. In such situations, the need to protect the patient overrides both the patient’s usual confidentiality rights and the rest of the usual screening procedures. (It is unnecessary to complete the screening process anyway, because patients who are
at imminent risk of suicide are excluded from enrollment in the trial). The interviewer is required to take the following steps:

If the patient is still in the hospital, both the physician and the nurse in charge of the patient’s care are to be notified immediately after the interview has been completed. If the patient has been discharged from the hospital, the patient’s physician is to be notified as soon as possible. If a suicide attempt is in progress, or if there is a substantial risk that a suicide attempt may be made before the physician would have time to intervene (e.g., the patient has swallowed a bottle of pills or is holding a weapon), the interviewer is required to call 911 immediately to dispatch emergency assistance. The interviewer is also required to notify the designated senior study staff as soon as possible and to discuss whether any other steps are necessary to protect the patient (e.g., notification of family members, caregivers, etc.)

Patients who are not at imminent risk, but who are possibly or definitely at elevated risk of attempting suicide within the next few weeks or months, are eligible to participate in the trial unless excluded on other grounds. If a patient is or may be at elevated risk of attempting suicide within the next few weeks or months, physician notification is mandatory, and it must be completed in a timely manner. Notification of the designated senior project staff member(s) is also mandatory. If the patient is randomized to the Treatment arm of the trial, the findings are to be discussed with his or her psychotherapist (and, if applicable, the project psychiatrist). If the patient is excluded from the trial or is randomized to the Usual Care arm, the designated project staff member should, if necessary, initiate a follow-up contact with the patient’s physician to confirm that the patient is being properly evaluated and/or treated.

Patients need not be excluded from participation in the trial simply because of a low-probability, long-term risk of suicide or because of transient or passive suicidal ideation. Furthermore, the interviewer’s duty to protect the patient’s confidentiality outweighs any potential need to notify the patient’s physician or other caregivers. For example, assume that the only evidence of any suicidality obtained from a patient is his statement that, “Once in a while, I wonder what I would do if things got a lot worse that they are now. I might think about killing myself, but I’d never do that. It’s just plain wrong, and I couldn’t do that to my family anyway.” In such a case, the interviewer would have no need, no responsibility, and no right to disclose this information to the patient’s physician or other caregivers.

2.2.3.7 Unwillingness to Provide Informed Consent

Patients who are not willing or able to provide written informed consent cannot be randomized in ENRICHD.

2.2.3.8 Inability to Complete Screening Visits

Patients who fail to complete ENRICHD screening visits or who cannot provide complete baseline data will not be randomized in ENRICHD. The inability to respond to a single item on the baseline questionnaires would not exclude a patient. However, patients who fail to complete a number of items should be excluded.
2.2.3.9 Inaccessibility for Intervention and/or Follow-up

Despite active efforts to accommodate patients' special needs, those who are have extreme difficulty attending therapy sessions and follow-up visits, and are therefore unlikely to be adherent with treatment and follow-up will be excluded from participation in ENRICHD. Establishing exclusion criteria to define accessibility is essentially related to such dimensions as the number of miles which a patient lives from an intervention or assessment site, the time that it takes to travel such distances, frequent business travel, plans to move from the area during the period of study, and not having access to a telephone for contact and follow-up. Nonetheless, differences between clinical centers in such factors as urban vs. rural location and availability of public transportation as well as differences in factors such as patient motivation and resources to overcome accessibility barriers preclude definitive criteria which are applicable to all centers and all patients. 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.

2.2.4 Ethnicity and Gender Composition of ENRICHD

One of the major selection criteria for a clinical site for ENRICHD was the ability to recruit women and minorities into the study. Clinical sites were selected to produce an overall study population of 50% women and 50% minorities, and will be monitored by the UNC Coordinating Center throughout the study to assure that our performance matches our expectations. Recruitment of women and minorities is essential at the beginning of the trial. If the overall proportion of women and of minorities appears to be falling significantly short of 50% for each, options and approaches to increasing the recruitment of women and minorities at some or all existing clinical sites will be reevaluated.

2.3 References


Table 1. Eligibility Criteria for ENRICHD

**Inclusion Criteria**

**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.

**Depression or social isolation as determined by:**

a. depressed - major or minor depression based on modified DSM-IV criteria (exclusive of requirement concerning depression being reactive to a physical condition; see Table 2 for modified DSM-IV criteria) during SV2

and/or

To meet the criteria for social isolation, 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) a score of 3 or less on two or more items, excluding items #4 and 7 (help with chores and marital status) and (c) a total score of 18 or less on items 1, 2, 3, 5 and 6.
Exclusion Criteria

1. Post-procedure MI (unless the procedure was performed to treat the acute infarction; see section 2.2.2.1)

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 or bipolar 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. Active Suicidal Ideation

7. Unwillingness to Provide Informed Consent

8. Inability to Complete Screening Visits

9. Inaccessibility for Intervention and/or Follow-up
Table 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; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. Those patients who meet these symptom criteria but not the two-week duration criterion and have had a previous episode of major depression, will be considered to have met criteria for major depression and be eligible for randomization if they meet all other eligibility criteria.

   (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).
e. 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. As in major depression, at least one of the symptoms must be either depressed mood or loss of interest or pleasure. Those patients who meet these symptom criteria but not the two-week duration criterion and have had a previous episode of major depression, will be considered to have met criteria for minor depression and be eligible for randomization if they meet all other eligibility criteria.

b. **Exceptional Criteria**

(1) **Dysthymia:** As defined by DSM-IV, dysthymia is a form of chronic, mild depression. Its features are very 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.
Figure 1. Overview of Proposed Screening/Recruitment Visits*