Manual 45
Field Center Procedures (Visit 1)

Last updated: February 14, 2024

Visit 1 Examination
Field Center Procedures
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1 OVERVIEW

This manual of operations on ARIC Gen2 Field Center Procedures is one of two manuals of operations specific to the ARIC Gen2 cohort baseline examination. ARIC Gen2 is funded by an NIH grant from the NHLBI, R01 HL158022 (Co-PIs: Elizabeth Selvin and Lin Yee Chen). The overarching goal of the grant is to evaluate the link between glucose patterns (hypo- and hyper-glycemia) with cardiac arrhythmias in adults with type 2 diabetes.

To accomplish this goal, we will use simultaneous 2-week continuous monitoring of heart rhythm (iRhythm Technologies*, ZioPatch*) and continuous glucose monitoring (Abbott, CGM) in adults with type 2 diabetes. As detailed within the ARIC Gen2 Screening and Recruitment Manual, older adults (aged 80 or older) will be recruited from within the ARIC Study, starting at Visit 10. ARIC does not currently include any participants younger than 80 years of age. Thus, ARIC Gen2 will involve additional recruitment of new participants with type 2 diabetes who are aged 50 to 80 years. Each of the four field centers will target to recruit at least 100 ARIC Gen2 participants (minimum N=400). The ARIC Gen2 study will be nested within the existing ARIC study and clinic visits for ARIC Gen2 participants will occur in parallel with ARIC participants. Highly trained staff at the four established ARIC field centers will be responsible for the ARIC Gen2 study as well.

To the extent possible, this first ARIC Gen2 visit is intended to mirror as many procedures as the ARIC Visit 10 exam with a few key differences in the study population (all ARIC Gen2 participants are newly recruited and are aged 50-80 years and have type 2 diabetes) and the visit procedures (e.g., no home visit offered for Gen2 participants). There are three ARIC Gen2 interviews (DEM, MHX, RHX) plus cognitive testing (ESU, WRAT, NCS, MME, CDPG, Trails A & B) that are not part of the ARIC Visit 10 field center procedures. In ARIC Gen2, audiometry, imaging, and accelerometry data collection will **not** occur. The ARIC Gen2 study is nested within the ARIC single Institutional Review Board (sIRB) protocols and is subject to ARIC sIRB requirements, as well as any local requirements.

This Manual details the interviews and clinical measurements conducted as part of the ARIC Gen2 visit field center examinations, cross-referencing the procedures set out in other ARIC manuals and the ARIC Gen2 Screening and Recruitment Manual. The procedures and interviews are presented below approximately in the order in which they occur, and in alphabetical order within blocks of interviews.

Similar to the ARIC cohort Visit 10, the ARIC Gen2 baseline visit will be conducted following strictly standardized protocols of the interviews and examination procedures across all field sites and throughout the duration of the study, to optimize data quality. Accordingly, all ARIC field center personnel must be fully familiar with this manual of procedures, be trained and certified in the procedures as described in this manual, and remain standardized throughout the data collection phase. With the exceptions noted earlier, most procedures in this ARIC Gen2 examination are the same as ARIC Visit 10. Procedures related to certification tracking and persons responsible for reporting certifications to the CC are described in Manual 2 visit 10. Mastery of the procedures described in this manual is required so that patterns in the ARIC Gen2 data can reflect differences between study participants and their characteristics as opposed to differences between study technicians or study center.

*GEN2 transitioned from the Abbott FreeStyle Libre Pro CGM to the Abbott FreeStyle Libre 3 CGM, and from the BioTel's ePatch heart sensor to the Zio XT Monitor ("ZioPatch") by iRhythm Technologies in January of 2024.

To the degree that this is applicable, the description of each interview/exam component in this manual includes a brief rationale for its use, operational procedures, a reference to training requirements and certification criteria, and mention of the quality assurance measures.

2 LIST OF ABBREVIATIONS

AFU	Annual follow-up
ARIC	Atherosclerosis Risk in Communities Study
BP	Blood pressure
CC	Coordinating Center
CDART	Carolina Data Acquisition and Reporting Tool
CDR	Clinical Dementia Rating Scale
CES-D	Center for Epidemiologic Studies Depression Scale
CGM	Continuous Glucose Monitoring
CIU	Contact Information Update form
DBP	Diastolic blood pressure
DMS	Data management system
EPICARE	Epidemiological Cardiology Research Ctr (ECG Reading Center at Wake Forest)
ER	Emergency room
Gen2	Generation 2
ICT	Informed Consent Tracking form
IRB	Institutional Review Board
LTCF	Long term care facility
MCI	Mild cognitive impairment
MRI	Magnetic resonance imaging
MSR	Medication Survey form
MTC	Medical Therapeutic Classification
NCS	Neurocognitive Study
NDC	National Drug Code
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
NIH	National Institutes of Health
NPI	Neuropsychiatric Inventory
OHRP	Office for Human Research Protections
PET	Positron-emission tomography
PSA	Participant Safety Screening form
QCC	Quality Control Committee
QxQ	Question by question
RTS	Recruitment Tracking and Scheduling form
sAFU	Semi-annual follow-up
sIRB	Single Institutional Review Board
SBP	Systolic Blood Pressure form
UBACC	University of California, San Diego Brief Assessment of Capacity to Consent
UDS	Uniform Data Set
UPC	Universal Product Code

3 RECRUITMENT TO THE ARIC GEN2 VISIT

Screening and recruitment of new participants to the ARIC Gen2 Study is detailed in a separate Manual (MOP44). Briefly, recruitment will be based at the four established ARIC field sites (Washington County, MD; Jackson, MS; Forsyth County, NC; Minneapolis Suburbs, MN). We will leverage the current contact with ARIC participants during to recruit family members and proxies (with a potential expansion to friends and neighbors) with **a history of diagnosed type 2 diabetes**, age 50-80 years old, community-dwelling, and fluent English-speakers. Each of the four field centers will target to recruit up to approximately 100 ARIC Gen2 participants (minimum N=400).

4 FIELD CENTER EXAMINATIONS

4.1 OVERVIEW

The ARIC Gen2 examination is a fully standardized sequence of interviews and procedures conducted according to a common protocol. The components of the visit examination are similar to ARIC Visit 10 (See table 0.1)

4.2 PRIORITY RANKING ASSIGNED TO VISIT DATA ELEMENTS

The priority ranking for Gen2 is different than for the main ARIC Visit 10 since all participants in Gen2 are **required** to wear the continuous glucose monitoring (CGM) and ZioPatch (ECG) sensors.

For specific procedure and training information about the Continuous Glucose Monitoring component, refer to Manual 39 Continuous Glucose Monitoring ARIC Visit 11.

For specific procedure and training information about the ZioPatch component, refer to Manual 21 ZioPatch.

The exam components are not listed in priority order.

The Field centers may reorganize the Exam Checklist (checklist can be found with the GEN2 forms on the ARIC website) to flow with their clinic set-up and to meet the individual needs of a given participant.

Orthostatic hypotension, ambulatory blood pressure monitoring (ABPM), and home blood pressure monitoring (HBPM) are Ancillary Studies that are optional and lower priority in Gen 2.

Peripheral neuropathy (MNSI) is an Ancillary Study but is a higher priority in Gen2 since peripheral neuropathy is a very important complication of type 2 diabetes.

Please note that the participant times in Table 0.1 are based on experiences in ARIC (much older population than Gen2) and are likely to be conservative. We anticipate that times will be lower for Gen2 participants as they will tend to be much younger (age range 50-80 years) than current ARIC participants.

Table 4.1. ARIC Gen2 Field Center Examination Components and Estimated Administration Times

Examination Components – Field Center	Forms	Ppt.Time (min)
Reception, informed consent, contact information, safety	ICTX, CIU, PSA	20
Medication Coding	MSR	5
Collection of urine specimen; Blood Draw*	BIO	15
Snack	--	15
Anthropometry	ANT	7
Seated blood pressure	SBP	10
Demographics, medical history	DEMG, MHXG	10
Break		5
Cognitive Battery A	ESU, MME, WRAT, NCS, CDPG,Trails A & B	60
Lunch/Snack		20
Physical function testing	PFX	20
Zeno Gait Mat	ZGM	15
ZioPatch/CGM (REQUIRED for Gen2)	EIO, CGMR	10
Peripheral Neuropathy	MNSA, MNSAQ	15
Orthostatic Hypotension (lower priority)	OBP, OSQ	20
HBPM (lower priority)	HBP, VAS	5
ABPM (lower priority)	ABP	15
Interviews: physical activity level	PAC	7
Exit interview (end-of-visit report; review of alerts; ZioPatch/CGM mailer; ABPM/HBPM mailer if applicable)	RARX	10
Total Time for Gen 2 Visit		4 hrs 40 mins
Total Time for Gen2 Visit with snack, including bathroom breaks and walking time		almost 5 hours

***** Fasting not required

4.3 PARTICIPANT SAFETY SCREENING

Verification of eligibility for all study procedures and a pre-screening to identify a participant's special needs and to ensure safety are part of the visit scheduling procedures. For this purpose, ARIC personnel use the Participant Safety Screening Form (PSA), supported by the ARIC data entry and management system (CDART). Following an explanation of the ARIC Gen2 study and the procedures involved, the interviewer requests an opportunity to verify the individual's eligibility for all procedures. The rationale for these questions is provided in the instructions for the PSA form, and explained to the participant if requested. **Note that there is no Participant Snapshot in GEN2.**

Any medication taken routinely by the participant – on any schedule – is recorded as Yes on item 1 of the PSA form. Only medications that are taken occasionally are recorded as No. The purpose of this question is to prompt ARIC staff to review the medications taken on a schedule with the participant at the time the clinic visit is scheduled. As described below, the participant is then asked to take specific medications on their prescribed schedule, or to defer others until after the blood draw during the exam visit. At the time the participant's visit is scheduled and at Reception after the informed consent is signed, arrangements are made for the participant to have access to medication that needs to be taken in the course of the exam at set times, and with food if required. This is specified on the Participant Exam Checklist found on the ARIC website.

The conditions reviewed during this interview (and listed on the form) include the participant's use of an implanted electronic device. Since participants with a pacemaker or neurostimulator are excluded from Gen2, the response to this question should be No. The responses of the safety screening questions are recorded on the PSA form and the participant is told of any procedures to avoid. In preparing for the participant's exam visit exclusions from a procedure are recorded on the Participant Exam Checklist and reviewed with the participant at the time of reception at the field center.

At the time of scheduling the exam, staff should inquire about special needs, such as any medical conditions or treatment that would affect the appointment time, difficulties in getting on or off an examination table, or impediments in hearing or reading. Arrangements for a safe and comfortable examination visit are made, inclusive of transportation, consulting with the Study Coordinator as appropriate. Participants should be reminded to bring all their medications to the field center, and the schedule of any medications to be taken on the day of the examination is reviewed.

4.4 SCHEDULING THE PARTICIPANT'S MEDICATIONS ON THE DAY OF THE EXAM

Refer to ARIC Visit 10 Manual 2

4.5 APPOINTMENT REMINDERS AND INSTRUCTIONS FOR THE CLINIC EXAMINATIONS

Refer to ARIC Visit 10 Manual 2

4.6 SPLIT FIELD CENTER EXAMINATIONS

Refer to ARIC Visit 10 Manual 2

4.7 SEQUENCE OF THE FIELD CENTER EXAMINATIONS

Refer to ARIC Visit 10 Manual 2

5 RECEPTION

Refer to ARIC Visit 10 Manual 2

6 INFORMED CONSENT

Informed consent is the first form administered during the examination. Its core content complies with guidelines from the National Heart, Lung, and Blood Institute and the ARIC Steering Committee. Its content and format also meet the specific requirements of the single Institutional Review Board, as well as any local requirements.

Informed consent will be obtained at the ARIC Gen2 examination, to inform the participant of the purpose and procedures of the study and the voluntary nature of their participation. Further, this form is intended to protect the rights of the ARIC Gen2 Study participants, meet Institutional Review Board requirements, and to identify the participant's instructions for the type of information and biospecimens to be collected, their long-term storage and disposition, and their wishes for sharing their data. The informed consent makes the study participant aware of the right to withdraw from the study, to not participate in a procedure, or to decline to answer any question(s) without penalty. Also, at this time the participant is asked for authorization for subsequent contacts by ARIC personnel, to access information in their medical records, and for instructions on distribution of their ARIC Gen2 study results.

It is not until informed consent is signed that the participant is assigned a GEN2 ID.

6.1 ADMINISTRATION

The purpose of the ARIC Gen2 study and the measurements to be made at this exam visit are reviewed with the participant. After introducing the consent form to the participant in a private area, staff asks whether the participant prefers to read the consent form or to have it read by the staff person. Record this preference on the Exam Checklist to make this information accessible to interviewers throughout the clinic visit and avoid repeated questions whether the participant is comfortable reading. Questions are encouraged, and time is allowed for the person to read and sign the informed consent document. Before proceeding, assess whether the participant uses reading glasses or a hearing aid. Record this information on the Exam Checklist and explain to the participant how to have the hearing aid / reading glasses conveniently and safely available throughout the clinic visit.

At the field centers' discretion, the informed consent can be mailed to the participant in the course of recruitment/exam scheduling. Staff should be attentive to the possibility that participants may have read the informed consent prior to their arrival. Questions of clarification should be solicited also under these circumstances and the consent portion of the form must be filled out and signed in the presence of the staff person who serves as witness. If a participant is visually impaired or otherwise incapable of reading the study description and informed consent page, the narrative portion is read to him/her and then the participant is asked to sign the document. The original informed consent document is filed in the participant's study folder. A copy of the informed consent is given to the participant.

6.2 TRAINING AND CERTIFICATION

Study coordinators are responsible for providing local staff training and certification by the Study Coordinator is required. Quality assurance is provided at each field center by means of observation by the local study coordinator.

6.3 DATA COLLECTION

The Informed Consent is a paper form. When the participant receives a copy of the informed consent, the field center has the option of providing a copy of the entire form, or merely the signed consent pages. In all cases, the original signature page must be kept at the field center and stored in the participant's study folder. Any restrictions noted on the informed consent form are keyed into the ICTX form (see below).

6.4 ABILITY TO COMPREHEND THE INFORMED CONSENT

Although the capacity to provide informed consent is required for an ARIC Gen2 examination to be conducted in an ethical manner it can be challenging to identify individuals who may not have the ability to comprehend the informed consent. There are no nationally recognized standards for this assessment and somewhat different findings have emerged when some states (and courts) have taken up this issue. As a result, each field center follows the guidance of the single IRB, as well as any local requirements. For instance, for participants in whom capacity to consent is uncertain, sites may be required to complete a University of California, San Diego Brief Assessment of Capacity to Consent (UBACC) to determine whether the participant can consent for themselves. A modified version of the UBACC is often used; modifications reflect ARIC's observational study design.

Unless impairment is obvious, recognizing cognitive impairment in a participant is difficult (even for professionals), particularly since social skills can remain intact for participants who otherwise do not perform well on testing. Given the age of Gen2 participants and our recruitment and screening procedures, we don't anticipant that many (if any) persons recruited for Gen2 will have overt cognitive impairments. But is worth noting that decision-making capacity is frequently task specific. As a result, depending on the type and extent of impairment, cognitively impaired individuals can remain fully capable of making a variety of decisions, including whether to participate in a study. Field center personnel should remain attentive to indicators of potential cognitive impairment, such as repetition (i.e., repeating questions/stories over the course of just a few minutes) and empty or poor responses (i.e., the participant who frequently responds with "I don't know").

To ensure that participants understand the informed consent staff can ask the participant to explain back (in their own words) certain portions of the study. This can be introduced by stating that it is very important that the participant understand his/her rights and the process by which the ARIC study protects the confidentiality of the participant's information. If the responses from the participant suggest that he/she has difficulty comprehending the consent process or the form contents, the staff person brings this to the attention of the supervisor. If it is determined that the participant cannot provide individual informed consent, the participant may be excluded from the Gen2 study.

7 INTERVIEWS UNIQUE TO GEN2

Refer to the GEN2 only forms on the ARIC website.

7.1 DEMOGRAPHICS (DEMG)

The Demographics (DEM) form collects information on participant characteristics and socioeconomic status. This questionnaire also records information any friends or family members of the ARIC Gen 2 participant who are part of the original ARIC study.

Rationale
Linkage to any original ARIC participants will enable the ARIC Gen2 study staff to maintain contact with the participants. It will also allow for potential analyses of multi-generational patterns in diabetes and heart disease.

Administration

The form is administered by trained and certified interviewers. Detailed procedures for administering the form are provided in the question-by-question instructions immediately following the form and in the central training manual.

7.2 MEDICAL HISTORY (MHXG)

The Medical and Health History (MHX) form of the clinic interview collects information on pertinent health conditions and the relevant medical histories of the participants' biological parents. The questionnaire is based on previous ARIC medical information forms.

A major objective of the ARIC Gen2 Study is to evaluate the link between glucose patterns and cardiac arrhythmias in adults with type 2 diabetes. The MHX form is a core data collection which is administered during the flexible component of the exam. This questionnaire documents the history of type 2 diabetes, heart disease, and other health conditions that are associated with diabetes and heart disease. The questionnaire also records information on the lifetime occurrence of head injuries which either resulted in loss of consciousness or required medical care and significant neurological conditions.

The Medical History form is administered by trained and certified interviewers with an understanding of the medical terms and diagnostic procedures referred to in this instrument. Detailed procedures for administering the form are provided in the question-by-question instructions associated with the form.

Training
Interviewers are trained centrally prior to the visit. The field center interviewer supervisor is responsible for the training and certification of new field center interviewers.

Certification
Certification is achieved by the demonstration of adequate technique on 5 taped interviews, reviewed and approved by the study coordinator or interviewer supervisor. Recertification is done annually and requires the successful completion of one taped interview of an actual participant. With participant approval, all interviews are taped for quality control. This tape is included in the round robin which is reviewed by the four interviewer supervisors selected to monitor each year's round robin tapes.

Quality Assurance
A non-systematic sample of Demographic and Medical and Health History forms are reviewed by the supervisor. Technique and adherence to protocol are also monitored by Coordinating Center Monitors; data quality is monitored by the Quality Control Committee.

Data Collection
Data from the Demographics and Medical and Health History form are collected by direct data entry in the DMS.

7.3 REPRODUCTIVE HISTORY (RHXG) (WOMEN ONLY)

The objective of the reproductive history questionnaire is to determine pregnancy history and any history of pregnancy complications, and to determine current and past history of gonadal function and exposure to exogenous hormones. The interview is administered to female participants only. It is completed during the interview portion of the participant's visit.

Rationale

Pregnancy is associated with significant hormonal and metabolic changes, which can result in both maternal and infant complications, including gestational diabetes, gestational hypertension, preterm birth, and newborns that are either too large or too small. It has been shown that these complications are associated with long-term health effects for the mother, particularly a higher risk for developing type 2 diabetes. In addition, there is evidence that age at onset of menstruation and age at onset of menopause (including from surgical removal of the ovaries) are associated with risk for cardiometabolic diseases.

The Reproductive History form (is administered by certified interviewers within the flexible sequence of the participant examination. Detailed instructions for administering each question are provided in the question-by-question instructions.

Questions on pregnancy history, menstrual history, and history of gynecologic surgery may be considered sensitive by participants and care must be exercised to administer each section in a nonjudgmental format.

The questionnaire is divided into 4 sections: (1) menstrual history and onset of menopause; (2) pregnancy history; (3) history of reproductive therapies; and (4) history of gynecological surgery.

Most of the questions on the form are closed-ended or pre-coded questions designed for direct entry into the computer by the interviewer. Open-ended questions are to obtain year of pregnancy, age, or number of pregnancies and births. The exact wording and order of the questions is followed to ensure standardization. Questions are not skipped unless indicated by the skip pattern.

Training
Interviewers are trained centrally prior to the visit. The field center interviewer supervisor is responsible for the training and certification of new field center interviewers.

Certification
Certification is achieved by the demonstration of adequate technique on 5 taped interviews, reviewed and approved by the study coordinator or interviewer supervisor. Recertification is done annually and requires the successful completion of one taped interview of an actual participant. With participant approval, all interviews are taped for quality control. This tape is included in the round robin which is reviewed by the four interviewer supervisors selected to monitor each year's round robin tapes.

Quality Assurance
A non-systematic sample of Reproductive History forms is reviewed by the supervisor. Technique and adherence to protocol are also monitored by Coordinating Center Monitors; data quality is monitored by the Quality Control Committee.

Data Collection
Data from the Reproductive History form are collected by direct data entry in the DMS.

7.4 SMOKING AND ALCOHOL USE FORM (ALCG)

Refer to ARIC Visit 10 Manual 2. The GEN2 ALCG form includes smoking questions where the ARIC visit 10 form does not.

7.5 COGNITIVE TESTING

Refer to ARIC Visit 10 Manual 2 and the Neurocognitive (NCG) Packet with the GEN2 Forms on the ARIC website.

8 INTERVIEWS & TESTS AS IN VISIT 10

8.1 BIOSPECIMEN COLLECTION (BIO)

The procedures used for the collection, processing and shipment of blood samples and urine samples are described in Manual 7. Biospecimen collection for ARIC Gen2 Visit 1 follows the same protocol as ARIC Visit 10 biospecimen collection.

8.1 ANTHROPOMETRY (ANT)

Anthropometric measures include height, weight, and body fat. These measures are used to assess the relationship between overweight and risk of disease. Anthropometry administration follows the protocol established in ARIC. GEN2 collects height which is not in the ANT form for ARIC visit 10.

8.2 SITTING BLOOD PRESSURE (SBP)

Refer to ARIC Visit 10 Manual 2.

8.3 MEDICATION SURVEY (MSR)

Refer to ARIC Visit 10 Manual 2.

8.4 PHYSICAL ACTIVITY (PAC)

Refer to ARIC Visit 10 Manual 2. Not that there are more questions in the GEN2 PAC form compared to the ARIC visit 10 PAC.

8.5 PHYSICAL FUNCTION TESTS (PFX)

For specific procedure and training information about the physical function tests component, please refer to Manual 32 Physical Function and Endurance.

8.6 GAIT MAT (ZGM)

For specific procedure and training information about the Zeno gait mat component, please refer to Manual 32 Physical Function and Endurance.

9 ANCILLARY STUDIES

9.1 PERIPHERAL NEUROPATHY

Because peripheral neuropathy is an important complication of diabetes, this ancillary component is high priority (but not required) for ARIC Gen2 participants. For specific procedure and training information about the Peripheral Neuropathy component, please refer to Manual 40 Peripheral Neuropathy – MNSI.

9.2 BLOOD PRESSURE MONITORING AND ORTHOSTATIC HYPOTENSION

The Blood Pressure Ancillary Studies are lower priority for ARIC Gen2 participants. But since hypertension and orthostatic hypotension are important complications of diabetes, ARIC Gen2 participants may be eager and willing to participate in these ancillary study protocols.

For specific procedure and training information about the Ambulatory Blood Pressure Monitoring, Home Blood Pressure Monitoring, and Orthostatic Hypotension components, please refer to Manual 38 Blood Pressure Monitoring and Manual 37 Orthostatic Hypotension.

10 DATA INVENTORY

Refer to ARIC Visit 10 Manual 2.

11 EXIT INTERVIEW

The end of visit debriefing provides an opportunity to ask for feedback about the visit and to identify aspects that the participant may have perceived as stressful or unpleasant. It also provides an opportunity to build rapport with the study participant and to seek commitment for a long-term association with the ARIC Gen2 study. The participant should be reminded of the six-month follow-up call, and at the field center's discretion the call can be scheduled at that time.

The participant is told that a written summary report, including additional tests, will be mailed to the participant and his/her physician (or alternate) six to eight weeks after the field center exam. It is important to establish who is authorized to receive the report of study results, according to the participant's instructions.

12 PARTICIPANT SAFETY

Refer to ARIC Visit 10 Manual 2.

13 OVERVIEW OF GENERAL QUALITY CONTROL PROCEDURES

Refer to ARIC Visit 10 Manual 2.

14 CONTINUED PARTICIPANT CONTACT

Generation 2 participants will be followed annually by site's local ARIC follow-up staff. Currently there are 2 follow-up forms under 'Administrative forms' (MCU & PHF) not related to the clinic visit. Follow-up staff will also be granted access to 'Contact Year Follow-up' in CDART where they will administer the annual only follow-up questionnaires to the participants (See Manual 2-Participant Follow-up). Furthermore, surveillance staff will then collect any hospital information in CDART similar to ARIC surveillance (See Surveillance manual 3 and 3a1).