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>
<thead>
<tr>
<th>Procedure/Workstation</th>
<th>Description</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed Consent</td>
<td>Obtain informed consent.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Reception</td>
<td>Greet the participant; determine fasting status; verify identifying information; obtain tracing data; collect medications.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Sitting Blood Pressure</td>
<td>Obtain sitting blood pressure before the participant has blood drawn.</td>
<td>Manual 11</td>
</tr>
<tr>
<td>Anthropometry</td>
<td>Measure weight, height, frame size, skin folds.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Venipuncture</td>
<td>Obtain blood samples for all laboratory tests.</td>
<td>Manual 7</td>
</tr>
<tr>
<td>Snack</td>
<td>Provide snack which contains no caffeine or stimulants.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>ECG</td>
<td>Obtain a 12 lead ECG and two minute rhythm strip.</td>
<td>Manual 5</td>
</tr>
<tr>
<td>Interview</td>
<td>Collect sociodemographic, food frequency and selected medical and personal history data.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Physical Exam</td>
<td>Obtain a brief systems review on each participant including neck, neurological, chest and lungs, breast (optional), heart, and extremities.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Pulmonary Function</td>
<td>Obtain spirometric measurements of timed pulmonary function (FVC, FEV1).</td>
<td>Manual 4</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>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.</td>
<td>Manual 6, Manual 11</td>
</tr>
<tr>
<td>Medical Data Review</td>
<td>Ascertaining 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.</td>
<td>Manual 2</td>
</tr>
<tr>
<td>Exit Interview</td>
<td>Return medication; thank participant.</td>
<td>Manual 2</td>
</tr>
</tbody>
</table>

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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.

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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 interviewer 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 feedback 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, triglycerides, 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


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 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

<table>
<thead>
<tr>
<th>Number of Times Eaten Per Week in Season</th>
</tr>
</thead>
<tbody>
<tr>
<td>Season Length</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>2 months</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>3 months</td>
</tr>
<tr>
<td>4 months</td>
</tr>
</tbody>
</table>

* 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.

ARIC PROTOCOL 2. Cohort Component Procedures Version 2.0 1/88
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 affect 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, Hartman 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

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<thead>
<tr>
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<th>Inches</th>
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<tr>
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<td>.81</td>
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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
graped. 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

Triceps:
A vertical fold on the posterior midline of the upper arm (over triceps muscle), halfway between the acromion and olecranon processes; the elbow should be extended and relaxed.
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.
Subscapular:
a fold taken on a diagonal line coming from the vertical border to 1 to 2 cm from the inferior angle of the scapula.

Figure 5. Location of Skinfold Measurements: Subscapula
Waist Girth at level of umbilicus

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 immovable 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
NOTE: Palm up and wrist straight

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 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 Tibia1 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

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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

<table>
<thead>
<tr>
<th>Referral Classification</th>
<th>Statement to Examination</th>
<th>Explanation to Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergency Referral</strong></td>
<td>See M.D.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immediately</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*SBP ≥ 260 mm Hg</td>
<td>BP very high</td>
</tr>
<tr>
<td></td>
<td>*DBP ≥ 130 mm Hg</td>
<td>BP very high</td>
</tr>
<tr>
<td><strong>Immediate Referral</strong></td>
<td>See M.D.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Today</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*SBP 240-259 mm Hg</td>
<td>BP very high</td>
</tr>
<tr>
<td></td>
<td>*DBP 115-129 mm Hg</td>
<td>BP very high</td>
</tr>
<tr>
<td></td>
<td>*Unstable angina</td>
<td>Your chest pains may be important</td>
</tr>
<tr>
<td></td>
<td>*Neurologic symptoms in past week</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td></td>
<td>*Other severe symptoms or findings</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td><strong>Urgent Referral</strong></td>
<td>See M.D. within a week</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>*SBP 200-239 mm Hg</td>
<td>BP high</td>
</tr>
<tr>
<td></td>
<td>*DBP 105-114 mm Hg</td>
<td>BP high</td>
</tr>
<tr>
<td></td>
<td>*Angina, stable but untreated/not being followed</td>
<td>Your chest pains may be important</td>
</tr>
<tr>
<td></td>
<td>*Neurologic symptoms, untreated, one week to six months ago</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td></td>
<td>*Acute congestive heart failure</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td></td>
<td>PFTs: FEV1 &lt; 65% or FVC &lt; 65% or FEV1/FVC &lt; 60% plus symptoms</td>
<td>Your lung function is diminished to % of predicted and warrants attention; M.D. will get a copy</td>
</tr>
<tr>
<td></td>
<td>*Other acute, but less severe symptoms</td>
<td>Your symptoms may be important</td>
</tr>
</tbody>
</table>
## Table 16 Referral Guidelines at Medical Data Review, continued

<table>
<thead>
<tr>
<th>Referral Classification</th>
<th>Statement to Participant</th>
<th>Examination Findings</th>
<th>Explanation to Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine Referral</td>
<td>See M.D. within month or at first convenient appointment</td>
<td>SBP 140-199 mm Hg</td>
<td>BP elevated into borderline range</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBP 90-104 mm Hg</td>
<td>BP elevated into borderline range</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Old MI (Rose Questionnaire), previously unrecognized</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your chest pain may be important</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Neurologic problem (stroke, TIA exam findings) &gt;6 months ago, unrecognized</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Claudication, previously unrecognized</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your leg pain may be important</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PFTs: FEV₁ &lt; 65% or FVC &lt; 65% or FEV₁/FVC &lt; 60% and not aware</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your lung function is diminished to ___% of predicted and warrants attention; M.D. will get a copy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Other symptoms or findings needing evaluation/not being followed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>No Referral</td>
<td>SBP &lt; 140</td>
<td>Normal BP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DBP &lt; 90 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PFTs: FEV₁ 65-79% or FVC 65-79% and FEV₁/FVC &gt; 60%</td>
<td>Your lung function is diminished to ___% of predicted. This does not warrant referral, but M.D. will get a copy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PFTs</td>
<td>Normal, M.D. will get a copy.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FEV₁ ≥ 80% and FVC ≥ 80% and FEV₁/FVC ≥ 60% of predicted.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 16 Referral Guidelines at Medical Data Review, continued

<table>
<thead>
<tr>
<th>Referral Classification</th>
<th>Statement to Participant</th>
<th>Examination Findings</th>
<th>Explanation to Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>*Angina, stable on treatment/being followed.</td>
<td>Confirm only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*MI, previously documented</td>
<td>Confirm only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Height, weight</td>
<td>Report only</td>
</tr>
</tbody>
</table>

**ECG**

<table>
<thead>
<tr>
<th>ECG Findings Requiring Review by M.D. Before Participant leaves the Field Center</th>
<th>Would like to review with M.D.</th>
<th><em>Acute pattern abnormalities (MI, ischemia...)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Rhythm disturbances</em> 2nd or 3rd degree block, ventricular tachycardia, any type of ectopic beat &gt; 6/minute, couplets bigeminy, R on T, multifocal premature ventricular contractions, atrial fibr/flutter with ventricular rate &lt; 60 or &gt; 110, sinus bradycardia &lt; 50, sinus tachycardia &gt; 110, PR interval ≥ 0.26 sec.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Any other ECG finding, alone or in conjunction with symptoms, causing concern.</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other ECG Findings or Normal ECG</th>
<th>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.</th>
</tr>
</thead>
</table>

* 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 feedback 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 feedback 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.

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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 database 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

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

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Type of Results</th>
<th>Type of Cover Letter</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D.</td>
<td>Normal results</td>
<td>M.D. Letter 1</td>
</tr>
<tr>
<td></td>
<td>Abnormal results, no earlier referral made</td>
<td>M.D. Letter 2a</td>
</tr>
<tr>
<td></td>
<td>Abnormal results, previous referral made</td>
<td>M.D. Letter 2b</td>
</tr>
<tr>
<td>Participant</td>
<td>Normal results</td>
<td>Participant Letter 1</td>
</tr>
<tr>
<td></td>
<td>Abnormal results, no earlier referral made</td>
<td>Participant Letter 2a</td>
</tr>
<tr>
<td></td>
<td>Abnormal results, previous referral made</td>
<td>Participant Letter 2b</td>
</tr>
<tr>
<td></td>
<td>Normal results, no M.D. designated</td>
<td>Participant Letter 3a</td>
</tr>
<tr>
<td></td>
<td>Abnormal results, no M.D. designated</td>
<td>Participant Letter 3b</td>
</tr>
</tbody>
</table>

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 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 \( \leq 2 \text{mm} \) 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: HDL₂, HDL₃, 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

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

\(^1\) 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

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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 (e.g. acute MI) require immediate evaluation of the participant at an acute care facility, some emergency measures may be required in the clinic before departure (e.g. 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 (e.g., 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.