3. EVENT CLASSIFICATION FOR COHORT COMPONENT

3.1 Identification of Events

In addition to information from the three-year clinic visits, three sources of identification of medical events are used for cohort members: (1) death certificates, (2) hospital discharge indexes and (3) annual follow-up interviews. The ARIC Study records the occurrence of several kinds of medical events: (1) hospitalized MI and stroke, and (2) death from CHD, stroke and all-causes. This section describes the identification, investigation and diagnosis of these hospitalized and fatal events. ARIC also records the occurrence of a number of non-hospitalized, non-fatal events, events identified through the routine operations of the ARIC clinics, such as angina pectoris and peripheral vascular disease, including intermittent claudication. These are generally defined using standard instruments, such as the Rose Questionnaire, and their identification and diagnosis are described in other sections of this manual.

The at risk period for an incident event begins at the baseline visit. Computer listings of death certificates and hospital discharges used for community surveillance are matched to the cohort membership list to identify cohort events. Additionally, when the annual follow-up interview indicates that the participant has either died or been admitted to a hospital, the death certificate or hospital record is obtained, and information abstracted onto appropriate forms.

3.1.1 Identification of Hospitalized Events

All hospitalized events occurring in cohort members are identified. Hospital admissions may be identified initially through review of hospital discharge indexes or information elicited during the annual follow-up interview. Hospital chart abstraction is carried out whenever needed to identify MI or stroke. All events discharged with specified diagnostic codes are abstracted onto the Hospital Record Abstraction Form (HRA) and/or the Hospital Stroke (STR) Form (See Appendix 8). In order to assure completeness of ascertainment, the discharge summary information is reviewed for events discharged with certain screening codes more remotely related to MI or stroke. If an MI or stroke is suggested, the chart is abstracted. In addition, all discharge diagnoses for all hospitalizations are recorded.

3.1.1.1 Obtaining Access to Hospital Medical Records

A critical feature of the process of hospitalized event identification among cohort members is obtaining information from medical records. Without complete cooperation of hospitals, the usefulness of event rates in the cohort at any time is limited. Hospital cooperation is sought for the cohort and community surveillance components of the ARIC Study simultaneously. However, the protocol sent to hospital administrators emphasizes the fact that, for cohort members, ARIC obtains signed hospital record release forms.
description of an approach for obtaining hospital cooperation for community surveillance is found in Manual 3, Section 2.2.1. On occasion, there may be a need to carry out special negotiations with out-of-area hospitals where an ARIC Study cohort member was hospitalized.

For both the cohort and the community surveillance components of the ARIC Study, it is important to keep the medical records directors, hospital administrators and cardiologists informed concerning the progress of the project. A periodic newsletter and reprints of publications from the project may help demonstrate the significance of the research and the lack of threat to the hospitals. This is also important because of turnover in staff both for the researchers and the hospitals. Thus the newsletters serve as a reminder to the continuing staff and an introduction to the newly hired staff.

3.1.1.2 Hospital Discharge Index

Eligible hospitalized events are identified from the discharge index of each hospital surveyed. Discharge indices are obtained directly from the hospital or from an indexing service such as CPHA.

When a person is discharged from a hospital, the physician must indicate the major illness from which the patient suffers. Usually one such diagnosis accounted for the hospitalization. This is the primary discharge diagnosis. Other old or new diagnoses may be listed as secondary discharge diagnoses. Discharge diagnoses are coded by the hospital medical records personnel according to the International Classification of Diseases (ICD). Most hospitals subscribe to a service which takes these diagnostic codes and produces an index of discharges classified by code.

The ICD was originally constructed to provide comparable international data on causes of death. It is now extended in many countries for use in coding hospital discharge diagnoses. The extension of the ICD currently being used by hospitals is called ICD9-CM (Clinical Modification). The hospital or "CM" modifications do not alter the basic codes, but provide additional codes so that diagnoses may be classified with more detail. For instance, ICD9 uses the code 410 for acute MI; ICD9-CM adds a decimal point so that location of the MI can be coded (e.g., an anterior wall MI is coded 410.1).

Using the discharge index for each hospital, all hospitalized events occurring in ARIC cohort members are identified. However, only special diagnoses require hospital chart abstraction. Hospital chart abstraction onto the Hospital Record Abstraction Form and/or Hospital Stroke Form is carried out for all of the hospitalizations with the following ICD9-CM primary or secondary discharge diagnosis codes:

1. MI: 402, 410-414, 427, 428 and 518.4
2. Stroke: 430-438

A list of diseases included in these ICD9-CM rubrics is presented in Appendix 9.

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Hospital chart discharge summaries are reviewed for the following screening codes:

1. Diabetes: 250
2. Diseases of the circulatory system (including pulmonary embolism and hypertensive heart disease): 390-459
3. Cardiac surgery: 35-39
4. Cardiac angiography: 88.5
5. Congenital abnormalities of the heart: 745-747
6. Cardiovascular symptoms, signs and ill-defined conditions: 794.3 (Abnormal function study); 798 (Sudden death, cause unknown); and 799 (other).

Should any mention of MI or stroke on the present admission (or synonyms for these conditions) be uncovered by the review of discharge summaries for the above conditions, hospital chart abstraction onto the Hospital Record Abstraction Form and/or Hospital Stroke Form is undertaken. For all other ICD9-CM codes, the discharge diagnoses are obtained from hospital discharge lists and recorded, but hospital records are not obtained or abstracted. A Cohort Eligibility Form (CEL, Appendix 8.1) is used to help determine eligibility.

A number of hospitalized events for cohort members are fatal. Hospital abstracting for these events is the same as for non-fatal events, regardless of whether the ICD9 code for cause of death from the death certificate satisfies the eligibility criteria for fatal events.

3.1.1.3 Hospitalized Events Occurring Outside the Study Community

Review of death certificates or annual follow-up interviews may reveal that the cohort member was hospitalized outside the study area. Hospitalization may occur outside the study area for the following reasons:

1. A major hospital catchment area for the region exists outside of the area (e.g., tertiary care hospital referral centers).
2. Residents who work outside of the geographic area may be admitted to an out-of-area hospital if they have an event requiring admission on an emergency basis.
3. A resident may have an event while in transit outside of the geographic area for recreation or social activities.
4. A cohort member may have moved from the study community.

Every effort is made to identify discharge diagnoses for such events and, if applicable, review the hospital chart. In soliciting access to discharge indexes and, occasionally, medical charts, a letter briefly describing the ARIC cohort study is sent to the hospital administrator as well as the director of medical records, along with a copy of the ARIC hospital record.
release form, signed by the participant at the time of the first exam. In some situations, it is also useful to send an abbreviated protocol. Additional contacts, including telephone conversations, with the hospital administrator or the head of the proper department (cardiology, neurology, etc.) may be necessary. No major obstacles are expected in obtaining access to medical charts, in view of the consent for such access provided by ARIC cohort members.

3.1.1.4 Range of Facilities Covered for Hospitalized Events

Events occurring to cohort members in acute care hospitals are investigated, regardless of where the hospital is located. Events in other institutions providing medical care (such as nursing homes, rehabilitation hospitals, long-term chronic disease hospitals and psychiatric hospitals) are not investigated. Cohort events in hospitals in the study community are identified by review of the discharge indexes from these hospitals and by the annual follow-up interview. The annual follow-up interview also allows identification of events occurring in, or leading to admission to acute care hospitals out of the study community. Events in out-of-area hospitals will generally have to be investigated by requesting a complete copy of the medical record to be mailed to the Field Center.

3.1.2 Identification of Deaths

3.1.2.1 Death Certificates

All deaths in the United States must be recorded on a death certificate which is filled out by a physician, medical examiner or coroner. The death certificate is a legally-mandated, public document which is filed in the county of the decedent's residence. A copy is also filed with the state. If a person dies away from his usual residence, a copy of the death certificate is (eventually) returned to the decedent’s county of residence for filing and is also filed at the state health department. In each state health department, trained nosologists code the cause of death given on the death certificate according to the International Classification of Diseases (ICD). The 9th revision of the ICD (ICD9) is currently used.

Each of the four states containing the ARIC communities assigns the specific "underlying cause of death" from the nosologist's coding of the death certificate using the Automated Classification of Medical Entities (ACME) system. Each ARIC center obtains a monthly printout of deaths in the community, from which cohort deaths are identified. Deaths occurring in cohort members are also identified if the member has moved out of the study community. Methods include systematic review of death certificates, annual follow-up interview, hospital chart review, use of obituary notices and other means. The corresponding death certificate is located and abstracted onto the ARIC Death Certificate Form (DTH), included in Appendix 8.3. ICD9 codes for both the underlying and contributory causes of death are recorded for all deaths, thus allowing computation of death rates for the underlying cause, as well as the contributory causes. This increases comparability between ARIC Study communities, as coding of death certificates and the decision to assign a cause to the underlying category may vary from community to community.
3.1.2.2 Deaths Occurring Outside the Study Community

Deaths outside of the study area but within the state are included on State Health Department monthly printouts, but some delay between the death and death registration is expected. The delay for out-of-state deaths is even greater, and they may appear only on final death files at the State Health Department. If the death certificate file is reviewed for the ARIC Study prior to receipt of the out-of-area certificates, a subsequent review is undertaken to identify these deaths. If the location of an out-of-area death is learned through the annual interview with a participant’s proxy, a copy of the death certificate can be obtained directly.

Deaths occurring outside the study community are also identified through the National Death Index and, in some centers, by monitoring of obituaries.

3.1.2.3 Identification of Deaths Requiring Special Investigation

Deaths in cohort members which occur out-of-hospital (as defined in Section 3.2.1.2) require a special investigation to determine whether or not they died of CHD if their death certificates have any of the following ICD9 codes for the underlying cause:

250, 401, 402, 410-414; 427-429, 440, 518.4, 798 and 799

For a listing of disease categories see Appendix 9.

Deaths in hospitalized cohort members which occur before an ECG or a complete set of enzymes is obtained also require special investigation, if the death certificate has one of the death certificate codes as shown.

The special investigation required for these deaths is described in Section 3.2.1.2.

3.2 Event Investigation

For the hospitalized events of MI and/or stroke, investigation entails review of the hospital record. Investigation of the fatal events occurring in cohort members (Section 3.1.2) includes review of the death certificate and hospital record where available. For out-of-hospital deaths and some inadequately diagnosed in-hospital events (defined in Section 3.2.1.2), investigations include physician questionnaires, interviews with next-of-kin and collection of other information.

3.2.1 Procedures for Fatal Events

The Cohort Eligibility Form and the Death Certificate Form are completed for all fatal events occurring in cohort members. One or more of the following forms may also have to be completed: (1) Hospital Record Abstraction Form (HRA), (2) Hospital Stroke Form (STR), (3) Informant Interview Form (IFI),
(4) Physician Questionnaire (PHQ), (5) Coroner/Medical Examiner Report Form (COR), and (6) a photocopy of the Autopsy Report (AUT). A Cohort Event Investigation Summary Form (CEI) is used to keep track of forms that are needed. Copies of these forms are included in Appendix 8.

The Death Certificate Form is completed and submitted to the Coordinating Center prior to or concurrent with submission of other forms. Occasionally it is necessary to obtain certificates for deaths occurring out-of-state to study area residents by writing to the state in which the death occurred.

Some proportion of fatal events -- either in-hospital or out-of-hospital -- are coroner or medical examiner's cases. This means that the county coroner or state medical examiner has performed an investigation of the circumstances of death in order to ascertain whether the causes were natural. In this case, the coroner/medical examiner signs the death certificate. In general, the coroner/medical examiner takes cases of unexpected death where no physician was in attendance during the 24 hours prior to death. During this investigation, the coroner/medical examiner may or may not perform an autopsy. Any death where a legal question is likely to arise (e.g., after surgery, during an automobile accident, etc.) will probably be a coroner/medical examiner case. If the death is certified by a coroner/medical examiner, the Coroner/Medical Examiner Form is completed and submitted to the Coordinating Center. When an autopsy is performed, the Autopsy Form is completed.

Specific procedures for investigating in-hospital and out-of-hospital deaths and requirements for completion of the other forms listed above are given in the next two sections.

3.2.1.1 In-Hospital Deaths

In-hospital deaths may be identified initially from death certificates or hospital discharge indexes. Hospital records for these events are abstracted if eligible as hospitalized events according to the rules described in Section 3.1.1.2. The Death Certificate Form is also completed and sent to the Coordinating Center for all deaths.

If the in-hospital death is initially identified from the hospital discharge index, the death certificate printout must be cross-checked to avoid duplication. If the in-hospital death is initially identified from the death index, the hospital discharge index must be cross-checked. Occasionally the hospital lies outside the catchment area for the ARIC Study community. In this case, this fact is noted on the Death Certificate Form and an attempt is made to find and, if eligible, abstract the hospital record.

Cohort members who die in the emergency room, are dead on arrival at the hospital, or are admitted without vital signs are reclassified as out-of-hospital deaths (as defined in Section 3.2.1.2). Only the administrative data of the Hospitalized Event Form are recorded for patients without vital signs. If the death is first identified from the death index and if the death certificate indicates "dead on arrival," an attempt is made to find the hospital record in order to verify this information.
If the hospital record indicates that the cohort member has been transferred directly from another acute care hospital or is transferring directly to another such hospital, the record for the other hospitalization is found and reviewed according to the rules given in Section 3.1.1.2.

3.2.1.2 Out-of-Hospital Deaths

Out-of-hospital deaths with one of the eligibility codes given in Section 3.1.2.3 require a special investigation into the cause of death. For this purpose out-of-hospital death is defined to include:

1. Deaths occurring outside of regular acute care hospitals.
2. Deaths occurring in hospital emergency rooms or outpatient departments.
3. Persons who were either dead on arrival or were admitted without vital signs. For purposes of defining out-of-hospital death "no vital signs" means no pulse rate and systolic blood pressure (or admitted on a respirator with no pulse rate or systolic blood pressure at any time off the respirator).

When the special investigation for out-of-hospital deaths is required, the information from the decedent's family and physician must be obtained within 6 months after death. The former is contacted for an interview, the latter by questionnaire. Often the informant is the spouse or other family member of the decedent. On other occasions the informant is someone else who witnessed the death or someone whose name is mentioned on the death certificate.

First an attempt is made to contact and interview the spouse or a first-degree relative (i.e., son, daughter, or sibling) of the decedent, or someone else who lived with the decedent. If another person witnessed the death, this person is interviewed as well. Using the information provided by the participant at the time of the clinic interview, the informant's telephone number can be identified, and a "Format 1" letter sent (Appendix 10.1). If a number cannot be found when reviewing information in the clinic interview, a reverse ("criss-cross") directory is used. If the informant's telephone number is still unavailable, a "Format 2" letter (Appendix 10.2) is sent asking the informant to provide a telephone number on the enclosed, self-addressed stamped post card (Appendix 10.3). A copy of the participant's consent form is attached to the letter to the informant. These letters are sent with both the interviewer and the Field Center Principal Investigator's signatures. After enough time elapses for the "Format 1" letter to arrive, or after receiving the reply post card to the "Format 2" letter, the interview is conducted using the Informant Interview Form. This interview may be conducted over the telephone, or if necessary, in person. If no reply is received, a "Format 4" letter (Appendix 10.4) is sent to next-door neighbors (identified by the reverse telephone directory) to request information on the whereabouts of the potential informant. The post card, to be returned by the neighbor(s), is shown in Appendix 10.5. A "Format 4" letter is also sent to the neighbor(s) when an informant's telephone number is initially available, but attempts at telephone contacts are unsuccessful. If no reply is received from the neighbor(s), no further effort is needed.
When the death is witnessed by someone other than a member of the decedent's family, both the family member whose name was given by the participant, and the witness recorded on the death certificate are interviewed. In such a case, the information from both interviews is recorded on separate Informant Interview Forms. Up to three (the three best) Informant Interview Forms may be completed for a given event.

Information is sought from physicians by sending the Physician Questionnaire. From both the clinic and informant interviews an attempt is made to identify the physician(s) who attended the decedent during the four week period prior to death. One questionnaire is sent to the physician who signed the death certificate. Another questionnaire is sent to the physician (if any, and if different from the first) who saw the patient for heart disease during the 28 days prior to death. Sample cover letters (Formats 7 and 8) for each of these physician contacts are provided in Appendix 10.7-8. Release-of-Information Forms, signed by the deceased cohort participant, are attached to these letters. If there is no response after four weeks of the initial mailing to the physician, a follow-up letter and another copy of the Physician Questionnaire are sent. If there is no response after eight weeks of the initial mailing, the physician is contacted by telephone. Up to two (the two best) Physician Questionnaires may be completed for a given event.

If the fatal event was a coroner's or medical examiner's case, his/her report is abstracted onto the Coroner Form. If the decedent died in a nursing home, personnel are asked to complete a Physician Questionnaire based on the nursing home record. Centers may offer to assist with abstraction if this would be helpful. A Release of Information Form may be needed.

If information provided by the informants or physicians indicates that a person who died out-of-hospital was hospitalized within 28 days prior to death for MI or heart surgery, an attempt is made to ascertain the discharge diagnoses and, if applicable, review and abstract the hospital record. Requests to hospitals include copies of the ARIC release forms.

3.2.2 Procedures for Hospitalized Events

For hospitalized events with one of the discharge diagnosis codes for MI or stroke, the Cohort Eligibility Form is completed. The selection codes are listed in Section 3.1.1.2. If a possible MI, the Hospital Record Abstraction Form is used for hospital record abstraction. If a possible stroke, the Hospital Stroke Form is completed. Both forms are completed if both a stroke and MI occurred. For the special case of MI, for events with discharge codes other than ICD9 410 or 411, if the patient was discharged alive with no ECGs taken and no cardiac enzymes measured, only the administrative information on the Hospital Record Abstraction Form is completed.

For certain ICD9 codes, specified in Section 3.1.1.2, which refer to conditions which are more remotely related to MI or stroke, the medical record is obtained and its discharge summary reviewed. Any evidence in the discharge summary of the occurrence of MI requires the use of the Hospital Record Abstraction Form. Any evidence of stroke requires the use of the Hospital Stroke Form.
For all remaining ICD9 codes, the discharge lists are perused and only the discharge diagnoses recorded. These latter codes do not lead to hospital abstraction.

There are a few cases in which the ICD9 code is recorded incorrectly, so that a code on the diagnostic index meets the ARIC Study criteria but none of the codes recorded on the discharge summary of the medical record meets the study criteria. The appropriate hospital forms are still completed in such a case.

Prior to abstracting any records from a hospital for the ARIC Study, information is collected on the normal ranges used for each of the cardiac enzymes abstracted. Many hospitals report use of more than one upper limit of normal for a particular enzyme, for example, when a different laboratory is used for determinations at night or on weekends.

ECGs are copied and sent to the University of Minnesota (as described in section 3.3.1.7) for full Minnesota coding.

If the hospital record indicates that the cohort member was transferred directly from another acute care hospital, or that the participant upon discharge was transferred directly to another acute care hospital, the discharge diagnoses for the other hospitalization are found and the rules described in Section 3.1.1.2 are followed.

3.2.3 Summary of Cohort Investigations

The following schema summarizes the forms completed for cohort events.

3.2.3.1 Out-of-hospital CHD death, as defined in Section 3.2.1.2
1. Cohort Event Investigation Summary Form, Cohort Eligibility Form, Death Certificate Form
2. One or more Physician Questionnaires and Informant Interviews
3. Coroner Form on all coroner/medical examiner's cases, Autopsy Report if autopsy was done, and Hospital Record Abstraction Form on cases hospitalized in the past 28 days with heart conditions meeting screening codes.

3.2.3.2 Hospital CHD deaths, no vital signs in-hospital*
1. Cohort Event Investigation Summary Form, Cohort Event Eligibility Form
2. First part of Hospital Record Abstraction Form, then investigate as 3.2.3.1 above.
3.2.3.3 Hospitalized CHD death, vital signs sometime in hospital*

1. Cohort Event Investigation Summary Form, Cohort Event Eligibility Form, Death Certificate Form, Hospital Record Abstraction Form

2. Autopsy Report (if applicable)

3.2.3.4 Hospitalized CHD case, discharged alive*

1. Cohort Event Investigation Summary Form, Cohort Event Eligibility Form, Hospital Record Abstraction Form

3.2.3.5 Hospitalized Stroke*

1. Cohort Event Investigation Summary Form, Cohort Event Eligibility Form, Hospital Stroke Form

2. Death Certificate Form (if death), Autopsy Report if applicable

3.2.3.6 Deaths from other causes

1. Cohort Event Investigation Summary Form, Cohort Eligibility Form, Death Certificate Form

*If also transferred to or from another hospital, the additional hospital forms are completed.

3.3 Diagnostic Criteria

This section describes the diagnostic criteria to define the major events studied as outcomes among ARIC cohort members: fatal coronary heart disease, hospitalized acute MI, or stroke. Note: A distinction is made between "chest pain", used in fatal diagnoses and "cardiac pain" used for MI.

3.3.1 Coronary Heart Disease

This section describes criteria for CHD events in cohort members.

3.3.1.1 Definite Fatal Myocardial Infarction (MI)

Must meet criteria 1. AND 2. below:

1. No known non-atherosclerotic or non-cardiac atherosclerotic process or event that was probably lethal.

2. Definite hospitalized MI within four weeks of death; use criteria in Section 3.3.1.7 (a) for Definite Hospitalized MI.
3.3.1.2 Definite Fatal CHD

Must meet ALL of the following criteria:

1. Lack of sufficient evidence to diagnose Definite Fatal MI according to criteria given in Section 3.3.1.1.

2. No known non-atherosclerotic or non-cardiac atherosclerotic process or event that was probably lethal.

3. Presence of one or both of the following findings:
   
a) A history of chest pain within 72 hours of death;

b) A history of ever having had chronic ischemic heart disease such as definite or possible MI, coronary insufficiency, or angina pectoris in the absence of valvular disease or non-ischemic cardiomyopathy.

3.3.1.3 Possible Fatal CHD

Must meet ALL of the following three criteria:

1. Lack of sufficient evidence to diagnose Definite Fatal MI or Definite Fatal CHD according to criteria in Sections 3.3.1.1 and 3.3.1.2.

2. No known non-atherosclerotic or non-cardiac atherosclerotic process or event that was probably lethal.

3. Death Certificate with consistent underlying cause, i.e., ICD9 codes 410-414, 427.5, 429.2, and 799.

3.3.1.4 Non-CHD Death

All deaths that do not meet the above criteria for Definite Fatal MI, Definite Fatal CHD, or Possible Fatal CHD.

3.3.1.5 Chronology of Death

All CHD deaths are classified, where possible, according to time interval from onset of acute symptoms to time of death.

3.3.1.6 Limitation of Activity

All out-of-hospital CHD deaths are classified according to whether in the month before death the decedent's activity was limited by sickness or illness.

3.3.1.7 Hospitalized Myocardial Infarction (MI)

The aim of the ARIC Study is a well-standardized process for event identification of hospitalized acute MI, allowing for valid inter-community and longitudinal comparisons, as well as the examination of associations with
risk factors. Although, as described in Section 3.1.1, all hospitalized events occurring in cohort members are identified, detailed chart abstraction is carried out only when acute MI or stroke is suspected. In addition, hospitalization for mild and chronic manifestations of ischemic heart disease, such as angina pectoris and congestive heart failure, are included in the screening process, only to aid in the identification of acute MI. (So-called silent infarctions are not identified from the hospital records, but from ECG changes occurring to cohort members between their baseline and follow-up examinations.) Both Q-wave (transmural) and non-Q-wave (non-transmural) infarctions are sought in all hospital records abstracted.

It is recognized that aggressive treatment of signs and symptoms of impending myocardial infarction, such as angioplasty, Coronary Artery Bypass Graft or streptokinase infusion, may prevent the development of the full diagnostic syndrome. In such cases, it may be difficult to diagnose the event accurately. The use of such modalities is recorded and subject to data analysis, but these modalities are not employed in the criteria for diagnosis.

3.3.1.7.1 Definite Hospitalized MI

Must meet one or more of the following criteria:

1. Evolving diagnostic ECG pattern (ED1-ED7, defined below in e).
   OR
2. Diagnostic ECG pattern (D1 or D2, defined below in e) and abnormal enzymes (defined below in f).
   OR
3. Cardiac pain (defined below in d) and abnormal enzymes and
   a) Evolving ST-T pattern (EV1 through EV8)
   OR
   b) Equivocal ECG pattern (E1 through E4)

3.3.1.7.2 Probable Hospitalized MI

Must meet one or more of the following criteria in the absence of sufficient evidence for Definite Hospitalized MI:

1. Cardiac pain and abnormal enzymes.
   OR
2. Cardiac pain and equivocal enzymes and
   a) Evolving ST-T pattern
   OR
   b) Diagnostic ECG pattern.
   OR
3. Abnormal enzymes and
   a) Evolving ST-T pattern

3.3.1.7.3 Suspect Hospitalized MI

Must meet one or more of the following criteria in the absence of sufficient evidence for Definite or Probable Hospitalized MI:

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1. Abnormal enzymes  
   OR
2. Cardiac pain and incomplete enzymes and  
   a) Diagnostic ECG pattern  
   OR
   b) Evolving ST-T pattern  
   OR
3. Cardiac pain and equivocal enzymes  
   OR
4. Equivocal enzymes and  
   a) Diagnostic ECG pattern  
   OR
   b) Evolving ST-T pattern  
   OR
   c) Equivocal ECG pattern

The criteria for Definite, Probable and Suspect Hospitalized MI are summarized in Table 3.1.

3.3.1.8 Definition of Cardiac Pain

Cardiac pain is defined as both 1. and 2. below.

1. Pain occurring anywhere in the anterior chest, left arm or jaw
2. Absence of a definite non-cardiac cause of chest pain

3.3.1.9 Definitions of Electrocardiographic Criteria:

The ECG series is assigned the highest category for which criteria are met, i.e., evolving diagnostic ECG patterns are higher than diagnostic ECG patterns, which are higher than evolving ST-T patterns, which are higher than equivocal ECG patterns, which are higher than other, which are higher than uncodable.

To fit an evolving ECG Pattern (Evolving Diagnostic and Evolving ST-T) two or more recordings are needed. Changes must occur within lead groups, i.e., lateral (I, aVL, V6), inferior (II, III, aVF), or anterior (V1-V5) and be confirmed for all codes by Serial ECG comparison.

Example

Reference ECG codes: 1-3-4 4-0 5-0 9-0
Follow-up ECG codes: 1-2-4 4-0 5-2 9-0

To be considered Evolving Diagnostic (pattern ED3) both the 1-2-4 and the 5-2 must be determined to be Significant Increase by Serial Change rules. If the 1-2-4 change is not Significant Increase and the 5-2 change is Significant Increase, then the change would fit Evolving ST-T (pattern EV3). If the 5-2 change is not Significant Increase, then pattern would be Diagnostic ECG (pattern DI) because of the 1-2-4, regardless of whether or not the 1-2-4 change is Significant Increase.
Table 3.1. Summary of ARIC Cohort Diagnostic Criteria for Hospitalized MI

<table>
<thead>
<tr>
<th>Cardiac Pain</th>
<th>ECG Findings</th>
<th>Enzymes</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>Present</td>
<td>Evolving Diagnostic</td>
<td>Abnormal</td>
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<td>ECG Pattern</td>
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<td>Incomplete</td>
<td>Definite MI</td>
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<td>Definite MI</td>
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<td>Diagnostic ECG Pattern</td>
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<td>Incomplete</td>
<td>Suspect MI</td>
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<td></td>
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<td>No MI</td>
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<tr>
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<td>Evolving ST-T Pattern</td>
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<td>Abnormal</td>
<td>Suspect MI</td>
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<td>Normal</td>
<td>No MI</td>
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</table>
3.3.1.9.1 Evolving Diagnostic ECG (Judged within lead group)

ED1 through ED7 cannot be assigned if a 7-1-1 code is present. ED2 through ED7 cannot be assigned if a 7-2-1 or 7-4 code is present.

ED1. No Q-code (no 1 code) in reference ECG followed by a record with a Diagnostic Q-code (Minn. code 1-1-1 through 1-2-5 plus 1-2-7), OR any code 1-3-X in reference ECG followed by a record with any code 1-1-X.

ED2. An Equivocal Q-code [(Minn. code 1-2-8 in the absence of 7-2-1 or 7-4) or (any 1-3 code)] and no major ST-segment depression in reference ECG followed by a record with a Diagnostic Q-code PLUS a major ST-segment depression (Minn. code 4-1-X or 4-2).

ED3. An Equivocal Q-code and no major T-wave inversion in reference ECG followed by a record with a Diagnostic Q-code PLUS a major T-wave inversion (Minn. code 5-1 or 5-2).

ED4. An Equivocal Q-code and no ST-segment elevation in reference ECG followed by a record with a Diagnostic Q-code PLUS an ST segment elevation (Minn. code 9-2).

ED5. No Q-code and neither 4-1-X nor 4-2 in reference ECG followed by a record with an Equivocal Q-code PLUS 4-1-X or 4-2.

ED6. No Q-code and neither 5-1 nor 5-2 in reference ECG followed by a record with an Equivocal Q-code PLUS a 5-1 or 5-2.


3.3.1.9.2 Evolving ST-T Pattern (Judged within lead group)

This diagnosis cannot be assigned if a 7-1-1 or 7-2-1 or 7-4 code is present.

EV1. Either 4-0 (no 4-code), 4-4 or 4-3 in reference ECG followed by a record with 4-2 or 4-1-2 or 4-1-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 4-2, 4-1-2 or 4-1-1 in reference ECG followed by a record with 4-0, 4-4 or 4-3 (confirmed by Significant Decrease). PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV2. Either 4-2 or 4-1-2 in reference ECG followed by a record with 4-1-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 4-1-1 in reference ECG followed by a record with 4-2 or 4-1-2 (confirmed by Significant Decrease), PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

ARIC PROTOCOL 2. Cohort Component Procedures - Visit 2. VERSION 3.0 8/90
EV3. Either 5-0, 5-4 or 5-3 in reference ECG followed by a record with 5-2 or 5-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 5-2 or 5-1 in reference ECG followed by a record with 5-0, 5-4 or 5-3 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV4. Code 5-2 in reference ECG followed by a record with 5-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 5-1 in reference ECG followed by a record with 5-2 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV5. Code 9-0 in reference ECG followed by a record with 9-2 (confirmed by Significant Increase) OR 9-2 in reference ECG followed by a record with 9-0 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV6. Code 4-1 in reference ECG followed by a record with 4-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 4-1 in reference ECG followed by a record with 4-1 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV7. Code 5-1-1 in reference ECG followed by a record with 5-1-1 (confirmed by Significant Increase) OR, for hospital ECGs only, 5-1-1 in reference ECG followed by a record with 5-1-1 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

EV8. Code 5-1-2 in reference ECG followed by a record with 5-1-2 (confirmed by Significant Increase) OR, for hospital ECGs only, 5-1-2 in reference ECG followed by a record with 5-1-2 (confirmed by Significant Decrease),

PLUS

either no Q-code in both the reference ECG and the follow-up ECG or Q-code(s) present in reference ECG or follow-up ECG but no Significant Increase in Q-code found.

ARIC PROTOCOL 2. Cohort Component Procedures - Visit 2. VERSION 3.0 8/90
3.3.1.9.3 Diagnostic ECG

D1. An ECG record with any Diagnostic Q-code (Minn. code 1-1-1 through 1-2-5 plus 1-2-7).

D2. An ECG record with ST-segment elevation code 9-2 PLUS (T-wave inversion code 5-1 or 5-2 in the absence of 7-2-1 or 7-4).

3.3.1.9.4 Equivocal ECG

E1. An ECG record with an Equivocal Q-code [(Minn. code 1-2-8 in the absence of 7-2-1 or 7-4) or (any 1-3 code)].

E2. An ECG record with ST-segment depression (code 4-1-X or 4-2 or 4-3 in the absence of 7-2-1 or 7-4).

E3. An ECG record with T-wave inversion (code 5-1 or 5-2 or 5-3 in the absence of 7-2-1 or 7-4).


3.3.1.9.5 Other ECG

01. Reference ECG coded 7-1-1.

02. Any ECG coded 7-1-1.

03. Normal ECG(s), defined as 1.0 in "clear" field of all ECGs.

04. Other findings including 1-2-6.

3.3.1.9.6 Uncodable ECG

U1. Technical errors coded 9-8-1 by Minnesota Code.

3.3.1.9.7 Absent ECG

A1. No ECG available for coding.

3.3.1.9.8 Minnesota Coding Procedures

The following ECG tracings are identified:

1. The first codable ECG after admission;

2. The last codable ECG recorded before discharge; and

3. The last codable ECG recorded on day 3 (or the first ECG thereafter) following admission or an in-hospital event.

Photocopies of the cohort hospital ECGs are sent to the Minnesota Coding Center in Minneapolis for Minnesota Coding, using the Minnesota Coding and Serial Change Form for hospitalized ECGs shown in Appendix O of Manual 5. Each ECG is read three times, blinded; the final codes are adjudicated by a senior coder. Minnesota Code criteria are in Appendix E of Manual 5.

After the data from the individual ECGs are entered, a determination is made at the Minnesota Coding Center by computer algorithm as to whether or not
Minnesota Code change criteria are met. A list of those IDs that fit the change criteria (i.e., any pattern ED1 through ED7 or EV1 through EV5, defined above) is generated. ECGs for these IDs are examined side by side for Serial ECG change.

Simultaneous ECG comparison is performed on the final Minnesota codes using the first codable ECG of the hospitalization as the reference. Serial ECG changes are determined two times, blinded. Serial change categories are (1) significant increase, (2) decrease (4-, 5-, and 9-2 codes, but not for Q-codes), (3) no change (this implies no increase for Q-codes) or (4) technical problem. The final categories are adjudicated by a senior coder and entered into the database. Serial Change criteria are in App. L of Manual 5.

As an example, the ARIC protocol defines a new Minnesota code 1-2-7 as a potential ischemic event. Persons with this severity of ECG change will have simultaneous ECG comparison. The ECG comparison procedure (for this case) requires a \( \geq 1 \) mm R-wave amplitude decrease between corresponding leads of the reference and comparison ECGs. The criteria for 1-2-7 are QS patterns in V1, V2 and V3. If the reference ECG has R-waves that are \( \geq 1 \) mm tall in V1 or V2 or V3, then when comparing these ECGs side by side, the R-waves in the reference ECG appear to decrease the appropriate amount (at least 1 mm) and a "significant increase" is recorded. If the reference ECG has R-waves < 1 mm tall, it cannot fulfill the change criteria and no change (or no increase) is noted. See Appendix L of Manual 5.

3.3.1.10 Definitions of Cardiac Enzyme Criteria

All pertinent enzyme results (as defined below) recorded in the hospital chart for days 1 through 4 after hospital admission, or days 1 through 4 after an in-hospital CHD event are abstracted. Information on non-ischemic cause for elevated enzymes is abstracted exclusively from the discharge summary on the medical chart.

3.3.1.10.1 Abnormal Cardiac Enzymes

Enzymes are classed as "abnormal" if any enzyme values recorded meet any of the three following criteria:

1. a) **CK-MB** is "present" (if laboratory uses the criterion of "present" or "absent" or similar technology without reporting a more specific value) or **CK-MB** is twice the upper limits of normal (if the laboratory gives a normal range) or, if no normal range is given, the **CK-MB** (heart fraction) is greater than or equal to 10% of the total **CK** value.

   **AND**

   b) There is no known non-ischemic cause (cardiac surgery, severe muscle trauma, rhabdomyolysis) for the elevated enzyme value.

   **OR**

   c) **Another enzyme** (such as **CPK**) is "present".

   **AND**

   d) There is no known non-ischemic cause (cardiac surgery, severe muscle trauma, rhabdomyolysis) for the elevated enzyme value.
2. a) The ratio $LDH_1 : LDH_2$ is $> 1$.
   AND
b) There is no evidence of hemolytic disease.
OR
3. a) Total CK and LDH are both at least twice the upper limit of normal. (These increases do not have to occur on the same day.)
   AND
b) There is no known non-ischemic cause (cardiac surgery, severe muscle trauma, rhabdomyolysis) for the elevated CK and no evidence of hemolytic disease.

If 1.b), 2.b), or 3.b) is present, but the criterion for abnormal is otherwise met, an MMCC physician reviews the enzymes to determine whether equivocal or normal applies.

3.3.1.10.2. Equivocal Cardiac Enzymes

Enzymes are classed as "equivocal" if the criteria for abnormal enzymes are not met and if:

1. Either total CK or total LDH are at least twice the upper limit of normal.
   OR
2. Both total CK and total LDH are between the upper limit of normal and twice the upper limit of normal. (These increases do not have to occur the same day.)
   OR
3. CK-MB is "weakly present" or between the upper limits of normal and twice the upper limits of normal or 5-9% of total CK.

A summary of the enzyme diagnostic criteria, as related to total CK and LDH is given in the following algorithm (Figure 3.1).

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<th>Twice the Upper Limit of Normal</th>
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<td>Twice Equivocal</td>
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<tr>
<td>T</td>
<td>Normal</td>
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<td>A</td>
<td>Normal</td>
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<td>Upper Limit</td>
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<tr>
<td>H</td>
<td>Twice Upper Limit of Normal</td>
</tr>
</tbody>
</table>

Figure 3.1. Algorithm for Total CK and LDH Enzyme Diagnostic Criteria
3.3.2 Stroke

This section describes the ARIC diagnostic criteria used to define strokes. Stroke is broadly defined as a clinical syndrome consisting of a constellation of neurological findings, sudden or rapid in onset, which persist for more than 24 hours or lead to death. This definition excludes events whose neurologic findings are due to traumatic, metabolic, toxic, vasculitic, neoplastic, or infectious processes of the central nervous system. Based upon objective diagnostic or pathologic findings, strokes are subcategorized into five major categories: (1) Subarachnoid hemorrhage, (2) Brain hemorrhage, (3) Brain infarction, thrombotic, (4) Brain infarction, embolic, and (5) Stroke of undetermined type.

3.3.2.1 Definite Subarachnoid Hemorrhage (SAH)

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet the criteria specified under at least one of the four paragraphs below:

1. Meets both criteria (a) and either (b) or (c) below:
   a) Angiographic identification of a saccular aneurysm or as the source of the bleeding (e.g., demonstration of a clot adjacent to aneurysm or reduced caliber of otherwise normal vessels),
   -AND-
   b) Bloody (not traumatic) tap or xanthochromic spinal fluid,
   -OR-
   c) Demonstration by computerized tomography of subarachnoid hematoma,
   -OR-
2. Demonstration by computerized tomography of a blood clot in Fissure of Sylvius, between the frontal lobes, in basal cisterns, or within a ventricle, with no associated intraparenchymal hematoma,
   -OR-
3. Demonstration at surgery of a bleeding saccular aneurysm,
   -OR-
4. Demonstration at autopsy of recent bleeding of a saccular aneurysm.

3.3.2.2 Probable Subarachnoid Hemorrhage

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet both criteria (1) and (2) below:

1. One or more of the following symptoms or signs occurred within minutes or a few hours after onset:
   a) Severe headache at onset, or severe headache when first conscious after hospital admission;
   b) Depression of state of consciousness;
   c) Evidence of meningeal irritation;
   d) Retinal (subhyaloid) hemorrhages;
   -AND-
2. Bloody (not traumatic) tap or xanthochromic spinal fluid.

3.3.2.3 Definite Brain Hemorrhage (IPH)

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet the criteria specified under at least one of the three paragraphs below:

1. Demonstration of definite intracerebral hematoma by computerized tomography, e.g., an area of increased density, such as seen with blood,

   -OR-

2. Demonstration at autopsy or surgery of intracerebral hemorrhage,

   -OR-

3. Evidence in the patient's clinical record that meet criteria (a), (b), (c), and (d) below:

   a) One major or two minor neurological signs or symptoms from the following list that lasted at least 24 hours or until the patient died:

      **Major**
      o Hemiparesis involving two or more body parts
      o Unilateral numbness involving two or more body parts
      o Homonymous hemianopia
      o Aphasia

      **Minor**
      o Diplopia
      o Vertigo or gait disturbance
      o Dysarthria or dysphagia or dysphonia

   -AND-

   b) Bloody (not traumatic tap) or xanthochromic spinal fluid,

   -AND-

   c) Cerebral angiography demonstrates an avascular mass effect and no evidence of aneurysm or arteriovenous malformation,

   -AND-

   d) No computerized tomography was performed or the CT was technically inadequate.

3.3.2.4 Probable Brain Hemorrhage

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet all criteria (1), (2), (3) and (4) below:

1. One major or two minor neurological signs or symptoms listed in Section 3.3.2.3, No. 3 above that lasted at least 24 hours or until the patient died,

   -AND-
2. Decreased level of consciousness or coma that lasted at least 24 hours or until the patient died, 
-AND- 
3. Bloody (not traumatic tap) or xanthochromic spinal fluid, 
-AND- 
4. No computerized tomography was performed or the CT was technically inadequate.

3.3.2.5 Definite Brain Infarction, Thrombotic (TIB)

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet the criteria specified under at least one of the two paragraphs below:

1. Demonstration at autopsy of nonhemorrhagic infarct in brain, 
   -OR- 
2. Evidence in the patient's clinical record that meet criteria (a), and (b) below:
   a) One major or two minor neurological signs and symptoms that lasted at least 24 hours or until the patient died:

   **Major**
   - Hemiparesis involving two or more body parts
   - Unilateral numbness involving two or more body parts
   - Homonymous hemianopia
   - Aphasia

   **Minor**
   - Diplopia
   - Vertigo or gait disturbance
   - Dysarthria or dysphagia or dysphonia 
   -AND- 

   b) Computerized tomography shows an area of decreased density which may indicate edema or ischemia, with no evidence of hemorrhage, or "infarct" on CT report.

3.3.2.6 Probable Brain Infarction, Thrombotic

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet all criteria (1), (2), and (3) below:

1. One major or two minor neurological signs or symptoms listed in Section 3.3.2.5 (a) above that lasted at least 24 hours or until the patient died, 
   -AND- 
2. Demonstration of negative or nonspecific findings and no evidence of hemorrhage by computerized tomography performed in the first 48 hours after the onset of symptoms or signs, 
   -AND-
3. A spinal tap was either not done, or was a traumatic tap, or yielded clear, colorless spinal fluid.

3.3.2.7 Definite Brain Infarction, Embolic (EIB)

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet the criteria specified under at least one of the two paragraphs below:

1. Demonstration at autopsy of:
   a) An infarcted area (bland or hemorrhagic) in the brain,
      -AND-
   b) A source of emboli in a vessel of any organ, or an embolus in the brain,
      -OR-

2. Evidence in the patient's clinical record that meet criteria (a), (b), and (c) below:
   a) One major or two minor neurological signs and symptoms that lasted at least 24 hours or until the patient died:

      Major
      o Hemiparesis involving two or more body parts
      o Unilateral numbness involving two or more body parts
      o Homonymous hemianopia
      o Aphasia

      Minor
      o Diplopia
      o Vertigo or gait disturbance
      o Dysarthria or dysphagia or dysphonia
      -AND-

   b) Establishment of a likely source for cerebral embolus, e.g.:

      o Valvular heart disease (including prosthetic heart valve)
      o Atrial fibrillation or flutter
      o Myocardial infarction with mural thrombus
      o Cardiac or arterial operation or procedure
      o Cardiac myxoma
      o Bacterial endocarditis
      o Arteriographic evidence showing an arterial branch occlusion
      -AND-

   c) Computerized tomography shows an area of decreased density which may indicate edema or ischemia, with no evidence of hemorrhage.

3.3.2.8 Probable Brain Infarction, Embolic

Evidence in the patient's clinical record of sudden or rapid onset of neurologic symptoms lasting for more than 24 hours or leading to death, plus must meet all criteria (1), (2), and (3) below:
1. One major or two minor neurological signs or symptoms listed in Section 3.3.2.7 (a) above that lasted at least 24 hours or until the patient died. -AND-

2. An identifiable source for the cerebral embolus as specified in Section 3.3.2.7 (b), -AND-

3. Demonstration of negative or nonspecific findings and no evidence of hemorrhage by computerized tomography performed in the first 48 hours after the onset of symptoms or signs,

3.3.2.9 Possible Stroke of Undetermined Type

Evidence in the patient's clinical record of sudden or rapid onset of at least one major or two minor signs and symptoms that lasted more than 24 hours or until the patient died:

**Major**
- Hemiparesis involving two or more body parts
- Unilateral numbness involving two or more body parts
- Homonymous hemianopia
- Aphasia

**Minor**
- Diplopia
- Vertigo or gait disturbance
- Dysarthia or dysphagia or dysphonia
- Severe headache at onset, or severe headache when first conscious after hospital admission;
- Depression of state of consciousness;
- Evidence of meningeal irritation;
- Retinal (subhyaloid) hemorrhages;
- Palsy of the iii cranial nerve;

-AND-

Clinical history, signs, symptoms and findings from diagnostic tests and/or autopsy are not sufficient to meet the criteria for classifying the case as a "Definite" or "Probable" case of one of the four specific diagnostic categories of stroke.

3.3.2.10 Undocumented Fatal Stroke

Must meet the following criteria:

1. Does not meet criteria for definite, probable, or possible stroke noted above -AND-

2. Underlying cause of death consistent with stroke (i.e. ICDA9: 430-438), but death occurred without hospitalization or hospital chart cannot be located.
3.3.2.11 Exclusionary Conditions for Diagnostic Criteria for Stroke

Cases are not considered a stroke if there is evidence in the patient's clinical record that the neurologic symptoms were the result of any of the following:

1. Major head (brain) trauma; e.g., epidural hematoma, subdural hematoma, skull fracture

2. Neoplasm; e.g., primary or metastatic brain/CNS neoplasia (malignant or benign)

3. Coma due to metabolic disorders or disorders of fluid or electrolyte balance; e.g., due to diabetes, hypoglycemia, epilepsy, hypovolemia, poisoning, drug overdose, uremia, or liver disease

4. Vasculitis involving the brain; e.g., SLE, radiation, etc.

5. Peripheral neuropathy

6. Hematologic abnormalities (considered exclusionary if present prior to event under consideration); e.g., DIC, thrombocytopenia, Heparin or Coumadin therapy

7. CNS infection: brain abcess, granulomas, meningitis, encephalitis, or any specific infection involving the brain or meninges.

The diagnostic algorithm for stroke is summarized in Table 3.2.
Table 3.2 Stroke Diagnosis Summary for ARIC Cohort Study

<table>
<thead>
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<th>Category</th>
<th>Specific Symptoms</th>
<th>Embolic Source</th>
<th>CT Scan</th>
<th>Angiogram</th>
<th>Lumbar Puncture</th>
<th>Pathology</th>
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<td><strong>Brain Infarction. Embolic</strong></td>
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<td>Definite</td>
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<tr>
<td><strong>Stroke of Undetermined Type</strong></td>
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<td>Possible</td>
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<tr>
<td><strong>Undocumented Fatal Stroke</strong></td>
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<td>Unconfirmed out-of-hospital</td>
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<tr>
<td>stroke death (ICD9 430-38)</td>
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</table>

+ — present/positive
- — absent
(+) — either one must be present
H — CT shows hemorrhage
S — CT shows SAH
I — CT shows infarction
O — CT not helpful
N — CT within 48 hours is negative

*All strokes must have neurologic finding(s) lasting at least 24 hours or until death, and no nonvascular cause.*
3.4 Event Determination

Final assignment of diagnostic categories for all cohort events of interest in the ARIC Study is made by the Morbidity and Mortality Classification Committee (MMCC), after initial assignment to diagnostic categories is carried out by computer algorithm. The diagnostic criteria used are given in Section 3.3 of this Manual. This section describes the procedures by which these determinations are made.

Computer-generated summaries of all relevant coded information from the data collection forms are provided to the MMCC in a convenient form for review. In addition, the MMCC considers remarks by family interviewers, hospital record abstractors, or clinic examiners or other uncoded information recorded on the data collection forms. These are photocopied for use by the committee.

All positive diagnoses made by computer for cohort members are reviewed by MMCC members to assure the specificity of the diagnoses. A sample of non-events diagnosed by computer is also reviewed. All differences between computer and MMCC diagnoses are reviewed by the full committee. If the MMCC determines that any change in the ARIC Study diagnostic criteria or refinement in the computer algorithm is needed to classify more accurately a given event, a recommendation is brought to the ARIC Steering Committee.

For types of events which often are not classifiable by computer algorithm, e.g., out-of-hospital deaths, the diagnostic criteria given in Section 3.3 may not be specific enough to permit unequivocal classification of each event by the MMCC. If the MMCC discovers a rule which helps standardize this process, it either (1) makes a recommendation to the ARIC Steering Committee for further specification of the ARIC Study diagnostic criteria or (2) records the rule as a part of the "case law" for its own use in classifying similar events.

In addition to diagnosing all cohort clinical events, the MMCC provides other information about these events. Examples include clinical judgments required prior to making diagnoses (e.g., concerning non-cardiac causes of chest pain, of elevated enzyme concentrations or death) and resolution of conflicting evidence regarding the time interval between onset of symptoms and death. These are discussed in the appropriate sections below.

All cohort events given ARIC Study diagnoses which differ substantially from the diagnosis coded at hospital discharge or on the death certificate receive special MMCC review for confirmation or correction. Events in which the difference cannot be confirmed or corrected are referred to the Field Centers for reabstraction of hospital records by a physician or the abstractor supervisor. This process serves as an additional quality control mechanism for the ARIC Study event investigation process.

The differences between the ARIC Study and the death certificate, or hospital record diagnoses which require MMCC review are listed in Table 3.3.
Table 3.3. Differences between ARIC diagnoses and diagnoses from other sources, which require review by the Mortality and Morbidity Classification Committee (MMCC)

<table>
<thead>
<tr>
<th>Diagnosis by ARIC Diagnostic Algorithm</th>
<th>ICD Codes Recorded as Final Diagnoses on the Death Certificate or Hospital Record</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Definite MI</td>
<td>No 410 - 414 codes on hospital record or, for fatal MI, no 410 - 414, 427.5, 429.2, 799 codes on death certificate</td>
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<tr>
<td>2. No MI</td>
<td>Codes 410 - 411 on hospital record</td>
</tr>
<tr>
<td>3. Fatal CHD, in hospital</td>
<td>No 410 - 414, 427.5, 429.2, or 799 codes on death certificate</td>
</tr>
<tr>
<td>4. Non-CHD Death, in hospital</td>
<td>Codes 410 - 414, 427.5, 429.2, or 799 on death certificate</td>
</tr>
<tr>
<td>5. Definite Stroke</td>
<td>No 430 - 438 codes</td>
</tr>
<tr>
<td>6. No Stroke</td>
<td>Codes 430 - 434</td>
</tr>
</tbody>
</table>

For each event requiring an MMCC judgement, the process begins with two MMCC members reviewing the information independently. If they agree, adjudication by the full committee is not required. If they disagree, the Coordinating Center informs them that they have disagreed (without specifying the exact nature of the disagreement). If, after review the two judges still disagree, adjudication by the full MMCC is undertaken. Selection of the two judges for each event is made by the Coordinating Center by a randomized process. The Coordinating Center also assigns specific tasks to the judges for each case (diagnosis, chronology of death, cause of elevated enzymes, etc.).

3.4.1 Diagnosis of Coronary Heart Disease

3.4.1.1 Hospitalized MI

Classification of hospitalized cohort events as Definite, Probable, Suspect or No MI is made by computer algorithm. MMCC members review all events assigned Definite, Probable and Suspect diagnoses and a sample of "No MI" diagnoses. In addition, the MMCC judges each event in which the chest pain or elevated enzymes is coded to be the result of non-cardiac causes. Records of all computer-MMCC differences are maintained, and any recommendations for changes in the diagnostic criteria or the computer algorithm are sent to the Steering Committee.
3.4.1.2 CHD Death

Narratives recorded by family interviewers and other uncoded information are important in diagnosing deaths which occurred out-of-hospital. For many out-of-hospital events, the MMCC must resolve conflicting information collected from several informants. In-hospital deaths meeting the criteria for "Definite MI" require MMCC review for a possible Non-CHD cause of death before being classified as "Definite Fatal MI".

A computer diagnosis of "Definite Fatal MI", "Definite Fatal CHD" or "Non-CHD Death" is provided for those events for which all the necessary coded information is available and unequivocal. Except for a sample of unequivocal computer diagnosed Non-CHD Deaths, all cohort deaths require MMCC review and classification.

All out-of-hospital deaths classified as "Definite Fatal CHD" or "Possible Fatal CHD" require an MMCC determination of the interval between the onset of symptoms and death.

3.4.2. Diagnosis of Stroke

Verbatim reports of lumbar puncture, cerebral angiography, CT scan, MRI scan, ultrasound, craniotomy, or autopsy abstracted from hospital records are interpreted by a study neurologist.

Classification of cohort events into "Definite", or "Probable", or "Possible" stroke for hospitalized events is made by means of a computer algorithm.

3.5 Diagnosis of Prevalent MI at Baseline and Interim MI Between Clinic Visits

3.5.1 Procedures

3.5.1.1 Minnesota Coding

Cohort 12-lead ECGs are taken during Field Center visits. One ECG is taken at the baseline exam and a second ECG is taken at the follow-up exam three years later.

Abnormal ECGs and a 10% selection of normal ECGs are transmitted from the Halifax Computer Center to the Minnesota Coding Center in Minneapolis. These ECGs are coded visually by the Minnesota Code as illustrated on the coding form in Appendix K of Manual 5. ECGs are read three times, blinded; the final codes are adjudicated by a senior coder.

3.5.1.2 Adjudication

The visual Minnesota Codes are entered and the Coordinating Center compares them with the computer generated codes. Adjudication between the visual code and the computer code is performed by two electrocardiographers only on ECGs that have a discrepancy involving any Q-code (1-code), or any 4-1, 4-2, 5-1, 5-2, 9-2, 6-4, 7-1-1 or 7-2-1 code. The Coordinating Center determines the IDs that have any of these discrepancies and sends a report form to the

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Minnesota Coding Center listing the ID, acrostic, date and time of ECG, the visual codes and the computer codes. These ECGs are examined and the adjudicated codes are recorded in the ECG database which is returned to the Coordinating Center.

3.5.1.3 Serial ECG Coding

When two ECGs from different Field Center visits are available, a determination is made at the Halifax ECG Coding Center as to whether or not Minnesota Code change criteria are met. A list of those IDs that fit the change criteria (i.e. any pattern ED1 through ED7) is sent to the Minnesota ECG Coding Center. ECGs for these IDs are examined side by side for Serial ECG change.

Simultaneous ECG comparison is based on the final Minnesota Codes. Serial ECG changes (significant increase, no increase or technical problem) are determined two times; the final categories are adjudicated by a senior coder and added to the database. The simultaneous ECG evaluation procedure uses the ECG of the first clinic visit as the reference ECG for comparison.

ARIC requires Minnesota Code change plus agreement by simultaneous ECG comparison before declaring the ECG pattern change meets ARIC criteria for an interim MI.

3.5.2 Definitions

A determination that an ARIC participant has had an MI, either prior to the initial clinic visit or between visits, can be made on ECG evidence alone, using the following criteria:

3.5.2.1 Prevalent MI at Baseline

Baseline ECG (initial cohort visit) coded:

a) any 1-1-X code.
   -OR-
   b) any 1-2-X PLUS 4-1-1 or 4-1-2 or 4-2 or 5-1 or 5-2.

3.5.2.2 Interim MI Between Cohort Visits

An Evolving Diagnostic ECG Pattern (ED1 through ED7) between the baseline ECG (initial cohort visit) and an ECG from a later cohort visit.