Atherosclerosis Risk in Communities Study Protocol

Manual 2

Cohort Component Procedures

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FOREWORD

This manual entitled, Cohort Component Procedures, is one of a series of protocols and manuals of operation for the Atherosclerosis Risk in Communities (ARIC) Study. The complexity of the ARIC Study requires that a sizeable number of procedures be described, thus this rather extensive set of materials has been organized into the set of manuals listed below. Manual 1 provides the background, organization, and general objectives of the ARIC Study. Manuals 2 and 3 describe the operation of the Cohort and Surveillance Components of the study. Detailed Manuals of Operation for specific procedures, including reading centers and central laboratories, make up Manuals 4 through 11. Manual 12 on Quality Assurance and Quality Control contains a general description of the study's approach to quality assurance as well as specific protocols for each of the study procedures.

The version status of each manual is printed on the title sheet. The first edition of each manual is Version 1.0. Subsequent modifications of Version 1 (pages updated, pages added, or pages deleted) are indicated as Versions 1.1, 1.2, and so on, and are described in detail in the Revision Log located immediately after the title page. When revisions are substantial enough to require a new printing of the manual, the version number will be updated (e.g., Version 2.0) on the title page.

ARIC Study Protocols and Manuals of Operation

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1. SAMPLING, RECRUITMENT, AND FOLLOW-UP IN THE COHORT STUDY

1.1 Introduction

The ARIC cohort sampling plan is designed to identify a representative sample of participants for this longitudinal study. Over a three year period, each field center selects and recruits from their community 4,000 men and women ages 45-64, for the baseline examination. Annually, thereafter, participants are recontacted by telephone in order to maintain correct addresses and to ascertain interim medical events. In the third year, participants are contacted for reexamination at the field center clinics.

An outline of the procedures employed follows:

A. Sampling and recruitment

1. Create sampling frame for each community
2. Probability sampling selecting households (Forsyth County) or individuals (Jackson, Minneapolis, Washington County).
3. Household enumeration for eligibility determination
4. Home interview with each age-eligible
5. Invitation to the clinic examination
6. Clinic examination

B. Follow-up

1. Annual contacts by telephone (or home visit)
2. Three year reexamination
3. Record abstraction for hospitalized events
4. Death certificate abstraction and mortality investigation for cohort deaths

1.2 Eligibility Requirements

Explicit inclusion criteria for the cohort study are established and uniformly applied across the four Field Centers. The criteria discussed below are applied during the sampling and recruitment phases of operation. The reference population for the ARIC cohort study is all noninstitutionalized persons currently living in the four Field Center areas who, by the time they are enumerated, are 45 through 64 years of age.

Application of the study's eligibility criteria first occurs during sample selection. Area and list frames from which the Field Center samples are drawn are confined to the boundaries of the following four areas as recognized at the time that the initial cohort sample is drawn.

1. Forsyth County, North Carolina, including the city of Winston-Salem.

2. The City of Jackson, Mississippi.

3. Washington County, Maryland, including the city of Hagerstown.

4. Seven suburban areas of Minneapolis (Brooklyn Center, Brooklyn Park, Crystal, Golden Valley, New Hope, Plymouth, Robbinsdale), Minnesota.

Within these four geographic areas, only those people living in residential units are included. The following definition from the 1980 Census has been adopted:

> Housing Unit---A house, apartment, mobile home or trailer, group of rooms or single room occupied or intended for occupancy as separate living quarters. Separate living quarters are those in which the occupants do not live and eat with any person in the structure and which have direct access from the outside of the building or through a common hall. The occupants may be a single family, one person living alone, two or more families living together, or any group of related or unrelated persons who share living arrangements (except as described by the definition of group quarters). For vacant units, the criteria of separateness and direct access are applied to the intended occupants whenever possible. If the information cannot be obtained, the criteria are applied to the previous occupants.

Explicitly excluded from the cohort study are all persons who live in residences called group quarters, in which relatively large groups of unrelated people live and share habitation together. Group quarters were defined as follows for the 1980 Census:

> Group Quarters---Living arrangements other than households. Includes institutions such as mental hospitals, homes for the aged, prisons, etc., plus other quarters containing ten (10) or more persons where 9 or more are unrelated to the persons in charge. Such quarters are commonly found in dormitories, military barracks, etc., but may also be in a house or apartment used as a rooming house or occupied on a partnership basis.

The Jackson Field Center includes only blacks in its cohort. The other Field Centers do not select their cohort samples on race or ethnicity.

The time marker for establishing a person's age and age-eligibility is the month in which the person is enumerated. Enumeration in ARIC involves recording all persons who usually reside in the selected household and are 18 years of age or older. A person is considered age-eligible if he is age 45 through 64 years during the month in which he is enumerated. See Table 1 for eligible dates of birth for each enumeration month.

The use of month and year (as opposed to month, day, and year) to determine age simplifies the procedures for the interviewers who must ultimately decide whether or not someone is age-eligible. Because of rescheduled examination

Table 1. Age eligibility rules for enumeration into the cohort of the ARIC study

Month of Enumeration	Dates of Birth Required to be Age Eligible
12/86	12/22 - 12/41
1/87	1/22 - 1/42
2/87	2/22 - 2/42
3/87	3/22 - 3/42
4/87	4/22 - 4/42
5/87	5/22 - 5/42
6/87	6/22 - 6/42
7/87	7/22 - 7/42
8/87	8/22 - 8/42
9/87	9/22 - 9/42
10/87	10/22 - 10/42
11/87	11/22 - 11/42
12/87	12/23 - 12/42
1/88	1/23 - 1/43
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3/89	3/24 - 3/44
4/89	4/24 - 4/44
5/89	5/24 - 5/44
6/89	6/24 - 6/44
7/89	7/24 - 7/44
8/89	8/24 - 8/44
9/89	9/24 - 9/44
10/89	10/24 - 10/44
11/89	11/24 - 11/44

appointments and the use of month and year to establish age, some age-eligible participants have not reached their 45th birthday and others will have celebrated their 65th birthday at the time of their first examination. The number of these departures from the intended 45-64 year age interval is relatively small. Finally, all age-eligible persons who consider the selected housing unit to be the place where they live most of the time, are included in the study. "Usual residence" is defined in Tables 2 and 3.

A number of other explicit exclusions from the study population are established. First, vacant and demolished housing units are excluded from enumeration in the North Carolina sample where compact segments are selected in the final stage of sampling. Second, the samples in each Field Center exclude persons who indicate that their permanent residence is somewhere outside of the study areas. Third, the study excludes persons who, in the judgment of the interviewer, would be physically or mentally incapable of full participation in the study. Fourth, persons currently living in the study area, but who indicate a definite relocation outside of the study area within the following three months are excluded, since follow-up of these persons would be difficult and incomplete.

There are several groups of people which will receive special enumeration, recruitment and scheduling efforts to ensure they are included in the cohort. The first group is all women who are in their third trimester of pregnancy or less than three months postpartum. Because of the infeasibility of certain measurements just prior to delivery, the examinations for these women are rescheduled for a later time when obtaining their measurements is more appropriate. A second group included is persons with language difficulties. Here, efforts are made to obtain an interview from the person, but with another family member or friend acting as interpreter. Persons with language difficulties but with no available interpreters are treated as eligible nonrespondents and dropped from the study. A third group not excluded is persons who are temporarily away from home (e.g. on vacation). As with the late pregnancies, examinations for this group are rescheduled for a more convenient time after they return.

To establish eligibility for the study, information can be obtained from any of the following sources:

1. Data available on the frame (Washington County and Minnesota list samples for age and household location, as well as race in Jackson);
2. A knowledgeable adult member of the selected housing unit during enumeration; or
3. A knowledgeable adult neighbor to the selected housing unit.

Gaining information by proxy under the third alternative is allowed only as a last resort (i.e. after all required call attempts have been made).

1.3 Sampling Procedures for Initial Cohort Selection

Probability sampling, with high coverage rates in each of the four Field Center areas, is used to select the cohort members. Although the sampling methods differ among areas, randomized selection methods from current sampling

frames are used in each design. The designs differ primarily by how the frames are constructed and in which units the sample is chosen. A summary of these differences among designs is given in Table 4.

Table 2. Enumeration rules for the ARIC study cohort: persons staying in housing unit at the time of enumeration

Type of person including members of family, lodgers, servants, visitors, etc.	Include in roster
1. Ordinarily stay here all the time (sleep here)	Yes
2. Here temporarily - no living quarters held for person elsewhere	Yes
3. Here temporarily - living quarters held for person elsewhere, but person spends (or expects to spend) largest part of the calendar year in this household	Yes
4. Regularly sleep greater part of week in another locality	Yes
5. Regularly sleep greater part of week in this household	Yes
6. Domestic servant who "lives in"	Yes
7. Student attending college in this locality - living in this household	Yes
8. Students away attending college - here only temporarily or on vacation	See Table 3
9. In Armed Forces - stationed at nearby installation, living in this household	Yes
10. In Armed Forces - temporarily here on leave - stationed elsewhere	No
11. Citizen of foreign countries - studying or working in the U.S. and living in this household	Yes
12. Citizen of foreign countries - temporarily traveling or visiting in the U.S	No

Table 3. Enumeration rules for the ARIC Study cohort for absent persons who would normally reside in this housing unit

Type of person including members of family, lodgers, servants, visitors, etc.	Include in Roster
Person in institution where people normally stay for shorter periods of time (e.g., general or VA hospitals, short-stay jails, etc.)	Yes
Person temporarily absent on a visit or vacation	Yes
Person temporarily absent on business trip or in connection with job (e.g., traveling salesman, bus driver, railroad man)	Yes
In Armed Forces - currently stationed elsewhere or assigned to naval vessel	No
Away attending school - living in a college dorm	Yes
Away attending school - living in a housing unit other than a college dorm	No
American citizen abroad	
1. Temporarily on vacation or away in connection with work	Yes
2. Employed by U.S. Government with place of duty abroad	No
3. Any other American working or living abroad for extended period of time	No

Table 4. Field Center sampling designs in the ARIC Cohort Study

Community	Sampling Units	Source of Frame
Forsyth County, North Carolina	Stage 1: Enumeration districts or block groups	1980 Census
	Stage 2: Compact segments of 6-8 housing units	Constructed for cohort study
Jackson, Mississippi	Persons in Jackson with a Mississippi drivers license or state identification card	Mississippi Highway Patrol
Minneapolis Suburbs, Minnesota	Persons eligible for jury duty in Hennepin County[1]	Hennepin County jury selection system
Washington County, Maryland	Persons enumerated in 1975	1975 Private Health Census of Washington County, MD
	OR	
	Persons in Washington County with a driver's license	Maryland Department of Motor Vehicles

[1]Possessing a Minnesota driver's license, Minnesota identification card, or registered to vote in Hennepin County.

In Forsyth County the sampling plan identifies a set of housing units to be enumerated. All age-eligibles in each housing unit are included in the cohort. In Suburban Minneapolis, Jackson, and Washington County, an age-eligible is sampled from a computer listing, the household to which the age-eligible belongs is enumerated and all age-eligibles in that household are included in the cohort. In Minneapolis and Jackson a computerized selection of age-eligibles is performed, but additional age-eligibles who are not on the computer listing are found through a half-open interval technique. Thus, the probability that a household is selected is not the same for the various sampling methods. In Forsyth County every household is equally likely to be selected; in Minneapolis Jackson and Washington County, the selection probability for the household is proportional to the number of household members (multiplicity) who are on the listing of the sample frame. When appropriate, the data are analyzed by weighting the observation inversely by the multiplicity.

The identification of household members on the sample lists is checked in Jackson, Minneapolis and Washington County by asking household members whether they have a current driver's license. Minneapolis enumerators also ask whether the household members are registered to vote.

1.3.1 Forsyth County, North Carolina

1.3.1.1 Population Sampled

Forsyth County is a single-county State Economic Area with clear census-based denominators and demographic descriptors. In the 1980 census, Forsyth County had a total population of 243,683 people, approximately 51,000 of whom were in the age group 45-64. The final cohort sample of 4,000 represents a sampling fraction of about 8 percent of the age-eligible population.

1.3.1.2 Design Summary

A total of 4,000 persons in the age group 45-64 is being examined during the three year period 1986-1989. Assuming that approximately 80 percent of all selected age-eligibles participate in both the home interview and the clinical examination, a sample of housing units containing approximately 5,000 eligible persons is selected. Approximately 9,000 housing units in Forsyth County will be contacted (1/10 sample) (Table 5).

A two-stage area probability sample of housing units located within the boundaries of Forsyth County was chosen as the sampling design. The sampling units in the first stage of selection are census-defined blocks. Within each selected block, a field interviewer lists housing units and forms geographically compact segments of six to eight housing units each. Sample segments are then selected for inclusion in the survey. Table 6 provides an outline of the method for sample selection.*

All eligibles in all housing units in a sample segment are included in the cohort. To identify cohort survey eligibles, a household enumeration is attempted for each selected housing unit. The eligibility requirements are specified in section 1.2 of this manual.

Both race and a measure or correlate of family income are used to stratify the census blocks prior to selection, though there is no disproportionate sampling by different strata. Since persons 45-64 years of age are selected, an estimate of the number of persons in this age group is used as the measure of size for selection blocks with probabilities proportional to size. The actual measure of size is estimates of the number of persons 38-57 years of age in 1980. This indicates approximately how many persons of age 45-64 to expect in 1987, midway through the three-year first-examination period.

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*It should be noted that the two-stage sample design proposed is statistically equivalent to a one-stage sequential sample of segments. This property can be used in setting up procedures for calculating estimates of sampling error, which, of course, must reflect the entire complexity of the sample design.

Table 5. Sampling rates and sample sizes needed to obtain 4,000 ARIC Cohort Study participants in Forsyth County, North Carolina

Sampling rates	Sample sizes
At 80 percent participation, number of eligibles needed	5,000
Number of housing units needed for sample	8,943
Number of segments of an expected 4 eligibles each	1,250
Average number of occupied housing units per segment	7.2
Overall sampling fraction	1/10.1

Table 6. Outline of sample selection methodology for the ARIC Cohort Study in Forsyth County, North Carolina

1. Using Census Summary File 1, obtain an estimate of the number of persons of age 38-57 in 1980 for each census block in the blocked portion of Forsyth County and each Enumeration District (ED) in the remainder. Divide this number by four and round to nearest integer greater than 0. This is the measure of size (number of segments) for the block or ED.

2. Stratify blocks by percent non-white, forming three strata of approximately equal population: High, Medium and Low non-white. The EDs constitute the fourth stratum.

3. Within each stratum, order blocks or EDs on an economic variable (estimated from housing characteristics) and form a serpentine ordering of blocks or EDs.

Stratum	Ordering on Variable Correlated with Income
High Non-white Blocks	Low to High
Medium Non-white Blocks	High to Low
Low Non-white Blocks	Low to High
EDs	High to Low

4. Cumulate number of segments and for each 10 segments randomly select 1.

5. Partition selected segments into 36 random subparts by randomly assigning the sample month to each selection, within each group of 36 selections.

6. Print out the identification of each census block or ED selected into the sample, its total number of segments, the number of segments selected, and the sample month assigned to each of the selections.

1.3.1.3 First Stage Sampling Frame

Although most of the population and, therefore, most of the sample lies inside the blocked area of the county (i.e., principally the city of Winston-Salem and its surrounding area), a small part falls in the area for which no block statistics are available. For that portion outside of the block statistics area, the smallest unit for which census counts are available is the enumeration district (ED), which is made up of a group of contiguous blocks and suitably serves as a primary sampling unit (PSU). The selection procedure for this portion of the county follows the same lines as described above, only selecting EDs instead of blocks at the first stage. One or more blocks within selected EDs are sampled. This type of procedure involves additional field work for the interviewers because it is necessary for them to visit the sample EDs and make counts of dwellings within each of the component blocks. These counts are then used to assign measures of size reflecting the number of dwellings (i.e., ignoring the age variable). Only about 7 percent of the Forsyth County population lived in the unblocked portion of the county in 1980, so the total impact of the sampling and interviewing complexities associated with this portion of the sample is minimal.

1.3.1.4 Listing and Enumeration

In Forsyth County blocks are selected by probability sampling, each selected block is mapped, and all housing units and those in selected segments are enumerated. This listing process is not done in the other study communities, since sampling takes place from already available lists of individuals. Household enumeration procedures, however, are essentially the same in all four communities.

1.3.1.5 Listing Sample Units in Forsyth County

Sample units (clusters of approximately 7 households) are selected as previously described. Accurate listing of all households in these units is performed by interviewers on a monthly basis, from November 1986 through July 1989. The listers attend a one-day training session on counting and listing procedures, conducted by a listing expert and the field supervisor. The listing process is directly supervised by the field supervisor.

1.3.1.6 Procedures to Increase Sample Size if Clinic Response is Low

The data in Table 5 show the samples required if an 80% clinic response rate is achieved. The actual sample is drawn using a lower bound of a 55% response, thus requiring a potential enumeration of 7286 persons. This sample is drawn to accommodate a poorer response and is used only if actual recruitment demonstrates that it is needed.

1.3.2 Jackson, Mississippi

1.3.2.1 Population Sampled

The population to be studied by the Jackson Field Center consists of all age-eligible black persons living within the city limits of Jackson,

Mississippi during the period of study. Census statistics are given for Jackson as a city within the Jackson standard metropolitan area.

At the time of the 1980 census there were 95,357 black persons living in Jackson of which 11,480 were between 45 and 65 years of age. A cohort of 4,000 persons would thus represent 35 percent of the estimated age eligible black population of Jackson.

1.3.2.2 Design Summary

The sampling frame for selection is the list of persons who hold a driver's license in Mississippi or who hold a Mississippi Identification Card. The list, furnished by the Mississippi Highway Patrol, includes all licensed drivers throughout the State of Mississippi and all who have secured an identification card through the Mississippi Highway Patrol. This list encompassed approximately 1.8 million persons on November 15, 1986. The information furnished includes name, address, zip code, race, sex and birthdate.

The list is updated yearly and file processing is performed each year to prepare a usable sampling frame. First, the subset of persons who are black and who are ages 45 through 64, and who either list Jackson, Mississippi as their address or who have a zip code of 392-- are extracted from the entire list. All of Jackson zip codes start with the prefix 392. This subset of persons is then sorted by name, by address, and by zip code and printed for visual inspection. This list is searched for duplicates, and these if found, are removed. One zip code 39208 serves only an area of Rankin County, not part of the city of Jackson. All addresses in the zip code, 39208. are searched for legitimate street addresses within the city of Jackson, and if found, are assigned a proper zip code. All remaining addresses for zip 39208 are then deleted from the list. There are certain addresses in zip codes 39209 and 39213 which also fall outside the city of Jackson, being on rural routes which cross the city borders on occasions. To the extent that those beyond the city limits can be identified, they are deleted from the sampling frame. One additional zip code was subsequently added to the sampling frame because a portion of persons within that zip code reside within the Jackson city limits. That zip is 39174. Some persons within 39174 give Jackson as their address; others list Tougaloo as their address. To the extent possible, persons living outside the city limits are deleted from the sampling frame, but where the distinction is not clear-cut, they are left on the sampling frame. For this reason there may be a few persons on the sampling frame who reside just outside the city limits of Jackson who will subsequently be ineligible for recruitment.

The list is updated on an annual basis for each of the three years of recruitment. For that reason, all persons who would become age eligible during the first 12 months are selected for the subset to be used as the sampling frame. In total there are 11,619 individuals on that list. Since not all persons are eligible for selection in every given month, a count was made of the frame size for each of the 12 months. The frame size varies from 10,826 in January to 11,255 by December of 1987. This corresponds rather closely with the 11,480 at the time of the 1980 census who were identified as being ages 45 through 64.

1.3.2.3 Sample Selection

A simple random sample (without replacement) is selected monthly from eligible individuals included in the driver's license and identification subset. Since the month and year of birth requirements change for each enumeration month, the population is considered dynamic and only those individuals who are age-eligible in a particular month will be selected. For each month those eligible are placed in a random permutation and the first "n" (approximately 120) individuals constitute the sample selected for any given month.

The frame is updated monthly prior to drawing the sample for the subsequent month. Updating means that indicator flags are set for those who have been previously selected, including both index subjects and age/race/sex eligibles residing in households with those index subjects. Concurrently with the sample selection every fourth person selected will be designated for the initiation of half-open interval procedures (see Section 1.3.2.4). In other words, in the initial phases of the study, i.e. the three months, half-open interval will be invoked one-fourth of the time in areas in which it is estimated that there is more than one eligible person on the block. If after this time it is found that the sampling frame is rather complete and that few eligibles are being found through half-open interval techniques, this will be dropped at that time. There are no plans to invoke the half-open interval when the index subject resides on a block which was estimated to have less than one age/race eligible person at the time of the 1980 census. The sampling information and expected response rates are presented in Table 7.

Table 7. Sampling rates and sample sizes needed to obtain 4,000 ARIC Cohort Study participants in Jackson City.

Sampling Information	Sample Size	
	List Sample	Half-Open Interval
Number of housing units enumerated	4243	3501*
Home Interviews (estimated 1.6 eligibles per housing unit and 80% participation from list sample).	5431	96
Participants examined at baseline (estimated 73% participation).	3965	70

* Includes some white households which are eliminated by a quick screen.

1.3.2.4 Dealing with Sample Coverage

The proportion of the Jackson City black population age 45-64 who are not on the sampling list is not known. The age-sex distribution of the list suggests that the list may under-represent females and older persons. Many of those persons missing from the list will be identified as living in the same household as an index person who is on the list, and thus will be recruited as participants.

The half-open interval technique provides an estimate of characteristics of the eligibles missed by the list sample, and of the coverage rate for the sample computed as the percent of persons who receive a home interview and who participate in the clinic visit but who are not identified by the list sample mechanism. The half-open interval technique is more completely described in the Minnesota sampling plan, Section 1.3.3.4.

The half-open interval was used during the first three months of the study to identify and recruit those who are not identified by the list sample (index persons and other household members). In one out of four households identified by the list sample, and in areas with one or more age-race eligible per block, the enumerator contacted adjacent households in a prearranged path until an age-race eligible was found and was also on the sample list. All age-race eligibles in the successive households not on the sample list were recruited and became part of the study. Because of the very low yield of study eligibles who were not identified by the list sample (less than 5 percent), the half-open interval technique was discontinued in Jackson City.

1.3.2.5 Procedures to Increase Sample Size Clinic Response is Low

The sampling procedure described above is planned assuming a 58% response rate. Since the sample is selected from the first "n" persons occurring on the random ordered list, the sampling fraction can be increased by increasing the selection number, "n".

1.3.3 Minneapolis Suburbs, Minnesota

1.3.3.1 Population Sampled

The population studied by the Minneapolis Field Center consists of all age-eligible persons living in eight contiguous suburbs in Minneapolis: Golden Valley, Robbinsdale, Crystal, New Hope, Plymouth, Brooklyn Center, Brooklyn Park, and Medicine Lake. Each of these suburbs is classified by the census as places of 10,000 to 50,000 population. It is estimated that about 40,000 persons aged 45-64 currently live in these areas. Thus, a final sample of 4,000 represents a sampling fraction of about 10 percent from the age-eligible population.

1.3.3.2 Design Summary

Using a list of persons eligible for jury duty in Hennepin County, a series of without-replacement stratified simple random samples of eligible persons is selected. A stratified simple random sample of individuals from the jury selection list is chosen monthly from a jury list which is updated annually. Members of each subsample are designated for examination during a particular one month period, although problems in scheduling due to respondent availability may require that the home interview and clinic examination take place in a later month. The criterion for stratification is age (45-49, 50-54, 55-59, 60-64). Simple random sampling is used within each stratum. The sample is proportionally allocated among strata (i.e., all stratum-specific sampling rates are equal).

Steps are taken to minimize the chances that one-month samples overlap. Starting with the second sample chosen, those persons selected (as well as age-eligibles in their housing units) in prior one-month samples are purged from the frame prior to sample selection. The computation of selection probability for use in analysis accounts for the purging, however, by having Field Center staff document the following (by stratum) each time a new sample is drawn: (1) the number of previously chosen individuals who were purged from the frame, (2) the number of remaining individuals on the frame, and (3) the number of individuals selected in the one-month sample.

Sixty percent of households of individuals selected are expected to contain another eligible participant, or stated differently, there are 1.6 eligibles per housing unit contacted. A participation rate of 70% is anticipated for the home interview and 93% for the clinic visit (65% overall). Thus, 3,840 housing units are enumerated to yield 4,000 participants (Table 8).

Table 8. Sampling rates and sample sizes needed to obtain 4,000 ARIC Cohort Study participants in the suburban Minneapolis area

Sampling Rates	Sample Size
Number of housing units enumerated	3,840
Home interviews (estimated 1.6 eligibles per housing unit and 70% participation)	4,301
Subjects examined at baseline (estimated 93% participation rate)	4,000

1.3.3.3 Frame Construction and Updating

The frame for selecting cohort participants in the Minnesota Field Center is extracted from a list of Hennepin County residents who are eligible for jury selection. The jury selection file includes all Hennepin County residents who either (1) have a Minnesota driver's license, (2) have a Minnesota identification card, or (3) are currently registered to vote in Hennepin County. This file is updated and screened for duplication on a quarterly basis and is thought to be 90-95 percent complete. The following information is included on each record of the file: name, address, zip code, birth date, and a person index number.

A data tape is obtained annually during the three-year recruitment period containing the most current jury selection list. Requested are those persons aged 43-64 years, as of April of that year, and listed with an address located in a zip code falling within one of the seven suburbs. The postal boundaries coincide almost exactly with geo-political boundaries in this part of Minneapolis. Duplicate names have been identified and removed by Hennepin County using a matching program which matches on exact last name and first initial, in combination with birth date and other identifiers. If a visual

inspection of a printed listing of the tape suggests that extensive duplication remains, a second matching using birth date, address and NYSIIS applied to name is performed and duplicates removed.

1.3.3.4 Dealing with Sample Coverage

Although thought to be quite good, the proportion of the study population included on the jury selection frame is not precisely known. Because coverage is not precisely known, Field Center staff employ a half-open interval technique for at least the first month's sample to document the frame's adequacy.

The half-open interval was originally designed for use in area samples of housing units. It is, however, easily adapted to the present sample design in which an individual chosen from the jury selection frame provides access to his or her home for the study. In principle, the object of the technique is to link, uniquely, each person missed by the frame to a person (or persons) included on the frame. Instructions to the interviewer making initial contact at the home of a selected individual follow:

1. Make contact and, if possible, enumerate the housing unit found at the address of the selected individual. If the selected individual no longer lives at that address, enumerate the housing unit of his new address, if it is within the study area, or drop the individual from the study if his/her new address is outside the study area.
2. If the selected individual lives in the study area, check for additional eligible persons in the housing unit at the address where you found him/her.
3. The half-open interval is applied by first deciding on some prearranged path to follow from the selected persons current address, and then moving around his/her neighborhood.
4. Following the prearranged path, determine for each housing unit in the path whether anyone living there would have been on the jury selection frame. This involves asking whether age-eligibles have a driver's license, Minnesota ID card or are registered to vote in Hennepin County. Any housing units with only "no" answers to these three questions for age-eligibles are included in the study. This process is discontinued once an age-eligible found along the path answers "yes" to one of the questions.

If coverage is good, relatively few additional housing units have to be contacted, unless the housing unit of the originally selected individual is located in a neighborhood with few age-eligibles.

The half-open interval gives the Minnesota Field Center additional useful information. By keeping a record of how many housing units are contacted in applying each interval, a direct estimate of the actual coverage of the jury selection list is obtained. For that reason and the improved coverage that is assured, Field Center staff apply this method during the first month of data collection. If the estimated coverage rate is found to be suitable after the first month, then the half-open interval method is not used in subsequent months. If the rate is low, the method is continued indefinitely.

1.3.3.5 Procedures to Increase Sample Size if Clinic Response is Low

The sampling procedure described above is planned assuming a 65% overall response rate. Since the sample is selected from a computer list, increased sample selection due to poor clinic response is achieved by redrawing the sample with a larger sampling fraction. Those already sampled are excluded.

1.3.4 Washington County, Maryland

1.3.4.1 Population Sampled

The census defined area chosen for the cohort sample in Maryland is Washington County. In the 1980 Census, Washington County had a total population of 113,068, with approximately 24,000 age 45-64 years. The final sample of 4,000 represents a sampling fraction of 17 percent of the age-eligible population.

1.3.4.2 Design Summary

The sample of housing units is chosen by simple random sampling from a list of individuals meeting both age and residency requirements for the study. The process of sample selection is repeated approximately every six months from a frame which has been updated to include only those individuals who would be ages 45 through 64 years during any time within the succeeding six month period for which the sample will be used.

The sample of individuals is chosen by first randomly ordering a sampling frame created by merging a list of age-eligible persons enumerated in a special 1975 census of the county, with a list of age-eligible county residents who have a Maryland driver's license. Selections for the sample are made by taking the first and subsequent members of the list until the desired sample size is achieved for the study. Stratification during sample selection is not used. As with the Minneapolis sample, selection probability for each selected age-eligible varies depending on the number of age-eligibles in his or her housing unit who appear on the frame.

The Washington County Field Center anticipates that 60 percent of households of individuals selected contain another eligible participant, or stated differently, there are 1.6 eligibles per housing unit contacted. A participation rate of 70% is anticipated for the home interview and 93% for the clinic visit (65% overall). Thus, 3,840 housing units are enumerated to yield 4,000 participants (Table 9).

Table 9. Sampling rates and sample sizes needed to obtain 4,000 ARIC Cohort Study participants in Washington County, Maryland

Sampling Rates	Sample Size
Number of housing units enumerated	3,840
Home interviews (estimated 1.6 eligibles per housing unit and 70% participation)	4,301
Subjects examined at baseline (estimated 93% participation rate)	4,000

1.3.4.3 Frame Construction

The frame of age-eligible individuals is constructed from two available sources. The data from one of these sources, a 1975 private health census done exclusively in Washington County, are available on tape to the Johns Hopkins School of Hygiene and Public Health. Age eligibility is determined from the birthdate which is available for all persons enumerated during that census. Other pertinent information available for each individual is full name, sex, and address. It is expected that this 1975 information is still accurate for most individuals, since both the county population and this age group are known to be geographically stable.

The second source for constructing the frame for the Washington County sample is the Maryland Department of Motor Vehicles. Age-eligible persons possessing a Maryland driver's license with a Washington County address are included. Each six-month frame constructed from this source is updated to reflect changes in the group of people with licenses, as well as the general aging in the population. The following relevant information for persons identified through this source is available: full name, sex, birth date, address, and an identification code (containing a SOUNDEX (or similar) code of the last name).

The census and driver's license lists are merged into a single frame with apparent matches between the two lists removed. Persons found on both are identified using sex, birth date, and a SOUNDEX code constructed from the last name and first initial as the matching keys (since no recognized unique identifier like social security number is available). Matching is done by first producing a computer generated list of potential matches and then verifying a match or nonmatch by visual inspection. For each confirmed match the record from the driver's license lists (which presumably is more current) is retained and the record from the 1975 census is dropped from the final frame. Failure at computer matching with the above keys is checked by visually comparing two alphabetic lists: driver's licenses and a list of age-eligibles with no driver's license as of the 1975 census. Persons who appear to be matches are flagged to ascertain at interview (if they are selected) whether the apparent match was real. A combined list, with cross-list duplicates removed, is produced every six months for sampling. Persons selected from these frames, along with all age-eligibles in this housing unit, are eligible for participation in the study.

Since a fresh sample of individuals is selected every six months from an updated sampling frame, effort is required to purge those persons (and the age-eligibles in their housing units) who were selected in previous six month samples. Maryland ID numbers or 1975 census ID numbers are used to do the necessary matching. To aid in the computation of selection probabilities for each sample, the Washington County Field Center computes the following three numbers for each six-month sample: (1) the number of individuals who were purged from the frame, (2) the number of remaining individuals on the merged frame, and (3) the number of individuals for whom contact attempts (for participation in the study) were made.

The frame for each six-month sample is also updated by removing all deaths which occurred during the previous six month period. This updating is done by matching an alphabetized listing of the previous six-month frame against

obituary listings and death certificates for deaths occurring since the last six-month sample was chosen.

1.3.4.4 Procedures to Increase Sample Size if Clinic Response is Low

The sampling procedure described above is planned assuming 65% overall response rate. Since the sample is selected from a computer list, increased sample selection due to poor clinic response is achieved by redrawing the sample with a larger sampling fraction. Those already sampled are excluded.

1.4 Sample Replication

To facilitate quality control of the laboratory methods used during the three-year examination period, samples in each Field Center are randomized so that the individuals examined during any one-month period are a random subset of the full sample and, therefore, a representative sampling of the study population in each area. This sample replication, serves to remove the effect of inherent differences in the observed sample through time.

Because sampling designs differ among Field Centers, the methods used to identify sample replicates differ as well. The replication method used in the Forsyth County sample is to choose the full sample prior to the start of recruitment, and partition it into 36 subsamples, one for each month of examination. Replicate allocation therefore, is of the block level. Frame construction and selection of the compact segments chosen in the second stage is not done until just prior to using the block group in one of the one-month replicates.

Sample replication is done in Jackson and Minneapolis by selecting a new sample each month. Sample replication is accomplished in each Washington County six-month sample by serial designating blocks of contiguously listed individuals on the randomly ordered frame, constructed by merging the driver's license and 1975 Census lists. Starting at the beginning of the list, the first block of names is designated for the first month of examination, the second block for the second month, and so forth through the sixth month.

Departures from the initial replicate assignments occur in those cases where the actual examination cannot be conducted in the assigned month due to scheduling conflicts on the part of the participant. These departures are not expected to alter significantly the original intent of the replication, however. Individuals examined each month are still a reasonably representative sampling of each study population.

Listers receive, for each block in their assignment, a sketch of the block and one or more maps showing its precise location. The estimated number of housing units within the block is indicated on the sketch.

When the lister arrives at a block, the boundaries are carefully identified and a count of housing units (HUs) completed. If any problems occur in a boundary identification, a call is made to the Field Center for resolution. Likewise, if a significant difference exists between the estimated number of housing units and the actual field count, the situation is discussed with a member of the sampling staff before further fieldwork is done.

Listing procedures generally begin in the northeast corner of the block. This point is noted on a final sketch sheet, which is completed as the lister moves in a clockwise direction around the segment. As each HU is encountered, a street address or HU description is recorded on a listing form and a corresponding sequential HU (line) number from the listing form is recorded on the final sketch sheet. HUs are listed as encountered on the right. Standardized procedures are developed to handle internal through-roads, dead-end roads, etc. The procedure continues until all HUs have been listed and recorded, both on the listing form and final sketch sheet.

Structures with more than one possible HU are frequently encountered during listing. Specified rules are applied to determine the correct listing order within multiple-unit structures, such as apartment buildings. Additional special instructions are prescribed for handling atypical structures, such as boarding houses, vacation cottages, group quarters, servants' quarters, etc. These rules are designed to include all units that meet the Census Bureau definition of a housing unit, while excluding units that do not meet this condition. (Note that this excludes persons living in institutions and those living in group quarters.)

When listing is complete and materials have been checked by the supervisor, they are mailed to the Field Center office. Upon receipt, the materials are checked by members of the survey operations and sampling staffs. Following the in-house review of materials, the segments within a block are delineated and the segments which are included in the sample are identified.

In spite of best attempts to achieve accuracy, occasional HUs may be missed in the listing process or new HUs may appear between listing and subsequent data collection. As part of standard field methods, a procedure is used to give a proper probability of selection to any such HUs discovered during the course of data collection. The method employed is an application of the half-open interval technique. In general terms, this procedure explicitly links any nonlisted HUs discovered after the initial listing of a segment with exactly one listed HU in that segment. Whether or not a nonlisted HU is added to the sample depends on the status of the listed HU with which it is associated. If the latter is an in-sample HU, any nonlisted HUs associated with it are automatically added to the sample. If the listed HU is not a sample HU, any associated nonlisted HUs are not included in the sample. Details of the listing procedures are included in the RTI Counting/Listing Manual.

1.5 Household Enumeration

Selectees chosen from the lists in Jackson, suburban Minneapolis and in Washington County, are first contacted by the ARIC Study using a letter sent to the selected individual at the listed address (see Appendix I, Form 1). The purpose of the letter is to introduce and explain the purpose of the study and to assure confidentiality. The field interviewers are given the selected individuals' names and addresses, grouped geographically to minimize travel. The household containing the selected individuals is found and the entire household enumerated for eligibility. If the address listed for the participant is incorrect, he/she is traced using phone directories, contacts with neighbors, etc. If the selectee still lives in the study community, the enumeration is complete; if the selectee lives outside the community

boundaries, he/she is considered ineligible. The enumeration form is in Appendix II.

In Forsyth County interviewers locate the sample segment and contact designated sample housing units to determine the eligibility status of members of the household. The sample households to be visited are clearly specified on the segment listing, and the location of each sample household is indicated on the segment sketch. An area map is also provided for each segment, showing the location of the segment within a larger geographical area. As described previously, application of the half-open interval technique is used by the interviewer to add certain hidden or newly constructed housing units that were not listed initially, but which are discovered in the enumeration process. (In Minnneapolis and Jackson a comparable half-open interval procedure is applied to a subsample of the housing units selected through an index person who was chosen from the sampling frame). Vacant housing units, nonresidential units listed erroneously as housing units, temporary or vacation homes, and group quarters are reported by the interviewer to the field supervisor. For each of these categories, the interviewer is required to obtain verification of the unit's status from either a neighbor, an occupant, or other reliable source. If approved by the supervisor, such units are dropped from the sample.

In all Field Centers, interviewers are instructed to make their initial visit to a sample household in the late afternoon or early evening on a weekday or on Saturday, since the chance of finding an eligible enumeration respondent (a knowledgeable household member aged 16 or older) is enhanced at these times. If no eligible enumeration respondent is at home on the first attempt, the interviewer attempts to learn from other household members (e.g., under age 16) or neighbors when an eligible household member is expected to be at home. If a suggested time cannot be obtained, the interviewer is required to make the second attempt between 5:30-9:00 p.m. on a weekday or during the morning of the following Saturday. Additional callbacks are made as necessary, with the interviewer continuing his/her efforts to learn from secondary sources when and how to contact an eligible enumeration respondent. In the absence of better information, successive attempts are made at varying time/day intervals in order to increase the probability of finding an adult at home.

When contact is made with an eligible enumeration respondent, the interviewer introduces him/herself, briefly describes the purpose of the visit, shows the respondent his/her credentials, and proceeds with enumeration. Enumeration is the process of completing a household roster to select the sample member(s). To be eligible to be a cohort member for a selected household, the person must be a member of the sample household and be ages 45 through 64, inclusive, at the time of enumeration.

Identification of the cohort sample participants is done by the interviewer. To assure proper selection, the enumeration respondent is asked to list all the persons 18 years of age or older who reside in the sample unit. From this listing, the number of eligibles per household is determined. As described previously, all eligible members of a household are selected for the cohort sample.

To assure that comparable efforts are made among Field Centers in obtaining participation for the study, a set of criteria for enumeration and clinic

recruitment has been established. Unless early attempts indicate that further efforts are fruitless (e.g., an unequivocal refusal), field staff are not allowed to consider a selected housing unit as a final noncontact until at least five (5) call attempts have been made, with at least one attempt made during a weekday, during a weeknight, and on a weekend (legitimate exceptions allowed). Initial nonrespondents not giving an unequivocal refusal are recontacted for possible clinic recruitment. Each Field Center is allowed to try to reschedule eligible persons for a period of up to six months after the month in which the person was initially assigned. If rescheduling is required for reasons such as illness or travel, this time period can be extended up to nine months.

1.6 The Home Interview

The Home Interview (Appendix IX) is administered to all age eligibles (45-64) within a sampled housing unit. After identifying those eligible to participate, the ARIC Study is explained and those who are eligible are asked to take part in it. The home interview is also designed to obtain certain demographic, socioeconomic, and medical information from the participant. Any questions the participant has about his/her clinic visit or about the study in general are clarified.

1.6.1 Home Interview Procedures

As eligible sample members (respondents) are identified through the enumeration process, the interviewer attempts to secure the home interview on the same visit to the household whenever possible. If a sample respondent is not home at the time of enumeration, callbacks are made, as necessary, in order to secure the interview.

When contacting an eligible respondent, the interviewer repeats the ARIC Study introduction (assuming the sample respondent is a different person from the enumeration respondent) and explains in somewhat more depth the purpose and importance of this study. A brochure and letter explaining the purpose of the study and the examination are used for recruitment. The voluntary nature of the study and the confidentiality of the collected data are stressed. If the sample respondent is not at home at the time of enumeration, callbacks are made, as necessary, to secure the household interview and schedule the clinic appointment.

1.6.2 Contacts with Participants

The first contact from the ARIC Study in Jackson, Minneapolis and in Washington County is by a letter sent to the selected individual at the listed address. The purpose of the letter is to introduce and explain the purpose of the study and to describe confidentiality assurances. In Forsyth County a postcard is mailed to the home to inform the resident that an interviewer will be calling. In Forsyth County, where area sampling is employed, and in the portion of Jackson sample identified through the half-open interval, the first household contact is for household enumeration.

In all areas, the ARIC interviewer, wearing an identification badge, visits the selected household, enumerates the household to determine eligibility, and recruits eligibles to the study. The ARIC Study enumeration protocol and form, as well as the eligibility requirements, are described elsewhere.

1.6.3 Making the Clinic Appointment

At the end of the home interview, the clinic visit is described to the participant and a request made for an appointment. The interviewer inquires about several items to assist in scheduling the appointment:

1. Any medical conditions (e.g., diabetes, dietary restrictions) which might affect the physical examination and/or type of snack provided;
2. Need for assistance in mobilization;
3. Preferred time and date of examination.

The interviewer schedules appointments for the examination during the 30 days following this household visit. The interviewer calls the clinic scheduler from the home of the respondent to set an appointment day and time. The appointment is recorded on a reminder sheet which is left for the participant. Participants are scheduled for appointments at their convenience, dependent upon clinic schedule. Whenever possible, eligible members of a single household are scheduled for examination on the same day. This makes the examination visit more attractive to the participants.

When examination arrangements have been made, the interviewer provides the participant with an ARIC Study brochure (if not already given), and a participant information sheet. The interviewer thoroughly reviews the brochure with the participant. Information provided in the brochure and information sheet includes the following: study overview, fasting requirements, description of the examination procedures, location of the clinic, and so forth. Participants are asked to fill a form containing their identifying information and social security number, as well as the names, addresses and phone numbers of contact persons. Once participants have signed the informed consent at the field center the information collected on this form is verified, and added to the data base. At the conclusion of the interview, sample respondents are thanked for their participation.

1.6.4 Instructions for the Baseline Clinic Examination

The instructions for the clinic visit are specified on the participant information sheet (Appendix I, Form 2) that each Field Center has prepared.

The instructions include:
1. Appointment date and time,
2. Directions to the clinic (a map) and to parking facilities,
   a) All Field Centers provide free parking or reimbursements.
3. Preparations:
   a) 12 hour fast
   b) No tobacco or vigorous activity
   c) Clothing to wear for the visit.

4. Things to bring:
   a) Eyeglasses for reading
   b) Name of physician and clinic
   c) Names, address, and phone number of contact persons
   d) Medication Instruction Sheet
      A script describing the need for medication information is on the home interview form and is read to the participant. The reminder sheet also indicates which medications should be brought. A bag is provided in which to carry the medications.
5. Clinic Operation
   a) A snack is provided after the initial part of the exam.
   b) Clinic hours and phone number.
6. Transportation
   a) Some centers provide transportation and arrange for participant pick-up.
   b) In Jackson, those who drive are asked to record mileage for reimbursement.

1.6.5 Scheduling Appointments

The interviewer delivers all materials from the household interview to the supervisor at the Field Center prior to the scheduled clinic appointment. The material is reviewed by office staff and entered into the data base on a regular basis. Sufficient appointments are scheduled each day for Monday through Friday, to meet the requirement of 30 appointments per week. The data base is updated on a regular basis. Each clinic maintains:

1. Assignment record of labels for the clinics.
2. A listing of telephone numbers and dates and times to conduct the telephone reminder calls.
3. Daily appointment schedule with participant name, ID number, appointment time, and special considerations such as health restrictions or child care requests. This schedule is used to structure that day's appointments and to check in participants as they arrive for their examination.
4. Clinic schedules are maintained by clinic schedulers and/or an answering service. In those centers where an answering service is used following clinic hours to schedule appointments, duplicate appointment books are kept and updated on a daily basis to avoid conflicts in schedules. In Jackson, interviewers use an answering machine after clinic hours to record appointments. When conflicts arise due to overbooking of an appointment, they are resolved by clinic personnel.

1.7 Instructions for Coding Occupation

Each center has two certified coders who assign occupational codes. All field interviewers are trained to ensure proper recording of occupational data for coders. Training includes probing for full and accurate responses.

1.7.1 The Alphabetical Index of Industries and Occupations

The basic resource for coding occupation is the Alphabetical Index of Industries and Occupations, 1980 Census of Population, Final Edition, November 1982. The document is available from the Superintendent of Documents, U.S.

Government Printing Office, Washington, D.C. 20402, or from any U.S. Department of Commerce District Office. (Prepayment is required if ordering by mail. Check price before ordering. For information call GPO, Washington, D.C. 202-783-3238.)

A companion volume, the Classified Index of Industries and Occupations (PHC 80-R4) is available from the same source.

Both indexes list some 20,000 industry and 29,000 occupation titles. The Alphabetical Index lists titles in alphabetical order, the Classified Index lists them in numerical order. The Alphabetical Index is the basic resource to use in identifying the appropriate occupational code. The Classified Index helps the user understand how the titles fit into the classification structure. This volume is also useful when dividing between two or more categories. It gives a broad picture of all the titles included within a category.

Both indexes are divided into two sections: the "white pages" list the industry codes; the "yellow pages" list the occupation categories. Each industry and occupation title has a 3-digit number or a letter which can be translated into a 3-digit number. The coder's task is to identify the 3-digit occupational code which best fits the respondent's answers to the occupation questions. The procedure is similar to looking words up in a dictionary. Once the coder is familiar with the index, the 3-digit code is relatively simple to assign for most cases. Few problems are expected with the cases and a mechanism is set up for resolving problem cases. Of note, the Industry "white pages" has a section on SELF-EMPLOYED with an extensive listing.

The Coder uses the description given by the Respondent to identify the occupational code in the "yellow pages". In those cases where specific industries are associated with an occupational title, the coder uses the industry information to select the appropriate code. Industry information, offered by the respondent but not coded directly, helps to identify the appropriate occupation code. If industry information happens to be incomplete, use the most general or "not elsewhere specified" category. The use of the 3-digit Census occupational codes provides maximum analytic flexibility. The codes can be aggregated into a common system across centers or into a system tailored to particular research objectives.

The Occupational Classification System developed by the Census contains 503 separate categories which include the 29,000 titles. The categories are contained in six summary groups and 13 major groups. This system, expanded to 15 major groups by separating out "writers, artists and athletes" and "farm operators and managers", is shown in Table 10.

Table 10. Occupational Classification System: 1980 Census; Fifteen Major Groups in Six Summary Groupings[1]

	Occupational Summary Groups	Occupational Codes
I.	Managerial and Professional Specialty Occupations	(003-199)
	1. Executive, Administrative, and Managerial Occupations	Codes 003-037
	2. Professional Specialty Occupations	Codes 043-179
	3. Writers, Artists, Entertainers, and Athletes	Codes 183-199
II.	Technical, Sales, and Administrative Support Occupations	(203-389)
	4. Technicians and Related Support Occupations	Codes 203-235
	5. Sales Occupations	Codes 243-285
	6. Administrative Support Occupations, Including Clerical	Codes 303-389
III.	Service Occupations	(403-469)
	7. Private Household Occupations	Codes 403-407
	8. Protective Service Occupations	Codes 413-427
	9. Service Occupations, Except Protective and Private Household	Codes 433-469
IV.	Farming, Forestry, and Fishing Occupations	(473-499)
	10. Farm Operators and Managers	Codes 473-476
	11. Other Farming, Forestry and Fishing Occupations	Codes 477-499
V.	Precision Production, Craft, and Repair Occupations	(503-699)
	12. Mechanics and Repairers, Construction Trades, Extractive Occupations, Precision Production Occupations	Codes 503-699
VI.	Operators, Fabricators, and Laborers	(703-889)
	13. Machine Operators, Assemblers, and Inspectors	Codes 703-799
	14. Transportation and Material Moving Occupations	Codes 803-859
	15. Handlers, Equipment Cleaners, Helpers and Laborers	Codes 863-889

[1] See Appendix III for the detailed Bureau of the Census Occupational Classification System.

1.7.2 Special Codes

The Bureau of the Census system includes occupation codes for persons in the labor force only. Other codes may be developed independently or special codes developed by the Census for other studies may be used. The following list of special cases (Table 11) is a combination of both. This list is updated from time to time.

Table 11. Occupational Codes for Selected Special Cases

Employment Status	If No Occupation Information is Given, Code as Follows	If Occupation Information is Given, Code as Follows
Armed Services	For: Military rank Military branch Military occupation (gunner, pilot, etc.) Code 905	For: Occupations that could be civilian or military, such as clerk, etc. Code according to regular instructions.
National Guard	Not considered part of Armed Services.	Code occupation according to regular instructions.
Retired	Code 913	Code occupation before retirement if information is given.
Disabled	Code 917	Code occupation before disabled if information is given.
Other		Codes Assigned
Homemaker or Housewife, Not in Labor Force		Code 997
Never Worked		Code 998
No Codable Information, or No Answer		Code 999

1.7.3 Specific Rules for Coding

1.7.3.1 Coding "Down"

When there is uncertainty or ambiguity in the responses to the occupation questions, code conservatively. There is apparently a tendency for people to inflate responses. When there is a choice in the selection of a code, follow the principle of "coding down" rather than "coding up".

Please note that "coding down" results in a higher 3-digit number not in a lower one. In the Occupational Coding system, lower 3-digit codes describe more professional occupations than the higher numbers. For example, "Managerial and Professional Specialty Occupations" range in codes from (003-199), whereas "Operators, Fabricators, and Laborers" range from (703-889).

1.7.3.2 Self-Employed

Note that the industry "white pages" include a section on SELF-EMPLOYED with an extensive listing of occupations. The listing starts on page I-140 of the Alphabetical Index, 1980 Census, and continues through the middle of page I-142.

In assigning an occupation code for a self-employed individual, first check the Self-Employed section, but do not limit search to these pages. If the appropriate code is not found in the SELF-EMPLOYED section, use the regular "yellow pages" to identify the appropriate occupation code.

1.7.3.3 Multiple Jobs

The interviewer probes for the main job if the respondent has more than one. The main job is defined as the job at which the person spends the most hours. If the hours are equal, the main job is the one the person considers the most important. If the person does not consider one job more important than the others, focus on the first job mentioned, making the assumption that the first job mentioned is the most salient one.

The Census Occupational Classification System includes a "homemaker" title, code T (407) under the heading "Private household cleaners and servants," which refers to work in someone else's home. The ARIC Study uses a special code, 997, for the unpaid homemaker or housewife who works in her own home.

1.7.3.4 Quality Control

At the start of the ARIC Cohort study, the first 100 cases assigned at the Field Centers are reviewed by a second person. Where there is disagreement, the cases are referred to the Study Coordinator.

1.8 Recruitment for Examination

1.8.1 Introduction

The projected clinic response rates (ranging from 60 to 80 percent) are dependent upon each clinic's ability to recruit eligible participants and to maintain their clinic attendance. Every effort is made to make the clinic visit as pleasant and burden free as possible. Additionally, the following features are part of the effort to maximize participation: (1) Qualified interviewers, (2) Preappointment contacts, (3) No show procedures, (4) Reimbursement, and (5) Publicity.

1.8.2 Qualified Interviewers

Standard survey procedures assist in maximizing the rate of participation. Experienced, well-qualified and sensitive interviewers are employed to conduct data collection activities. They generally live in or near the area in which they are working.

Interviewers are thoroughly trained to overcome objections and concerns. The training includes two-three days of classes covering the content of the clinic visit, the materials used for the interviews, and procedures to be used for probing and overcoming objections and/or concerns.

Interviewers make initial contact with households at optimal times (i.e., late afternoons, evenings, or weekends), and schedule appointments for interviews as needed. Additionally, interviewers make callbacks as necessary, at varying times of the day and week. No unlocatable code may be entered until a minimum of five contacts have been made.

1.8.3 Pre-appointment Contacts

To increase respondent participation following recruitment by an interviewer, a preappointment postcard is mailed prior to the scheduled appointment. This card reviews the fasting requirements, the examination data and time.

Reminder calls are made to each participant one or two days prior to the examination. At this time, the information concerning the fasting requirements, medications bags, and other details is reviewed with the participant. Participants are asked if they have any special needs and every effort is made to answer participant's questions.

When appropriate, a letter is sent to the participant's employer explaining the ARIC Study (see Appendix I).

1.8.4 Contacts for No Shows

Eligible participants who fail to arrive for a scheduled appointment or who cancel their appointments are contacted by telephone to reschedule the appointment. At that time, the scheduler attempts to address any concerns or fears that the participant may still have.

Each no-show case is individually reviewed by the interviewer and when necessary by the supervisory staff. Conversion efforts include a combination of telephone contacts, in-person visits, and/or conversion letters. A participant is considered a refusal following three broken appointments.

1.8.5 Reimbursement

Each center provides for, or reimburses transportation and/or parking. For those who are reimbursed, detailed records are maintained for accounting purposes according to OMB and each university's guidelines.

1.8.6 Publicity

To enhance participation, the Field Centers maintain close contact with the media in their communities. Attempts are made to provide them with updates of the study and to enhance community support.

1.8.7 Supervision

Throughout the entire process from initial interview to final examination or refusal, close supervision helps maximize the rate of response. Supervisors record reasons for nonresponse, and examine performance trends by interviewer and by area. When deemed appropriate, supervisors initiate recontact with refusing participants to attempt their conversion. Detailed records of all contacts are maintained.

1.9 Recruitment Management System

To facilitate and standardize the bookkeeping on the large housing unit and person samples in the study, a computer-based system is used. Two separate control files are established for this and maintained by each field center. The file for the housing unit sample is called the Housing Unit Control File (HUCF), and the file for the sample of persons who complete the initial enumeration is called the Person Control File (PCF).

The interface between sample selection and this control system depends on the sample design used. In the Washington County, Jackson, and Minneapolis samples where eligible individuals are chosen initially and all eligible persons in their households are included, the HUCF is a file of housing units defined by the eligible member of that housing unit who was chosen from the frame. As these housing units are located and solicited for participation in the cohort study, other eligible members of their housing units are identified through the household enumeration form. Also added are housing units not included on the sampling frame but discovered through the half-open interval technique. The PCF contains a record for each of the initially chosen eligibles, plus any other eligibles in their housing units who are listed on the household roster during the household enumeration. For the Forsyth County city area sampling, housing units selected from the household listing frames constitute the HUCF. The PCF is created from the roster of study eligibles produced as part of the household enumeration in each responding housing unit.

The format for the HUCF is the same for each Field Center, although different sampling frames cause corresponding data items to differ. The comparable items appear on the HUCF for each field center are shown in Table 12.

Briefly summarized, some of the uses of the HUCF are:

1. To generate reports to summarize the status of recruitment for household enumeration (e.g., computing interviewer-specific refusal rates).
2. To store selection probabilities and other sampling information for each sample housing unit.
3. To compute housing unit response rates and weight adjustments for nonresponse.
4. To create an interviewer assignment log to be used during recruitment for enumeration.

Data from the PCF may be used for the following purposes:

1. To generate status reports for the process of recruiting for the field examination and follow-up.
2. To produce printed mailing addresses for reminder letters sent just prior to the first examination, and each subsequent follow-up call.
3. To produce response rates and adjustments for nonresponse occurring during the process of recruitment for the examination.
4. To link the sampling ID number (generated from the housing unit identification number used in the HUCF) and the clinical ID number (generated for labels needed for storing specimens taken during the examination). The PCF, therefore, is the file used to link study data back to the original selection probabilities and other sampling information (e.g., stratum and PSU in the Forsyth County sample).
5. To produce the daily appointment log for the examination centers in each Field Center.

Table 12. Comparable Housing Unit Control File Items by ARIC Field Center

Forsyth County Field Center (Area Sample)	Minnesota, Washington County, and Jackson Centers (List Samples)
Field Center Identifier	Field Center Identifier
Unique Housing Unit ID Produced During Sample Selection	Unique Individual ID Number Produced During Sample Selection
Full Name of Head of Housing Unit (if available)	Full Name of Selected Individual as Available
Street Address as Recorded During Second Stage Listing (if available)	Complete Mailing Address Available on Sampling Frame
Sampling Design Information (Primary Stratum; PSU; SSU)	Sampling Design Information (which six-month sample; stratum)
Housing Unit Selection Probability	Individual Selection Probability
Operational Replicate (Nos. 1-36 for each month during the three years of the examination)	Operational Replicate (Nos. 1-36)
Final recruitment status code (e.g., home interview completed, refusal, no no eligibles present, not at home, vacant, demolished, etc.)	Final recruitment status code for home interview in individual's housing unit (same code categories as in area samples)

The PCF is created for each Field Center using data obtained from study eligibles, recorded on the Household Enumeration and Home Interview forms. The PCF in each Field Center includes the following items: (1) the unique housing unit ID number, (2) the individual's unique clinical ID number, (3) participant's operational replicate, (4) participant's full name and permanent address, (5) intended exam date, (6) final exam status code (e.g. exam completed at scheduled time, exam completed at rescheduled time, exam no-show), (7) status code for subsequent follow-up date/time of rescheduled exam (if applicable), (8) telephone number, and (9) several items related to tracing for follow-up.

In order to facilitate the study's ability to locate study participants during follow-up, certain items of information must be obtained either during the recruitment phase of operations or during the first examination. Since obtaining a significant amount of personal information during recruitment may reduce the chances that a person will participate in the study, tracing information is obtained during the examination. Although all of the following items may not be feasibly collected from participants, they collectively increase the chances of locating that small percentage of hard-to-locate individuals:

1. Full name, current mailing address, and telephone number.
2. Social security number.
3. Name of current employer.
4. Name, address, and phone number of two close friends or relatives.
5. Driver's license number.
6. Maiden name (for females) and other names.
7. Birth date.
8. State of birth.

1.10 Annual Follow-Up

1.10.1 Annual Contacts Between Exams

Each study participant is recontacted approximately 12 months after his or her initial examination and then again, approximately 12 months after that. These two follow-up contacts review the health-related developments occurring since the last contact. Each follow-up is completed by telephone (preferred) or in person (if necessary). The follow-up call is preceded by a letter sent by mail about two weeks in advance of the call (See Appendix I). Information for this mailout is taken from the study database.

1.10.2 Follow-up Procedures

Annual follow-up of the ARIC Study cohort is used to (1) maintain contact and correct address information on cohort participants and (2) ascertain vital status and interim medical events between the three-year comprehensive examinations.

The basic procedure for interim contacts is described below and summarized in Figure 1.

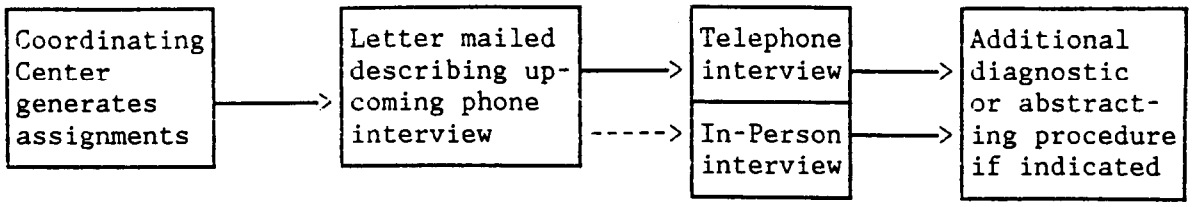

Figure 1. Interim Contact Procedures Between Clinical Examinations in the ARIC Cohort Study

At the baseline examination the following information is collected and stored in the data base to facilitate future contacts:

1. I.D. Number
2. Name, address, telephone number
3. Age
4. Physician/hospital name, address, telephone number
5. All tracing information, such as the names of close friends, social security number, employer, etc.

This file is used for preparing results letters, annual contact letters, and rescheduling second exams.

The preferred time-window for making interim contacts is within a month of the anniversary date of the original examination. Letters are mailed out two to three weeks before the anniversary date, and telephone interviews start one week before the anniversary.

The initial letter (see Appendix I, Form 5), sent first class with address correction requested, is on ARIC Study stationery and includes:

1. A reminder that the addressee is in the study and that annual contact is involved.
2. A description of the purpose of the contact.
3. Information that the participant should obtain to assist with the interview (e.g., hospitalizations, physicians visits).
4. The approximate time of day the call is made and the length of the telephone interview.

For persons not reached by phone, in-person interviews are attempted. Extensive efforts are made to maintain contact with every cohort participant.

1.10.3 Annual Cohort Interview

The annual follow-up interview of the ARIC Study cohort updates address and tracing information of cohort participants, ascertains vital status, interim

hospitalizations, and new cardiovascular symptoms. (See Appendix IX, Annual Follow-up Form). Its main purpose is to identify possible cardiovascular events or treatment requiring hospitalization or physician visit. Every hospitalization is verified and the discharge diagnoses recorded. Potential cardiovascular events are reviewed further for ARIC Study endpoint criteria by abstraction of hospital records.

Every attempt is made to identify cohort deaths before the annual contact, through regular review of death certificates. For those who have died, a mortality interview is conducted at an appropriate time.

2. THE BASELINE VISIT

2.1 Introduction

Upon completion of the home interview, eligible participants are invited to take part in the baseline examination at the field center. Six or more participants are scheduled daily. Field centers offer Saturday sessions when required.

Chapter Two, the Baseline Visit, presents an overview of the baseline examination, a detailed description of certain baseline examination components, and a reference to the pertinent manuals of the protocol for those examination procedures not covered in detail in Manual 2. Separate protocol manuals are available for baseline examination components that require lengthy description and technical specification, or are of intrinsic substantive interest as stand-alone documents.

Table 13 identifies the main components of the ARIC baseline examination, presents a summary description of each work station, and cross-references the respective sections of the protocol.

2.2 Participant Flow

At each field center the flow of participants follows a common plan. This plan is aimed at minimizing the participant time burden and reducing variability in the various baseline measurements. The participant flow pattern begins with a fixed sequence of steps, adhered to at each field center, followed by a flexible sequence of work stations after the snack.

2.2.1 Fixed Sequence

The fixed sequence of participant flow reflects the following requisites: signed informed consent prior to any examination; participant time is to be kept within four hours; twelve hours of fasting and one hour of abstinence from smoking are required for venipuncture and measurement of sitting blood pressure; sitting blood pressure and anthropometry to be measured before venipuncture; and both the interviews and the physical examination are to be completed prior to the medical data review.

After the participant has been welcomed and has signed the consent form, s/he is asked to change into a surgical scrub suit, provided by the field center. Each field center also provides a safe place to store clothing and valuables for the duration of the visit. After changing, anthropometry and sitting blood pressure are measured, and then the participant is taken to the venipuncture area. Following venipuncture, the participant is shown to the snack area and provided with a caffeine-free snack.

Table 13. Components of the ARIC Cohort baseline examination and location of the descriptions in the Manuals of Operation

Procedure/ Workstation	Description	Location
Informed Consent	Obtain informed consent.	Manual 2
Reception	Greet the participant; determine fasting status; verify identifying information; obtain tracing data; collect medications.	Manual 2
Sitting Blood Pressure	Obtain sitting blood pressure before the participant has blood drawn.	Manual 11
Anthropometry	Measure weight, height, frame size, skin folds.	Manual 2
Venipuncture	Obtain blood samples for all laboratory tests.	Manual 7
Snack	Provide snack which contains no caffeine or stimulants.	Manual 2
ECG	Obtain a 12 lead ECG and two minute rhythm strip.	Manual 5
Interview	Collect sociodemographic, food frequency and selected medical and personal history data.	Manual 2
Physical Exam	Obtain a brief systems review on each participant including neck, neurological, chest and lungs, breast (optional), heart, and extremities.	Manual 2
Pulmonary Function	Obtain spirometric measurements of timed pulmonary function (FVC, FEV1).	Manual 4
Ultrasound	Obtain B-mode scan and arterial wall distensibility measurements in carotids and a popliteal artery. Measure heart rate and blood pressure changes as participant arises from supine position.	Manual 6 Manual 11
Medical Data Review	Ascertain the completeness of the exam and verify abnormal results. Review results of the medical history and exam with the participant. Refer participant for diagnosis or treatment elsewhere if appropriate.	Manual 2
Exit Interview	Return medication; thank participant.	Manual 2

2.2.2 Flexible Sequence

The remainder of the baseline examination follows a flexible sequence. This allows field centers to optimize participant flow according to the local work station configuration, staffing pattern, and the scheduled number of participants per day. Procedures not subject to a specified sequence are interviews, ultrasound examination, physical examination, electrocardiogram, and pulmonary function.

Upon completion of these stations, the flow pattern reverts to the fixed sequence in that the physician assistant or nurse practitioner reviews the results of the medical history and physical examination with the participant. Results are explained and referrals are made as appropriate. The participant then changes to street clothes, while the information is checked for completeness.

2.3 Informed Consent

2.3.1 Administration of the Informed Consent Form

The informed consent form is administered by staff certified for this purpose by the Study Coordinator at each Field Center. A comfortable area near the reception station is provided for the review of the form. Five topical areas are covered in the consent form: a description of the baseline examination, risks, benefits, annual follow-up and re-examination schedules, and release of medical records for review by the ARIC Study. A copy of the ARIC informed consent form can be found in Appendix IV.

2.3.2 Training

Training for the administration of the informed consent form consists of background study of the protocols and role playing with the Study Coordinator, and ARIC staff familiar with each of the cohort study work stations.

2.3.3 Certification

After observing the practice and role playing sessions, the Study Coordinator certifies (up to) three persons for administration of the informed consent form. The Study Coordinator may also choose to administer the informed consent form or serve as back up.

2.3.4 Quality Assurance

During the first month the Study Coordinator observes once or twice per week all recently certified staff as they administer the informed consent form. A record of all refusals is kept.

2.4 Reception

2.4.1 Introduction

At the reception workstation ARIC staff greet and welcome the participant, obtain Informed Consent, and collect information corresponding to three study forms: Identification (IDN), Fasting/Tracking (FTR), and the Medications

Survey (MSR). Copies of these forms are included in Appendix IX. The order in which these forms are completed may vary between field centers. The reception procedures take place in a private area, administered by one of several field center staff trained for this purpose.

2.4.2 Description of Procedures

The personal information recorded on the Identification Form is obtained during the Home Interview by the field interviewer, and keyed onto the participant's diskette prior to the clinic visit. During reception the staff member verifies this identifying information by reading it aloud to the participant. Correct entry of names, addresses, telephone numbers, and birthdate are confirmed or corrected at this time.

The fasting time is recorded on the Fasting/Tracking form. If participants have not fasted a minimum of 12 hours as instructed during the Home Interview, venipuncture is performed but the participant is offered the opportunity to repeat blood drawing in the fasting state at a later date. During the Home Interview participants are also given a form to record tracking information such as friends, relatives and contacts, and the name and address of their provider of medical care. This information is verified as part of the reception procedures and added to the participant's record. After showing a disclosure statement and explaining that provision of this information is voluntary, participants are also asked their social security, and driver's license numbers.

The remaining portion of the Fasting/Tracking Form identifies the person or agency designated to receive the participant's study results. A summary sheet of the results to be reported and their schedule is presented to the participant at this time. It indicates that some results will be reviewed with the physician assistant or nurse practitioner at the end of the clinic visit, and a written summary report mailed to the participant's physician (or alternate) three to four months after the clinic visit date, as described in Section 2.10. Samples of the report and accompanying letters are included in Appendix VIII. Information collected during reception also includes the Medications Survey, described in Section 2.5.

2.5 **Medications Survey**

2.5.1 Introduction

The purpose of this component of the ARIC baseline examination is to assess medication usage in the two weeks preceding the examination date. Both prescription and non-prescription drugs are ascertained. Knowledge of the use of medications by the participant will assist during analyses in measuring the following: patterns of medication use in the study communities and over time, changes in medical care practice, diagnostic classification of cardiovascular diseases, interpretation of laboratory test results, frequency and type of vitamin/mineral supplement use (to complement the dietary questionnaire), and predictors of study end points.

The participant is asked during the home interview to bring to the field center all medications taken during the two-week period prior to the baseline examination. To assist in this process the home interviewer provides verbal and written instructions, a list of candidate medications, vitamins and dietary supplements, and a medication carrying bag. The appointment reminder to the study participants, prior to their visit to the field center, makes specific reference to the medications to be brought to the field center.

2.5.2 Reception of Medications at the Field Center

When the participant arrives at the Field Center, the medication carrying bag is logged in at the Reception work station, and identification labels are placed on the medication bag and the medication forms. If the participant has not brought any medications, the receptionist inquires whether s/he has taken any medications during the past two weeks, and probes for possible reasons for noncompliance. In case of inadvertent omissions, arrangements are made for obtaining the information over the telephone or through a visit by a field interviewer. In case of deliberate omission to bring medications to the Field Center, this is indicated on the Itinerary Sheet and conversion is attempted later during the medical review of results with the participant.

2.5.3 Transcription of Medication Names

While the participant proceeds through the examination, the receptionist transcribes medication names onto the study form. Names are printed (onto the Medication Survey Form, Appendix IX) in block capital letters, including all parts of the medication name, identifying letters and/or numbers that refer to strength. Flavors of products and whether preparations are sugar-free or sodium-free are not recorded. The receptionist and his/her back-up for medication transcription are trained and certified for this purpose. Only study personnel certified for transcription of medications by the Study Coordinator are allowed to carry out this function.

2.5.4 Medication Use Interview

After completing the medication name transcription, the Receptionist verifies that the medication forms and carrying bag are clearly identified with ID labels. The medications and corresponding forms are placed in the carrying bag and taken to the work station designated for the completion of the medication survey. The physician assistant, nurse practitioner, or a trained interviewer conduct a brief medication use interview by asking two questions for every medication listed. One of these questions classifies each medication as prescription, nonprescription, or shared. The other identifies medications taken during the preceding 24 hours. If the participant has declined to bring all his/her medications, conversion is attempted at this time.

When preparing to ask about each medication, the interviewer removes them all from the bag and sets them in front of the participant. As each medication is asked about, it is shown to the participant while keeping the other medications in view. After the questions are answered for each medication, it is placed back in the carrying bag to minimize confusion and to assure that all medications are returned.

In the process of asking these questions about each medication, the staff member verifies the transcription of medication names and makes corrections on the paper forms as required. At this time, unknown and incomplete names are checked against the American Drug Index and Physician's Desk Reference. The medication interview concludes with a probe on the completeness of the medications reported for the prior two weeks, and a probe on medications taken for specific cardiovascular disorders.

If in response to the probe the participant recalls additional medications taken during the preceding two weeks, the interviewer records the name with as much detail as possible. If any doubt exists as to the accuracy of the recall, the interviewer makes arrangements with the participant for a phone call to verify the prescription label information, and records this on the form. The medications are returned to the participant with other personal belongings, as part of the exit procedures.

2.5.5 Medication Coding at the Field Center

After the participant has left, the medication names are coded by trained Field Center personnel, using a (hard copy) translation dictionary. Only exact matches and specific spelling variants listed in the dictionary are coded, by entering the corresponding numeric code on the form. During data entry on screens only the codes are keyed (matching names are not kept in the data base). A missing code status is entered for nonmatching names, and the latter are keyed into the Problem Log. A print out of these names is provided with the participant ID or a quality control ID, and sent for central coding.

2.5.6 Central Coding of Medication Names

Unresolved matches and a quality control sample of medication names are coded at the central medications coding center at the University of North Carolina, affiliated with the Coordinating Center. The medication coding tape service of Medi-Span is used for this purpose. This coding system provides a very comprehensive and up to date list of generic and brand name, prescription and over-the-counter products. Medications are coded into similar pharmacologic classifications, by generic equivalents, and considering multiple ingredients.

2.5.7 Quality Assurance

A record is kept of the number (and proportion) of participants who did not receive an adequate explanation of the medication survey instructions during the home interview; of refusals to bring medications to the field center; of incomplete medication bags; and of medication names transcribed incorrectly. At each Field Center a 10% sample of one month's medication forms is recoded every six months. In addition, Field Centers resubmit a 10% sample of the cumulative six months total of (nonmatching) medication name printouts for central coding. Reports of these quality control procedures are forwarded to the Coordinating Center for central processing.

2.6 The Clinic Interviews

The field center clinic interviews are designed to obtain a medical and reproductive history, information on dietary and health habits and verify selected items of information obtained during the home interview. The clinic interviews also provide the participant with an opportunity to ask questions or alleviate apprehensions concerning the examinations.

The ARIC Study utilizes computer-assisted direct data entry as the primary mode of data collection for the clinic interview. Paper forms are available for situations in which direct data entry is not possible. Separate instructions and training procedures prepare each interviewer to conduct standardized interviews using direct data entry and paper forms. In order to be certified as interviewers ARIC personnel must demonstrate knowledge of the instructions on interviewing technique included in the ARIC training materials, familiarity with the interview instruments, and proficiency in each data collection mode.

In this section a brief description is presented of the topical areas covered by the clinic interviews, together with a summary of the training, interview, and quality assurance procedures specific to each interview form.

2.6.1 Medical History

The Medical History form of the clinic interview collects information on access to medical care, chest pain on effort, unstable angina pectoris, congestive heart failure, pain of possible infarction, intermittent claudication, and vasectomy. Information on stroke and transient ischemic attack (TIA) is collected on a separate form described in Section 2.6.7. Study forms are provided in Appendix IX. The ARIC Study has placed emphasis on standardization in the identification of the condition or the signs and symptoms alluded to above. This is reflected in the training materials and the requirements for certification/recertification of the clinic interviews. The Medical History form uses portions of the questionnaire developed at the London School of Hygiene and Tropical Medicine, commonly called the Rose Questionnaire, to collect interview information pertaining to angina on effort, myocardial infarction and intermittent claudication. This document contains materials abridged from Cardiovascular Survey Methods, Rose, G.A. and Blackburn, H., World Health Organization, 1968. The original questionnaire and the training materials developed by Dr. Rose and adopted by the ARIC Study are intended as an evaluation of a participant seen for the first time. On repeat evaluations a modified questionnaire is used by ARIC that applies to the interval since the participant's last visit, or previous annual contact. For the annual contacts and the re-examination questionnaire inquiry is restricted to any chest pain occurring within the appropriate time interval. Otherwise the instruments are the same.

The ARIC Study has allowed for an additional possible response to the question "Do you get it when you walk uphill or hurry?" contained in the questionnaire on chest pain on effort. The added response category reads "Never hurries or walks uphill". Interviewers are instructed to take the word "never" quite literally, not including responses such as "almost never" or "rarely".

2.6.1.1 Required Training

A manual was developed to assist in training ARIC personnel who administer these standardized data collection instruments embedded in the Medical History Form. All interviewers complete this training and are certified before data collection begins. This training includes a set of test interviews. Separate certification materials are kept at the Coordinating Center, which is responsible for administering the certification/recertification program at all ARIC Field Centers. Before interviewers are certified to administer the Medical History interview, they are required to:

1. Attend a training session conducted for this purpose by the Coordinating Center and pass the tests administered there, or
2. Be trained by the pertinent ARIC Study Coordinator and pass equivalent tests administered with the approval of the Coordinating Center.

Before certification, all interviewers are required to practice administering the questionnaire. Because of infrequent positive responses to most of the questions among the general population, it is recommended that this practice be obtained with specially selected subjects (such as hospital patients), or other volunteers. Each interviewer observes interviews conducted by trained interviewers and conducts interviews in the presence of a trained interviewer.

2.6.1.2 Procedure for Certification of Interviewers in Administration of the Rose Questionnaire

1. An annual certification/recertification exam is provided to the field centers by the Coordinating Center. All staff administering the Rose Questionnaire are expected to take this exam.

2. The staff at the Coordinating Center grades the exam and notifies the examinees promptly of their performance (pass or fail). Those who pass the exam receive corrected copies of their test. Those who fail do not receive the answers to the questions until they pass a re-examination, but feed-back to study coordinators is provided to assist them in training the interviewers.

3. ARIC staff who fail the exam continue to take the same exam until they pass it or until the Study Coordinator recommends a different course of action. The training coordinator may go over the training material with these individuals, but does not provide the answers to the exam. The same restriction applies to other ARIC personnel.

4. New interviewers take the most current certification exam when they are ready to begin seeing participants. They are re-certified annually along with the other clinic staff.

2.6.2 **Respiratory History**

The assessment of pulmonary function conducted at the baseline visit is described in Manual 4 of the ARIC protocol. Since the diagnosis of most chronic respiratory conditions relies to a considerable degree on symptoms,

the baseline visit also includes a set of standard questions on the presence of common respiratory symptoms. The component of the clinic interview which ascertains chronic respiratory disorders is described briefly in this section. The interviewer-administered questionnaire records the presence, salient characteristics of cough, phlegm, wheezing, and breathlessness. In addition, historical information on the presence of chronic bronchitis, emphysema, and asthma is obtained.

The ARIC Respiratory Symptoms Form has been adopted from the Epidemiology Standardization Project. The wording and structure of the questionnaire, as well as the detailed instructions to the interviewers, are taken directly from that source. Interviewers are instructed to follow the actual printed wording for each question, and to accept unequivocal answers as provided by the participant. The wording of the questions, and the instructions by the interviewer before starting this portion of the interview, lead to simple "yes" or "no" answers. Probing is limited to a repetition of the question when possible, and equivocal answers are recorded as "no".

Training of the interviewers is based on a common training manual, practice scripts, and role-playing. Interviewers are certified by the ARIC Study Coordinators. After obtaining approval from the participant, the ARIC clinic interview is recorded on tape for purposes of quality assurance. As is the case with the other components, quality control for the Respiratory History component is based on four main elements: (1) the editing features of the direct data entry system; (2) a review of tape-recorded interviews by the Study Coordinator at each field center; (3) site visits by clinic monitors from the Coordinating Center; and (4) quality analysis at the Coordinating Center of the data collected by each interviewer.

2.6.3 **Physical Activity**

2.6.3.1 Introduction

Physical inactivity has been shown in several epidemiologic investigations to be directly associated with coronary heart disease incidence. The ARIC requirements for physical activity assessment were that the instrument be (1) a questionnaire measuring usual activity, (2) relatively valid and reliable, and (3) as brief as possible (less than 10 minutes). The ARIC Physical Activity Questionnaire is based on a self-administered questionnaire developed for a Dutch population by Baecke et al. (Am J Clin Nutr 1982;36:932-42). The questionnaire was adapted for ARIC (see Appendix IX) by making the following modification or clarifications in the version translated from Dutch:

1. The instrument was modified to be interviewer-administered because of concern by ARIC investigators that not all subjects could complete a self-administered questionnaire. Response cards are used to aid the participant.
2. The original questionnaire had no time reference. Pretesting indicated confusion by respondents on how to include activities that were seasonal, just taken up, or just given up. To clarify this, the ARIC instructions specify that the interest is in physical activity in the past year. This is consistent with original question 9.

3. The question on "main occupation" was dropped from the questionnaire, because this question is asked in the Home Interview. Occupation is coded using 1980 Census codes. Activity level (low, medium, high) of each occupation was assigned in the following fashion:

   a) Two exercise physiology research assistants reviewed the documentation provided by the original Dutch investigators.
   b) The two exercise physiologists independently assigned low, medium, or high intensity ratings to the occupations, using the Labor Department's Dictionary of Occupational Titles as a reference.
   c) Disagreements between the exercise physiologists were adjudicated by an industrial hygienist.

4. Original question 2 ("At work I sit") was allowed to have a response "Does not work". Persons who do not work are given the minimum score for the Work Index.
5. In original question 6, "tired" was changed to "physically tired", based on pretest experience.
6. Original question 9 was changed from "Do you play sport" to "Do you play sports or exercise?", based on a clarification from the original investigators of the Dutch meaning of "sport".
7. The original question 9 allowed for only two sports or exercises to be listed. The Dutch investigators report that this is because the Dutch rarely do more than two. The investigators indicated through personal communication that if additional activities are performed, they ought to be listed. The ARIC questionnaire, therefore, allows for four activities in order of frequency. The Sport Index scoring scheme was modified accordingly.
8. The assignment of intensity codes was based on standard references, for example Passmore and Durnin. The categories of frequency in original question 9 and question 10 were more clearly defined so as to be non-overlapping.
9. Original question 12 ("During leisure time I play sport: never/seldom/sometimes/often/very often") was felt to be redundant with question 9 ("Do you play sport"). We, therefore, changed the wording of original question 12 slightly and do not ask it if the response to original question 9 is "no".
10. Original questions 15 and question 16: "cycle" was changed to "bicycle".
11. An additional question was added: "How many flights of stairs do you climb up each day?" This question is incorporated into the overall activity index.

2.6.3.2 Administration

1. The ARIC Physical Activity Questionnaire is interviewer administered. Response cards are used to help the subject respond.
2. The interviewer introduces the questionnaire by reading the introduction given on the form.
3. The interviewer reads each question slowly, pointing to the corresponding Response card for each question, designated as [rc].
4. If completed on a paper form, the interviewer edits the form immediately for completeness while the participant is still present.

2.6.3.3 Scoring

The scoring of the original Physical Activity questionnaire by Baecke is shown in Appendix V.

2.6.4 Reproductive History

2.6.4.1 Introduction

The objective of the reproductive history questionnaire is to determine current and past history of gonadal function and exposure to exogenous hormones. The questionnaire addresses both endogenous and exogenous hormone exposure in women because each may play different roles in the development of atherosclerosis. The interview is administered to female participants only. It is completed during the interview portion of the participant's visit. Questions on menstrual history are included because of the associated fluctuations in lipoprotein, lipids, and apoproteins in relation to menstrual cycles. It has been reported that women with CVD have had more childbirths and abortions than women who do not have CVD. Some data suggest a higher frequency of premature menopause among women with CHD than those without CHD. The risk of MI in current oral contraceptive users is reported to be 3 to 4 times higher than that of non-users. Also, higher levels of LDL-cholesterol, triglyceride, systolic and diastolic blood pressure have been found in current users of oral contraceptives. A question on hot flashes is included in the questionnaire to obtain an approximate measure of postmenopausal endogenous production of estrogen.

2.6.4.2 Survey Format

The questionnaire is interviewer-administered and contains 52 questions. It is divided into 4 sections:

1. Menstrual history and pregnancy,
2. Past and present use of birth control pills,
3. Past and present use of estrogen hormone preparations, and
4. History of gynecological surgery and age at surgery.

Ten questions are included in the Menstrual History and Pregnancy Section to obtain information on age of first menstrual period, number of pregnancies and deliveries, frequency of missed periods, menstrual periods, and menopause status.

Present and past birth control use is determined from questions 11-15. Past and present frequency of hormone use is assessed from questions 16-44. The survey allows for the coding of past and present frequency information for four different hormones. The gynecological surgery section, questions 45-49, is to determine whether the ovaries or uterus were/was removed, and to determine the age at surgery.

Most of the questions are closed-ended or precoded questions designed for direct entry into the computer by the interviewer. Open-ended questions are to obtain names of female hormones being used.

The exact wording and order of the questions is followed to ensure standardization. Questions are not skipped unless indicated by the skip pattern instructions. Because there are many skip patterns in this survey, the interviewer should be very familiar with the flow of the survey to ensure smooth administration with a conversational tone. Medication names are coded as described in Section 2.5.

2.6.5 Dietary Assessment

2.6.5.1 Introduction

Dietary intake has a significant effect on risk of atherosclerotic diseases. ARIC collects dietary data to characterize the nutrient intake of individual cohort members and to determine its relationship to atherosclerosis and cardiovascular risk factors. Secondarily, ARIC explores dietary differences among the four cohorts over time. The nutrients of primary interest are total calories, carbohydrate, protein, total fat, saturated, polyunsaturated and monounsaturated fatty acids, cholesterol, alcohol, and calcium.

Dietary data are collected in ARIC using a food frequency questionnaire developed by Walter Willett. This questionnaire was chosen for ARIC because (1) it has been demonstrated to have reproducibility and validity compared with more extensive dietary methods (Willett et al, Am J Epi 1985; 122:51-65), (2) it is brief, and (3) compared to other brief dietary assessments, it was believed to be better able to characterize individual dietary patterns. It is recognized that use of a brief food frequency questionnaire may sacrifice some nutrient precision.

There are several versions of the Willett Questionnaire, all designed for self-administration. The ARIC Study uses a shorter version of the form, with few modifications (Appendix IX). The major modification is that, in ARIC, the questionnaire is interviewer administered. The primary reason for this is to accommodate less literate participants. Interviewer administration also enhances consistency and accuracy by having trained staff asking the questions, thus reducing the effects of individual interpretations.

The interviewers are provided with "help screens" for portion size/frequency adjustments, and for specification of foods to be included in or excluded from each category. The food items listed in the help screens are expected to occur with sufficient frequency to warrant clarification.

The other modifications made in the Willett questionnaire were minor:

1. Additional questions are asked about consumption of fish.

2. Questions on vitamins are covered in the ARIC medications questionnaire.

3. The questions on cooking fats are expanded.

4. A category is added allowing participants to include other foods which they eat frequently, as is done in more recent versions of the Willett questionnaire.

5. The alcohol questions are covered in a separate ARIC questionnaire, incorporated into the Dietary Assessment form.

6. The interviewer is provided with sheets to assist in conversion of non-standard portion sizes into appropriate frequency categories and to convert seasonal intakes (Table 14).

2.6.5.2 Training and Certification of Interviewers

Interviewers are centrally trained to use a standardized procedure for administering the dietary questionnaire. Training includes instructions in research interviewing techniques and in completing the form. Interviewing skill training includes:

1. adherence to the standardized protocol
2. use of non-judgmental attitude
3. degree and nature of prompting permitted
4. dealing with problem interviewing situations
5. use of portion size-frequency conversion screen and seasonal intake
6. use of response cards for participant
7. handling participants' comments and recording relevant information on the note log
8. post-interview responsibility for the data

2.6.5.3 Quality Control

To ensure consistency and accuracy in data collection and to minimize inter- and intra-interviewer differences, clinic supervisors monitor 5% of the interviews done by each interviewer. In addition, a brief written worksheet/quiz on portion size/frequency or interviewing problems is completed by each interviewer every three months. The quiz emanates from the Coordinating Center.

2.6.5.4 Preparation for Interview

The interview takes place in a quiet and private physical setting to put the participant at ease. The standard food unit models, help screens, and participant response cards are readily accessible.

Note: The ARIC receptionist alerts the interviewer in advance if a participant is illiterate or has any problem in reading. In those instances, response cards are read by the interviewer.

2.6.5.5 Conduct of Interview

2.6.5.5.1 Instructions for Introduction of Questionnaire

Greet the participant cordially. Explain that the purpose of the interview is to obtain information about usual dietary intake, that there are questions on specific foods and portion sizes, and that you need to find out how often, on average, the specified amount was consumed during the past year. Explain that any difference from the stated portion size must be reported only if it is at least twice as much or half as much. Frequency of consumption is based on number of times either per day, week or month. State that any foods not

mentioned which he/she eats frequently may be added at the end. Assure the participant that he/she may feel free to have instructions repeated or to ask questions.

The interviewer must show an interest in the interview, using a pleasant non-judgmental tone and posture. In introducing the questionnaire, the interviewer reads verbatim the following statement: Statement to Participant:

In this part of the clinic visit we want to obtain information on your usual eating habits. We will go over some specific foods by groups. I'll name a food and a portion size and you tell me how often, on average, you ate that during the past year. If your portion size was much different from the amount I say, please tell me if it was at least twice as much, or half as much. We have a few sizes of cups and glasses here for reference.

Here are the choices for 'how often' (give participant response card with frequencies listed). The choices are number of times a day or week or month. Please respond with the appropriate letter response. For example, 'once a day' would be 'D'. If you ate or drank something less than twelve times a year, that would be the same as 'less than once a month' which is 'I'. It is important that your reply be brief in order to save time, but we want you to be as accurate as possible. If we miss food items that you usually eat often, we will list those at the end. Feel free to ask questions or have me repeat instructions if I am not being clear.

First, the dairy group: "In the past year, how often on average did you consume...?"

2.6.5.5.2 Instructions to Interviewer for Data Collection:

All interviewers must be consistent in reading the Food and Amounts list to the participant. Read the questions clearly, using the exact wording on the form. It is imperative that there be no exclusions or inclusions in reading the food list. Do not add any interpretations. If the participant asks if he/she should include certain food items, refer to the help screens which list items that may be included for each category. For example, the participant may ask if skim or low fat milk includes cocoa. By calling up the help screen, the interviewer can see that it does.

Periodically the interviewer may have to reiterate the comment "on average, the number of times in the past year", or may remind the participant of the stated portion size.

Standard portion size models are required at each interview station at clinic sites to enhance the reliability of the dietary information and ensure consistency across centers:

1. 12 oz. beverage tumbler marked with gradations for 8 oz., 12 oz.

2. 6 oz. beverage tumbler marked with 4 oz. and 6 oz. levels

3. Set of standard measuring cups: 1 cup, 1/2 cup, 1/3 cup, 1/4 cup

4. Set of 2 standard measuring spoons, 1 teaspoon, 1 tablespoon

5. Soup bowl for cereals, stews, hot dishes with levels marked for 1 cup and 1/2 cup

6. Salt-clay models: 1/2 cup portion.

Offer the models as examples to assist in portion size definition.

Problem items are recorded in the note log. Resolution of these items are handled by a nutritionist at the Coordinating Center.

Enter frequency of intake in the appropriate column utilizing the help screen for portion/frequency conversions. For example, the portion size for ice cream is 1/2 cup. If the participant reports a portion of 1 cup, 2-4 times per week, the interviewer calls up the portion/frequency help screen and finds the 2X Row in the Multiple of the Amount column. The interviewer reads across to the 2-4 Week column to obtain the adjusted frequency. The adjusted frequency is entered as 5-6 per week.

If the participant reports a seasonal intake of a food item which would total to more than 12 times per year, the average frequency is calculated for the year. For example, if peaches are eaten only in season, but two peaches are eaten every week for three months, the frequency would be calculated as follows: 2 peaches x 4 weeks x 3 months = 24 divided by 12 (months in year) = 2 per month. The following table is a guide.

Table 14. Seasonal intake guide for administering the food frequency questionnaire

	Number of Times Eaten Per Week in Season			
Season Length	1 time /week	2 times /week	3 times /week	4 times /week
2 months	Almost Never (I)*	1/m (H)	2/m (H)	2-1/2/m (H)
3 months	1/m (H)	2/m (H)	3/m (H)	1/w (G)
4 months	1/m (H)	3/m (H)	1/w (G)	5/m (G)

* I, H, G identify these responses on the flash card used during the interview

C. Closing the Interview

Thank the participant. Escort participant to next procedure.

2.6.5.6 Scoring the Questionnaire

The nutrient data base and software for scoring the food frequency data are provided by Dr. Willett and adapted for ARIC use by the Coordinating Center.

2.6.6 Alcohol Consumption

2.6.6.1 Introduction

An association among alcohol consumption, CHD and all-cause mortality has been observed in several prospective studies; however, data regarding the relationship of alcohol intake and extent and progression of atherosclerosis are not available. In addition, alcohol consumption may effect the primary risk factors of interest in the ARIC study (lipoproteins, apolipoproteins and hemostasis factors). Therefore, alcohol consumption is assessed in the ARIC Study clinic interview.

2.6.6.2 Survey Format

The Alcohol Consumption Form (Appendix IX) contains 13 questions. The first questions determine whether the participant consumes alcohol or did so in the past. According to the participant's responses, habitual past intake of alcohol and/or habitual present consumption is assessed. Alcohol intake over the preceding 24 hours is also ascertained. Past and present consumption is determined for wine, beer, and drinks made with hard liquor since these are the three major types of alcoholic beverages.

Frequency of alcohol consumption is determined as usual weekly intake. The serving sizes are different for beer, wine, and hard liquor. The definition of serving size, while consistent for measuring both present and past intake, is made more precise for present intake. This is done because recent intake is recalled better than past intake, and is probably more important for the ARIC study questions. For past intake serving sizes are defined as "one beer", "one glass of wine", or "one shot of liquor or one mixed drink". For present intake serving sizes are "12 oz. bottles or cans of beer", "4 oz. glasses of wine", or "1 and 1/2 oz. shots of hard liquor". For the final questions, which relate to the most recent 24 hours, the more precise definition of serving size is used.

The total amount of absolute alcohol ingested weekly for past alcohol consumption is determined by multiplying the number of servings by the amount of alcohol in one serving of the type of alcohol ordinarily drunk. If more than one type is ordinarily drunk, this calculation is made assuming an equal number of drinks of each type.

The total amount of absolute alcohol ingested weekly for present alcohol consumption results from the addition of absolute alcohol consumed for wine, beer, and hard liquor (questions 96-98). The total amount of absolute alcohol drunk during the 24 hours prior to the clinic interview is determined by multiplying the number of drinks (Question 99) by the amount of absolute alcohol in the type of drink consumed (Question 100).

All questions are closed-ended, designed for direct data entry by a trained interviewer. In order to ensure standardization, exact wording and order of questions are followed. Questions are skipped only if specified in the questionnaire instructions.

2.6.7 Stroke and TIA

Stroke and transient ischemic attack (TIA) have been identified as important endpoints in the ARIC Study. During the baseline clinic visit, a history of TIA and stroke is determined by a standardized Stroke/TIA questionnaire. At follow-up these endpoints are assessed both by the Stroke/TIA questionnaire and by abstracting hospital records.

The Stroke/TIA questionnaire (Appendix IX) is based on a self-administered questionnaire reported in Sahs AL, Hartmen EC (eds): Fundamentals of Stroke Care (DHEW Publication No. HRA 76-14016). Washington, D.C. Departments of Health, Education, and Welfare, 1976, pp. 41-47. The version used by the ARIC Study has been modified for use as an interviewer-administered form. In addition, the revised form includes the diagnosis of stroke and allows the incorporation of multiple events. It also provides more detailed information, aimed at the identification of the vascular distribution. The Stroke/TIA form is divided into seven sections: (1) medical history, (2) sudden loss or change of speech, (3) sudden loss of vision, (4) double vision, (5) sudden numbness or tingling, (6) sudden paralysis or weakness, and (7) sudden spells of dizziness or loss of balance.

The first section determines whether the participant has a history of physician-diagnosed stroke or TIA. Sections 2-6 ask a series of similar questions about each category of symptoms. The first question of each section determines if the participant has ever experienced the sudden onset of the particular symptom. If the response is No or Don't Know, the rest of the questions in that section are skipped and the interviewer proceeds to the first question in the next section. If the answer is Yes, the rest of the questions in that section are asked. Subsequent questions explore whether more than one episode has occurred, the frequency, duration and onset of all episodes, and some specific characteristics about the worst episode of the symptom. The definition of worst is left to the discretion of the participant, but should include such factors as duration, severity and occurrence in conjunction with other symptoms. The last question in each section asks about associated symptoms. The last section, Section 7, asks similar questions about dizziness, as those in Sections 2-6 but they are presented in a different order to screen out those participants who have experienced symptoms of sudden dizziness or loss of balance of a non-neurologic etiology.

The form is administered by the clinic interviewers at the time of the clinic visit. Any positive symptom is flagged for review during the Medical Data Review at the end of the clinic visit, as described in Section 2.8. At that time a TIA/Stroke Summary form (Appendix IX) with additional questions seeking non-cerebrovascular explanations is administered by the physician assistant or nurse practitioner. This form and the participant's records are later reviewed by the ARIC physician. Both the physician assistant/nurse practitioner and the physician record their assessment on whether the symptoms are attributable to a non-cerebrovascular cause. This additional information is designed to enhance the specificity of the diagnosis of stroke and TIA, which is based on a clinical algorithm established a priori.

2.6.7.1 Training and Certification of Interviewers

Training and compliance with study-wide certification criteria are required. Training materials include general statements on interview technique, question-by-question instructions, and practice scripts. Trainees have access by conference call to study neurologists for clarification and questions. Certification takes place by administering three sets of scripts to each interviewer, with coding of the responses by the Coordinating Center. Yearly recertification scripts for the Stroke/TIA questionnaire are administered by the Coordinating Center.

2.6.7.2 Quality Control

To ensure consistency and accuracy in data collection and to minimize inter- and intra-interviewer differences, interviewer supervisors and/or study coordinators monitor 5% of the interviews done by each interviewer.

2.7 Examinations

2.7.1 Anthropometry

Anthropometry is performed before the clinic snack with the participant's bladder empty. All measurements are made with the participants wearing light-weight, nonconstricting underwear. (Hip measurements may be taken over the scrubsuit if done consistently.) Height and weight measurements are not taken with the participant wearing shoes.

Measurements are taken by either a team of two persons (one acting as observer and the other as recorder) or by one technician using a full length mirror to aid in placement of the tape measure. If two technicians are available, the first observer takes the measurements, calling out the name of the next measurement. The first observer keeps the measuring instrument in place until the recorder repeats the number. The recorder also checks the examinee's position during the procedure. If a single technician performs the measurements, each should be recorded immediately after they are taken. Values taken are rounded down to the unit indicated for each measure. Anatomical landmarks for body size measurement can be found in Figure 2. The Anthropometry Form is included in Appendix IX.

2.7.1.1 Height and Weight

2.7.1.1.1 Standing Body Height

The participant stands erect on the floor or the horizontal platform with his/her back against the vertical mounted metal centimeter ruler, heels together and against the vertical ruler, looking straight ahead with his/her head in the Frankfort horizontal plane (the horizontal plane which includes

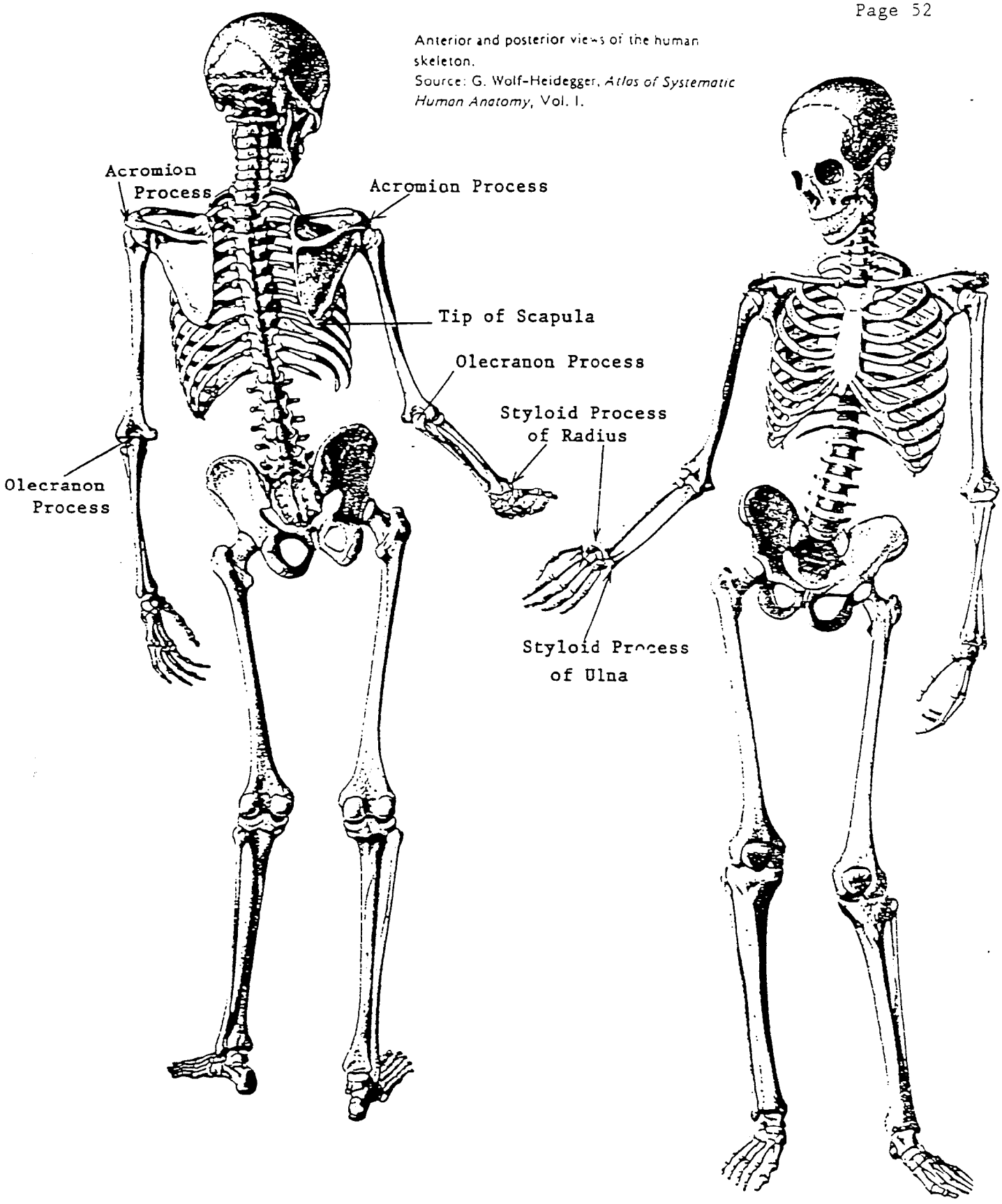

Figure 2. Bony Landmarks for Anthropometric Measurements

the lower margin of the bony orbit--the bony socket containing the eye--the most forward point in the supratragal notch--the notch just above the anterior cartilaginous projections of the external ear) (Figure 3). The right angle is brought down snugly but not tightly on the top of the head. A foot stool is used if the examiner is shorter than the participant such that the examiner's view is level with the point of measurement on the head of the participant. The participant's height is recorded to the centimeter, rounding down. The participant is instructed to stand as straight as possible but with feet flat on the floor. A chart converting centimeters to inches is on the wall or available for use in informing the participant of his/her height in inches (Table 15).

2.7.1.1.2 Sitting Height

Sitting height measurement provides an adjustment for pulmonary function tests. The measurement is made with the participant seated on a sturdy flat-seated stool or chair approximately 32" high. After standing height is measured, the stool is set in front of the height ruler. Two of its legs are placed against the wall and the seat is centered against the ruler. The height of the stool seat is measured and verified daily or when moved. The participant is seated on the stool with the sacrum, thoracic spine, and back of the head against the ruler. The participant's lower legs should hang unsupported. The muscles of the thighs and buttocks should be relaxed. The participant is encouraged to sit up as straight as possible to achieve his/her maximum sitting height. The measurement is made with the head in the Frankfort plane (Figure 3) and the participant looking straight ahead. The right angle is brought down along the centimeter ruler until it is snug, but not tight, on the top of the head. The unadjusted sitting height is read to the centimeter, rounding down. During data analysis, the actual sitting height is calculated by subtracting the stool seat height from the unadjusted sitting height.

2.7.1.1.3 Body Weight

Before a participant is weighed, the scale is balanced so that the indicator is at zero when no weight is on the scale. The scale must be level and on a firm surface (not a carpet). The participant is instructed to stand in the middle of the platform of the balance scale (Detecto, model #437) with head erect and eyes looking straight ahead. Adjust the weight on the indicator until it is balanced. Record the results down to the pound, rounding down. To maintain accuracy, the scale is zeroed daily and must be calibrated with a known weight (50 lbs.) every week or whenever the scale is moved.

2.7.1.2 Skinfolds

The Lange caliper is used for all skinfold measurements, and caliper calibration is checked with the calibration block prior to taking measurements on each participant. A chart of percent body fat computed from the sum of triceps and subscapular skinfolds is available if the participant asks for the interpretation. See Appendix VI.

All measurements are taken on the participant's right side and positions are marked with a marking pen. A fold of skin one (1) cm above the pen mark is

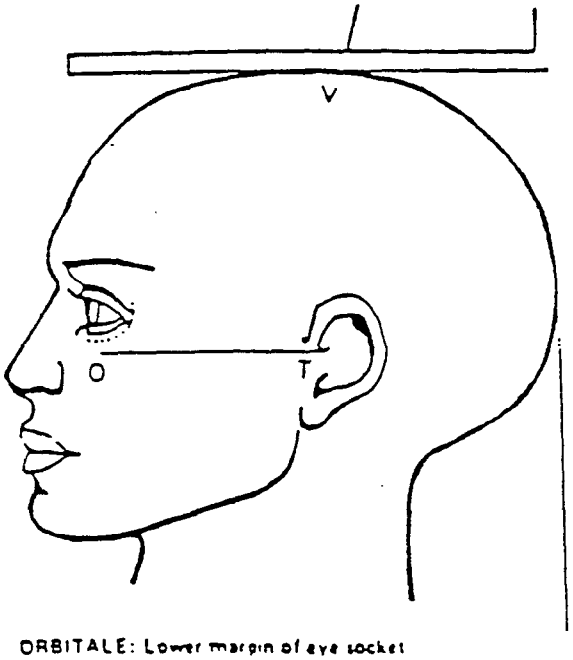

Figure 3. Frankfort Plan for Measuring Body Height

Table 15. Body Size Measurements: Body Height in Centimeters and Inches[1]

Centimeters	Inches
122.0	48
124.5	49
127.0	50
129.5	51
132.0	52
134.5	53
137.0	54
139.5	55
142.0	56
145.0	57
147.5	58
150.0	59
152.5	60
155.0	61
157.5	62
160.0	63
162.5	64
165.0	65
167.5	66
170.0	67
172.5	68
175.0	69
178.0	70
180.5	71
183.0	72
185.5	73
188.0	74
190.5	75
193.0	76
195.5	77
198.0	78
200.5	79
203.0	80
205.5	81

[1] 1 inch = 2.54 centimeters; 1 centimeter = .39 inches

firmly grasped between the left thumb and first two fingers and then gently lifted away from the body only to the extent to determine that no muscle is grasped. A firm grip is necessary but it must not exceed the pain threshold. Do not stretch the skinfold away from the body. Grasp and gently lift the fold two or three times to make certain that no musculature is grasped. The observer then grasps and continues to hold a skinfold firmly as the calipers are placed on the pen mark. Do not let go of the fold. Release the grip on the caliper completely, allowing the spring to compress the fold. Count silently 1-2-3 (approximately 2 seconds) and then take a reading on the caliper dial to the millimeter, rounding down. Keeping the left hand above the skinfold (see Figure 4) allows the dial to be read easily. Remove the caliper, then release the fold.

The width of the skin that is enclosed between the fingers is an important factor. It will vary, however, from one site on the body to another. With a thick subcutaneous layer, a wider segment of the skin must be "pinched" than when there is little adipose tissue. For a given site the width of the skin is the minimum needed to yield a well defined fold.

The depth of the skinfold at which the calipers are placed on the fold also requires comment. The two sides of the fold are not likely to be parallel, being narrower near the crest and broader toward the base. When the calipers are placed at the base, the resulting measurement is too large. The correct location is approximately midway between the crest and the base, where surfaces are approximately parallel to each other. The contact surfaces of the calipers should be parallel and applied perpendicular to the grasped skinfold.

It is important to measure skinfolds accurately. Even after extensive practice, it is possible to make errors due to slight misplacement of the caliper or misreading the dial. To avoid such errors, the following procedure is recommended:

1. Skinfolds are lifted two or three times to determine the fold to be measured before placing the calipers. Too many individuals put the calipers in place before determining what is really to be measured.
2. Two measurements at each site are to be performed on each participant. The skinfold is released between measurements.

2.7.1.2.1 Triceps Skinfold

The observer determines and marks the posterior tip of the acromion process. The observer then has the participant flex the right arm 90 degrees, to determine and mark the tip of the olecranon. Using the tape measure, the observer measures from the tip of the acromion process on the right shoulder to the tip of the olecranon process on the back of the elbow with the elbow flexed at 90 degrees. The participant then straightens the arm, allowing it to hang loosely at the side. Make a mark (+) at the midpoint between the acromion process and olecranon marks in the midline of the back of the arm (Figure 4). Using thumb and first two forefingers, the observer grasps a skinfold parallel to the long axis of the straightened, relaxed arm one centimeter above the mark. The caliper is applied at the mark perpendicular to the grasped skinfold. The observer silently counts 1-2-3 (approximately 2 seconds), takes the reading, and records it. Measurements must be read two

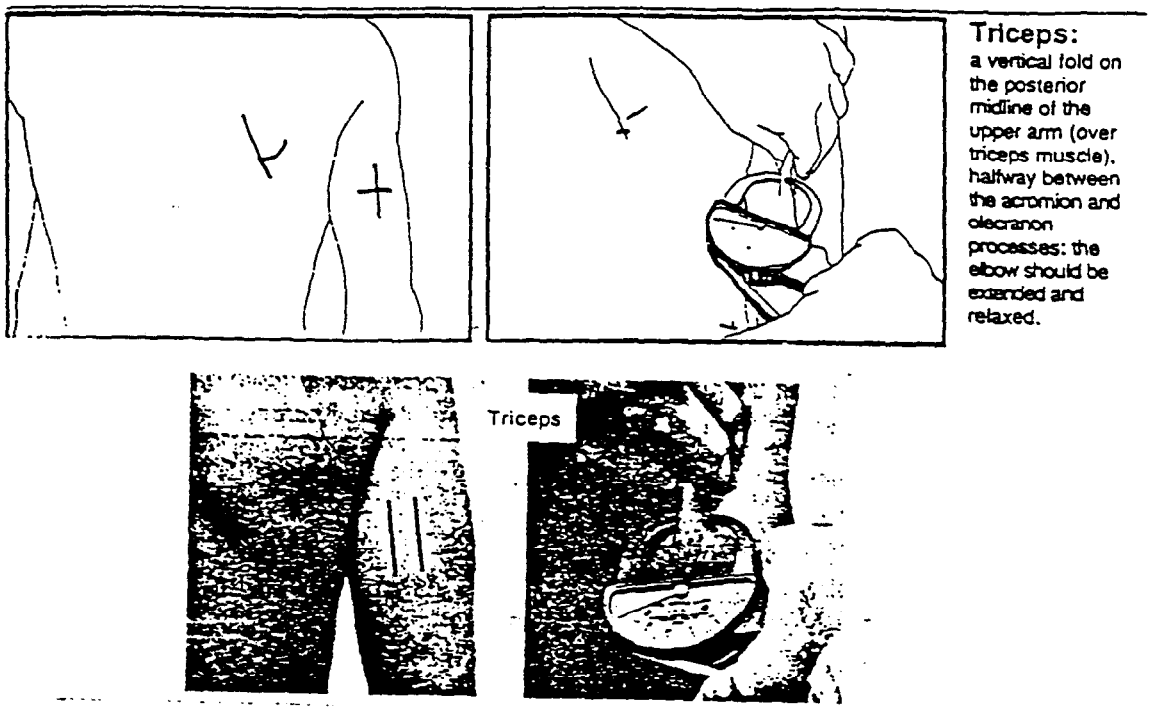

Figure 4. Location of Skinfold Measurements: Triceps

seconds after the full pressure of the caliper jaws is applied to the skinfold; if a longer interval is allowed, the jaws may "creep" or fat may compress and the reading be inaccurate. The measurement is repeated one more time, releasing the skinfold between measurements. The two measurements are recorded to the millimeter, rounding down.

2.7.1.2.2 Subscapular Skinfold

This measurement is made one centimeter below the inferior angle (tip) of the right scapula (Figure 5). To find the right medial scapular border, have the participant place the back of his right hand on the middle of his back. The observer locates the medial border of the right scapula moving his/her fingers down the full length until the inferior angle is located. With the subject's arm relaxed, make a pen mark 1 cm below the inferior angle on a diagonal line coming down from the medial border. The observer then grasps a skinfold 1 cm above the mark on and in the direction of the diagonal line coming down from the medial border of the scapula with two fingers on top, thumb below. The skinfold should be angled about 45 degrees from the horizontal, going medially upward and laterally downward. The calipers should be placed on the pen mark perpendicular to the grasped skinfold. Measurements are performed two times and recorded to the millimeter, rounding down, as for the triceps skinfold.

2.7.1.3 Waist (Abdominal) Girth

Have the participant lift the scrub suit top just high enough to make the area visible. An anthropometric tape is applied at the level of the umbilicus (navel) (Figure 6) and the participant is instructed to "breathe quietly". The technician verifies that the participant is standing erect and the tape kept horizontal.. The recorder, or use of a mirror, helps verify the position of the tape. One measurement is made and recorded to the centimeter, rounding down.

2.7.1.4 Hip Girth

Instruct the participant to stand erect yet relaxed with weight distributed equally over both feet. The hip girth is measured at the level of maximal protrusion of the gluteal muscles (hips) (Figure 7). Keep the anthropometric tape horizontal at this level and record the measurement to the centimeter, rounding down. Only one measurement is made. The greatest source of error for this measurement is due to not having the tape horizontal. Technician(s) should check the position of the tape to assure its correct position from both the front and back.

2.7.1.5 Lower Leg (Calf) Circumference

The participant sits on a table or stool such that the right leg hangs freely. The observer applies the tape measure horizontally. Find the spot of maximum circumference over the calf muscle by moving the tape vertically up and down the calf (Figure 7). Record the measurement to the centimeter, rounding down.

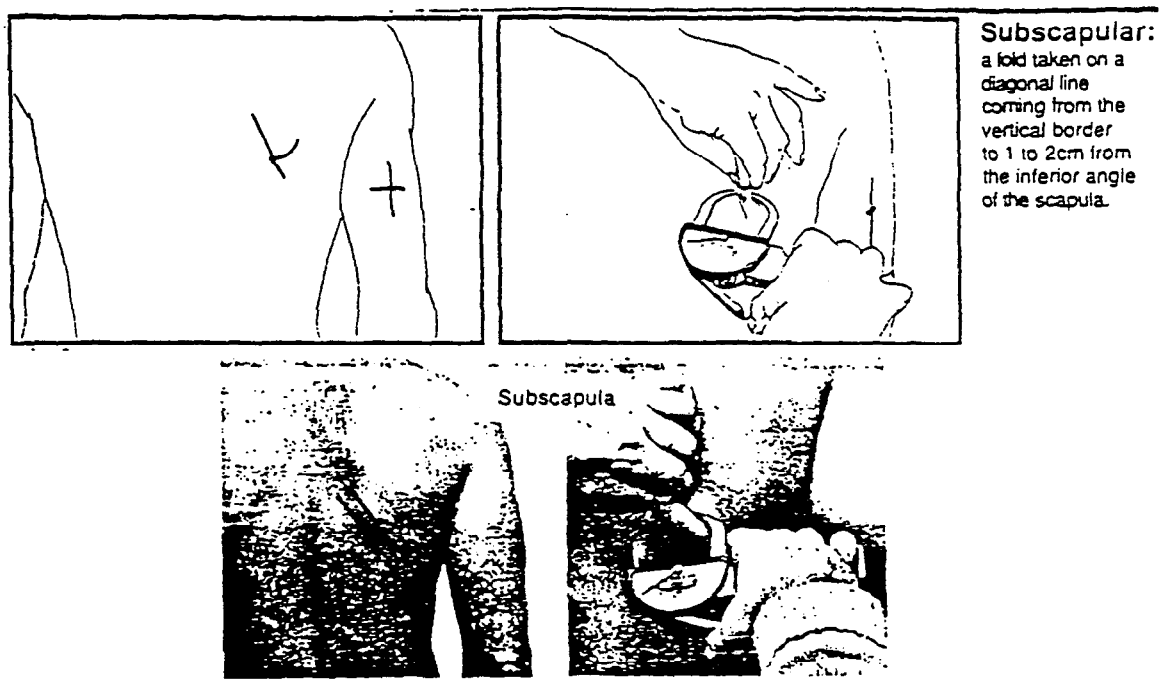

Figure 5. Location of Skinfold Measurements: Subscapula

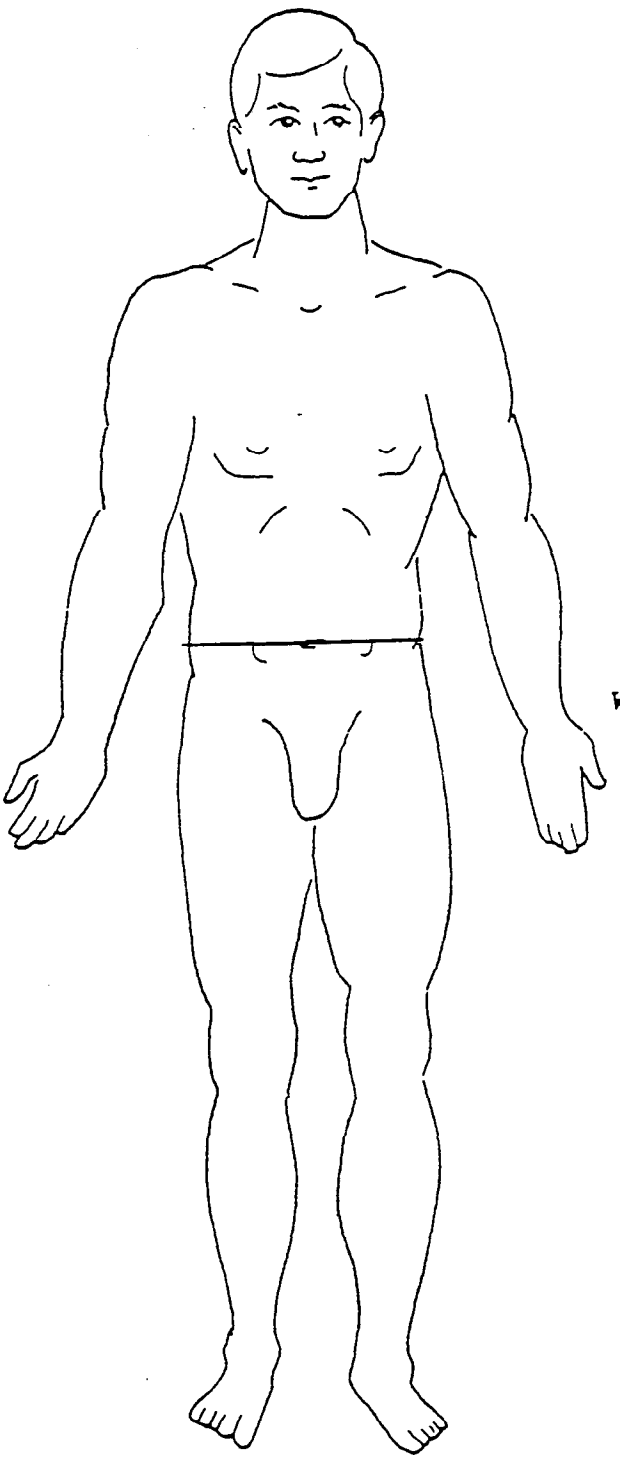

Figure 6. Location of Waist Girth Measurement

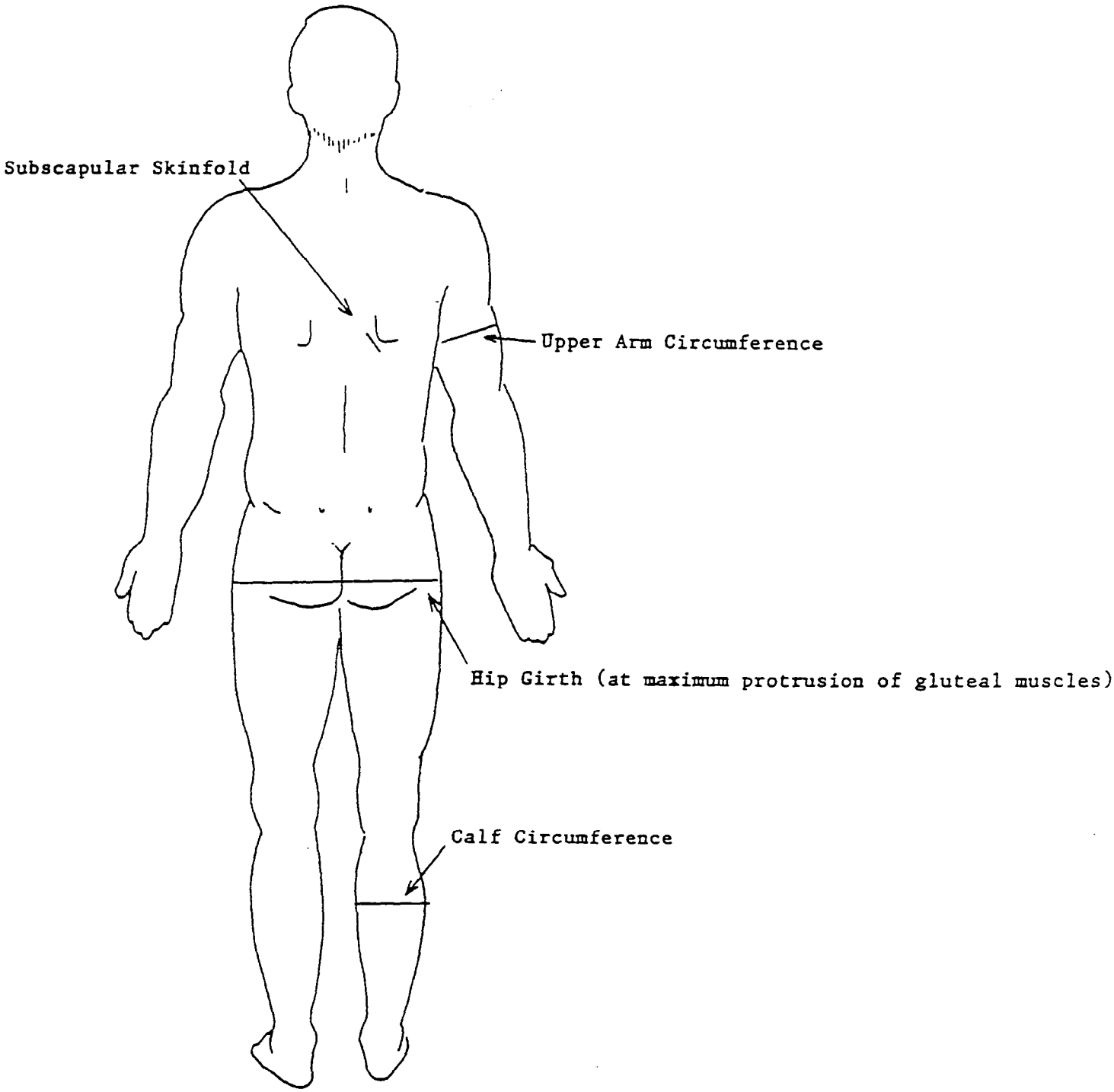

Figure 7. Location of Upper Arm, Hip and Calf Circumferences; and Subscapular Skinfold

2.7.1.6 Wrist Breadth

Identify the styloid processes of the right radius and ulna, with the palm upward and parallel to the floor. The wrist may be flexed upward or downward to help identify the styloid processes. (Figures 8 and 9). Locate the styloid processes of the radius and ulna. With the wrist straightened and the palm upward, hold the body of the sliding caliper above the wrist, place the immoveable jaw on the styloid process of the ulna and gently side the moveable jaw snugly to the styloid process of the radius. Read measurement to the millimeter, rounding down. Observe caliper dial millimeter marks and slide centimeter marks carefully to obtain accurate reading, to the millimeter, rounding down. The sliding calipers should be checked using a standard aluminum step wedge set at 50 mm, before measuring wrist breadth on each participant. If the calipers are more than 1.0 mm off the standard, they should be repaired.

2.7.1.7 Training and Certification

Each technician must undergo training and certification by an anthropometry expert. The training program for taking body size measurements consists of the following components (adapted from the Health Examination Survey, 1966-70, and the CARDIA Study Protocol).

1. Training is conducted centrally by an expert in anthropometry. One full day or two half-days are required.

2. Each field center trains two or three individuals before the baseline examination. One individual from each center is designated the center's anthropometry supervisor.

3. If additional personnel are needed by a center to perform anthropometry, training is provided by the center's anthropometry supervisor.

4. Training includes:

   a) Introduction - rationale for body size measurements, overview of technique, expected limits of reproducibility, and pitfalls related to anthropometry.

   b) Demonstration of technique - an expert demonstrates the proper technique of each measurement on a volunteer subject. This includes a description of proper and improper techniques, as well as recording of data.

   c) Practice - technicians divide into groups of three, with two performing measurements on the third in a round-robin fashion. This is done under the observation of a trained anthropometrist. Differences in technique and clarification of problem areas are discussed.

   d) Testing - several volunteer or paid subjects are assessed independently and blindly by each technician. Each technician's measurements are compared with the expert's measurements and the results discussed in class. The four subjects examined have four distinctly different body types: lean, obese, athletic, and aged.

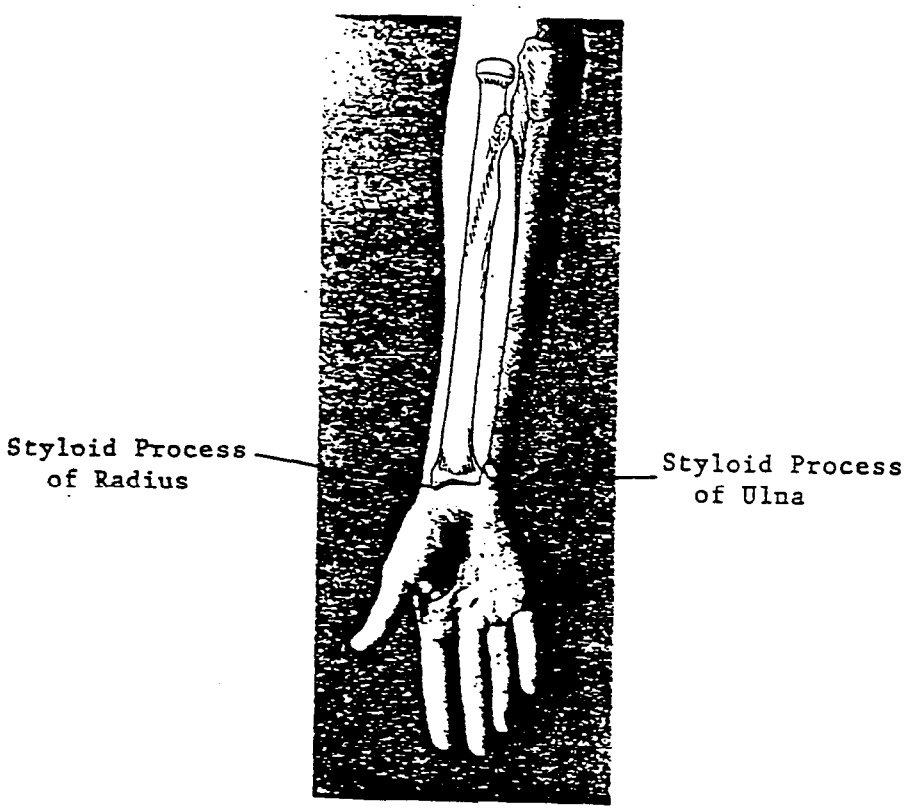

Figure 8. Bony Landmarks for Wrist Breadth Measurement

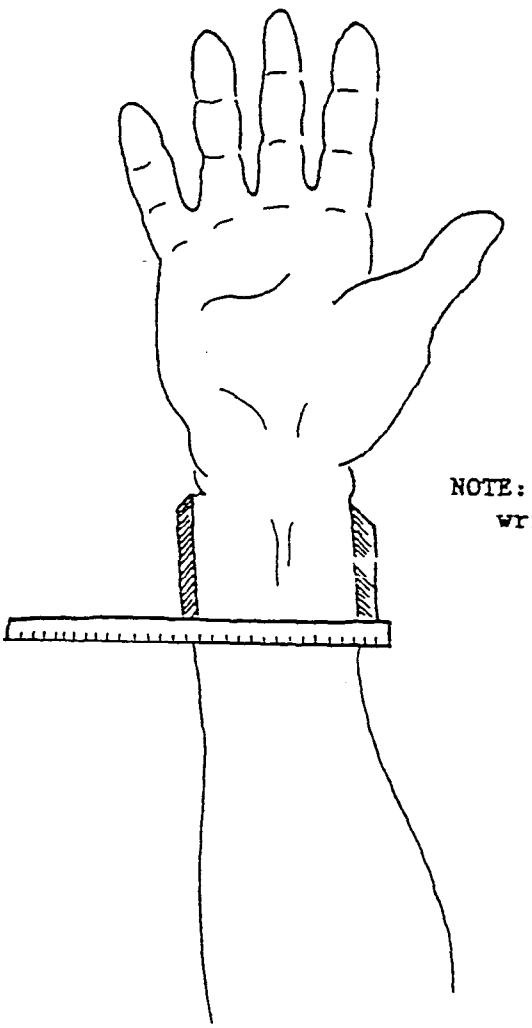

Figure 9. Wrist Breadth Measurement

e) Certification - technicians must measure one or more test subjects and be within certain standards of error:

1) Each skinfold measurement must agree within ± 2 mm of the expert on each subject (an average difference with ± 1 on both subjects).

2) The arm, waist, hip and calf circumference measurements must agree within ± 1 cm on each subject (± 2 cm on arm and calf; ± 1.5 cm on waist and hip; average difference within ± 0.75 cm for both subjects)

3) Weight must agree within ± 0.5 lb. Height and sitting height within ± 1 cm.

4) Wrist breadth must agree within ± 1 mm.

When these are met, the technician receives preliminary certification for field work. Technicians who have problems are identified, and they are allowed to practice and try again to be certified.

Final certification is made at a later date after additional practicing at the local centers. This final certification also is done by comparing technicians versus an expert on blind measurements.

2.7.1.8 Quality Control

The quality control scheme for anthropometry involves equipment calibration and monitoring, as well as between-technician and within-technician assessments of reliability. The detailed quality control procedures are found in Manual 12.

2.7.2 **Physical Examination**

2.7.2.1 Introduction

All examinations are performed by trained clinicians, either nurse practitioners, physician assistants or physicians. All examination items are within the scope of training that these providers have received and are usual, if not daily, parts of physical examinations. This implies that detailed descriptions and training are aimed at achieving reliability from examination to examination, and among centers. This is the main goal of this component of the ARIC protocol.

The training of the nurse practitioners, physician assistants and physicians on the ARIC protocol is centralized at the Coordinating Center and is based on the written protocol. Each Field Center has designated a primary examiner and at least one other person who is available to perform examinations in the absence of this primary person. The second examiner may be the medical director or an ARIC physician.

Certification requires adequate performance of the components of the examination as validated by the chief trainer. Quality control focuses on the potential for false positive examinations. Because most participants are

healthy, the frequency of abnormal findings is relatively small. The presence of real abnormalities among those with normal examinations is also small (a low false negative rate), and this makes it inefficient to re-examine the many individuals with normal findings. The review of positive findings is part of the Medical Data Review. While only a few items are targeted for confirmation, a sampling of positive findings for review by a physician provides for an on-going quality assurance program.

After the initial training, continuing education includes regular review of the protocol, followed by conference calls with the trainer at approximately six month intervals.

2.7.2.2 Item by Item Specification

Participants wear a surgical scrub suit and socks for the examination. It is helpful to have them wear large scrub pants to enable the pant legs to be rolled up for the ultrasound and ECG examinations. The Physical Examination Form is included in Appendix IX.

2.7.2.2.1 Walking/Standing

Use of cane/wheelchair - ascertained at the time the participant enters the examination room.

Gait - If the person uses a cane for normal walking, the cane is part of the examination. If the walking cannot be performed, this is noted on a note log. The participant walks ten steps along a line in the center of a hallway at a rapid rate. A dystaxic gait is present if the individual passes one ankle more than six inches away from the other in walking. A hemiplegic or paretic gait is noted when the normal leg is on the ground and the abnormal leg swings in a circular motion to place the opposite foot on the floor. A limp is usually apparent. If an arm is affected, it usually does not swing and may be held flexed at the elbow.

Arm strength/Romberg - The participant stands with feet together, ankles and big toes of each foot touching. He or she is asked to fix gaze on a distant location with arms outstretched horizontally, palms up, and hands and fingers extended. If the individual cannot balance with the feet together, have the person stand so that balance is achieved. If the person cannot balance, this is recorded on a Note Log. When balance is achieved, the participant is asked to close eyes and balance for ten seconds. Weakness in one arm is noted by a downward drift in that arm of one foot or more, or pronation of the hand toward the vertical position. A positive Romberg sign is one in which the individual has to move a foot from the starting position to maintain balance. During this procedure the examiner stands close to the participant, to assist in case of loss of balance.

2.7.2.2.2 Invasive Procedures

During or after the physical examination, the participant is asked about past invasive procedures on the cardiovascular system. Questions addressed to the participant include "surgery to the heart, or the arteries of (the) neck or legs," various arterial revascularization procedures, and carotid endarterectomy.

2.7.2.2.3 Sitting

Lungs - Rhonchi, Rales - The participant is in the sitting position. It may be best for men to remove the scrub top entirely and for women to lift it. The stethoscope diaphragm (which should be warmed in the palm of the hand) is used. The participant is instructed to take deep breaths through the mouth. After the first five or six breaths and as needed thereafter, the participant is asked about symptoms of lightheadedness. Auscultation takes place over the posterior lung fields, beginning at the apices with at least one full breath in each location. Three locations on each side are examined: apex, mid-lung field (approximately at the 6th intercostal space) and the base, which may need to be determined by percussion. Rhonchi are described as coarse breathing noises. Rales are fine moist noises. Basilar rales are reported as those within two stethoscope diameters of the base of the lung. "Lower lung" means from above the base to mid-lung, at the 6th space posteriorly.

Heart - The diaphragm of the stethoscope is placed consecutively at the apex, the left sternal border at the 5th intercostal space, the left sternal border at the 2nd intercostal space, and the right sternal border at the 2nd intercostal space. The examiner listens for at least five beats in each location. This is repeated at each of the four spaces with the bell of the stethoscope lightly applied to each area. The location of a systolic or diastolic murmur is reported in the area in which it appears loudest. More than one location of equal intensity is acceptable. A grade one murmur is barely audible. Grade two is just easily audible. Grades three and four are intermediate and increasing in intensity; grade four is palpable as a thrill. Grade five is louder, palpable, but still requires the stethoscope on the chest, lightly applied. Grade six can be heard with the stethoscope off the surface of the chest. Other findings include the radiation and the character of the murmur. Other - Other findings include changes in breath sounds and evidence of surgery.

2.7.2.2.4 Supine

Heart - Systolic and Diastolic Murmur - Auscultation is performed in the supine position as described under 2.7.2.2.3, above. Record findings if present in either the sitting or supine position.

Other Findings - Other findings include evidence of surgery.

Neck, Carotid Bruits - The participant remains supine. She/he is asked to stop breathing momentarily. With the stethoscope bell, the examiner listens first above the clavicle for the common carotid artery and second, at the angle of the jaw for carotid bifurcation. In each position, the stethoscope is placed for three cardiac cycles, alternating sides of the neck.

Other Findings - Other findings include venous pulsations or other arterial sounds.

Breasts - A breast examination is not part of the ARIC protocol, but is an option offered by some field centers. The recommended procedure includes (1) Palpable Mass, (2) Location - Using the pads of the fingertips, examination

begins at the nipple, using a spiral motion outward and alternate soft and deep pressure. Palpation is extended into the axillae with arms abducted. A mass is defined as palpable tissue different from surrounding breast tissue. Masses are reported as central, meaning in contact with the nipple or areola, or into quadrants, centered at the nipple.

Other Findings - Other findings include discharge, retraction and description of any masses that are felt.

Ankle Edema - At this point the socks or other foot covering are removed. The participant is examined in the supine position. Gentle but firm pressure is applied along the mid-tibia, anteriorly down to the ankle in each leg. Pitting or indentation remaining after pressure is removed constitutes definite edema. The examiner identifies the mid-point between the prominence of the medial malleolus and the inferior border of the patella. Pitting at or above that mid-point is recorded as "marked" edema. Pitting only below that point is recorded as "mild" edema.

Posterior Tibial Pulse - The examiner palpates inferior to the medial malleolus of each foot. The presence or absence of arterial pulsation is recorded. If in doubt, the examiner compares with the radial pulsation.

Babinski - The lateral surface of the sole of the foot (plantar surface) is stroked with pressure beginning at the heel and going forward along the lateral surface, crossing the forefoot (ball of the foot) toward the big toe.

The absence of Babinski reflex is a plantar flexion of the great toe. If the leg is withdrawn (a tickle response), the lateral surface of the foot (not the sole) is stroked similarly beginning at the heel and going forward toward the little toe. The Babinski sign is present when the great toe extends on these maneuvers (dorsiflexion).

2.8 Medical Data Review Procedures

2.8.1 Introduction

Three levels of review of a participant's medical data take place at the field center. The first (described in section 2.8.2) is designated Medical Data Review and occurs at the conclusion of the clinic interview and examinations. ARIC personnel responsible for this review process are physician assistants or nurse practitioners.

The next level of review (the Medical Review, described in Section 2.8.3) involves an ARIC physician and, when needed, the Field Center Ultrasound Director. The ARIC physician's review takes place within 48 hours of the participant's visit. In addition to the baseline examination data, the participant's folder contains at this time the results from the hematology tests. The Ultrasound Director's review is initiated in the event of an alert value report from the Ultrasound Reading Center.

In the course of the four to six weeks following the participant's visit, study results from the central agencies are received at the field center. Central agencies notify the field centers by telephone of results requiring

expedited notification (alert values). These are reviewed by the ARIC physician or field center director within 24 hours of receipt. Routine results are obtained via the Coordinating Center, and are assembled for review with the field center director once a complete set of study results is available for a participant. At this time a letter of notification of results is prepared. The field center director or the ARIC physician determines the type of notification required, and the corresponding source letter is selected according to the criteria described in section 2.10 of this manual. The letter of notification is personalized, signed by the field center director or person designated by him/her, and copies of study results are included.

2.8.2 Medical Data Review

The purpose of the medical data review is (1) to summarize the results of selected measurements obtained at the clinic for the participant and answer questions, (2) record the impression of the nurse practitioner or physician assistant (or physician) on the presence of noncerebrovascular causes of any positive TIA symptoms, and (3) identify potential medical problems. If any are found, referral procedures are initiated.
The medical data review is conducted by a physician assistant, a nurse practitioner, or a physician. Prior to meeting with the participant the interview note logs, the electrocardiogram, and the pulmonary function test results are examined. In addition, the Medical Data Review Printout (Appendix IX) is generated from the participant's diskette, and examined by the physician assistant or nurse practitioner. This printout displays the participant's average blood pressure and all items from the interviews and physical examination which are flagged for inclusion in this review. Listed on this printout are any positive responses to the TIA, stroke and chest pain queries, and associated questionnaire items that facilitate their clinical evaluation. Also listed on this printout are positive answers to the history of medical conditions obtained during the home interview, and abnormal findings from the physical examination. Finally, the printout identifies the participant's physician. The results from the pulmonary function test, and a preliminary interpretation of the electrocardiogram are recorded by hand on the printout by the physician assistant or nurse practitioner.

Data collected on paper forms are transcribed on the medical data review printout at this time. During the home and clinic interviews historical information (e.g., previous illnesses, treatment), and symptoms (e.g., chest pain) are obtained through standardized interviews. During the medical data review selected affirmative answers to these standardized questions are confirmed through additional, non-standardized, clinically-oriented questions. The physician assistant or nurse practitioner also records his/her impression on the presence of noncerebrovascular causes for positive TIA symptoms. The physician assistant or nurse practitioner also determines whether any condition reported by the participant is already under treatment.

Factual information is then given to the participant about his/her results, identifying any abnormalities and referral as needed, but avoiding medical advice about prognosis, prevention, or therapy. The first Participant Report (see Appendix VIII) is completed at this time and given to the participant with his/her results. When a non-physician conducts the review, adequate medical back-up is available at all times. Participant values, referrals and

the reviewer's impression on noncerebrovascular causes for TIA symptoms are reviewed by a physician twice a week (see section 2.8.3, Medical Review).

2.8.2.1 Referral Levels at Medical Data Review

ARIC refers participants only if there is medical consensus on need, using established guidelines for referral where available. The ARIC Study considers referrals for initial care, as well as the circumstances under which it is necessary to advise the participant to return for care. Uniform criteria for referral of participants are implemented at all ARIC centers. Immediate, urgent, and routine referrals are made. Methods for referring participants who have no physician are established with the participant. All referrals are documented on a separate log (see Appendix IX). The following are the levels of referral established for the Medical Data Review.

1. Emergency: Emergency referral or emergency squad.

2. Immediate Referral: The participant is urged to see his/her physician within one day.

   The physician assistant consults with the ARIC physician, and the participant's physician is called by the appropriate person. The participant is provided with an "immediate referral" letter (Referral Letter 1), to take to his/her physician.

3. Urgent Referral: The participant is urged to see his/her physician within one week.

   The physician assistant confirms the decision with the ARIC physician, and gives the participant an "urgent referral" letter (Referral Letter 2) to take to his/her physician's office. The ARIC physician calls the participant's provider of care, and sends copy of Referral Letter 2 to him/her.

4. Routine Referral: The participant is asked to see his/her physician within one month, or at first convenient appointment.

   The physician assistant advises a visit to the participant's physician. A "routine referral" letter (Referral Letter 3) is sent to the participant's physician.

5. No Referral: The study results are summarized for participant and held for routine results letters.

2.8.2.2 Referral and Review Guidelines

Guidelines for referral at medical data review are provided in Table 16 below. Certain interview items or measurements (identified with an asterisk) require confirmation. The reviewer determines the acuteness of the findings, as well as whether or not the condition is being followed by a physician. If the participant is aware of and being followed medically for a condition, judgement is exercised about whether to refer.

Table 16. Referral Guidelines at Medical Data Review

Referral Classification	Statement to Participant	Examination Findings	Explanation to Participant
Emergency Referral	See M.D. Immediately	*SBP ≥ 260 mm Hg *DBP ≥ 130 mm Hg	BP very high BP very high
Immediate Referral	See M.D. Today	*SBP 240-259 mm Hg *DBP 115-129 mm Hg	BP very high BP very high
		*Unstable angina	Your chest pains may be important
		*Neurologic symptoms in past week	Your symptoms may be important
		*Other severe symptoms or findings	Your symptoms may be important
Urgent Referral	See M.D. within a week	*SBP 200-239 mm Hg *DBP 105-114 mm Hg	BP high BP high
		*Angina, stable but untreated/not being followed	Your chest pains may be important
		*Neurologic symptoms, untreated, one week to six months ago	Your symptoms may be important
		*Acute congestive heart failure	Your symptoms may be important
		PFTs: FEV1 < 65% or FVC < 65% or FEV1/FVC < 60% plus symptoms	Your lung function is diminished to ___% of predicted and warrants attention; M.D. will get a copy
		*Other acute, but less severe symptoms	Your symptoms may be important

Table 16 Referral Guidelines at Medical Data Review, continued

Referral Classification	Statement to Participant	Examination Findings	Explanation to Participant
Routine Referral	See M.D. within month or at first convenient appointment	SBP 140-199 mm Hg	BP elevated into borderline range
		DBP 90-104 mm Hg	BP elevated into borderline range
		*Old MI (Rose Questionnaire), previously unrecognized	Your chest pain may be important
		*Neurologic problem (stroke, TIA exam findings) >6 months ago, unrecognized	Your symptoms may be important
		*Claudication, previously unrecognized	Your leg pain may be important
		PFTs: FEV1 < 65% or FVC < 65% or FEV1/FVC < 60% and not aware	Your lung function is diminished to ___% of predicted and warrants attention; M.D. will get a copy
		*Other symptoms or findings needing evaluation/not being followed	Your symptoms may be important
No Referral		SBP < 140 DBP < 90 mm Hg	Normal BP
		PFTs: FEV1 65-79% or FVC 65-79% and FEV1/FVC > 60%	Your lung function is diminished to ___% of predicted. This does not warrant referral, but M.D. will get a copy.
		PFTs FEV1 ≥ 80% and FVC ≥ 80% and FEV1/FVC ≥ 60% of predicted.	Normal, M.D. will get a copy.

Table 16 Referral Guidelines at Medical Data Review, continued

Referral Classification	Statement to Participant	Examination Findings	Explanation to Participant
		*Angina, stable on treatment/being followed.	Confirm only
		*MI, previously documented	Confirm only
		Height, weight	Report only
ECG			
ECG Findings Requiring Review by M.D. Before Participant leaves the Field Center	Would like to review with M.D.	*Acute pattern abnormalities (MI, ischemia...)	
		*Rhythm disturbances 2nd or 3rd degree block, ventricular tachycardia, any type of ectopic beat > 6/minute, couplets bigeminy, R on T, multifocal premature ventricular contractions, atrial fib/flutter with ventricular rate < 60 or > 110, sinus bradycardia < 50, sinus tachycardia > 110, PR interval ≥ 0.26 sec.	
		*Any other ECG finding, alone or in conjunction with symptoms, causing concern.	
Other ECG Findings or Normal ECG	I am reviewing this ECG only for major abnormalities and see none. Dr. ___ and I will review this ECG in detail within ___ days. A copy will be sent to your physician with the other results.		

* Interview items or measurements require confirmation.

2.8.2.3 Training and Quality Review

It is the responsibility of the medical director of each field center to ensure that ARIC protocol is followed appropriately during medical data review, referrals, and reposting of results. Physician assistants and nurse practitioners are trained and certified for this purpose by the medical director and/or the field center principal investigator. As described in the next section, frequent review by the ARIC physician or medical director is a feature of the ARIC protocol, providing assurance for participant safety and quality control. In addition, a library of electrocardiographic tracings, prepared by a cardiologist to supplement the training of the ARIC nurse practitioners and physician assistants in the recognition of key electrocardiographic patterns, is used at each field center under the supervision of the ARIC physician.

2.8.3 Medical Review

Medical review consists of a general medical review and, when needed, a review by the Field Center Ultrasound Director.

2.8.3.1 General Medical Review (Review by ARIC Physician)

The purpose of the medical review is to (1) provide a physician interpretation of the study results, (2) record the impression of the ARIC physician on the presence of noncerebrovascular causes for positive TIA symptoms, and (3) provide an overview of referrals and reports from the field center. This is the responsibility of the ARIC physician or the clinic director, assisted by the nurse practitioner or physician assistant.

The medical review is an ongoing activity at the field center. Twice a week the physician reviews the data of participants seen in the preceding two to three days. After reviewing the participant's Medical Data Review printout, the physician reads the ECG, records the interpretation on the Medical Data Review printout, and reviews the preliminary interpretation by the physician assistant. The physician also reviews the local hematology results for alert values, and assumes responsibility for any referrals. If any referrals were made during Medical Data Review, these are reviewed at this time with the physician.

As "alert values" (see section 2.10.6) are returned from the central laboratories and reading centers, the physician reviews them and assumes responsibility for referrals. Routine results may bypass physician review until the final report is generated. The ARIC physician or clinic director reviews all letters and reports sent to participants and their providers of health care.

2.8.3.2 Field Center Ultrasound Director Review

The purpose of the medical review by the Ultrasound Director is to: (1) provide clinical review of all alert values reported by the Ultrasound Reading Center; (2) recommend appropriate course of action to field center director or

ARIC physician in instances of ultrasound alert values; and (3), provide clinical back up to field center sonographers.

The Ultrasound Director reviews all alert values notified by the Ultrasound Reading Center within two days of notification. Verification ensures that the participant's video tape has been identified correctly and that the center's half-inch video tape is confirmatory of the alert value. It is the responsibility of the Ultrasound Director, assisted by the sonographer and the Ultrasound Reading Center, to resolve any discrepancies found and recommend a course of action concerning participant referral.

It is also the role of the Ultrasound Director to perform ad hoc reviews of video tapes identified by the center's sonographers because of safety, or data quality concerns. In addition, the director periodically reviews a sample of half-inch video tapes for quality of data, provides feed-back to each sonographer, and a report to the Ultrasound Reading Center.

2.9 Exit Interview

Prior to the time the participant finishes with the last physical exam or interview, a check is made to determine if any quality control repeat measures are necessary. If required, these must be done before the participant changes into street clothes. If not, the participant is directed to change at any time after all exams requiring a loose gown are completed. The last interviews, medical data review and pulmonary function may be conducted in street clothes.

There is usually a short wait after the last exam or interview and before the medical data review while results are being printed and the physician, physician assistant, or nurse practitioner reviews the results. An appointed staff person takes the participant to the change room, and explains that the summary of results will be ready in a moment. Some centers return medications at this time. In other centers, the medications are returned by the person conducting the medical data review.

In most centers there is no formal "exit" interview. Several questions regarding clinic procedures and home interview procedures are incorporated into the medical data review interview done by the physician, physician assistant, or nurse practitioner. The person conducting this interview thanks the participant and sees that all personal items and medications are returned. In some centers, the participant is then escorted to the reception desk where reimbursement for parking fees is provided.

2.10 Report of Study Results

2.10.1 Introduction

It is the policy of the ARIC Study to hold meetings with local physicians to explain ARIC's reporting policy and seek their advice and support. In each study community the local medical society(ies) provide the mechanism to obtain specific recommendations on the test results to be reported, and to define the local ARIC referral policy. Some ARIC field centers have established a

medical advisory board of community physicians who provide this important link to the practitioners in the ARIC study communities.

Within this context, reporting methods and participant referral are standardized across field centers. All results of routine medical tests (normal and abnormal) are reported to the participant's physician. Routine medical tests are those which, according to standard medical practice in the ARIC study communities, are considered to have empirical value for diagnosis and/or treatment.

All reports to participants or physicians are factual. If verification or follow-up is needed, the participant is advised to discuss the results with his/her physician. If additional tests and procedures are performed by participants' physicians as a result of ARIC reporting, this is considered an acceptable and necessary consequence.

The ARIC Study makes referrals according to the criteria described in sections 2.8 (during the clinic visit) and 2.10.6 (when alert values are received). Referrals for emergencies are described in section 2.11. Beyond this responsibility ARIC provides no specific medical advice or interpretation. This type of advice is the prerogative and responsibility of the participant's physician. Consistent with this policy, clear instructions are given to all ARIC staff to avoid interpreting study results. If detailed information is requested, the participant is referred to his/her physician for interpretation.

Whenever the therapeutic implications of results are not known, a statement to that effect is included in the report to the physician. Copies of all reports and letters concerning examination results sent to participants and physicians are kept at each field center.

2.10.2 Overview of Results Reporting

Either at home or during the clinic visit, participants receive a schedule that indicates which study results will be reported back to them, and at what time (See Appendix VIII). In the course of the examinations at the field center, the participant is given immediate verbal feed-back on his/her blood pressure, height, and weight. During the medical data review at the end of the examination, the participant receives a report on the results from the physical examination and anthropometry, as well as preliminary results from the electrocardiogram and pulmonary function test. Results from other measurements are not available for review with the participant at that time. Instead, the participant is reminded that a letter containing a report on the study results will be mailed three to four months later, as well as to the physician identified by the participant. The reasons for this delay are explained, and the participant is told that any abnormal results will be reported on an expedited schedule, either by letter or telephone. The physician and the participant are notified of any "alert value", specifying the test or measurement at issue and the observed result that requires verification. The participant is asked in this communication to follow-up on this finding with his/her physician. Once all study results are received at the field center, a letter is sent to the participant and to the physician reporting on all routine results, and restating any alert values previously notified.

Figure 10 provides an overview of this process and illustrates the interface between the review of medical data, the referral process, and the notification of study results. The figure also indicates that certain results are reported on a routine basis, whereas potentially abnormal study results are quickly reported to participants and their physicians.

At all field centers the reports to the participant and/or the physician provide a minimum, standard, set of study results. Reports to participants include a statement indicating either that all study results are within ranges considered normal, or that a study result requires confirmation or further study. Brief explanatory statements are provided. Physicians receive a copy of this report, and are thus aware of any results flagged as being outside of the ARIC reference range, and of the wording and explanations provided to their patients. Reports to participants and physicians include the ARIC reference ranges for all results. The wording of these statements can be found in the prototype letters and reports included in Appendix VIII and are listed here briefly.

1. At reception, the participant is given the document Schedule of ARIC Results Reporting, describing the tests to be reported to the participant and the physician.

2. At Medical Data Review, a Participant Medical Data Review Printout and all note logs are generated summarizing findings for the Medical Data Review. Items flagged for review are automatically retrieved from the data base and printed on this form. The physician assistant, nurse, or physician conducts the Medical Data Review with the participant, as described in section 2.8.2. A preprinted First Participant Report is given to the participant to summarize exam results.

3. At the Medical Data Review, a referral may be necessary. Three levels of referral are designated: Immediate (Letter 1), Urgent (Letter 2), Routine (Letter 3), and the corresponding referral letters are sent to the participant's physician. In some cases, a phone call may be indicated.

4. Twice a week, a medical review occurs during which the ARIC physician reviews the participant's data and interprets ECG, as described in section 2.8.3. If an abnormality is detected at this time, a report or referral letter, such as the ones described above, is sent.

5. Subsequent to the exam, results will return from various labs and reading centers as described below. If there are "alert values", the participant is notified using a Alert Value Referral Letter (Letters 4 & 5) and his/her physician is notified using either the Urgent, or Routine Letter, or a phone call if indicated. If there are no "alert values", the results are entered in the database for final Results Letters.

6. A record is kept of all alert values and referrals (Alert/Referral Log) and a copy of all referral letters.

7. When all results are available, the Summary Report to the Participant and Physician and accompanying cover letters are generated. The several types of cover letters are summarized in Table 17.

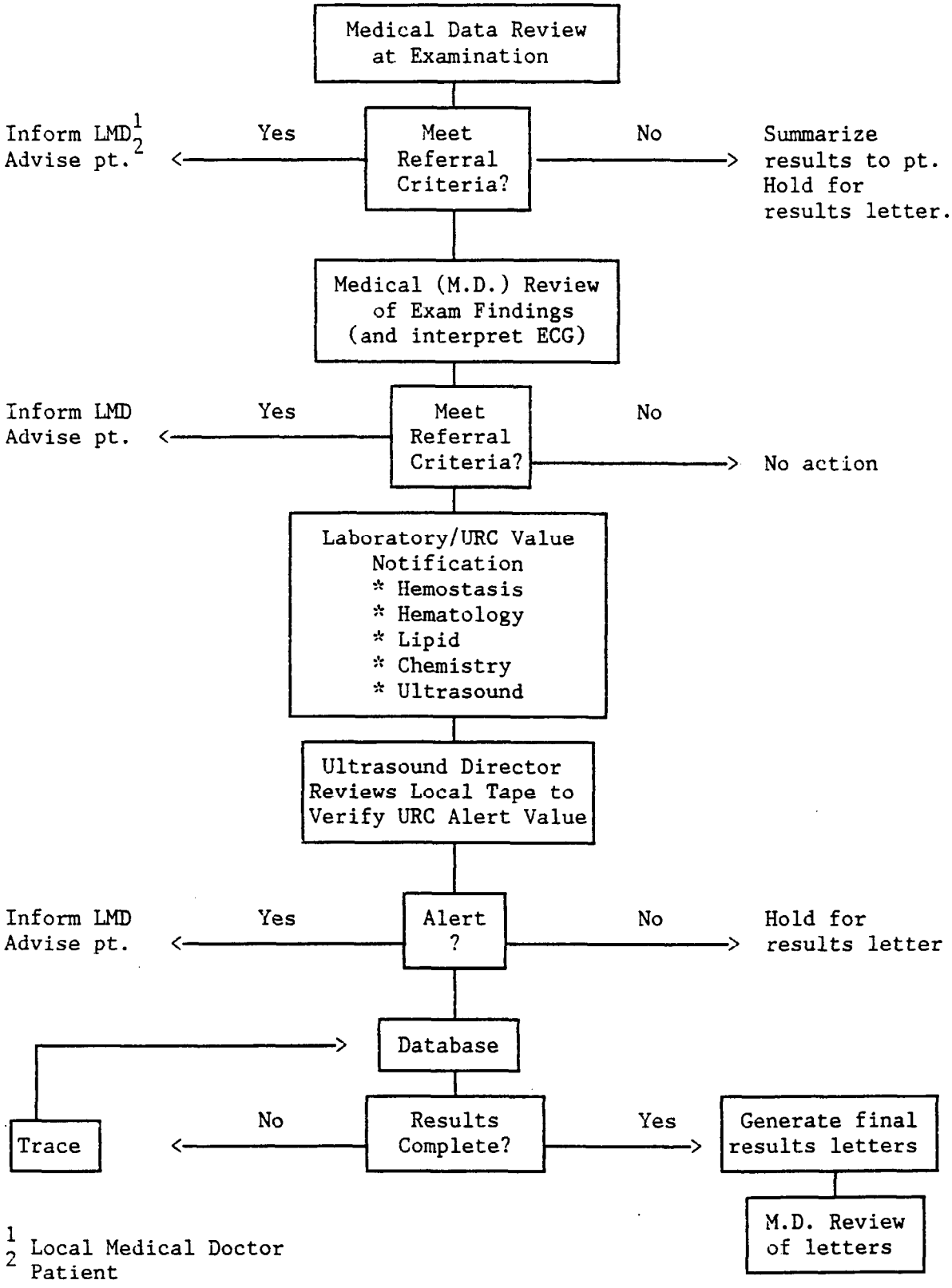

Figure 10. Summary of Review of Results, Reporting, and Referral

Table 17. Cover Letters for the Summary Reports to Participants and Physicians

Recipient	Type of Results	Type of Cover Letter
M.D.	Normal results	M.D. Letter 1
	Abnormal results, no earlier referral made	M.D. Letter 2a
	Abnormal results, previous referral made	M.D. Letter 2b
Participant	Normal results	Participant Letter 1
	Abnormal results, no earlier referral made	Participant Letter 2a
	Abnormal results, previous referral made	Participant Letter 2b
	Normal results, no M.D. designated	Participant Letter 3a
	Abnormal results, no M.D. designated	Participant Letter 3b

8. The field center director or a field center physician reviews all results and takes responsibility for letters before they are mailed. If the participant is currently participating in another medical research project, possible unblinding by reporting ARIC results is considered.

2.10.3 Report of Ultrasound B-Mode Scan Measurements

The ARIC ultrasound examination is oriented toward the detection of early changes in the arterial wall and does not provide clinical documentation of the extent of isolated lesions which might be of medical importance. Portions of the internal carotid artery, which may have disease, are not visualized at all. Some of the early arterial changes documented for ARIC (changes in arterial distensibility, for example, or non-lumen encroaching wall thickness) are not, at present, of known medical value and are of research interest only. Such results are not routinely reported to the participant and his/her physician. In the process of obtaining consent, the participant is informed of this fact.

No consensus exists as to the most effective treatment of atherosclerotic lesions in the carotid arteries, and surgery has no proven benefit at present. Neither the ARIC ultrasound examination protocol, nor the training of the the ARIC sonographers, provide an adequate capability to detect clinically significant arterial lesions in the study participants. If in the course of the highly standardized ultrasound scanning protocol lesions are found that occupy the carotid artery lumen, the ARIC study is not able to adequately characterize such lesions. False positives cannot be ruled out, and a significant risk would be incurred if "abnormal findings" were reported to participants and their physicians under such circumstances.

For the above reasons, participants and their physicians are notified only if: a) participants report recent (six months) symptoms indicative of TIA or stroke, verified during the medical data review; or b) the Ultrasound Reading Center notifies the field center of a residual lumen of $\leq$ 2mm in a carotid artery segment measured according to the ultrasound reading protocol and the Ultrasound Director at a Field Center confirms this finding. In addition, the routine report to participants and their physician includes a brief summary statement on the B-Mode findings in the carotid system, together with appropriate explanatory material in the case of an "alert value" (See Appendix VIII).

The medical and ultrasound experts of the ARIC Study agree that these criteria are consistent with local medical practice for each of the ARIC study communities. It is an explicit requirement of the participant safety criteria of the ARIC Study that this section of the protocol be reviewed periodically, and modified as needed according to advances in the state of the science and evolving medical practice.

2.10.4 Routine Notification of Study Results

All results of routine medical examinations, normal or abnormal, are reported to the participant and his/her physician, unless the participant has not identified a personal physician or has specifically asked to receive all study results. This is explained to the participant during the visit to the ARIC field center, and the participant is provided a schedule for results reporting (see Appendix VIII).

2.10.4.1 Results Routinely Reported to the Participant

Results reported to the participant during the clinic visit include height, weight, blood pressure, lung function test (preliminary report), and ECG (preliminary report).

Three to four months after the visit, the following are reported to the participant by mail: Height, Weight, Blood Pressure, Electrocardiogram (summary report only), Lung Function Test (summary report only), Ultrasound Examination (summary report only), and Blood Tests: total cholesterol, LDL cholesterol, total HDL cholesterol, triglycerides, hematocrit, hemoglobin, white blood cell count, platelet count, total protein, albumin, calcium, phosphorous, magnesium, sodium, potassium, creatinine, urea nitrogen, uric acid, glucose.

2.10.4.2 Results Routinely Reported to the Physician

The participant's physician receives a copy of the report sent to their patients, as indicated in Section 2.10.2. In addition, physicians are notified of any important symptoms reported by the participant and they are provided with the participant's electrocardiogram (copy and interpretation), and lung function test (copy and interpretation).

2.10.5 Results Reported Only by Request

The following are considered measurements of research value only, and are reported only if requested by the participant or his/her physician. The selection of study results of research value reflects the views of local practitioners and of the medical societies at the ARIC study communities, and is subject to revision in response to local medical practices.

Blood tests of research value only: HDL_2, HDL_3, Lipoprotein Lp(a), insulin, Apolipoproteins AI and B, Activated PTT, Fibrinogen, Factor VII, vWF-Antigen, Protein C, Antithrombin III.

Ultrasound measurements of research value only: Arterial distensibility measurements, postural changes in heart rate and blood pressure.

Anthropometric measurements of research value only: skinfold thickness.

2.10.6 Study Results Requiring Special Notification

The ARIC protocol identifies certain potentially abnormal findings that require expedited notification to the participant or his/her physician. These include flagged responses to the medical history questionnaire and findings during the physical examination. These items, and the corresponding referral and notification criteria, are described in section 2.8. Similarly, "alert value" levels have been defined for the functional tests and laboratory measurements.

Laboratory and ultrasound results are not available at the time of the clinic visit. Local hematology results are scrutinized at the Field Center for alert values, on the day following the clinic examination. Notification in response to an alert value in hematology results occurs by telephone after review of the participant's record by the Field Center physician. Central laboratories and the Ultrasound Reading center notify field centers directly of any "alert values". Notification of alert values to field centers is by telephone or electronic mail; confirmation and acknowledgment is required. The laboratory alert values are listed below.

Table 18. Laboratory Alert, and Normal Reference Values

Test	Alert Value[1]	Reference Range, ARIC Laboratory[2]
Total cholesterol (mg/dL).....	--	< 240
LDL cholesterol (mg/dL).....	--	< 165
Total HDL cholesterol (mg/dL)....	--	Male > 31 Female > 40
Triglycerides (mg/dL).....	>1,000	Male < 250 Female < 220
Hematocrit (%)	<30,>60	Male 41 - 51[3] Female 37 - 47[3]
Hemoglobin (g/dL).....	<8,>20	Male 13 - 17[3] Female 12 - 16[3]
White blood cell count ($x10^3/mm^3$)..	<2,>20	4.8 - 10.8[3]
Platelet count ($x10^3/mm^3$).....	<40,>800	140 - 440[3]
Total protein (g/dL).....	<5,>9	6.0 - 8.3
Albumin (g/dL).....	--	3.8 - 5.3
Calcium (mg/dL).....	<8,>12	8.4 - 10.4
Phosphorous (mg/dL).....	--	2.0 - 5.0
Magnesium (mEq/L).....	>3	1.3 - 2.1
Sodium (mmol/L).....	<130,>155	136 - 147
Potassium (mmol/L).....	<3.0,>6.0	3.5 - 5.2
Creatinine (mg/dL).....	>2	Male 0.5 - 1.3 Female 0.5 - 1.1
Urea nitrogen (mg/dL).....	>30	7 - 23
Uric acid (mg/dL).....	<0.5,>10	Male 3.5 - 7.6 Female 2.6 - 6.0
Glucose (mg/dL).....	<60,>140	70 - 130

[1] Laboratory notifies field center; field center MD takes referral or notification action

[2] Reference ranges are provided on ARIC reports to participant and their physician

[3] Center-specific reference ranges

2.10.6.2 Ultrasound Scan Alert Values

A minimal residual carotid artery lumen of ≤ 2 mm is reported as an alert value by the Ultrasound Reading Center. Notification occurs by electronic mail or telephone, followed by a letter signed by the director of the Ultrasound Reading Center. Records of this notification are kept at the Reading Center and the field center. The field center's Ultrasound Director reviews an alert value notified by the Ultrasound Reading Center according to procedures described in Section 2.8.3.2.

2.10.6.3 Criteria for Reporting Alert Values to Participants and their Physicians

At the field centers, alert values require special mention to participants and their physicians. The degree of urgency of notification or referral depends upon the type of finding and level.

1. Immediate/Urgent Referrals - These are based on neurologic symptoms, major ECG abnormalities, or physical examination findings. Alert values received from an ARIC central agency are reviewed by the ARIC physician and/or Ultrasound Director in the context of other data in the participant's record. In this process, extreme laboratory results and readings performed at the ARIC central agencies can lead to urgent notifications to participants and their physicians.

2. Routine Referrals - All confirmed alert values require at least a routine referral, i.e., a notification by the field center director or physician to the ARIC participant and his/her physician. Such alert values include those reported by the ARIC laboratories as well as the URC reports of minimal residual lumen ≤ 2 mm in any segment of the carotid system, once confirmed by the field center Ultrasound Director. All communication between the central laboratories, the field centers, the participants, and their referring physicians is documented in writing, and copy kept in the participant's file.

2.11 Participant Safety

The safety and welfare of the ARIC examinee is assured by (1) specific measures taken in the design or conduct of the examination for his/her protection, (2) the mechanisms established for handling potential emergencies, (3) routine notification of examinees and their physicians regarding the results of the examination and (4) the procedures ARIC staff use to review all potentially medically important results and make the appropriate referrals.

An important factor in the participant's welfare involves his/her expectations regarding the examination. If he/she believes the ARIC examination is a substitute for a clinical examination, he/she could delay seeking medical care that is needed. Provision of adequate information is a requisite to the ARIC informed consent procedures (described in section 2.3).

2.11.1 Measures to Protect the Participant

Examination procedures which convey potential risk to participants include the fasting requirement, venipuncture, pulmonary function test, ultrasound scan and measurement of postural changes in blood pressure. Methods by which participant risk is minimized (more fully described elsewhere in ARIC Manuals) include the following.

The possibility of hypoglycemia with a 12-hour fast is diminished by routine inquiry during the home interview about diabetes. Other medical conditions or dietary restrictions which may be incompatible with the snack provided in the clinic are also ascertained.

Hematomas or prolonged bleeding may result from venipuncture. These are usually avoided if well-trained technicians follow the procedures for blood drawing and take the precautions described in ARIC Manual 7. Prior to venipuncture, the participant is asked the question "Do you have any bleeding disorders?" If the participant answers affirmatively or is uncertain, he/she is asked about whether he/she has had blood drawn previously and if so, whether there were any problems such as swelling or continuing to bleed at the venipuncture site. If the answer to this question is "yes", or if the participant has never had a previous blood test, the clinic supervisor is summoned and will approve the venipuncture only if so advised by a physician.

Occasionally, with any participant, bleeding persists after venipuncture. Procedures described in Manual 7 are followed. If bleeding persists, the clinic supervisor is alerted, and if the measures taken have not stopped all bleeding within 30 minutes, and there is no obvious explanation for the prolonged bleeding, a medical referral is made. Also, the participant is instructed to seek medical care promptly if bleeding recurs after leaving the ARIC clinic. Participants may experience syncope during the venipuncture. Methods for handling minor and major emergencies are described in section 2.11.2.

The exertion and hyperventilation sometimes associated with the pulmonary function test can also produce a syncopal attack. Routine precautions are described in ARIC Manual 4. Procedures followed in the event of syncopal attack are described in this Manual, section 2.11.2.

The ARIC ultrasound exam involves no more ultrasound exposure than is usually the case when examining superficial arteries clinically. The output of the ultrasound instrument in each Field Center is measured periodically with a hydrophone probe to assure that the exposure does not increase unexpectedly. See ARIC Manual 6 for details.

The American Institute for Ultrasound in Medicine has issued the following statement concerning the safety of ultrasound.

> Safety Statement for Training and Research
>
> Diagnostic ultrasound has been in use for over 25 years. No confirmed adverse biological effects on patients resulting from this usage have ever been reported. Although no hazard has been identified that would preclude

> the prudent and conservative use of diagnostic ultrasound in education and research, experience from normal diagnostic practice may or may not be relevant to extended exposure times and altered exposure conditions. It is therefore considered appropriate to make the following recommendations:
>
> In those special situations in which examinations are to be carried out for purposes other than direct medical benefit to the individual being examined, the subject should be informed of the anticipated exposure conditions, and of how these compare with conditions for normal diagnostic practice.

Following the 45 minute ultrasound examination, the participant is asked to stand so that postural changes in blood pressure and pulse rate can be measured. These procedures are described in ARIC Manual 11. The precautions against adverse effects of orthostatism are summarized here.

Before beginning, the procedures for measuring postural changes are explained to the participant. The participant is asked whether or not he or she ever feels faint on standing. If the question is answered in the affirmative, permission to make the measurement (postural change) is still sought. Should the patient decline, the procedure is not performed. In the absence of a reason not to continue, however, the participant is asked if he or she is taking medications that produce postural effects. When the postural changes are measured, two clinic staff members are in attendance with one positioned closely behind the patient as a protective measure should he or she become faint. A sturdy chair is close at hand so that the participant may sit down promptly should s/he feel the need. Furthermore, examinees are advised to notify staff immediately if not feeling well and to ask for the chair. Clinic staff are instructed to watch the participant constantly for signs of distress. In the event that the participant faints, the procedures described in section 2.4.2 are followed.

2.11.2 Methods for Handling Emergencies

While all life threatening emergencies (eg. acute MI) require immediate evaluation of the participant at an acute care facility, some emergency measures may be required in the clinic before departure (eg. cardiac arrest). In addition, there are minor emergencies (hypotension, fainting, etc.) which may require treatment in the clinic only. Although most emergencies are of the less severe nature, ARIC Field Center clinics are prepared for both types.

2.11.2.1 Major Emergencies

In a serious event the primary concern of the clinic staff is to implement pre-established procedures to get the participant to the nearest medical facility. All ARIC clinics are located within a few city blocks of a large general acute-care hospital. At every clinic session a physician, physician assistant or registered nurse with certification in basic life support is on duty and physically present. Needed life support procedures are continued until emergency care arrives or the participant is transported to a hospital. Each ARIC clinic, depending on its location and staffing patterns, has specific emergency procedures, which define:

1. Who is in charge during the emergency.
2. Who is to administer treatments.
3. Who is to be notified.
4. What action clinic staff is to take.
5. Which reports are to be filed.

Each clinic has, in addition to trained personnel and emergency equipment, posted in a conspicuous place (eg. the reception area): **PHONE NUMBERS OF POLICE AND FIRE STATIONS; AMBULANCE SERVICES; AND SPECIFIC PHONE NUMBERS OR CODES TO ALERT MEDICAL TEAMS IF APPLICABLE.**

In each participant's folder, the name and phone number of his/her physician or usual source of health care is available on a standard ARIC form. The home and work telephone numbers of the next of kin are also listed. Each field center clinic is required to have on site at all times during which participants are interviewed and examined either a **PHYSICIAN** or a **PHYSICIAN ASSISTANT** or a **REGISTERED NURSE.**

All emergency situations are coordinated by a physician if present in the clinic. In the physical absence of the latter, this role are assumed by the charge nurse or senior physician assistant (to be designated by the clinic Principal Investigator). Each center has a designated physician on duty for each clinic session. If not physically present in clinic, he or she is within immediate reach by phone or paging system and within a short distance to the clinic. The physician duty roster is posted with the clinic secretaries and in the office of the head nurse and/or senior physician assistant so that the name of the responsible physician is readily accessible. However, in no case is emergency referral and/or care deferred while staff is attempting to locate a clinic doctor.

All personnel are trained to carry out their specific responsibility during an emergency. Retraining is conducted at least yearly.

All emergencies, whether serious or minor, are to be documented. This requires filling out a form identifying the type of emergency. This is done by the person in charge at the time, and all reports are co-signed by a clinic physician. These reports are filed at each clinic, and copies sent to the Coordinating Center.

2.11.2.2 Minor Emergencies

The most common minor emergency is simple syncope (fainting) and near syncope. These events may occur during the postural blood pressure measurements, venipuncture, or the pulmonary function test. Management of simple syncope or near syncope is the same whether associated with measuring postural blood pressure changes, drawing blood or performing the pulmonary function test.

Many syncopal episodes can be prevented if clinic staff are alert to early signs. In any situation in which syncope is likely, e.g. before the venipuncture, staff verify that the participant does not look or feel faint. If the participant looks faint or feels faint in the venipuncture area:

1. Have the person remain in the chair and sit with head between the knees.

2. Crush an ampule of smelling salts and wave it under the participant's nose for a few seconds;

3. Provide the participant with a basin and a towel if he/she feels nauseous;

4. Have the participant stay in the chair until he/she feels better and the color returns.

If the participant continues to feel sick, recline the chair, place a cold wet towel on the back of the person's neck, and notify the supervisor. If a participant faints, he/she is cautiously lowered to the supine position on the floor and one attendant immediately calls for an in-house physician assistant or nurse to assist the patient. The remaining attendant raises the patient's legs above the plane of the body to increase venous return. Prior to this, the staff member momentarily palpates for a carotid pulse and checks to be sure the subject is breathing. If life support measures are needed, the procedures outlined in section 2.11.2.1 are followed.

2.11.3 Emergency Equipment

A basic first aid kit is maintained at each Field Center. The kit contains a reference guide of its contents, and is checked every six months and immediately after each use. At each Field Center the Study Coordinator identifies a person responsible for this task.

2.11.4 Notification of Study Results

Before informed consent to be examined is obtained, the ARIC participant is told about each component of the examination. It is emphasized that the ARIC examination is not a substitute for clinical examination. The participant is told, however, that one of the benefits of participation is possible early detection of warning signs of certain diseases.

As described in section 2.10, the ARIC notification mechanism is designed to provide a clear statement to the participant to seek medical care, when confirmation or further investigation of study results indicates this course of action. An additional criterion built into the notification mechanism is to avoid anxiety in the study participants when presented with medical information, and any unnecessary consultation to practitioners.

All letters of notification conform to common procedures stipulated in the ARIC protocol. Appendix VIII of this Manual includes a schematic overview of the notification process, and prototype letters of notification. The wording of these letters can be modified by the principal investigators of the ARIC Field Centers, to conform to the referral practices of each ARIC study community. Only the Field Center director or an authorized ARIC field center physician sign the notification letters.

Section 2.10 of this Manual identifies the minimum set of significant findings and the alert values of laboratory results to be reported to participants and/or their physicians. It also specifies the schedule followed by the ARIC central agencies and field centers in notifying study participants, according to an expedited and a routine notification procedure. Described in section 2.8 in this Manual is the medical data review mechanism that generates a referral, and the report to the participant and his/her the physician.

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 IX). 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. A detailed

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 X.

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 IX) 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 IX. 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 X.

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) Autopsy Form (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 IX.

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 VII). 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 VII) is sent asking the informant to provide a telephone number on the enclosed, self-addressed stamped post card (Appendix VII). 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 VII) 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 VII. 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 6 and 7) for each of these physician contacts are provided in Appendix VII. 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 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.

Cohort ECGs are coded by abstractors and recorded on the HRA Form. ECGs are also 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 <u>from</u> another acute care hospital, or that the participant upon discharge was transferred directly <u>to</u> 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 Form 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 Form (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 Form (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.

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 are recorded and subject to data analysis, but 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 EV5)
      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:

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 19.

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 D1) because of the 1-2-4, regardless of whether or not the 1-2-4 change is Significant Increase.

Table 19. Summary of ARIC Cohort Diagnostic Criteria for Hospitalized MI

Cardiac Pain	ECG Findings	Enzymes	Diagnosis
Present	Evolving Diagnostic ECG Pattern	Abnormal	Definite MI
		Equivocal	Definite MI
		Incomplete	Definite MI
		Normal	Definite MI
	Diagnostic ECG Pattern	Abnormal	Definite MI
		Equivocal	Probable MI
		Incomplete	Suspect MI
		Normal	No MI
	Evolving ST-T Pattern	Abnormal	Definite MI
		Equivocal	Probable MI
		Incomplete	Suspect MI
		Normal	No MI
	Equivocal ECG Pattern	Abnormal	Definite MI
		Equivocal	Suspect MI
		Incomplete	No MI
		Normal	No MI
	Absent, Uncodable, or Other	Abnormal	Probable MI
		Equivocal	Suspect MI
		Incomplete	No MI
		Normal	No MI
Not Present	Evolving Diagnostic ECG Pattern	Abnormal	Definite MI
		Equivocal	Definite MI
		Incomplete	Definite MI
		Normal	Definite MI
	Diagnostic ECG Pattern	Abnormal	Definite MI
		Equivocal	Suspect MI
		Incomplete	No MI
		Normal	No MI
	Evolving ST-T Pattern	Abnormal	Probable MI
		Equivocal	Suspect MI
		Incomplete	No MI
		Normal	No MI
	Equivocal ECG Pattern	Abnormal	Suspect MI
		Equivocal	Suspect MI
		Incomplete	No MI
		Normal	No MI
	Absent, Uncodable, or other	Abnormal	Suspect MI
		Equivocal	No MI
		Incomplete	No MI
		Normal	No MI

3.3.1.9.1 Evolving Diagnostic ECG

ED1. No Q-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 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.

ED7. No Q-code and no 9-2 in reference ECG followed by a record with an Equivocal Q-code PLUS a 9-2.

3.3.1.9.2 Evolving ST-T Pattern

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 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 found.

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 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 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 found.

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.

3.3.1.9.4 Equivocal ECG

E1. An ECG record with an Equivocal Q-code (Minn. code 1-2-8 or any 1-3 code).
E2. An ECG record with ST-segment depression code 4-1-X or 4-2 or 4-3.
E3. An ECG record with T-wave inversion code 5-1 or 5-2 or 5-3.
E4. An ECG record with ST-segment elevation code 9-2.

3.3.1.9.5 Other ECG

01. Reference ECG coded 7-1-1, 7-2-1, or 7-4.
02. Any ECG coded 7-1-1, 7-2-1, or 7-4.
03. Normal ECG(s)
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 Cohort Hospital ECG Form (ECG) shown in Appendix P of Manual 5. ECGs are read three times, blinded; the final codes are adjudicated by a senior coder. Minnesota Code criteria are in Appendix E of Manual 5.

The data from the ECG form is entered and a determination is made at the Coordinating Center by computer algorithm as to whether or not the 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 sent to the ECG Coding Center. 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 three 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 added to the EKG Form. Serial Change criteria are in Appendix 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 noted on the Appendix O form. 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 X 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" without reporting a numeric value) or the CK-MB (heart fraction) is $\geq$ 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

2. a) The ratio LDH_1 : LDH_2 is $\geq$ 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.

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 = 5 - 9% of total CK or "is weakly present".

A summary of the enzyme diagnostic criteria, as related to total CK and LDH is given in the following algorithm (Figure 10).

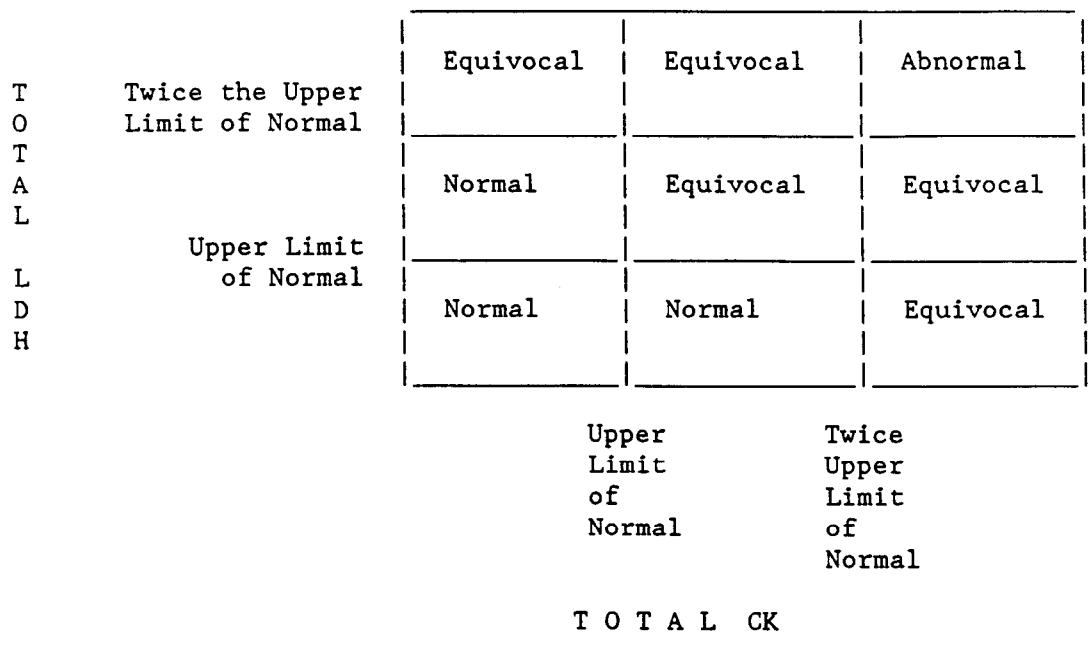

Figure 10. Algorithm for Total CK and LDH Enzyme Diagnostic Criteria

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 Dysarthia 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
      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 Dysarthia 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 Dysarthia 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
- 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 Dysarthia or dysphagia or dysphonia
- o Severe headache at onset, or severe headache when first conscious after hospital admission;
- o Depression of state of consciousness;
- o Evidence of meningeal irritation;
- o Retinal (subhyaloid) hemorrhages;
- o 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.

Table 3. Stroke Diagnosis Summary for ARIC Cohort Study[1]

Category		Specific Symptoms	Embolic Source	CT Scan	Angiogram	Lumbar Puncture	Pathology
Subarachnoid Hemorrhage							
Definite	a.		-	(H)	+	(+)	
	or b.		-	S			
	or c.		-				+
Probable		+	-			+	
Brain Hemorrhage							
Definite	a.		-	H			
	or b.		-				+
	or c.	+	-	O	+	+	
Probable		++	-	O		+	
Brain Infarction, Thrombotic							
Definite	a.		-				+
	or b.	+	-	I			
Probable		+	-	N		-	
Brain Infarction, Embolic							
Definite	a.		+				+
	or b.	+	+	I			+
Probable		+	+	N		-	
Stroke of Undetermined Type							
Possible		+	±				
Undocumented Fatal Stroke							
Unconfirmed out-of-hospital stroke death (ICD9 430-38)							

\+ = 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

[1]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 21.

Table 21. Differences between ARIC diagnoses and diagnoses from other sources, which require review by the Mortality and Morbidity Classification Committee (MMCC)

Diagnosis by ARIC Diagnostic Algorithm	ICD Codes Recorded as Final Diagnoses on the Death Certificate or Hospital Record
1. Definite MI	Codes other than 410-411
2. No MI	Codes 410 - 411
3. Definite Stroke	Codes other than 430-438
4. No Stroke	Codes 430 - 434

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 on the coding form shown 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 sent to the Coordinating Center for data entry and comparison 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, or any 4-2, 4-1-2, 4-1-1, 5-2, 5-1 or 9-2. The Coordinating Center determines the IDs that have any of these discrepancies and sends a report form to the 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 on the report form which is returned to the Coordinating Center.

3.5.1.3 Serial ECG Coding

The Coordinating Center adds the adjudicated codes to the database as the definitive Minnesota Codes for the ID involved.

When two ECGs from different Field Center visits are available, a determination is made at the Coordinating 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 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 three times; the final categories are adjudicated by a senior coder and added to the Appendix O form, Manual 5. 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.

4. ARIC Clinic Visit Data Management

4.1. Overview

The data management tasks for the ARIC cohort baseline visit are designed to ensure the accuracy of the study data and to facilitate the smooth execution of the visit. These activities can be conveniently grouped into three categories: (1) those tasks which are performed before the visit, (2) those performed during the visit, and (3) those performed after the visit.

This section is organized according to these categories. Section 4.2 deals with activities which take place prior to the visit, including those involving the Recruitment Management System, preparation of the participant's folder and diskette, and periodic "special" preparations for the visit. Section 4.3 describes certain data management activities which must be handled during the visit. These largely involve the use of the Participant Itinerary Form and the Inventory Review process; the latter is intended to check that the data is complete and to prepare it for the Medical Data Review. Section 4.4 details tasks which follow the conclusion of the visit, which include the continued management of inventory information, as well as the uploading of data to the local data base and its subsequent transfer to the Coordinating Center.

Data coordinators either perform, or oversee the performance of these activities. Any questions on their part should be referred to the clinic monitors at the Coordinating Center.

4.2 Pre-Visit Activities

Pre-visit data management tasks begin with entering sampling and recruitment data into the Recruitment Management System (RMS) and continue with those activities necessary to prepare for the participant's visit. Both of these tasks involve using the RMS and Data Entry System (DES) software. This protocol describes the RMS and DES functions to be performed, but does not give full operational details. Complete documentation for the required functions can be found in the RMS, DES, or Data Coordinator manuals.

4.2.1 Entering Enumeration Information

Sampling, recruitment, and enumeration data are keyed into the RMS in stages. First the sample information is either keyed or read from the sample selection file. Enumerator ID and date assigned are entered when a sample is assigned. After the completed Enumeration Form is returned, the data for all enumerated persons are recorded in the RMS. The remainder of tasks in Section 4.2 pertains to those eligible for whom a Home Interview form was initiated.

4.2.2 ID Assignment / Folder Creation

When a Home Interview (HOM) form is received for a participant, the following tasks are performed.

4.2.2.1 Assign the ARIC participant ID

Check the HOM form Final Result code. If the respondent refused to participate (Final Result code 04), go to section 4.2.3, enter the Interview Status and Date Changed and stop.

If the respondent agreed to participate (Final Result code 01), take the next set of ID labels and place one of the large labels in the upper left hand corner of the HOM form in the area marked "Coordinating Center Participant ID LABEL".

4.2.2.2 Create Participant Folder

Place one of the large ID labels on the participant folder and put the remaining labels and the HOM form inside the folder. The folders can be accumulated at this point for batch processing of the remaining tasks.

4.2.3 Enter Recruitment Management System Portion of Home Interview Information

From the RMS Main Menu, select 5, the "Change Participant Record" task, and enter the Household ID and Participant ID from the Assignment Information label on the HOM form. Confirm that the name on the HOM form and the name displayed on the screen match and then enter the following variables from the HOM form:

1. ARIC Participant ID - from the label in the top left hand corner of page 1.

2. Home Interviewer ID - Question 3, Page 1.

3. Interview Status - from the Final Result Code circled on page 1. If interview was completed (Code 01), continue entering the rest of the data. If respondent refused (Code 04), enter the Final Result code and Date Status Changed, then stop.

4. Date Status Changed - For Result Code 01, enter Question 1 and continue. For Result Code 04, enter the date of the Final Result Code and stop.

5. Time Interview Began - Question 2, Page 1.

6. Name - Question 66, Parts a, b, c, d, Page 12

7. Telephone Information - Questions 68-71, Page 13.

8. Clinic Visit Information - Questions 72-81, Pages 13-15.

9. Interview Remarks - Questions 82-84, Page 17.

4.2.4 Diskette Initialization

Before a diskette can be used as a work disk for the ARIC Data Entry System it must first be initialized. The DES Initialize task creates the Cohort Examination Inventory (CXI) form, work data base, and parameter files needed to Log on and Log off a participant at a DES work station. Either a blank, DOS formatted diskette, or a participant work disk that has been uploaded to the local data base and cleared for reuse is suitable for initialization. See Section 4.4.5 for criteria on when to reuse diskettes.

1. Carefully remove any existing label from the diskette and add a label containing the ARIC participant ID. Do not use sharp metal objects to remove label.

2. Initialize the diskette using the Initialize task on the DES data coordinator mode task menu. See Data Coordinator Manual for details.

3. Place the initialized diskette and jacket in the pocket of the participant folder.

4.2.5 Entering of Home Interview Information

Information from the paper version of the Home Interview Form is keyed in three different places: the Recruitment Management System, the Identification Form, and the Home Interview Form. Keying instructions are provided in the right margin on the form. The RMS portion was described in Section 4.2.3. Prior to the visit, the remainder of this form must be entered on the participant diskette at a DES workstation as described below.

4.2.5.1 Identification Form

Home Interview items 4, 66, 67, 68, and 70 are keyed into the Identification Form on the DES. The "IDN" form code is provided in the margin of the Home Interview next to these items. Specific instructions are provided in the Q by Q instructions for the Identification Form.

4.2.5.2 Home Interview Screens

The following data from the HOM form are keyed into the Home Interview screens: Household ID, Participant ID, and responses to questions (data fields) 1, 3, 5, 6, 9-60, 62-65. For questions 1 and 3, the "HOM" form code is provided in the margin as a keying instruction. The remaining data fields do not have this type of instruction, but the rule is as follows: Any question which is either in "multiple choice" or "fill-in-the-boxes" format, and which is not keyed into either the RMS or IDN form, is to be keyed into the Home Interview screens. Note that questions 7, 8, and 61 are not in either format, and thus are not keyed. The pertinent question numbers are given on the DES screens as an additional aid.

4.2.6 Itinerary Form Preparation

The Participant Itinerary Form is found in Appendix IX. The following portions of the form should be completed prior to the visit and the form should be attached to the outside of the participant folder.

4.2.6.1 Identifying Information

Using the completed Home Interview and Household Enumeration Forms, fill in the participant's ID, name, sex, race, date of birth, and age at the top of the Itinerary Form. This will avoid the awkward situation of having to ask these same questions again. The information will be needed at certain stations (e.g., Pulmonary Function, ECG). Again, the purpose of recording it here is to avoid asking the questions repeatedly at these times.

4.2.6.2 Sequence of Visit

The sequence in which the participant is to visit each station should be entered on the form prior to the visit. Part of that sequence is fixed and is indicated by preceding those sequence numbers on the Itinerary Form. The block at the beginning of the visit includes Reception, Sitting Blood Pressure, Anthropometry, Venipuncture, and Snack. The ending block includes Inventory Review, Medical Data Review, and Exit Interview. The remaining stations (Physical Exam, Pulmonary Function, Ultrasound, ECG, and the various interviews) may be ordered in any way, as long as they remain between the Snack and the Inventory Review. This order is recorded in the blanks provided on the form.

This portion of the form is also somewhat flexible in that none of the sequence information is actually kept as data once the visit is over. Thus, one may denote flow sequences in slightly different ways if it is convenient to do so. For example, if the interview is always done entirely at one time, a single entry could denote this (rather than assigning a number to each interview segment).

4.2.7 Periodic Tasks

This section describes several tasks that must be performed on a routine schedule. Although the exact frequency is determined by the participant load and other factors, a weekly schedule is assumed.

4.2.7.1 Schedule for Clinic Visits

A list of all participants scheduled for clinic visits in the next week must be prepared. This list will be used to prepare for the visit as described in the next two sections.

4.2.7.2 Label Preparation (Venipuncture Station)

The labels required for the blood collection and processing tubes must be sent to the lab in time for the labels to be attached before the participant visit.

Remove the labels required for the specimen tubes from the participant folders and send them to the blood processing lab along with a copy of the clinic visit schedule.

4.2.7.3 Special Handling Items

In order to be prepared for any special needs or arrangements required, the responses to Questions 72-79 of the HOM form must be reviewed for each participant and appropriate action taken. The RMS participant record contains the "YES/NO" responses to these questions and may be used to screen the participants. The details of any Yes responses should be examined in the HOM form itself.

4.3 Visit Flow and Information Inventory

Certain data management procedures are necessary during the visit itself. These tasks center around the Itinerary Form and the Inventory Review.

4.3.1 Use of Itinerary Form

Part of the Participant Itinerary Form is completed before the visit (see Pre-Visit Activities). The form is then attached to the front of the participant's folder for use during the visit. Additional information is recorded on it as the participant proceeds through the stations as described below.

4.3.1.1 Completion of Times and Code Numbers

The three right-hand columns of the Itinerary Form must be completed at each station. These are start and stop times and code numbers. The times should reflect the actual time spent on a procedure. Thus, any "waiting" time should not be included. The "Observer Code Number" is the three-digit code number of the staff member in charge of each station. This will usually (but not always) be the same individual who records his/her code number on the form(s) completed at the given station.

4.3.1.2 Additional Notations

There is additional information which should be recorded on the Itinerary Form at various times. At Reception, the date and time of visit are recorded, as well as an indication that the Informed Consent, Identification, and Fasting/Tracking Forms have been completed. Also, check the appropriate box indicating whether the participant brought his/her medications.

Some information is collected at the beginning of the visit, and becomes useful again later in the visit. For example, the arm circumference is determined in the Sitting Blood Pressure station, and is also needed when the Postural Changes procedure is done in the Ultrasound station. Similarly, the height is measured in Anthropometry, and is required again for Pulmonary Function. In these cases, a space is provided on the Itinerary Form to record the information so that it will be easily available later in the visit.

At times it may not be possible to perform certain procedures during the visit. For example, the participant may refuse to take a pulmonary function test, or the ECG machine may be malfunctioning. In these cases, it is very important that this information be recorded on the Itinerary Form. This can be done by writing "REFUSED" or "RESCHEDULE" where the times are usually recorded on the form. This information will be needed at the Inventory Review, so it must be clear whether or not the procedure will be rescheduled.

4.3.2 Inventory Review Procedures

The Inventory Review takes place near the end of the visit, after all of the "data-gathering" procedures but before the Medical Data Review. It may be convenient to allow the participant to change clothes during this time, since a waiting period will generally be involved. The Inventory Review is performed by the data coordinator or an appropriate designate. However, it must be performed on a workstation PC-XT, not the database PC-AT. The tasks involved are described below.

4.3.2.1 Keying of Paper Forms

Any forms collected on paper during the visit should be keyed on a workstation PC-XT at the beginning of Inventory Review. The highest priority is to key those forms used to generate the Medical Data Report:

Sitting Blood Pressure (SBP)
Anthropometry (ANT)
Respiratory Symptoms / Physical Activity (RPA)
Medical History (MHX)
Physical Exam (PHE)
Stroke / TIA (TIA)
Medication Survey (MSR)

Identification (IDN)
Home Interview (HOM) } keyed before visit

If time permits, any other forms which were collected on paper should also be keyed at the Inventory Review. Note that the Medication Survey Form is keyed even if the medication names have not yet been assigned a code, as this can be done later in batch mode.

4.3.2.2 Printing the Cohort Examination Inventory (CXI) Form

Print the CXI form by choosing the "PRINT" option in the task menu, and entering "CXI" on the ID screen. Once in the form, enter Esc-6. A prompt appears asking whether you wish to print the whole form. Answer by entering "Y".

4.3.2.3 Completeness Check of DES Data

Check that those forms which were collected on the Data Entry System (or keyed as above) are present by reviewing the Cohort Examination Inventory Form

(CXI). Each form that was scheduled for completion should now show a "C" status in the CXI. If any forms do not have this status, investigate further by attempting to browse the form and/or review the participant transaction file. Also, look for the procedure on the Itinerary Form.

4.3.2.4 Completeness Check of Data Not Collected on DES

Any data not collected on the DES is also reviewed for completeness at the Inventory Review. This consists of paper forms which are not yet keyed and data which are sent to some central labs and reading centers.

4.3.2.4.1 Paper Forms

All paper forms require quality control to ensure that they are complete and consistent. The following items should be checked by the supervisor on all forms:

1. Legibility.

2. Presence of interviewer ID and participant ID on all forms.

3. Form completeness: all necessary questions answered and skip rules followed correctly.

Do not alter the status of these paper forms in the CXI form. This is done automatically when the form is keyed. An example is the Medication Survey Form (MSR), which is collected on paper and keyed after the visit. Make sure that the MSR form has been completed and is in the folder. The Itinerary Form should be helpful as a reference.

On some forms, there are specific items that must be verified. These forms include Home Enumeration and Home Interview. The checklists for each form follow.

<u>HOUSEHOLD ENUMERATION FORM</u>

Section B

1. If the Sample Person is no longer living there, Code 12 must be entered in Section D.

Section D

1. Check to ensure that this section is complete.

2. Each contact must have a Code and Field Interviewer ID.

3. Check codes for correctness.

Section F

1. Check to ensure that the number in question 2 is smaller than the response to question 1.

2. Check to be sure that only one Enumeration Respondent (ER) is checked (Question 4).

3. Double check eligibility of all persons based on birth (Question 5).

4. Double check that spouse pairs are recorded correctly in column 7.

5. Ensure that the Participant ID numbers of all eligible respondents have been circled and that the number of circled respondents is the same as the number noted in question 8.

6. Ensure that the form has been keyed as a Household Record into the RMS system.

7. Ensure that all circled Participant ID numbers have a record created in the Person Control File in the RMS.

HOME INTERVIEW

1. Coordinating Center Participant ID label must be placed in the upper left corner of the first page of the form.

2. A label for the index person in the household with the subject's name written in (if it is not the same) and ID (both original and Participant ID) must be immediately below the Coordinating Center label.

3. Check to ensure that the Record of Calls section is complete.

4. Each contact must have a code and ID.

5. Check all result codes for correctness:

   IF Code 01 (Interview Complete), ensure that the entire form is completed.

   IF Code 04 (Refusal) this is a final code and no more information is required.

   IF Code 11, ensure that a Home Interview time was set.

6. Question 1: double check that the year was entered correctly.

7. Question 3: Interviewer ID MUST be entered.

8. Question 5: If subject responds yes, double check answer in question 6 to be sure move is in next 3 months, otherwise subject is eligible and form should be completed.

9. Question 14: If stroke, heart attack, or cancer is written in the line for response d (Other), double check with interviewer.

10. Question 52: May be blank if subject is a smoker.

11. Question 54: There should be only one answer for this question, either a number for grades 1 - 12, or a circled number for GED, Vocational, or College. If both, check with the interviewer.

12. Question 56: This question must be answered if the response to Question 55 was F or G - the subject is retired.

13. Question 63: Must be answered if from Maryland or Mississippi, otherwise blank.

14. Question 64 & 65: Must be answered if from Minnesota, otherwise blank.

15. Questions 72 - 79: Must be reviewed prior to clinic visit to ensure any special needs of the subject are met.

16. Double check that interviewer has given the subject everything required (i.e. Medication Bag, Brochure, etc.). Note the checklist on page 16.

17. Double check that all skip rules have been followed correctly, and all questions have been answered.

Checks for forms currently not available on the DES are shown in Appendix X.

4.3.2.5. Reading Center Data

The Cohort Examination Inventory (CXI) Form must be updated to reflect the status of those procedures which do not involve the DES. To do this, write the appropriate status on the paper copy of the CXI form which was printed in step 2 above. (This information will be entered into the DES after uploading; do not attempt to enter it now.) The second screen of the CXI form contains the following list:

SAMPLE NAME	CODE	NEEDED	STATUS
CLINICAL CHEM	CCS	S	
ECG	ECS	S	
HEMATOLOGY	HYS	S	
HEMOSTASIS	HSS	S	
LIPIDS	LIS	S	
PULMONARY	PLS	S	
ULTRASOUND	ULS	S	

Update the status column by writing in a "C" if the given procedure was completed.

If the procedure was not completed and will not be rescheduled, write a "P" for "Permanently Missing". If the procedure was not completed but will be rescheduled, write a "T" for "Temporarily Missing".

To determine which code to use, review the participant's folder for each procedure. Use the Itinerary Form as a guide. If a procedure was not completed, the Itinerary Form should state this. For example, if "REFUSED" has been written on the form next to Pulmonary Function, write a "P" on the CXI form. If "RESCHEDULE" has been written next to ECG, leave that status blank and reschedule the procedure at the Exit Interview. If a procedure has been completed according to the Itinerary Form, check that any relevant documents are in the folder (e.g., Pulmonary Function output), and write a "C" on the CXI form.

4.3.2.6 Medical Data Review (MDR) Preparation

The Medical Data Review requires that information from various sources be compiled and organized in the participant's folder before the MDR can take place. The MDR report can be generated by running the MEDREVU program or by transcribing the necessary data from the DES records or paper forms.

4.3.2.6.1 Transcribing MDR Report Data

A blank MDR form (see Appendix IX) can be used for transcription of the MDR data from the necessary data records or forms. Each item on the MDR is followed by the form and question number containing the data value. The data values can be transcribed from the paper forms or by using the BROWSE function of the DES.

4.3.2.6.2 Generating the MDR with the MEDREVU program.

The MEDREVU program can be used to extract the data values from the participant diskette. Any data values from records not on the diskette are displayed as "_" and the values must be transcribed from the paper forms.

4.3.2.6.2.1 From the C:> prompt, key MEDREVU and strike Enter
The Medical Data Review Screen will be displayed; insert the participant diskette in Drive A and strike Enter. The MDR program will run and then start DW3; strike enter twice and the DW3 main menu will be displayed.

From the DW3 main menu, depress ALT-F9 to generate the report. After the report has printed, strike Enter to exit DW3 and return to the C:> prompt.

4.4. Post-Visit Tasks

Those data management tasks which are completed following the participant's visit are described in this section. They focus on completing and uploading the data, and sending it to the Coordinating Center.

4.4.1 Keying of Remaining Paper Forms

Any forms which were completed on paper, but were not keyed into the Data Entry System at the Inventory Review, must be keyed as soon as possible after the visit. This is done using the work diskette on a workstation PC, not the data base machine.

4.4.2 Uploading Data

The forms collected on the participant's work diskette are not part of the local data base until the information has been added to it via the "DBUPDATE" procedure. It is vital that each participant's disk update the local data base as soon as all remaining paper forms have been keyed to the work diskette. Prompt updates ensure that all information collected on a participant are secure and available for other data management programs to use.

4.4.3 Further Inventory Tasks

Four additional tasks are related to modifying the inventory form (CXI) and generating sample inventory information for the Reading Centers. These tasks must be done with the participant's CXI form after the work diskette has updated the local data base.

1. Using the CHANGE task on the local data base machine, update the status column on the second screen of the CXI form to indicate which procedures were completed, or will never be rescheduled. Use the paper copy of the CXI screen produced earlier during the completeness check to key the appropriate codes (e.g. "P" for permanently missing and "C" for completed). See the example below.

SAMPLE NAME	CODE	NEEDED	STATUS *
CLINICAL CHEM	CCS	S	C
ECG	ECS	S	
HEMATOLOGY	HYS	S	C
HEMOSTASIS	HSS	S	C
LIPIDS	LIS	S	C
PULMONARY	PLS	S	P
ULTRASOUND	ULS	S	C

* (Note: When the ECG procedure is completed in the future, the CXI form on the local database should be updated to reflect that fact. If it becomes apparent that it will not be completed, the status should be changed to "P".)

It is very important that this information be accurate, because it is the only way the Coordinating Center can know whether to expect certain data on a participant. Discrepancies are resolved periodically between the appropriate centers.

The next three tasks related to producing inventory lists for Reading Centers can be performed as needed (such as preparing a batch of samples for shipment).

2. The SHIPLIST utility program (see Data Coordinators' manual) should be run whenever a current list of samples collected, but not yet shipped to a Reading Center, is needed. The SHIPLIST report produces a specific listing for each procedure completed on all participants. For instance, if a batch of ultrasound tapes is being prepared for shipment, SHIPLIST can generate a report of ultrasound tapes collected and needing shipment to a Reading Center. Use the SHIPLIST report to facilitate packing samples for shipment. Mark in the space provided on the SHIPLIST report whether a sample was "PACKED" or "NOT PACKED". This information is needed for sample inventory control and is discussed in the next task.

3. The SHIPPING task of the DES (see Data Coordinators' manual) is used to update each participant's inventory form (CXI) to indicate which samples are being shipped to a Reading Center. This task only allows changes to the CXI form. Key a "S" in the status column for each procedure to indicate that the collected sample is now being shipped to a Reading Center. In the example below, the hematology and lipids samples have been changed from the sample CXI completed on the previous page.

SAMPLE NAME	CODE	NEEDED	STATUS*
CLINICAL CHEM	CCS	S	C
ECG	ECS	S	
HEMATOLOGY	HYS	S	S
HEMOSTASIS	HSS	S	C
LIPIDS	LIS	S	S
PULMONARY	PLS	S	P
ULTRASOUND	ULS	S	C

* (Note: When the ECG procedure is completed in the future, the CXI form on the local database should be updated to reflect that fact. If it becomes apparent that it will not be completed, the status should be changed to "P".)

4. The PRNTLIST utility (see Data Coordinators' Manual) produces a printed listing of the batch of inventory records being sent to a Reading Center, and copies the corresponding inventory file to diskette. This provides each Reading Center with inventory information that can be used manually or automated. Use PRNTLIST only after all samples for a batch have had their status changed to "S" with the SHIPPING task (see part 3 above). The utility can be run once for each batch of samples being mailed.

4.4.4 Sending Data to Coordinating Center

The SENDDATA utility is used to send the current reporting period's collection of participant data to the Coordinating Center. The procedure makes backups of journal and data transfer files, starts PRINTCOM so that a listing of the data records is printed, and copies the data transfer file to diskette. A series of 5 data transfer diskettes are used in rotation to send data to the Coordinating Center. SENDDATA prompts the user for a specific diskette in the series. Once the procedure has ended, pack the data transfer diskette into a mailer and send it to the Coordinating Center. Keep the PRINTCOM listing of records sent filed at the Field Center for future reference to this batch of data.

4.4.5 Maintenance of Work Diskette Until Notification to Reuse

All participant work diskettes should be kept on file while the data transfer disk for their batch is in shipment to the Coordinating Center. The Field Center should save the work diskettes and not reuse them until authorized by the Coordinating Center. The Coordinating Center returns to the Field Center the data transfer diskettes.

4.4.6 Update Clinic Visit Status on RMS Participant Record

Once the participant visit is complete, the Clinic Visit Status and Date Status Changed fields of the RMS participant record can be updated using the Change Participant record task in the RMS Main Menu. This is normally the last entry made for a participant in the RMS system.

4.4.7 Send RMS Data to the Coordinating Center

The RMS data for each reporting period is sent to the Coordinating Center on a formatted diskette. This can be done on the same schedule as the DES data transmittal and the diskettes can be mailed in the same package. To generate the RMS transfer data file, select Task 12, Utility Task Menu, from the RMS Main Menu screen. Insert the data transfer diskette and select sub-task 2 to generate the data file.

5. MEDICAL CARE ASSESSMENT

Several medical care variables are assessed for cohort members. Information is collected through clinic interviews, annual follow-up interviews, hospital chart abstraction and investigations into the cause of death. Detailed data collection procedures are not available for distribution at this time. Requests for an updated version of this section of Manual 2 should be addressed to the ARIC Coordinating Center.