5. Chapter 5: Medical Measures and Endpoints Follow-up
Data Collection Procedures

5.1 Introduction to Screening, Eligibility, and Baseline Medical Forms

The Medical Eligibility form (MEA) will be used for screening all patients admitted to hospital for acute MI. Information to be collected includes basic demographic information (age, race sex) plus the detailed inclusion and exclusion criteria defined for the study. For patients who are eligible by meeting the medical criteria, a Medical History form (MHA), and Baseline Examination form (BEA) are also complete. The MHA and BEA are intended to be completed as fully as possible from patient chart review prior to conducting the interview portion of the forms.

5.2 Medical Eligibility Form -- Screening, Inclusive/Exclusive criteria- MEA
Version C

A) Demographics.

1a.) Age- record the patient age in years as noted in the chart.

1b.) Sex- note gender from chart or other screening log sources.

1c.) Race- record using the standard NIH ethnic group guidelines (see section 5.3).

B) Acute MI criteria.

The criteria for myocardial infarction, which is the criteria for the inclusion in the study, is outlined in section 3.3.1 of the protocol and is newly restated below.

2) Acute myocardial infarction must have one of the following characteristic enzyme profiles:

a. Cardiac enzymes are 2 times the upper limit of normal or greater for either peak CK, troponin or LDH. The CKMB level will take priority over CK alone or troponin if more than one assay is performed.

b. Include patients as meeting the criteria for the diagnosis of acute myocardial infarction if: (a) MBCK values are increased above the upper bound of the reference range as assessed by the site cardiologist even if they are not two-fold greater than the upper limit of normal, provided a rising and falling pattern is manifested, and (b) acute myocardial infarction has been diagnosed locally, and if symptoms compatible with acute MI and/or characteristic ECG findings are present as defined in the ENRICHD eligibility criteria.

c. Acute angioplasty. (a) Include patients who present with ST segment elevation and classic signs and symptoms of MI if these patients meet ENRICHD criteria for marker protein elevations even if an acute angioplasty had been done so long as the diagnosis of
acute infarction is confirmed by the site cardiologist; (b) NOT include patients with ST segment elevation if no elevations of marker proteins occur; (c) Include patients who present with chest pain, ST segment depression, a local diagnosis of acute myocardial infarction, if a three-fold increase in any of the biomarkers of myocardial injury is present and if the site cardiologist concurs with the diagnosis of acute infarction; (d) NOT include patients with less severe elevations. In the situation where ST segment depression is present, it is more difficult to know whether acute infarction has occurred from the initial history, physical and electrocardiogram or whether or not elevations could be due to the acute interventional procedure. However, recently, criteria have been proposed to diagnose acute myocardial infarction during the periprocedural time period if a three-fold increase in any of the marker proteins occurs.

3) The characteristic evolutionary electrocardiographic ST changes or new Q-wave are defined in section 3.1 of the protocol.

4) The symptoms compatible with myocardial infarction will include those of chest pain, burning, tightness, squeezing, or pressure in chest which may radiate to arm, neck, or jaw lasting 20 minutes or greater or unrelieved by three nitroglycerin tablets which may be accompanied by nausea, vomiting or angina equivalent including shortness of breath, syncope, or excessive fatigue.

C) Medical exclusive criteria for patients with documented MI.

5) Patients who have a condition in which the probability of death is greater than 20% at one year will be excluded from the study. This would include cancer such as lung cancer, lymphomas, leukemia, advanced liver disease, and advanced rheumatologic disease. 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. If there is a question regarding the potential eligibility of the patient, this should be directed towards the project clinician at the Coordinating Center.

6) Severe cardiac complications are present such that the patient cannot either physically withstand assessment for eligibility, or communicate because of current condition (e.g. on a ventilator).

7) Conditions likely to limit physical capacity. Every effort should be made to include these patients in the study. However, it is likely that some of these patients will not be candidates because they are bedridden, or have physical limitations such that they could not be brought to the clinic by any support system or other methods and thus would result in exclusion from the study. Otherwise, we would encourage all patients, even those with important physical limitations option to participate.

8) Patient is not fluent in either English, or Spanish and either cannot comprehend the study instruments, or able to participate in therapy due to language barrier.
9) Major psychiatric comorbid illness present, except depression. Patients with current illnesses such as dementia, schizophrenia, active suicidal ideation, alcoholism can present problems for long term follow-up and adherence to therapy.

10) Patients who are in current research protocols involved in the investigation of the depressed or socially isolated post MI patients including the testing of antidepressant pharmacologic therapies would be excluded from this study. However, all 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.

11) Patient refuses consent-- self explanatory.

12) Physician refusal for patient to participate. Self explanatory.

13) Patients cannot have a post procedural MI. This includes procedures such as CABG, and PTCA. These procedures are associated with enzymes leaks that have a different outcome than patients with de novo myocardial infarction. Patients who have undergone noncardiac surgery (orthopedic, abdominal or vascular) and suffer a subsequent myocardial infarction will be candidates for the study. Thus, only those procedures that affect the coronary arteries will be excluded from the study.

14) Patient able to complete screening visits. If the patient is not able to complete all of the medical and psychological screening, then they are not eligible for the study.

15) Patient accessible for follow-up visits. If the patient is not accessible either by telephone, or in person for collection of follow-up data they are ineligible.

16) Death before randomization, self explanatory.

17) Screening window of 28 days elapsed before the entire baseline assessment of patient could be completed. The limit on age of the index MI intended to limit the eligibility of patients to the more recent, acute, phase following the qualifying event.

18) Patient is currently taking antidepressant medications less than 14 days. Short duration antidepressant use is still an exclusion. However, patients can be rescreened within the 28 day window and if the depression diagnosis evaluated at that time meets DISH criteria, then the patient could be included in the trial.

19) Patient assessed as having good social support and nondepressed by ESSI and DISH is self evident, and is used as a screening aid in recording the outcome of assessment.

5.3 Medical History Form
A) Demographics - The questions in this section are intended to be based on patient interview. Response cards will be used for the sensitive questions of race and income.

1) Birth Date of the patient may be present in the chart, but confirmation should be obtained to get as consistent and accurate information.

2) Gender of the patient should be self-explanatory.

3) Racial group of the patient will be recorded using ethnic categories defined by NHLBI guidelines. Hand or show the patient the queue card listing the 5 racial groups and have them select the group with which they identify that is consistent with the guidelines.

A synopsis of those guidelines follows: **Black** refers to a person having origins in any of the Black racial groups of Africa. In the United States this definition includes native-born Black Americans, Africans, West Indians, and Haitians. **Hispanic** refers to people born in North, Central, and South America, and in the Caribbean whose language is Spanish or Portuguese, and people born in Brazil, French Guyana, British Guyana, and Dutch Guyana although they are part of South America. The most common Hispanic groups in the U.S. are Mexican Americans, Puerto Ricans, and Cubans. **Native American** refers to a person having origins in any of the original peoples of North America and who maintains cultural identification through community recognition or tribal affiliation in one of the tribes residing in the lower 48 states. NHLBI classifies Native Hawaiians as Native Americans in addition to American Indians, Alaska Eskimos, and Aleuts. **Pacific Islander** refers to a person having origin in any of the peoples of the Pacific Islands (except Hawaii). **Asian** refers to a person having origin in any of the peoples of the Far East, Southeast Asia, and the Indian subcontinent.

4) Marital Status and living arrangement is self explanatory.

5) Highest grade of regular schooling completed is self explanatory.

6) Employment Status refers to being employed for wages, full or part-time basis.

7) Income for the past year should be presented to the patient as a category selected from the queue card. Mark the letter associated with the total household income range selected either on an annual basis, or the monthly equivalent which is in parentheses.

B) Risk factors - comorbid illness. These data items will generally be present in the patient chart. In general, a failure to mention the presence of a problem means the problem did not exist. However, asking the patient is always recommended for confirmation.

8) Hypertension is defined as a history of or currently diagnosed hypertension either treated or untreated, usually with blood pressure measurements of a systolic blood pressure measurement of 140 mmHg and/or a diastolic blood pressure 90 mmHg. There should be evidence of a diagnosis of hypertension either in the chart or from the patient; a random blood pressure measurement above these thresholds is not adequate.
9) Diabetes Mellitus - A history of diagnosis of diabetes mellitus. Check yes for insulin treated, if insulin given currently or has been given anytime prior to index myocardial infarction.

10) Smoking history - Check yes if patient smokes now or has ever smoked regularly. Indicate whether the patient is a current smoker or has quit smoking. If he/she has quit, give the year he/she last smoked. Provide the number of years smoked and average number of cigarettes per day. The definition of a current smoker is anyone who has smoked or taken a puff of a tobacco product within the month prior to hospitalization.

11) Hypercholesterolemia - A prior diagnosis of hypercholesterolemia treated or untreated or a history of or currently documented serum cholesterol > 200 mg/dl or a LDL cholesterol > 130 mg/dl.

12) Estrogen use - Check yes if patient has taken Estrogen within two years of index MI either as an oral contraceptive or hormone replacement therapy. Also indicate if Estrogen is currently being used by patient. Provide the age of menopause onset.

13) Family history of heart disease - Definite MI or sudden death before 55 years of age in the father or other 1° relative, or before 65 years of age in mother or other female 1° relative.

14) Renal insufficiency - Only patients with creatinine > 1.8 mg/dl should be defined as having renal insufficiency.

15) Malignancy - The presence of a malignant neoplasm should be noted in the chart. If not, and the patient is unsure please check with the attending physician since a severe malignancy could exclude the patient from ENRICHD.

16) Pulmonary disease - a history of or diagnosis of pulmonary disease such as asthma, COPD, pulmonary fibrosis or other diagnosis.

17) Rheumatologic disease - A history of or diagnosis of rheumatologic diseases such as arthritis, or other collagen - vascular diseases. Joint aches and pains do not qualify as true rheumatologic disease.

18) History of thyroid disease - history of hypothyroidism or hyperthyroidism, diseases such as thyroiditis, goiter, myxedema, or exophthalmos.

19) Depression - Patients on medication for depression prior to index myocardial infarction. Patients on antidepressants for other reason will have the drug reflected in their medications but should not be included here.

20) Liver cirrhosis - Patients with advanced liver disease with an expected survival that is reduced.

21) Other comorbid illnesses - Provide other clinically important comorbid illnesses using standard diagnostic medical terminology when possible.
C) History of Cardiovascular Diseases / Procedures

22) History of a definite myocardial infarction - prior to current symptom episode - Record number of previous MIs, and the date of the most recent. Check type (Q-wave, non Q-wave) if known, and check location of most recent MI (anterior, inferior etc.) if it is known.

23-26) Previous angina, prior stroke, CABG, PTCA - A history occurring prior to index MI. PTCA includes all percutaneous interventions. Record number of prior CABG or PTCA and date of the most recent procedures.

27) CHF, NYHA Class: a condition classifiable on a NYHA scale. Check the worse classification during the six weeks prior to the six week MI. Asking for physician help if clarification is needed is recommended.

   a) NYHA Class I - Patients with cardiac disease, but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.

   b) NYHA Class II - Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

   c) NYHA Class III - Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitations, dyspnea, or anginal pain.

   d) NYHA Class IV - Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

28) Previous history of atrial fibrillation - A history of atrial fibrillation occurring prior to the index MI.

29) Previous times when the patients were resuscitated from cardiac arrest prior to index MI. Record date of prior event from chart if available.

30) Peripheral vascular disease- A history of prior PVD characterized by symptoms such as claudication, gangrene, or a record of surgical procedures or angioplasty to restore blood flow to the extremities.

D) Current Medications
Check the patient chart just prior to, or immediately after discharge, and record the medications currently prescribed for the patient. Use the medications dictionary that groups drugs by class for recording on the form.

5.4 Baseline Examination Form

The Baseline Examination form is completed primarily from a review of the patient’s chart associated with hospitalization for the index MI event that qualifies that person for enrollment into the trial. A limited physical examination is performed, noting vital signs along with ascertainment of specific signs and symptoms of heart failure. However, when questions arise, they should be directed to the attending physician or one of the ENRICHD medical investigators.

A. INDEX MYOCARDIAL INFARCTION:

1) Hospital Admission Date: record the date associated with admission of the index event.

2) Hospital Discharge Date: once the patient has been discharged for the index event, complete this item.

3) Index MI date-indicate the confirmation date of the myocardial infarction based upon enzyme elevation and physician documentation in History and Physical (H&P). On occasion, it is difficult to determine the exact onset of a heart attack. Often the major event is preceded by multiple small events. If there is confusion about the date of the index MI, choose the date and time that the patient came to the hospital.

4) Infarct Type: Q waves- A development of new Q waves in 2 or 3 leads in anterior, inferior or lateral regions. The easiest way to preserve these data would be to xerox the recording. In the absence of that, indicating whether the infarction is Q-wave or non Q-wave. should be entered. If help is needed, the attending physician or ENRICHD cardiologist should be consulted.

5) Infarct Location-Anterior: loss of R waves or development of QS complexes in leads V1-3, Inferior: development of new Q waves in leads II, III, or AVF. Other: Lateral, defined as development of new Q waves in leads I, AVL, or 2 of 3 leads of V4-6.

6-7) Ejection fraction-% left ventricular ejection fraction: If the ejection fraction has been measured, the number should be indicated in number 6 and the method in number 7. If no ejection fraction measurement is available, but a catheterization, echocardiogram or radionuclide imaging study has been done and it is indicated whether or not the diminution in ejection fraction is severe, moderate, mild or if the ejection fraction is normal, it should be indicated in 7A. If such tests have been done but no report indicates the severity of LV dysfunction, one of the ENRICHD investigators should be asked to investigate whether an estimation can be obtained.
8) Killip class - At the time of index MI should be recorded in the chart; if not delineated in the chart, determinants are listed in the bottom of the form and can be used to determine the appropriate class.

B. TREATMENT OF INDEX MI

Simply check those procedures which have been done during the patient's hospitalization for acute myocardial infarction. These may not necessarily be those that occurred in the intensive care unit but should include the entire hospitalization. Note the dates for cardiac catheterization and CAGB if performed.

9) IV thrombolytic therapy-enter use of any thrombolytic agent such as streptokinase as a yes or no answer.

10) PTCA-indicate percutaneous transluminal coronary angioplasty (PTCA), stent or atherectomy and the hours that procedure occurred after admission to hospital. Note elapsed time since admission for performance of procedure.

11) IABP-enter use of aortic balloon pump during early course of recovery as a yes or no answer.

12) Swan Ganz-Self Explanatory.

13) Defibrillation-Indicate use of defibrillator for ventricular tachycardial or fibrillation during hospitalization course as a yes or no answer.

14) Temporary Pacemaker-Self Explanatory.

15) Intubation-Indicate whether intubation was performed at any time during hospitalization as a yes no answer.

16) CPR-Cardiopulmonary resuscitation-Indicate whether CPR was performed at any time during hospitalization as a yes or no answer.

17) Cardiac Catheterization-Indicate whether cardiac catheterization was performed during hospitalization for index myocardial infarction and date of catheterization.

18) CABG- Coronary Artery Bypass Graft performed associated with the index MI. Record date the procedure was performed.

C. ENZYME LEVEL/LABORATORY/UPPER LIMIT OF NORMAL

Laboratory values should be recorded from the chart. Values that are not available cannot be included. If values are available from a referring hospital, it would be optimal to obtain those laboratory values for completeness of the baseline data.
19-22) Peak CK-Characteristic elevation of creatinine kinase (CK) and creatinine kinase MB fraction above upper limits of normal for each hospital laboratory.

23-26) LDH-characteristics highest elevation of lactic acid dehydrogenase isoenzymes: recording of LDH 1 and 2 and hospital upper limits of normal.

27-28) Troponin T or I - characteristic elevation of the markers troponin T or I.

29) Creatinine-Self Explanatory.

30) Total cholesterol- Document earliest recorded measurement of lipoproteins at time of myocardial infarction.
D. MI COMPLICATIONS

Complications during hospitalization should be indicated in the boxes for questions 31-41.

Questions with interpretation of these data should be checked with the attending physician or ENRICHD cardiologist.

31) Congestive Heart Failure-Syndrome of heart failure manifested by dyspnea, rales, jugular venous distention, gallop rhythm, or evidence of cardiomegaly or pulmonary vascular redistribution on chest X-ray.

32) Pulmonary Edema-Defined as either pulmonary vascular redistribution or frank pulmonary edema as noted by the radiologists interpretation on chest X-ray.

33) Respiratory Failure-as defined by H&P or intubation during early course of recovery.

34) Sustained Ventricular Tachycardia/Ventricular Fibrillation-episodes of either rhythm of greater than 30 seconds duration.

35) Advanced Heart Block (2\textsuperscript{0} or 3\textsuperscript{0}) - Mobitz 1-classical Wenchebach with increasing prolongation of the PR interval with a dropped beat Mobitz 2-a dropped sinus beat without prolongation of PR interval 3\textsuperscript{0} heart block-dissociation of the arterial and ventricular rhythms.

36) Cardiogenic Shock-Persistent hypotension and tachycardial despite treatment with intravenous fluids and inotropic agents.

37) Ventricular Septal Defect-Positive only if presence is documented by a diagnostic test such as an angiogram, right heart carth, echo-doppler, or radionuclide study.

38) Severe Mitral Regurgitation-Holosystolic murmur at the cardiac apex as indicated by physical exam, catheterization or non-invasive study such as echo.

39) Supraventricular Arrhythmias-Characteristic widening of QRS complexes associated with RBBB or LBBB.

40) HR<45 beats/minute-Self Explanatory.

41) Stroke - Documented evidence of a cerebrovascular accident.
E. PHYSICAL EXAM AT BASELINE

The majority of these data can be garnered from the chart or by a nurse. All except for number 49, the presence of an abnormal cardiac sound can easily be obtained by well qualified nursing personnel. If there is difficulty appreciating whether an S3 gallop is present, one of the physicians caring for the patient or one of the ENRICHD investigators should be asked to do an examination.

At this time a baseline electrocardiogram should be obtained for comparison with future electrocardiograms to be taken during follow up. This ECG may be taken by the ENRICHD staff (see section 5.5 that follows for protocol for obtaining electrocardiograms) which would permit the best comparison to be made. However, if the ENRICHD team is unable to obtain an electrocardiogram themselves, a xerox copy of one taken several days after the index event could be scanned into a mini computer or copied to preserve the data for transmission to the data center and ECG core laboratory.

42) Date of Examination-- record date the patient physical exam was performed.

43) Height (in inches or in meters)-- stated height can be used if measurement impractical.

44) Weight (in pounds or kilograms) -- weigh patient without shoes, heavy clothing.

45-46) Systolic and Diastolic blood pressure—Measurement of blood pressure should be recorded in sitting position using a mercury sphygmomanometer, with appropriate cuff width for pts arm. After 5 minutes of rest, 1st measurement and 2nd measurements should be taken at least 2 minutes apart using same arm for measurement.

47) Heart Rate- Measured for 15 seconds and recorded in beats per minute.

48) Pulmonary Rales-The presence of a rales more than bibasilar with or without elevated neck pains or a third heart sound gallop.

49) S3 Gallop-Low pitched sound heard at apex in the left decubitus position.
5.5 ENRICHD ECG Procedures

Introduction

At baseline after randomization preferably and after follow-up at 6, 18, and 30 months, a standard supine 12-lead resting ECG should be recorded.

5.5.1 Electrode Position Measuring and Marking

Because it is essential for the study to be able to compare baseline ECG data with subsequent records, a uniform procedure for electrode placement and skin preparation is required. The method and procedure for standardizing electrode locations are outlined below.

The participant, chest bared, is instructed to lie on the recording bed with arms relaxed at the sides. The individual is asked to avoid movements which may cause errors in marking the electrode locations, but encouraged to converse with the technician. Prior experience with electrocardiograms is discussed, as is the purpose of the ECG recording. The participant should be told this is a research ECG to be used for analysis.

For best electrode/skin interface, place the electrodes on the skin at least 2-3 minutes before taking the ECG.

A good felt tip pen is used to mark the six chest electrode positions. Wipe the general area of the following 10 electrode sites with a sterile alcohol prep to remove skin oil and perspiration. It is extremely important that care be taken to locate these positions accurately. Therefore, the procedure given below must be meticulously followed. Electrode positions in women with large, pendulous breasts must be determined in relation to the anatomic points described below - as for all participants. The electrodes must then be placed on top of the breast (in the correct position).

Limb Leads

Locate electrode LL on the left ankle (inside).
Locate electrode RL on the right ankle (inside).
Locate electrode LA on the left wrist (inside).
Locate electrode RA on the right wrist (inside).
Electrode V1

Locate electrode V1 in the fourth intercostal space at the right sternal border. This should be at the same level as V2 and immediately to the right of the sternum.

Electrode V2

Locate the sternal angle and second left rib between the index and middle fingers of your right hand. Count down to the fourth rib and identify the fourth intercostal space below it. Locate V2 in the fourth intercostal space immediately to the left of the sternal border.

Electrode V3

Using a flexible ruler, mark the location of electrode V3 midway between the locations of V2 and V4.

Electrode V4

Electrode V4 is located using the E-V6 Halfpoint Method (3). Using a medical tape measure (American Hospital Supply, Cat. No. 30940), measure the distance between the E point and the V6 marking. The tape should be resting lightly on the skin, not pressing into the flesh. The E and V6 marks should clearly be seen above the tape. Without moving the tape, mark the location of electrode V4 midway between E and V6.

Electrode V5

Using a flexible ruler, mark the location of electrode V5 midway between the locations of V4 and V6.

Anterior 5th Interspace Marker (E Point)

Identify the fifth rib and fifth intercostal space below V2 by counting down ribs as described for V2. Follow this space horizontally to the midsternal line and mark this point. This is the "E" point.

Electrode V6
With the chest square held lightly against the body (see Figure 2) locate the V6 electrode at the same level as the E point in the midaxillary line (straight down from the center of the armpit). If breast tissue is over the V6 area, mark the V6 location on the breast.

Do not attempt to move the breast in order to mark V6 on the chest wall.

Figure 2. Location of V6 Electrode Using the Dal-Square

5.5.2 Skin Preparation

Prepare the skin for applying electrodes by wiping with alcohol, then briskly with a gauze pad. If technical problems are observed due to poor electrode contact, it is necessary to do further preparation as described below:

1. With the participant's consent, remove any excess hair from each electrode site on the chest and legs using an electric shaver.
2. At each electrode location in turn, the outer horny layer of the epidermis is removed by gentle dermal abrasion with a piece of 6-0 (220) sandpaper. Only three passes (in the form of an asterisk) at each site using light pressure are required.

If the skin preparation has removed the felt pen marking at any of the electrode sites, these are accurately re-established by carefully repeating the procedure described in Electrode Position Measuring and Marking. It is important that the electrode sites be marked using the exact technique described.

5.5.3 Application of Electrodes

Disposable electrodes or suction cups may be used. When placing each electrode, massage it in a small circular motion to maximize the pre-gel contact with the skin but avoid overlap of gel from one electrode to the next.

Center the four limb electrodes on the inside of the wrist or ankle with the tab for the clip pointing toward the head. Center the six chest electrodes on the chest markings with the tabs pointing down. Do not let the electrodes overlap or touch each other if possible.

Clip the appropriate leadwire to each electrode (Figure 1). Do not pull or jerk tangled wires. To untangle wires, disconnect lead wires from electrodes.

Recording the 12-lead ECG

Hit the record button on your ECG machine. Make sure that a standard 10 mm pulse is recorded as a standard.

5.5.4 Self-Evaluation of Technical Performance

This section allows technicians to monitor their own ECG technique. It is intended to help technicians who are having difficulty meeting the quality standards set by the ECG Reading Center. These data are not intended to be collected by the study.
The technician examines the ECG tracing to estimate the noise level and baseline drift. Based on the requirements of the Minnesota Code, acceptable and unacceptable levels of noise and baseline drift have been established. These levels are scored using the following table:

<table>
<thead>
<tr>
<th>Quality Grade</th>
<th>Noise (mm)</th>
<th>Overall Drift (mm)</th>
<th>Beat-to-beat Drift (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt; .25</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>2</td>
<td>&lt; .50</td>
<td>&lt; 2</td>
<td>&lt; 1.5</td>
</tr>
<tr>
<td>3</td>
<td>&lt; 1</td>
<td>&lt; 3</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>4</td>
<td>&lt; 2</td>
<td>&lt; 4</td>
<td>&lt; 3</td>
</tr>
<tr>
<td>5</td>
<td>≥ 2</td>
<td>≥ 4</td>
<td>≥ 3</td>
</tr>
</tbody>
</table>

The grade levels given in this table are related to the ability of the analysis program to achieve the required accuracy. **Quality Grade 5 is unacceptable.** ECGs of Quality Grade 5 must be deleted from the machine's memory and retaken immediately.

1. First, the tracing is examined for obvious errors such as right arm/left arm and other common lead misplacements (see Figure 3, negative p-waves in I indicate lead switch). These ECGs must be deleted from the machine's memory and retaken immediately.

Figure 3. Right Arm/Left Arm Lead Switch
2. The Quality Grade for noise is obtained by measuring the noise level as vertical peak-to-peak values in terms of number of small paper divisions (smallest grid squares). Note that recording sensitivity is 1 mv per centimeter, (one small paper division = 1 mm = 0.1 mv). A noise level of more than 2 small paper divisions (> 0.2 mv peak to peak) is unacceptable (Figure 4).

3. The Quality Grade for overall drift is obtained by searching each of the 12-leads for the maximum and minimum baseline levels within that lead (as determined by the PR and/or TP segments) over the 10 second recording and measuring the vertical distance between them. A distance of more than 4 small paper divisions is unacceptable (Figure 5).

4. The Quality Grade for beat-to-beat drift is determined by searching for the pair of successive QRS complexes having the largest amplitude difference (vertical distance) between successive PR segments. A difference of more than 3 small paper divisions (> 0.3 mv) indicates an unacceptable record (Figure 6).

Improvement in technical quality will indeed result if the prescribed procedure for electrode position marking, electrode and skin preparation, electrode replacement and equipment use are carefully followed. Baseline drift problems, which are essentially caused by poor electrode-skin contact are particularly easy to remedy, as is 60-cycle interference.

Sixty-cycle interference is characterized by perfectly regular fine oscillations occurring at the rate of sixty per second (Figure 7).

Electrical equipment of any kind may be the source of AC interference on an ECG in all leads or only certain ones. Check quality of skin preparation and electrode contact. Check leadwires and resecure attachment of the alligator clip to the electrode. Make sure participant does not touch any metal part of the bed or other equipment. Proximity to a wall with hidden wiring or a partially broken cable may also cause this problem.

Muscle Tremor causes irregular oscillations of low amplitude and varying rapidity superimposed upon the ECG waveform (Figure 8). Muscle tremor is the involuntary muscle activity of a participant whose state is tense, apprehensive, or uncomfortable. This is why a clear explanation of the electrocardiogram test and reassurance are necessary for the participant. The participant is asked if the temperature of the room is too low for her/him and is covered with a blanket if so.

5.5.5 Original Hard Copy Record

The original 12-lead ECG record is copied and the copy filed at the field center. The original is sent to the coordinating center. Make sure the patient's ID number is on each.
Figure 4. Unacceptable Noise Level

Figure 5. Unacceptable Overall Baseline Drift

Figure 6. Unacceptable Beat-to-Beat Baseline Drift
Figure 7. Sixty-Cycle Interference

Figure 8. Artifact Caused by Muscle Tremo
5.6 Follow-up and End Points Data Collection

Since the primary objective of the ENRICHD 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 social support, medical information must be collected uniformly on all patients who experience suspected end points during the course of the trial to evaluate outcomes. Secondary objectives include evaluation of the effects of the intervention on a number of medical endpoints of interest which also must be supported by the underlying data. This chapter describes the forms used to document those endpoints, and the procedures that the Events Classification Committee will follow in review of reported events. Clinical center staff need to be alert to detection of potential primary and secondary endpoints, either through direct patient contact at a follow-up visit, or via secondary sources (newspapers, electronic media, etc.) on an ongoing basis for the duration of the trial.

5.6.1 Primary Endpoint

The primary endpoint of this study is the first occurrence of a nonfatal myocardial infarction or mortality for any reason (“all cause”).

5.6.2 Secondary Medical Endpoints

The secondary medical endpoints in this study are:

1. All cause mortality (death of the patient from any cause)
2. Cardiovascular mortality (due to sudden death, fatal MI, or intractable heart failure death)
3. Recurrent nonfatal myocardial infarction (occurrence of another nonfatal MI since baseline)
4. Revascularization procedures (PTCA, CABG, cardiac transplantation)
5. Cardiovascular hospitalizations (a hospitalization having a discharge ICD-9 code of 401, 404, 411-414, 428 or 429 is a cardiovascular hospitalization)
6. HCFA quality of care process indicators (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)
7. Risk factor profile change (blood pressure change, self-report of compliance with medical regimens, and smoking status)

(See Appendix F of the ENRICHD protocol which contains specific definitions for the primary and secondary medical endpoints outlined above.)
5.7 Event Reporting and Submission of Events

The documentation for potential endpoint events that will be collected will be the occurrence of death, suspected MI, other cardiovascular events, and revascularization. Reporting of events to the Coordinating Center can occur directly as the result of information collected during routine follow-up visits and phone calls, in which 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. Once a suspected event is detected by the clinical center, complete Notification of Event (NOE) form to alert the Coordinating Center that a potential event has been detected, and that more detailed information is to follow pending a chart review and collection of supporting documentation surrounding the event. The NOE form lists the specific information required to be sent to the Coordinating Center for compilation into a case file for the Event Classification Committee to review. Detailed information concerning a hospital admission is to be recorded on a separate Hospitalization and Secondary Events forms (HOS) along with a copy of the discharge summary and determination by the PI or ENRICHD cardiologist. In the event of a patient death, obtain a copy of the official death certificate and complete a Death Certificate form (DCI) along with a copy of the discharge summary and determination by the PI or ENRICHD cardiologist. Reports of non-fatal events can also be initiated by the patient notifying the clinical center directly of a hospitalization, and will constitute a back-up method of notification. Specific instructions for completion of the end points related forms are detailed in section 5.8 of this chapter.

5.8 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 Events Classification Committee. The committee will be chaired by a cardiologist and consist of eight cardiologists as members with at least one representative from each clinical center. The committee will meet on a six month basis to adjudicate all deaths and potential MIs. Each suspected event will be reviewed by two cardiologists who are not affiliated with the clinical center from which the patient was recruited. Each reviewer will be provided with summary and original materials to support determination of end points. Information will be provided from hospital records, including enzyme measurements, and accompanying ECG strips. In the event of death, relevant records will be obtained from hospital, or primary care physician, and a copy of the death certificate will be abstracted. The Coordinating Center will blind all supporting end points information submitted to it so that no indication of treatment assignment remains. Full agreement on the primary and secondary events by both reviewers must be reached in order to classify an event. In case of a disagreement by the reviewers, a third independent reviewer will adjudicate the end points determination. The judgment of the adjudicator is final in event classification. The decisions of the committee will be facilitated by development of case law guidelines for standardized classification of end points.

5.9 Collection of End Points Measurements
Medical measurements for the determination of end points are recorded by the clinical center on the Notification of Admission, Hospitalization and Secondary Events, and Death certificate forms (see section 5.8.1). The Events Classification Committee will record the results of their determination on the Clinical Events ECG (ECG), and Clinical Events Review (CER) forms during a semi-annual meeting (see section 5.8.2). Detailed explanation for completion of the two groups of end points data collection forms follows. For all suspected events, and without specific request from the Coordinating Center, each clinic will forward the copies of ECGs and ECG reports clearly labeled by patient ID number along with supporting HOS and/or DCT forms abstracted from hospital records, death certificates, or coroner’s reports.

5.9.1 Follow-up, Notification of Event, Hospitalization, and Death Reporting Forms

Data collection forms associated with routine follow-up of the patient for monitoring any change in health status over the course of the trial are the Follow-up Examination (FUX), Notification of Event (NOE), Hospitalization and Secondary Events (HOS), and Death Certificate forms (DCT). The scheduled collection of information in clinic during a follow-up examination is at 6 months and 18 months after randomization, and annually after that period (30, 42, 54 months post-randomization).

The remainder of the forms are event driven, only completed upon the basis of patient self report of hospitalization, or based on reports from the patient’s physician.

5.9.1.1 Instructions for Completing the Follow-up Examination Form (FUX Version A)

This Follow-up Examination form is to be completed during routine scheduled follow-up of the ENRICHD patient. Responses to questions 1, 2, and 17-21 flag circumstances where a suspected end point may have been reached. Instances of suspected endpoints include whenever a hospital admission or specific cardiac related procedure occurs.

Center: use 2 digit ENRICHD center ID number

Patient ID: use 7 digit patient ID number

Patient Initials: first middle and last initials (enter “X” if patient has no middle initial)

Visit Code: use boxes provided to identify visit number

Date: use 2 digit codes for month, day and year

Staff ID number: use your assigned ENRICHD 3 digit staff ID#

Health Status and Risk Factor Changes

1) Hospitalization: Has the patient been hospitalized since the last visit? If, Yes, first complete a preliminary notification of event form, and then complete Hospitalization Form, and include send supporting end points review information to the coordinating center. Last visit is the last ENRICHD contact including scheduled phone contacts which are given visit numbers.
2) Serious Illness: ER - Has the patient been to the emergency room since the last ENRICHD Visit, but did not require hospitalization?

3) Angina: Since the last ENRICHD Visit, has the patient had angina; if so, characterize in questions 3a, 3b, 3c. Be aware that all chest pain is not angina and that ischemic symptoms or anginal equivalents need not be typical but may be shortness of breath or fatigue, especially in older patients. Specific questions should be handled locally by the ENRICHD physician.

4) Cigarette Smoking: Any self report by the patient of smoking within the last week. Obtain confirmation from the patient's confidant.

5) Drinking: If the patient reports any alcohol intake within the last week, check yes. If yes, ask the patient how many drinks they had? Enter the average number of drinks consumed. If the patient does not report any alcohol intake during the week check the corresponding box. Any self report of alcohol consumption within the last week should be noted. Obtain confirmation from the patient's confidant about the alcohol consumption.

6) Fatigue: Early onset with minimal physical exertion, or at rest.

7) SOB: Any report of shortness of breath either at rest or with minimal physical effort.

8) Orthopnea or PND: Report if patient is having difficulty breathing at night (this is usually episodic and called PND, paroxysmal nocturnal dyspnea), or sleep using pillows to elevate themselves while sleeping at night (this need is known as orthopnea).

9) Hours employed for wages: Probe to see if the patient has returned to work and is earning a wage. If retired at baseline, or on disability, confirm employment status. Record average number of hours worked per week. Record 0, if not presently working or retired.

10) Participation cardiac rehabilitation: Answer yes if during the period since the last visit, has the patient participated in a supervised cardiac rehabilitation programs.

11) Regular exercise: Record self report of patient exercising regularly on a weekly or daily basis, not monthly.

12) Counseling, psychotherapy, or stress management: Answer yes if patient is engaging in any of these activities and is professionally supervised. Counseling and therapy includes therapy through the ENRICHD intervention.

13) Diet modification: Ask the patient if he/she is presently following any kind of dietary modification. If so, was the diet modification plan made on the advice of a doctor or health care worker? Record any modification of the patients diet to follow the AHA active partnership guidelines, and the change is effected, not if only contemplated.
14) Cognitive strategies: Record self report of patient practicing CBT strategies to counter depression or low social support. Is the patient involved in any routine that is designed to help them feel better about her/himself. The question is posed in terms of problem solving to avoid complex terms possibly unfamiliar to patients in usual care or the intervention arm.

15) Medications for anxiety or depression: Ask the question, “Are you taking any medication for anxiety or depression?” If yes, ask the patient when they started to take the medication? Enter the name of the medication, dose, and if use is current at time of the visit. Please note that medicine being recorded should be for anxiety or depression. Any other medications that are taken for other reasons should not be included.

16) Depression: Ask if patient is feeling low, or depressed. This is by patient report only; it is not a clinical diagnosis to be made by the ENRICHD staff. Probe to determine duration of this reported episode if reported.

Any of the following procedures in questions 17-21 should alert you that a suspected event may have occurred, and a hospitalization form will need to be completed with supporting documentation from the patient’s medical records.

17) CABG: Coronary artery bypass graft.

18) IV Thrombolytic Therapy: IV therapy administering tPA or streptokinase for example to improve coronary circulation.

19) PTCA: Balloon angioplasty of any coronary arteries.

20) Coronary Angiogram: Use of this diagnostic imaging procedure may indicate worsening condition of patient, or associated with a related surgical intervention.

21) Vascular Stent: Placement of this device during an interventional procedure may also indicate worsening condition of patient.

22) Other Cardiovascular procedure: Any other reported cardiovascular procedure.

22-27) Physical Exam: Repeat of the physical exam given at baseline visit. Height, weight, BP, heart rate, heart sounds recorded using the same procedures described earlier under the baseline examination.

28) Killip Class: Determination of Killip class based on the exam as described in the baseline section of the manual of operations.

29) NYHA CHF Class: Determination of CHF severity, using 1-4 scale and 0 if no signs, and not on medication for heart failure as described at baseline. This NYHA Classification refers to the patient’s typical status over the last two weeks prior to hospitalization (or to the acute episode that lead to hospitalization).
**Class I No limitation:** Ordinary physical activity does not cause undue fatigue, dyspnea, or palpitations, e.g., can walk one level mile without symptoms.

**Class II Slight limitation of physical activity:** Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitations, dyspnea, or angina, e.g., walking two level blocks or one flight of stairs causes symptoms.

**Class III Marked limitation of physical activity:** Although the patient is comfortable at rest, less than ordinary activity will lead to symptoms, e.g., walking from the living room to the bedroom causes symptoms.

**Class IV Inability to carry on any physical activity without discomfort:** Symptoms of congestive heart failure are present even at rest. With any physical activity, increased discomfort is experienced.

30-50) Medications: Use of medications within the last two weeks. Encourage patient to bring pill bottles into clinic so that actual drug names can be verified instead of relying on patient recall. This should also include over the counter medications (which may include ASA which is being taken for prescription, but is purchased over the counter).
5.9.1.2 Instructions for Completing the Notification of Event Form (NOE, Version A)

This form is to be completed whenever a suspected end point has been reached when hospital admission or death occurs. This form should be completed, entered on the computerized Data Management System (DMS), and also faxed to the coordinating center which will then notify the End Point Clinical Event Review Committee chairman.

Center: use 2 digit ENRICHD center ID number

Patient ID: use 7 digit patient ID number

Patient Initials: first middle and last initials

Visit Code: use boxes provided to identify visit number

Sequence Number: use boxes provided to identify sequential event number

Date: use 2 digit codes for month, day and year

Staff ID number: use your ENRICHD 3 digit staff ID#

1) Complete date of event using 2 digit code for month, day and year.

2) Indicate whether the event is fatal cardiac, fatal non-cardiac, or a non-fatal event.

3) For hospitalized events, enter the most appropriate class of suspected event based on available information.

4) Check appropriate boxes for ancillary documents to be forwarded to Clinical Event Review Committee via the Coordinating Center.
5.9.1.3 Instructions for Completing the Notification of Event Form (NOE, Version B)

The same procedures for the Version B Notification of Event form apply whenever a suspected end point has been detected by clinical center personnel (hospital admission or patient death). This form is to be completed whenever a suspected end point has been reached when hospital admission or death occurs. This form should be completed, entered on the computerized Data Management System (DMS), and also faxed to the coordinating center which will then notify the End Point Clinical Event Review Committee chairman. The effective date for use of this form begins August, 1997.

Center: use 2 digit ENRICHD center ID number
Patient ID: use 7 digit patient ID number
Patient Initials: first middle and last initials
Visit Code: use boxes provided to identify visit number
Sequence Number: use boxes provided to identify sequential event number
Date: use 2 digit codes for month, day and year
Staff ID number: use your ENRICHD 3 digit staff ID#

1) Complete date of event using 2 digit numeric codes for month, day and year.

2) Indicate whether the event is (a) fatal cardiac/fatal non-cardiac, or (b) a non-fatal event of either cardiac or non cardiac nature. If the case is not totally clear-cut, assume that the event is cardiac so that it can be reviewed.

3) For hospitalized events, check all suspected events based on available information.

4) Enter responses in appropriate boxes for ancillary documents to be forwarded to Clinical Event Review Committee via the Coordinating Center. If documents are not available to review for this event enter code letter “N”, or if not applicable enter “A”. Send complete information about event to the Coordinating Center once sufficient documents become available to answer responses on the Hospitalization and Death Certificate forms. Should information about an event (e.g., missing enzymes or hard to located ECG’s) suddenly become available, update the NOE hardcopy and change the electronic version as well. Forward the updated documents to the Coordinating Center for inclusion in the patient event file.
5.9.1.4 Instructions for Completing Death Certificate Forms (DCT Version A)

In the case of a patient death, cardiac arrest records, related hospitalization and discharges summaries should be appended to the death forms. In addition, records from the ambulance, paramedics or emergency medical technician should be obtained and forwarded along with the death form to the Coordinating Center. If the death occurred in hospital, a Hospitalization form should also be completed. If death occurs outside the hospital, a Notification of Event (NOE) should accompany the Death Certificate (DCT) form.

**Center:** use 2 digit ENRICHD center ID number  
**Patient ID:** use 7 digit patient ID number  
**Patient Initials:** first middle and last initials  
**Visit Code:** use boxes provided to identify visit number  
**Date:** use 2 digit codes for month, day and year  
**Staff ID number:** use your ENRICHD 3 digit staff ID#

**Information from Death Certificate**

1) **Death certificate number:** This should be obtained from the State death certificate.

2) **Social security number:** This should be obtained from the death certificate and matched to the to the social security number obtained from the initial enrollment form. The coordinating center should be notified of any discrepancies between the two.

3) **Date of birth:** Use 2 digit code for month, day and year

4) **Date of death:** Use 2 digit code for month, day and year

5) **Age at death:** Use age at last birthday in years

6) **Time of death:** Use 24 hr format

7) **Where did the decedent die?** ENRICHD affiliated hospitals can be identified from directory of affiliated hospital (where does the list exist in the manual). The address of place of death is listed on the death certificate; should include apartment number, street, number, city, state and zip code.
8) If **decedent died in hospital** circle place of death within the hospital:

   - **A** = dead on Arrival
   - **E** = if died after admission into ER
   - **I** = if died as an Inpatient
   - **N** = None of the above
   - **R** = if not Recorded

9) **Name and location of hospital:** Should include full name, city location and state.

10) If this were a coroner nurse or medical examiner’s case check “yes” or “no”. If no, go to item 12.

11) Please list a name of the coroner’s or medical examiner’s complete address including street number, city, state and zip code. If the answer to number 10 is yes.

12) Indicate by “yes” or “no” whether or not an autopsy was performed.

13) Physician's belief of the **cause of death** record most appropriate code from group below:

   - **A** = MI
   - **B** = Sudden Death
   - **C** = Intractable failure
   - **D** = Stroke
   - **E** = Vascular non-cardiac
   - **F** = Unobserved
   - **G** = Non-Cardiovascular
   - **H** = Malignancy
   - **I** = Suicide
   - **J** = Accident
   - **K** = Other

14) Please use **ICD9 codes for underlying cause of death**.

15) **ll other listed ICD9 codes** on the death certificate should be included.

16) Transcribed directly from the death certificate the immediate cause of death and **two other diagnosis that may be listed as due consequences of the immediate cause of death**.

17) Transcribe other significant conditions as they were recorded on the death certificate.

18) **Name and address of certifying physician.**

19) Check off whether emergency medical services (Paramedical services) report is enclosed.

20) Check off whether the copy of the **death certificate is enclosed** with the form.

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**5.9.1.5 Instructions for Completing Hospitalization and Secondary Events Form**

(HOS, Version A)
The follow up hospitalization form should be completed at the end of hospitalization and in the case of death a copy of the death certificate should be obtained. These should be forwarded to the coordinating center. Ancillary documents to be included in the case of a hospitalization include copies of all ECGs, a complete record of all cardiac enzyme determination including CKMB, LDH1, LDH2 values, and troponin I or T values where available.

Discharge summaries, emergency room notes, procedural reports such as coronary angiograms or echocardiograms and operative procedural note in the case of angioplasty or coronary artery bypass graft should be appended to the hospitalization form. In the case of a death, cardiac arrest records, related hospitalization and discharges summaries should be appended to the death forms. In addition, records from the ambulance, paramedics or emergency medical technician should be obtained and forwarded along with the death form.

**Center:** use 2 digit ENRICHD center ID number

**Patient ID:** use 7 digit patient ID number

**Patient Initials:** first middle and last initials

**Visit Code:** use boxes provided to identify visit number

**Sequence Number:** use boxes provided to identify event number, beginning with 01

**Date:** use 2 digit codes for month, day and year

**Staff ID number:** use your ENRICHD 3 digit staff ID#

**A. DISCHARGE DIAGNOSIS**

1) **Name and location of hospital:** use complete hospital name, city and state

2) **ENRICHD-affiliated hospital:** please refer to ENRICHD-affiliated hospital list to determine if this hospital is in an affiliated hospital, if so enter lower case “a” in the given box, if not enter “b”.

3) **Medical record number:** please use the medical record number of the admitting hospital

4) **Indicate whether the hospital chart has been located** by checking the appropriate box

5) **Date of hospital arrival:** use 2 digit code for month, day and year

6) **Time of arrival at hospital:** use emergency room time of admission, except for patients who are directly admitted. Use 24 hour format.

7) **Date of discharge:** use 2 digit codes for month, day and year

8) **Please complete the disposition of the patient on discharge** and fill in the appropriate letter in the given box.

9) **Record causes of death** as they appear on the discharge summary. This does not pertain to death certificate causes of death

10) **For patients transferred** from another hospital record the entire hospital name, city and state for the referring hospital
11) **Discharge Diagnosis:** for the boxes designated by the letters “A thru E”, fill in the hospital discharge codes as they appear on the front page of the discharge summary. The actual discharge diagnosis should be written as they appear the lines designated by the letters “F thru J”; these should correspond directly to the codes that are listed in the boxes designated to “A thru E”.

12) **CHD refers to Coronary Heart Disease.** It will include diagnoses such as acute myocardial infarction, non Q wave myocardial infarction, stable angina pectoris and unstable angina. It may also include diagnosis of ventricular or supraventricular arrhythmia and heart failure. As best as you can determine, estimate the time from the onset of the presenting complaint to arrival at this hospital.

13) **CHD events** will include recurrent angina pectoris, subsequent myocardial infarction, sudden cardiac death, and heart failure. Indicates as follows:

   - **A** - indicate the date of the CHD event
   - **B** - whether it occurred following a surgical procedure
     (if yes, complete items C & D)
   - **C** and **D** - indicate the date and time of surgery
   - **E** - list the type of surgery

14) Ascertain the presence of pain is consistent with angina pectoris occurring any time within 72 hours prior to arrival or during the hospitalization. If this is answered “yes”, list as follows:

   - **A** - the date of onset of pain using 2 digit code
   - **B** - whether the pain was in the chest
   - **C** - whether nitrates were used to treat the episode
   - **D** - whether the nitrate is effective and
   - **E** - whether the physicians indicated in the medical record as to whether this was felt to be of non cardiac origin

15) Indicate the actual level of **cardiac enzymes drawn within 1st 24 hours** of arrival, or after a suspected event and indicate the appropriate unit as follows:

   - **A** - peak CK would refer to the highest value of CK reported in the first 24 hours after arrival
   - **B** - CK ULN refers to the upper limited normal for that laboratory item
   - **C** - peak CKMB would be the highest absolute CKMB for the first 24 hours after admission, also indicate if reported as CKMB index and indicate the appropriate units
   - **D** - CKMB ULN represent the upper limit of normal for your laboratory
   - **E** - the peak LDH value in units per liter
F - the upper limit of normal for LDH for your laboratory
G - LDH1 - please use the peak value within the first 24 hours of arrival, indicate units
H - LDH2 - use the peak value within the first 24 hours, indicate the appropriate units
I - if Troponin T is used in your hospital please indicate the peak value in milligrams per ml.
J - if Troponin I is used in your hospital please indicate the peak value in nanograms per liter.
K - indicates the date of enzyme determination during day one.

16.) **Diagnostic Cardiac Enzymes occurring after 1st 24 hours of Arrival, or after a suspected in hospital CHD event:** these items should be completed as in item 15. The highest values on day 3 or after an in-hospital CHD event should be used.

17) This should be completed as in item 15 and using the highest value obtained on the last day after arrival or after an in-hospital CHD event again, the highest values should be used.

18) Indicate the **first codable ECG** after arrival or in-hospital CHD event:

A - whether or not a **codable ECG** is available for this hospitalization
B - indicate the date of the first ECG
C - indicate whether there are other codable ECGs for this hospitalization

19) Indicate whether or not a **third day codable ECG** is available after arrival or after in-hospital CHD event:

A - indicate the date of the third ECG
B - indicate whether there are any other codable ECGs hospitalization

20) Indicate the date of the **last codable ECG** after arrival or after in-hospital CHD event.

21) Indicate the number of ECGs sent for end points coding.

### 5.9.1.6 Instructions for Completing Hospitalization and Secondary Events Form (HOS, Version B)

The effective date for use of the version B Hospitalization and Secondary Events forms is July 1997. The same circumstances and supporting documentation surrounding a suspected event apply in the use of the HOS version B form. Additional response areas appear to capture information about the original and up to two transfer for an event.

**Center:** use 2 digit ENRICHD center ID number

**Patient ID:** use 7 digit patient ID number
Patient Initials: first middle and last initials

Visit Code: use boxes provided to identify visit number

Sequence Number: use boxes provided to identify event number, beginning with 01

Date: use 2 digit codes for month, day and year

Staff ID number: use your ENRICHD 3 digit staff ID#)

A. DISCHARGE DIAGNOSIS

1) Number of hospitalizations related to event: use 1 digit code, enter 1 if no transfer.

2) Name and location of first hospital: use complete hospital name, city and state for the first (or only) hospital in the treatment series.

3) ENRICHD-affiliated hospital: please refer to ENRICHD-affiliated hospital list to determine if this hospital is in an affiliated hospital, if so enter lower case “a” in the given box, if not enter “b”.

4) Medical record number: please use the medical record number of the admitting hospital

5) Indicate whether the hospital chart has been located by checking the appropriate box

6) Date of hospital arrival: use 2 digit code for month, day and year.

7) Time of arrival at first hospital: use emergency room time for admission, except for patients who are directly admitted. Use 24 hour format.

8) Date of discharge at first hospital: use 2 digit codes for month, day and year.

9-15) Documentation of second hospital in treatment series: skip if no transfers; otherwise, complete as in questions 2 through 8 above.

16-22) Documentation of third hospital in treatment series: skip if not applicable; otherwise, complete as in questions 9 through 15, and 2 through 8 above.

23) Please complete the disposition of the patient on final hospital discharge and fill in the appropriate letter in the given box.

24) Record causes of death as they appear on the discharge summary. This does not pertain to death certificate causes of death.

25) Discharge Diagnosis: for the boxes designated by the letters “A thru J”, fill in the hospital discharge codes as they appear on the front page of the discharge summary. The actual discharge diagnosis should be written as they appear using the lines lines designated besides...
the corresponding ICD-9 code. The diagnoses must correspond directly to the codes that are listed in the boxes labeled A thru J.

26) CHD refers to Coronary Heart Disease. It will include diagnoses such as acute myocardial infarction, non Q wave myocardial infarction, stable angina pectoris and unstable angina. It may also include diagnosis of ventricular or supraventricular arrhythmia and heart failure. As best as you can determine, estimate the time from the onset of the presenting complaint to arrival at this hospital.

27) CHD events will include recurrent angina pectoris, subsequent myocardial infarction, sudden cardiac death, and heart failure. Indicates as follows:

A - indicate the date of the CHD event
B - whether it occurred following a surgical procedure (if yes, complete items C & D)
C and D - indicate the date and time of surgery
E - list the type of surgery

28) Indicate if pain is consistent with angina occurred any time within 72 hours prior to arrival or during the hospitalization.

29) Indicate the actual level of cardiac enzymes drawn within 1st 24 hours of arrival, or after a suspected event and indicate the appropriate unit as follows:

A - peak CK would refer to the highest value of CK reported in the first 24 hours after arrival
B - CK ULN refers to the upper limited normal for that laboratory item
C - peak CKMB would be the highest absolute CKMB for the first 24 hours after admission, also indicate if reported as CKMB index and indicate the appropriate units
D - CKMB ULN represent the upper limit of normal for your laboratory
E - the peak LDH value in units per liter
F - the upper limit of normal for LDH for your laboratory
G - LDH1- please use the peak value within the first 24 hours of arrival, indicate units
H - LDH2 - use the peak value within the first 24 hours, indicate the appropriate units
I - if Troponin T is used in your hospital please indicate the peak value in milligrams per ml.
if Troponin I is used in your hospital please indicate the peak value in nanograms per Liter.

- indicates the date of enzyme determination during day one

30) **Diagnostic Cardiac Enzymes occurring after 1st 24 hours of Arrival, or later than 24 hours after a suspected in-hospital CHD event:** these items should be completed as in item 29. The highest values on day 3 or after an in-hospital CHD event should be used.

This should be completed as in item 29 and using the highest value obtained on the last day after arrival or after an in-hospital CHD event again, the highest values should be used. *Skip if no further enzymes drawn prior to 48 hour or peak enzyme values after day 3.*

32) Indicate the first, i.e., legible codable ECG after arrival or in-hospital CHD event:

A - whether or not a codable ECG is available for this hospitalization
B - indicate the date of the first ECG
C - indicate whether there are other codable ECGs for this hospitalization

33) Indicate whether or not a third day codable ECG is available after arrival or after in-hospital CHD event:

A - indicate the date of the third day ECG
B - indicate whether there are any other codable ECGs hospitalization

34) Indicate the date of the last codable ECG after arrival or after in-hospital CHD event.

35) Indicate the number of ECGs sent for endpoints coding.

36-46) **Medications prescribed at discharge:** check medication prescribed for patient at time of discharge for this hospitalization.

### 5.9.2 End Points Classification Forms

The Clinical Event Review (CER) and Clinical ECG Interpretation (ECG) forms are completed by members of the Events Classification Committee during review of information compiled to document suspected events. A blinded events review packet will be compiled for each designated reviewer to use during the semi-annual subcommittee meeting by the Coordinating Center.

#### 5.9.2.1 Instructions on Completing Page 1 of 2 ENRICHD Clinical Event Review and End Point Assignment Form

*This form is to be completed by the blinded reviewers after each individual event review.*
1) **Center:** Use 2 digit ID number

2) **Patient ID:** Use 7 digit patient ID number

3) **Patient initials:** Use first, middle and last initials.

4) **Visit:** Use the 2 boxes provided to identify visit number.

5) **Date form completed:** Use 2 digit codes for month, day and year.

6) **Staff ID:** Provide 2 or 3 digit ENRICHD staff ID number

7) The primary end point of non-fatal myocardial infarction or death should be completed by checking off the appropriate box. Non fatal myocardial infarction should be further differentiated among unrecognized, symptomatic or hospitalized infarction. More than one box may be applicable.

8) In the case of death the appropriate box should be checked and differentiation between noncardiovascular and cardiovascular death should be made. Cardiovascular deaths are to be distinguished among sudden cardiac deaths, death due to MI, death due to heart failure, or other cardiac deaths using definitions provided in the operation manual. Date of death should be completed using 2 digit codes for month, day and year. The time of death should be provided in military time.

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**5.9.2.2 Instructions for Completing Page 2 of 2 ENRICHD Clinical Event Review End Point Assignment Form**

1-6) Identification and date of form should be performed as page one.

7) The observation of a secondary end point should be designated by an appropriate check in the boxes provided and the date should be provided using two digit codes for month, day and year.

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**5.9.2.3 Instructions for ENRICHD Clinical Event Review ECG Interpretation**

1-6) Identification and date of form should be performed as page one.

7) **Baseline:** If this is a baseline ECG at enrollment please indicate by checking the appropriate box.

8) If this is a suspect new clinical event after randomization please check the appropriate box.

9) **Date:** This refers to the date the event occurred, use 2 digit numbers for month, day and year.
10) **Old Q waves:** Indicate the presence of old Q waves used by checking the “yes” box. Please check the appropriate leads in which the old Q was observed.

11) **New Q waves:** New Q waves as defined by modified Minnesota code criteria should be designated by checking the “yes” box. The leads in which they occur should be checked in the appropriated box.

12) **ST segment elevation > 1mm:** Refers to ST segment elevation in excess of 1mm occurring approximately 80 msec after the J point. If present designate by checking off the “yes” box and check off the leads where the ST segment elevation was observed.

13) **ST depression segment > 1mm:** If present please designate by checking off the “yes” box and check off the leads where the ST segment depression was observed.

14) **Final interpretation:** Please indicate whether the ECG diagnostic of either old MI or new MI by using the appropriate yes box.
## Appendix A: ENRICHD Medical Measures Data Collection

<table>
<thead>
<tr>
<th>Name of Form</th>
<th>Form Mnemonic</th>
<th>Time Point</th>
<th>Visit Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tracking</td>
<td>TRK</td>
<td>Screening</td>
<td>01</td>
</tr>
<tr>
<td>CAGE</td>
<td>CAG</td>
<td>Screening</td>
<td>01</td>
</tr>
<tr>
<td>Medical Eligibility</td>
<td>MEA</td>
<td>Screening</td>
<td>01</td>
</tr>
<tr>
<td>Medical History</td>
<td>MHA</td>
<td>Baseline</td>
<td>02</td>
</tr>
<tr>
<td>Baseline Examination (with ECG)</td>
<td>BEA</td>
<td>Baseline</td>
<td>02</td>
</tr>
<tr>
<td>Randomization Worksheet</td>
<td>RAN</td>
<td>Baseline</td>
<td>02</td>
</tr>
<tr>
<td>Telephone Contact</td>
<td>TCF</td>
<td>Follow-up</td>
<td>3, 9, 24, 36</td>
</tr>
<tr>
<td>Follow up Examination with ECG (6, 18, 30, 42 &amp; 54 mo)</td>
<td>FUX</td>
<td>Follow-up</td>
<td>4, 7, 9, 10, 13</td>
</tr>
<tr>
<td>Notification of Event</td>
<td>NOE</td>
<td>Follow-up</td>
<td>per event</td>
</tr>
<tr>
<td>Hospitalization and Secondary Events</td>
<td>HOS</td>
<td>Follow-up</td>
<td>per event</td>
</tr>
<tr>
<td>Death Certificate</td>
<td>DCT</td>
<td>Follow-up</td>
<td>per event</td>
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### Follow-up Visit Collection Schedule

<table>
<thead>
<tr>
<th>Month:</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>30</th>
<th>36</th>
<th>42</th>
<th>48</th>
<th>54</th>
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</thead>
<tbody>
<tr>
<td>Visit #:</td>
<td>03</td>
<td>04</td>
<td>05</td>
<td>06</td>
<td>07</td>
<td>08</td>
<td>09</td>
<td>10</td>
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<td>12</td>
<td>13</td>
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</table>

### Clinic Visit Post Randomization

<table>
<thead>
<tr>
<th>Month:</th>
<th>6</th>
<th>19</th>
<th>30</th>
<th>42</th>
<th>54</th>
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<tbody>
<tr>
<td>Visit #:</td>
<td>04</td>
<td>07</td>
<td>09</td>
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<tr>
<td>Month</td>
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<td>12</td>
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<td>03</td>
<td>05</td>
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