



MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

EXAM 7

Field Center Manual of Operations

**August 8, 2023
Version 12**

MOP Version Change Log

Version Date	Summary of Changes
V1 1/12/2020	<p>Added New Sections</p> <ul style="list-style-type: none"> • Section 5: Clinic Reception and Consent • Section 6.11: Neighborhood Questionnaire • Section 7.5: Clinician’s Physical Exam • Section 7.6 SPPB • Section 7.8 Arterial Stiffness Measures (VaSera Device) • Section 11.1 Data Collection Tablet Best Practices • Section 13.1-13.4: Certifications overview
V2 1/21/2022	<p>Added New Sections</p> <ul style="list-style-type: none"> • Section 6.8 Environmental Exposures Form • Section 7.1.4 Neck Circumference • Section 7.2.4 OMRON 10 Series BP Monitor • Section 8.5 24H Blood Pressure Monitor • Section 13.5 Summary of Certification Requirements
V3 1/24/2022	<p>Added New Sections</p> <ul style="list-style-type: none"> • Section 6.2 UBACC • Section 7.10 Hair follicle collection • Section 8.5.10 Instructions for OnTrack ABPM Monitor (v7 1/18/2022 from SRC) <p>Updated Sections</p> <ul style="list-style-type: none"> • Section 4.3 Added “Participants should remove nail polish or acrylic nails for pulse oximetry, and not have any metal in their hair (hair clips, hairpins) for brain MRI.” • Section 5.1 Added consent decision diagram • Section 8 Heart Monitor Patch <ul style="list-style-type: none"> ○ 8.4.10 and 8.4.13 Added details for automated phone surveys ○ 8.4.18 updated variables for completion form
V4 2/10/2022	<p>Added New Sections</p> <ul style="list-style-type: none"> • Section 4.2 COVID-19 Screening Policy • Section 5.4.1 Print and Provide the Exit Report • Section 6.5 Sleep PSG Questionnaire • Section 7.9 Spirometry • Section 7.11 Nasal Brushing Sample Collection • Section 8.7 Participant Diary <p>Updated Sections</p> <ul style="list-style-type: none"> • Section 4.4 Instructions to Participants before the Clinic Visit • Section 4.7 Guidelines for Examination of Diabetic Participants • Section 6.8 Added METHODS section to Environmental Exposures Questionnaire • Section 6.11 Added post-script to Neighborhood Questionnaire • Section 8.1.11-14 Hip Activity Monitor introductory script, instructions, and completion form • Section 8.4.6, 8.4.15 Skin Tac for heart monitor patch, trouble shooting • Section 8 Combine reminder calls for all devices • Section 13.5 Summary of Certification Requirements
V5 3/7/2022	<p>Added New Sections</p> <ul style="list-style-type: none"> • Section 6.8 Family History Form • Section 8.9 Home Sleep Study (v1.2, 3.6.22)

	<ul style="list-style-type: none"> Section 13.6 Submitting Certification Materials for Review <p>Updated Sections</p> <ul style="list-style-type: none"> Section 6.6: Added new Q3 to Personal History (Language spoken at home), clarified Q9 and 10 (If the participant does stocks or investments and their family does, and they receive no benefits from their family having these things, the participant should respond “no.”) Section 6.9: Removed Q7 from Environmental Health (Was a secondary address reported on the Participant Tracking Form. Section 7.11: Nasal Brushing Materials and Procedure Section 8.4.6, 8.4.7, 8.4.10: Updates to Cardea SOLO sensor placement, cleaning and prepping skin, Daily Stress phone survey callerID, participant take home materials 8.4.13 Clinic Staff Reminder Calls. Section 13.5: Added certification contacts for all components included in the table, added certification details for nasal brushing and hair collection.
V6 3/17/2022	<p>Updated Sections</p> <ul style="list-style-type: none"> Section 8.6.3 ABPM monitoring should NOT occur on the same night as the PSG
V7 3/23/2022	<p>Updated Sections</p> <ul style="list-style-type: none"> Section 8.6: Updates alerts reporting forms and procedures. Section 8.7: Participant Diary is collected for only the first 8 days of monitoring. Section 7.3: Pulse oximeter should be placed on the opposite side that the blood pressure is placed.
V8 4/18/2022	<p>Updated Sections</p> <ul style="list-style-type: none"> Section 1.2 Updated table of labs and reading centers Section 3.3 Updated Data collection forms table to include Cognitive Function and Neighborhood Completion Forms. Added alert and quality summary forms that are completed by Reading Centers. Section 5.1.1 and 6.2 The outcome of UBACC screening is recorded in the Clinic Reception Form. The term “Dementia” should not be used with participants. Section 5.2: Forms will only be displayed if the appropriate consent is recorded in the Clinic Reception Form. Section 5.4.1: Updated instructions for printing Exit Report Section 6.11 and 6.12 Updated Sleep and Sleep PSG Questionnaire QxQs. Section 7.7: Added Cognitive Function Testing Completion Form. Section 8.3.4, 8.6.4: place sticker on outside of sensor pouch. Section 8.4.11: updated take home materials for heart monitor patch. Section 9: Alerts notifications. Section 13.5 Added PSG and Cognitive Function Testing certification details to table. <p>New Sections</p> <ul style="list-style-type: none"> 6.10.2 Neighborhood Questionnaire Completion Form 11.4 Data Transfer reference table
V9 5/4/2022	<p>Updated Sections</p> <ul style="list-style-type: none"> Section 4.1 added scheduling script Section 8.3 Substantial updates to all parts. Please tracked changes here. Section 8.4.7-10 Clarification for heart monitor patch procedures. Section 8.5 ABPM inflates every 30 minutes (not 20min during the day).
V10 5/12/2022	<p>Updated Sections</p> <ul style="list-style-type: none"> Section 7.9.5: printing the spirometry report to PDF and uploading to Spirometry Completion Form in REDCap. Section 7.9.15 and 7.11.1 instructions for Spirometry and Nasal Swab Collection Form. Section 7.10.1 instruction for Hair Collection Completion Form.

<p>V11 6/27/2022</p>	<p>Updated Sections</p> <ul style="list-style-type: none"> • Section 3.3: Added Participant Tracking and COVID-19 forms to form completion table. • Section 3.5: Hip and wrist monitors must be worn together over the same time period. • Section 4.4.2: Call log displays warning if LAR is required for consent, allows tracing for participants who prefer a home or remote visit. • Section 6.3.1: Added Study Informant contact script and designating one of the listed MESA Contacts as the MESA MIND Study Informant. • Section 6.5 In the Medical History Form, if the participant reports having a condition (other than shortness of breath) that makes them unable to walk, skip the shortness of breath questions. • Section 6.13: Question 38 on the PSG Sleep Questionnaire was split into two parts for activities in bed and in the two hours before bedtime. • Section 7.7: Added completion of MESA MIND Study Informant interview to the Cognitive Function Testing Completion Form. • Section 8.7: Added time of blood pressure medications in the Participant Diary. <p>New Sections</p> <ul style="list-style-type: none"> • Section 4.2 Optional verbal consent for Exam 7 Questionnaires • Section 6.10 Added COVID-19 History Questionnaire • Section 11.4.1 Instructions for downloading monitor data files to OneDrive.
<p>V12 8/8/2023</p>	<p>Updated Sections</p> <ul style="list-style-type: none"> • Section 5.2 Clinic Reception form updated to include information about Clinic, Home, Remote and Phone visits. • Section 7.7. Cognitive Function testing is disabled when participant had adjudicated result of “dementia” in MIND Visit A • Section 8.5 ABPM Home Monitoring • 13.5 Certification requirements updated for Heart Monitor, Lung CT, and Spirometry certifications • <p>New Sections</p> <ul style="list-style-type: none"> • Section 4.3 Alternative Visits • Section 6.8 Physical Activity Questionnaire <p>Removed Section</p> <ul style="list-style-type: none"> • COVID-19 Questionnaire – this is now asked on FU24/FU25

Multi-Ethnic Study of Atherosclerosis

Exam 7 Field Center Manual of Operations

1	OVERVIEW	11
1.1	PURPOSE AND OBJECTIVES	11
1.2	BRIEF DESCRIPTION OF MESA	11
1.3	EVENTS	12
1.4	HOW TO USE THIS MANUAL	13
2	EQUIPMENT AND SUPPLIES	14
3	EXAM 7 PROCEDURES	20
3.1	PURPOSE OF EXAM COMPONENTS	20
3.2	EXAM 7 COMPONENTS DESCRIPTIONS BY ANCILLARY STUDY:	21
3.3	DATA COLLECTION FORMS	24
3.4	ORDER OF EXAM COMPONENTS	25
3.5	EXAM COMPONENT SELECTION REQUIREMENTS AND PRIORITIZATION	26
4	PREPARING FOR THE EXAM 7 VISIT	27
4.1	SCHEDULING	27
4.2	OPTIONAL VERBAL CONSENT FOR EXAM 7 QUESTIONNAIRES	28
4.3	ALTERNATIVE VISITS	29
	<i>Some participants may not wish or be unable to come to the clinic for an Exam visit. In this case you can offer a couple of options for Exam 7:</i>	29
	• Home Visit	29
	• Remote Visit	29
	<i>Home Visit: A home visit option allows participation for those who are unable or unwilling to come to the clinic. Home visits improve retention rates and provide an additional way to help keep participants connected to MESA. See the Home Visit MOP for specifics.</i>	29
	<i>Remote Visit: The MESA Exam 7 Protocol includes a remote visit option to allow participation for those who are unable or unwilling to come to the clinic and do not want field center technicians to come to their home. Remote visits improve retention rates and provide an additional way to help keep participants connected to MESA. In general, it may take more than one remote visit to complete the examination. See the Remote Visit MOP for specifics.</i>	29
	<i>Phone Visit: If a participant is unable or unwilling to complete a home or remote visit a phone visit may be an option. A phone visit only includes completion of the following:</i>	29
	• Environmental Exposures Questionnaire	29
	• Medical History	29
	• Personal History	29
	• Neighborhood Questionnaire (and Neighborhood Questionnaire Completion form)	29
	• Health and Life	29
	• Sleep Questionnaire	29
	<i>In the Clinic Reception form select Phone Visit. This will activate the appropriate questionnaires. All questions are read to the participant over the phone and data is entered directly into REDCap. If the participant expresses interest in completing more of the Exam then a Clinic, Home or Remote visit can be scheduled.</i>	29
4.4	COVID-19 SCREENING POLICY	29
4.5	PRE-VISIT REPORTS AND FORMS	30
4.5.1	Administration of Forms	31
4.5.2	Call Log Form	31
4.5.3	Participant Information Form	34
4.5.4	Exam 7 Notes Form	34

4.6	INSTRUCTION TO PARTICIPANTS BEFORE THE CLINIC VISIT	34
4.7	SET UP PARTICIPANT SUPPLIES	35
4.8	STAFFING	35
4.9	GUIDELINES FOR EXAMINATION OF DIABETIC PARTICIPANTS.....	35
5	PARTICIPANT RECEPTION AND CONSENT	36
5.1	CONSENT PROCEDURES	36
5.1.1	<i>Consent for Participants without cognitive impairment</i>	<i>37</i>
5.1.2	<i>Consent for Participants with known cognitive impairment</i>	<i>37</i>
5.2	CLINIC RECEPTION	38
5.3	REDCAP RECORD STATUS DASHBOARD	39
5.4	POST EXAM ACTIVITIES.....	40
5.4.1	<i>Print and provide the Exit Report.</i>	<i>40</i>
6	PARTICIPANT QUESTIONNAIRES.....	40
6.1	GUIDELINES AND TECHNIQUES FOR SUCCESSFUL INTERVIEWS	40
6.2	UNIVERSITY OF CALIFORNIA, SAN DIEGO BRIEF ASSESSMENT OF CAPACITY TO CONSENT (UBACC)	42
6.3	PARTICIPANT TRACKING	45
6.3.1	<i>Section A: Participant Information:.....</i>	<i>45</i>
6.3.2	<i>Section B: Secondary Residence:</i>	<i>46</i>
6.3.3	<i>Section C: Contacts Information:.....</i>	<i>46</i>
6.3.4	<i>Section D: Health Care Providers Information:.....</i>	<i>47</i>
6.4	MEDICATIONS.....	49
6.4.1	<i>Section A: Medication Reception.....</i>	<i>50</i>
6.4.2	<i>Section B: Prescription Medications.....</i>	<i>50</i>
6.4.3	<i>Section C: Over-the-Counter Medications</i>	<i>53</i>
6.4.4	<i>Section D: Vitamins and Supplements.....</i>	<i>53</i>
6.5	MEDICAL HISTORY	54
6.6	PERSONAL HISTORY	58
6.7	HEALTH & LIFE (SOCIAL DETERMINANTS OF HEALTH)	63
6.8	PHYSICAL ACTIVITY	67
6.9	FAMILY HISTORY QUESTIONNAIRE.....	72
6.10	ENVIRONMENTAL EXPOSURES QUESTIONNAIRE	74
6.11	NEIGHBORHOOD QUESTIONNAIRE	81
6.11.1	<i>General Instructions.....</i>	<i>81</i>
6.11.2	<i>Neighborhood Questionnaire Completion Form</i>	<i>81</i>
6.11.3	<i>Specific Instructions</i>	<i>81</i>
6.12	SLEEP QUESTIONNAIRE	87
6.13	SLEEP STUDY PSG QUESTIONNAIRE	92
7	EXAMINATION PROCEDURES	100
7.1	ANTHROPOMETRY	100
7.1.1	<i>Standing Body Height.....</i>	<i>100</i>
7.1.2	<i>Body Weight.....</i>	<i>101</i>
7.1.3	<i>Girth Measurements</i>	<i>102</i>
7.1.4	<i>Neck Circumference Measurement.....</i>	<i>103</i>
7.2	SEATED BLOOD PRESSURE	105
7.2.1	<i>Blood Pressure Classification.....</i>	<i>105</i>
7.2.2	<i>Preparation</i>	<i>106</i>
7.2.3	<i>Dinamap Methods.....</i>	<i>107</i>
7.2.4	<i>OMRON 10 Series Methods.....</i>	<i>109</i>
7.2.5	<i>BP Measurement Instructions for Participants With Short, Thick Arms.....</i>	<i>111</i>
7.2.6	<i>Reporting Blood Pressure Results to Participants</i>	<i>112</i>
7.3	PULSE OXIMETRY.....	113
7.4	BIOSAMPLE COLLECTION	115
7.5	CLINICIAN’S PHYSICAL EXAMINATION	116
7.6	SHORT PHYSICAL PERFORMANCE BATTERY	118

7.6.1	Introduction.....	118
7.6.2	Equipment.....	118
7.6.3	Balance Tests.....	118
7.6.4	Side-by-Side Stand.....	119
7.6.5	Semi-Tandem Stand.....	119
7.6.6	Tandem Stand – Short and Long.....	119
7.6.7	One Leg Stand.....	119
7.6.8	Gate Speed Tests.....	120
7.6.9	Narrow Walk Test.....	120
7.6.10	Chair Stand Test.....	120
7.6.11	Video Certification.....	121
7.7	COGNITIVE FUNCTION TESTING.....	123
7.8	ARTERIAL STIFFNESS MEASURES.....	124
7.8.1	Introduction.....	124
7.8.2	Technician Certification.....	124
7.8.3	Guidelines for Acquisition of Arterial Stiffness Recordings.....	124
7.8.4	Attachment of the Heart Sound Microphone (Phonocardiogram).....	127
7.8.5	Performing the Examination.....	128
7.8.6	Assessing the Quality of the Signals.....	131
7.8.7	Instructions for Electronic Transfer of Arterial Stiffness Waveforms to the Local PC and to the Penn CL.....	137
7.8.8	Core Lab Quality Review.....	141
7.8.9	References.....	141
7.8.10	Contact Information.....	141
7.8.11	VaSera Arterial Stiffness Transmittal Form.....	142
7.9	SPIROMETRY.....	143
7.9.1	Background.....	143
7.9.2	Equipment and Supplies.....	144
7.9.3	How to Test Participants.....	148
7.9.4	Post-Bronchodilator Testing.....	155
7.9.5	How to Print a Report.....	158
7.9.6	Quality Assurance.....	163
7.9.7	Safety Procedures.....	167
7.9.8	References.....	167
7.9.9	Appendix A: The OMIWSP Setup Program.....	169
7.9.10	Appendix B: Flow Chart for Determination of Post-Bronchodilator Test.....	171
7.9.11	Contact Information.....	172
7.9.12	Definitions and Symbols.....	174
7.9.13	Methods Summary.....	176
7.9.14	Spirometry and/or Albuterol Exclusion Criteria.....	177
7.9.15	Spirometry and Nasal Swab Completion Form.....	179
7.10	HAIR SAMPLE COLLECTION.....	182
7.10.1	Hair Collection Completion Form.....	183
7.11	NASAL BRUSHING SAMPLE COLLECTION.....	184
7.11.1	Nasal Swab Collection Completion Form.....	185
8	HOME MONITOR PROCEDURES.....	186
8.1	ACTIGRAPH HIP ACTIVITY MONITOR.....	186
8.1.1	Overview of the MESA 24H-ACT Study.....	186
8.1.2	Study Leadership Contact Information.....	187
8.1.3	Summary of MESA 24H-ACT Study.....	188
8.1.4	Wearable Devices.....	189
8.1.5	Quick Links.....	190
8.1.6	Labeling and Charging Activity Monitors for Field Data Collection.....	190
8.1.7	Recruitment and Eligibility Criteria for the Activity Monitor Component.....	191
8.1.8	ActiGraph wGT3X-BT Initialization Process.....	191
8.1.9	ActiGraph wGT3X-BT Download Process.....	194
8.1.10	Preparing the Data Collection Package.....	196

8.1.11	Activity Monitor Overview	196
8.1.12	Activity Monitor Overview and Participant Instruction	197
8.1.13	2-3 Day Check-in Telephone Call.....	198
8.1.14	Completing the Hip and Wrist Activity Monitor Completion Form	199
8.1.15	Recovery Protocol	200
8.1.16	Appendix A: Recruitment Materials.....	203
8.1.17	Appendix B: Take-Home Package Materials.....	204
8.1.18	Appendix C: Tracking Activity Monitors in the Field	209
8.1.19	Appendix D: Research Staff Certification Checklist	210
8.1.20	References Cited	210
8.2	GENEACTIV WRIST ACTIGRAPHY SLEEP MONITOR	212
8.2.1	Purpose	212
8.2.2	Equipment and Supplies.....	213
8.2.3	Staff Training and Certification	213
8.2.4	Actigraphy Data Acquisition.....	213
8.2.5	Participant Instructions.....	217
8.2.6	Downloading Data from the GENEActiv Software	219
8.2.7	Equipment Maintenance, Cleaning and Disinfection	221
8.2.8	Data Transmission to the CC.....	221
8.2.9	Repeat Studies.....	221
8.2.10	Sleep Reading Center Contacts	221
8.2.11	Appendix A: Participant Diary.....	222
8.2.12	Appendix B: Participant Instructions.....	223
8.2.13	Appendix D: Actigraph Device Completion Form	224
8.2.14	Appendix D: Actigraph Device Completion Form	225
8.3	CONTINUOUS GLUCOSE MONITOR.....	227
8.3.1	Background, Rationale and Context.....	227
8.3.2	Objectives.....	227
8.3.3	Methods and Measures.....	227
8.3.4	Reports for Participants	228
8.3.5	Training and Certification Procedures.....	228
8.3.6	Procedures for Placing and Removing CGM Sensors.....	229
8.3.7	Glucose Software: FreeStyle Libre Pro.....	236
8.3.8	Appendix C.1. Script for CGM Removal Call	240
8.4	HEART MONITOR PATCH MONITOR AND DAILY STRESS QUESTIONNAIRE.....	241
8.4.1	Introduction and Background.....	241
8.4.2	Eligibility and Exclusion Criteria for the MESA Stress Reactivity Study	241
8.4.3	Supplies:	241
8.4.4	Heart Rhythm Monitor: Introduction	242
8.4.5	Prepare Materials.....	242
8.4.6	How to Prepare the Skin and Apply the Cardea SOLO Patch.....	242
8.4.7	Step-by-step instructions for applying the sensor and what to tell the participant.....	248
8.4.8	Explain how to care for the Sensor (show inside-left of brochure).....	249
8.4.9	Show Participant Instructions	249
8.4.10	Daily Phone Surveys.....	250
8.4.11	Removal and Return of the Sensor.....	251
8.4.12	Fill out the Stress Reactivity Study Completion Form.....	252
8.4.13	Clinic Staff Reminder Calls	254
8.4.14	Spanish or Chinese language materials	255
8.4.15	Troubleshooting.....	255
8.4.16	Technician Certification	257
8.4.17	Contact information.....	257
8.5	24-HOUR BLOOD PRESSURE MONITOR	258
8.5.1	Purpose	258
8.5.2	Introduction to the Ambulatory BP Monitoring	258
8.5.3	Recruitment and Eligibility	258
8.5.4	Training and Certification.....	259

8.5.5	Equipment and Supplies	259
8.5.6	Method.....	260
8.5.7	Alerts and Referrals.....	269
8.5.8	Calibration of ABPM Monitors	270
8.5.9	Form Completion.....	270
8.5.10	Appendix A: Participant Instructions.....	271
8.5.11	Appendix B: Instructions for OnTrak ABPM Monitor	276
8.6	HOME SLEEP STUDY.....	286
8.6.1	Brigham Sleep Reading Center Introduction	286
8.6.2	Staff training and certification	286
8.6.3	Overview of the Multi-Ethnic Study of Atherosclerosis (MESA) Sleep study	287
8.6.4	Sleep Study Data Collection Overview.....	288
8.6.5	Preparing the Nox A1s for Data Collection.....	296
8.6.6	Supplies and Equipment Required for the Study Visit	303
8.6.7	Preparation for the Study Visit, Arrival in the Home, and after Visit Overview	304
8.6.8	Suggested Order of Nox A1s Sensor Application.....	307
8.6.9	Applying the Nox A1 Equipment to the Study Participant.....	315
8.6.10	Starting the Nox A1 Sleep Study Recording	323
8.6.11	Receiving and Cleaning/Disinfecting the Nox A1 kit.....	323
8.6.12	Downloading Sleep Study Data and Sending the Study to the Coordinating Center	325
8.6.13	Scored Reports, Study Acceptability and Urgent Alerts	329
8.6.14	No Show or Blank Studies	330
8.6.15	Device Accountability Logs.....	330
8.6.16	Training and Certification	330
8.6.17	Ongoing Quality Control	331
8.6.18	Appendix A. Definitions and Descriptions of Common Sleep Terms	333
8.6.19	Appendix B. Nox A1 Equipment Removal Instructions.....	336
8.6.20	Appendix C. PSG Tracking Form	338
8.6.21	Appendix E. PSG Accountability Log.....	340
8.7	PARTICIPANT DIARY	341
9	ALERTS	343
9.2	MESA ALERTS AND ALERT LEVELS	345
9.3	HEART RHYTHM MONITOR ALERTS	347
9.4	CHEST CT ALERTS.....	347
9.5	BRAIN MRI ALERTS	349
9.6	GERIATRIC DEPRESSION SCALE ALERTS.....	349
9.7	CONTINUOUS GLUCOSE MONITORING ALERTS	349
9.8	AMBULATORY BLOOD PRESSURE MONITORING ALERTS	349
9.9	POLYSOMNOGRAPHY (PSG) ALERTS.....	349
10	REPORTING PARTICIPANTS' RESULTS	351
10.1	MESA CORE EXAM	351
10.2	MESA STRESS REACTIVITY	351
10.3	MESA LUNG.....	351
10.4	MESA-MIND.....	351
10.5	MESA CONTINUOUS GLUCOSE MONITORING.....	352
10.6	MESA SLEEP.....	352
10.7	MESA 24H-ACT.....	352
11	DATA MANAGEMENT.....	353
11.1	DATA COLLECTION TABLET BEST PRACTICES.....	353
11.2	MICROSOFT SURFACE PRO 4 BASICS	353
11.3	MESA EXAM 7 REDCAP INSTRUCTIONS.....	360
11.3.1	Using REDCap	360
11.3.2	Data Entry Practice	362
11.4	DATA TRANSFER.....	363

- 11.4.1 Transferring monitor data from devices to OneDrive 363
- 11.4.2 Transferring monitor data from OneDrive to the Coordinating Center 366
- 12 EVENTS SURVEILLANCE 367**
 - 12.1 PURPOSE 367
 - 12.2 FOLLOW-UP CALL 367
 - 12.3 CONTINUING PARTICIPANT SURVEILLANCE 368
 - 12.4 USE OF PROXY 368
 - 12.5 ADMINISTERING AND PROCESSING FOLLOW-UP FORMS 368
- 13 CERTIFICATION 369**
 - 13.1 STANDARDIZATION OF CLINICAL PROCEDURES 369
 - 13.2 RESPONSIBILITIES AND QUALIFICATIONS OF COORDINATORS AND DATA ENTRY PERSONNEL 369
 - 13.3 DATA ENTRY AND CLINICAL OPERATIONS TRAINING AND CERTIFICATION 369
 - 13.4 HUMAN SUBJECTS PROTECTION TRAINING 369
 - 13.5 SUMMARY OF CERTIFICATION REQUIREMENTS 370
 - 13.6 SUBMITTING CERTIFICATION MATERIALS FOR REVIEW 377
 - 13.6.1 MESA E7 Certification Recording Submission Form 377
 - 13.6.2 NextCloud Certification Materials..... 378
 - 13.6.3 NextCloud Data Transfer 378
 - 13.6.4 Arterial Stiffness Data Transfer..... 378

1 OVERVIEW

Welcome to Exam 7 of the Multi-Ethnic Study of Atherosclerosis (MESA)! This is a continuation of a vitally important national research project that will influence diagnosis and treatment of cardiovascular diseases over the next several decades. The study enrolled 6814 participants at six field centers and has so far consisted of six examinations, periodic surveillance phone calls, and collection of data from Events (new diagnosis of a clinical cardiovascular disease)

As we continue, keep the above in mind when you perform the procedures on those gracious and willing participants. The ultimate value of this study depends on *you* and on the quality of the data that you collect.

1.1 Purpose and Objectives

The purpose of MESA is to study subclinical cardiovascular disease (CVD). Subclinical diseases are those detected by non-invasive procedures, such as MRI, CT, ECG and ultrasound, before they have produced any clinical signs or symptoms.

The primary objectives of MESA are to determine:

- What factors influence the progression of mild subclinical disease to more severe subclinical disease?
- What factors influence the progression of subclinical disease to clinical disease?

The secondary objectives of MESA are to:

- Assess ethnic, age, and gender differences in subclinical CVD prevalence and risk of progression
- Describe the interrelationships of established risk factors for subclinical CVD with new risk factors that are identified by the MESA study
- Develop population-based methods, suitable for application in future screening and intervention studies, to identify asymptomatic individuals who are at high risk for subclinical CVD.

1.2 Brief Description of MESA

MESA is a large and complex long-term study. Of the 6814 men and women ages 45–85, approximately 38% of the cohort are Caucasian, 28% African American, 23% Hispanic, and 11% Asian, predominantly of Chinese descent.

The cohort was recruited from the following six field centers (site ID number in parentheses):

- Wake Forest University, Winston-Salem, NC (3)
- Columbia University, New York, NY (4)
- Johns Hopkins University, Baltimore, MD (5)
- University of Minnesota, Minneapolis-St. Paul, MN (6)
- Northwestern University, Chicago, IL (7)
- UCLA, Los Angeles, CA (8)

Exam 7 includes the following Reading Centers and Labs:

Ancillary Study	Data/Samples Collected	PI	Institution
Core	<ul style="list-style-type: none"> • Biosamples 	Russell Tracy	University of Vermont
Core	<ul style="list-style-type: none"> • Lipid labs 	Mike Tsai	University of Minnesota
24-H Act	<ul style="list-style-type: none"> • ActiGraph hip monitor data • Daily Diary data 	Keith Diaz	Columbia University
Glucose Homeostasis	<ul style="list-style-type: none"> • FreeStyle Libre Continuous Glucose monitor data • Daily Diary data 	Morgana Mongraw-Chaffin	Wake Forest University
Lung	<ul style="list-style-type: none"> • Lung CT 	Eric Hoffman	University of Iowa
Lung	<ul style="list-style-type: none"> • Spirometry data 	R. Graham Barr	Columbia University
MIND	<ul style="list-style-type: none"> • Arterial Stiffness data 	Julio Chirinos	University of Pennsylvania
MIND	<ul style="list-style-type: none"> • Brain MRI data 	Nick Bryan	University of Pennsylvania
MIND	<ul style="list-style-type: none"> • PET data 	Robert Koeppe	University of Michigan
MIND	<ul style="list-style-type: none"> • MRI reading center 	Joao Lima	Johns Hopkins University
MIND	<ul style="list-style-type: none"> • MESA MIND Neurocognitive Operations 	Tim Hughes Bonnie Sachs	Wake Forest University
Neighborhood	<ul style="list-style-type: none"> • Neighborhood questionnaire data; participant address 	Jana Hirsch	Drexel University
Sleep	<ul style="list-style-type: none"> • GENEActiv Wrist Actigraphy Sleep monitor data • Daily Diary data • 24-H ABPM data • Home Polysomnography data 	Susan Redline	Brigham Sleep Reading Center (SRC), Harvard University
Stress	<ul style="list-style-type: none"> • Cardea Solo heart monitor data • Daily Stress questionnaire data 	Kiarri Kershaw	Northwestern University

The Coordinating Center at the University of Washington (Seattle) continues to coordinate all aspects of the study, including development of the Manual of Operations, development of data entry and management software, quality control, and statistical analysis of the data for publication in academic journals.

Funding for MESA is provided by the National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health. The Project Office from NHLBI also provides scientific leadership to the study.

MESA began more than 20 years ago. The first 18 months of the study were devoted to protocol development, staff training, and pilot testing. MESA Exam 1 (i.e., the “Baseline Exam”) took place over a two-year period, beginning in late July 2000. The second and third exams started in late 2002 and early 2004 and each required about 18 months to complete. The fourth exam required just under two years to complete, starting in late 2005. The fifth exam was completed in early 2012 and ran for just under two years. The sixth exam began in September 2016 and took place over a 22-month period. Since the first exam, participants have also been contacted by telephone every 9-12 months to determine whether any medical events have occurred.

1.3 Events

In MESA, an “event” is the development of a medical condition requiring participant hospitalization or other specified types of treatment, or the death of a participant. In MESA, we are particularly interested in collecting data about myocardial infarction (MI or “heart attack”), stroke, transient ischemic attack (TIA or “mini-stroke”), angina, congestive heart failure (CHF), peripheral vascular disease (PVD), and death. When an event occurs, we will collect a separate set of data based on hospital and physician records and on interviews with participants or their proxies.

1.4 How to use this manual

This manual contains step-by-step instructions for completing all the components in MESA Exam 7. Many of the steps and clinic procedures are the same as in previous exams; thus, where appropriate the previous manuals of operation may also be consulted.

You should carefully study all sections that relate to procedures that you will be performing, and you should keep this manual handy as a reference. If you have questions about anything in the manual, please direct them to your Study Coordinator.

2 EQUIPMENT AND SUPPLIES

Most supplies and equipment needed for Exam 7 are similar to that of previous exams. Each clinic should be equipped with the following supplies and equipment:

Exam equipment & supplies on hand at Field Centers

Item	Procedure
Clean sheets, pillowcases, blankets	General
Consent forms (and participant folders/files)	General
Examining table disposable paper	General
Gowns or scrubs & slippers	General
Disposable face masks	General
Paper (PDF) copies of forms (backup)	General
Reading glasses or magnifying glass	General
Snacks	General
Surge Protectors	General
Desks/tables and chairs	Consent
Field Center specific consent forms	Consent
1 Detecto Platform Balance Scale in lbs/kg	Anthropometry
Portable scale for home visits (SECA)	Anthropometry
Printer	Anthropometry
Stadiometer (Accu-Hite Measure Device with level bubble)	Anthropometry
Full length mirrors	Anthropometry
Gulick II 150 cm anthropometric tapes	Anthropometry
Four 50-pound weights (certified prior to first MESA visit) to calibrate scale	Anthropometry
Germicidal cleanser and wipes	Anthropometry
Current version of PDR	Medications
Tables/desks	Medications
Chairs and two footrests (2 stations)	Seated Blood Pressure
Copies of Critikon chart for choosing correct BP cuff size	Seated Blood Pressure
Dinamap automated blood pressure devices (Dinamap Monitor Pro 100, which includes printer paper, power cable, and power converter).	Seated Blood Pressure
OMRON 10 Series Wireless Bluetooth Upper Arm blood pressure monitor (model BP7450) Quantity 2	Seated Blood Pressure
Storage case for OMRON blood pressure Monitor Quantity 2	Seated Blood Pressure
Measuring tapes (for arm circumference).	Seated Blood Pressure
Watch or stop watches (to time five-minute rest and resting heart rate)	Seated Blood Pressure
Blood pressure cuffs in a variety of sizes (Dura-cuf Adult Assortment Pack [#2699]).	Seated Blood Pressure
Felt tip non-toxic washable markers	ECG patch application
CardeaSolo Information Packet (includes razor, cleaning supplies, return postage pack)	ECG patch application
Devon Medical Handheld Pulse Oximeter PC-66	Oximetry

Examination equipment provided by the Coordinating Center

Item	Procedure
Tablet PC computers	General
3 digital audio recorders	General
MESA medication bags	General
Questionnaire response option flip book	Questionnaires

Core exam phlebotomy and laboratory supplies and equipment

Item	Procedure	Provided by:
Lab coats and gloves	Blood Collection	FC
Phlebotomy chair	Blood Collection	FC
Washcloths/Towels	Blood Collection	FC
Smelling salts	Blood Collection	FC
Lab mats and wipes	Blood Collection	FC
10% bleach solution or approved biohazard disinfectant	Blood Collection	FC
Plastic cart with wheels for phlebotomy supplies (or plastic tray with compartments)	Blood Collection	FC
Butterfly needles (21 G) with luer adapter (BD# 367281)	Blood Collection	FC
Vacutainer barrels	Blood Collection	FC
Tourniquets	Blood Collection	FC
Alcohol prep pads	Blood Collection	FC
Gauze (2x2)	Blood Collection	FC
Surgical tape - paper tape (easier on participants)	Blood Collection	FC
Band-Aids	Blood Collection	FC
Blood collection tubes:	Blood Collection	FC
10 mL Serum tubes (BD# 367820)	Blood Collection	FC
10 mL EDTA tubes (BD# 366643)	Blood Collection	FC
5 mL Serum tubes (BD# 367814)	Blood Collection	FC
2 mL EDTA tubes (BD# 367841)	Blood Collection	FC
2.5 mL PAXgene RNA (BD# 762165)	Blood Collection	Lung AS
6 mL EDTA tubes (BD# 367863) NWU only	Blood Collection	FC
8.5 mL Heparin CPT (BD 362753) NWU only	Blood Collection	Epi AS
Draw tube rocker	Blood Collection	FC
Draw tube racks	Blood Collection	FC
Ice bucket and crushed ice - filled 10 min before draw	Blood Collection	FC
Stopwatches or timers	Blood Collection	FC
Scissors	Blood Collection	FC
Pens and Sharpie pens	Blood Collection	FC
Participant barcode labels (from Coordinating Center)	Blood Collection	CC

MESA Phlebotomy and Processing Forms (from Coordinating Center)	Blood Collection	FC
Blood Spill Kit	Blood Collection	FC
Biohazardous waste container	Blood Collection	FC
Needle/sharps container	Blood Collection	FC
Covidien Sterile Midstream Urine Collection Systems (Covidien2090SA), 14-375-143 (Fisher Scientific)	Urine Collection	FC
Lab coats	Sample Processing	FC
Nitrile or latex gloves	Sample Processing	FC
Splash shield and/or safety glasses	Sample Processing	FC
Lab mats and wipes	Sample Processing	FC
10% bleach solution or approved biohazard disinfectant	Sample Processing	FC
Emergency eye wash station	Sample Processing	FC
Biohazards waste container	Sample Processing	FC
Ice bucket with crushed ice, filled before start of processing	Sample Processing	FC
Draw tube racks	Sample Processing	FC
0.5 mL cryovials	Sample Processing	UV
2 mL cryovials	Sample Processing	UV
Blue cryovial caps	Sample Processing	UV
Red cryovial caps	Sample Processing	UV
Yellow cryovial caps	Sample Processing	UV
Orange cryovial caps NWU only	Sample Processing	UV
10 mL Transport Tube	Sample Processing	UV
White Cap with O'Ring for 10 mL Transport Tube	Sample Processing	UV
2 mL Sterile Cryovials	Sample Processing	LUNG AS? Or UV
Pooling Tube Rack (Globe Scientific 456930 Fisher Catalogue #21-200-285)	Sample Processing	FC
Cryovial/tube racks (Fisher 96 slot rack # 05-541-37 with Fisher cover # 05-541-28 OR Fisher 50 slot rack # 05-669-45 no cover)	Sample Processing	FC
15 mL Pooling tubes (Fisher #05-539-12 15 mL)	Sample Processing	FC
50 mL Pooling tubes (Fisher #05-539-8 50 mL)	Sample Processing	FC
Fixed-volume pipettes with tips (MLA). (Volumes to be pipetted: 0.5 mL, 1.0 mL, and 1.5 mL) Note: calibrated adjustable pipets may be used.	Sample Processing	FC
Cryovial freezer boxes (Revco boxes 2" with 9 x 9 grids Fisher #110678-24A [Mfr.No. Thermo Scientific #5954] with 9 x 9 grid Catalog# 13-989-218, Mfr.No. Thermo Scientific 6212 ordered separately) and REVCO 3"	Sample Processing	FC (UV may have extras to share)
Bench Top -20C Cooler (Fisher #05-405-11)	Sample Processing	Lung AS
Pens and Sharpie pens	Sample Processing	FC
Clock	Sample Processing	FC
Stopwatch or timer	Sample Processing	FC
Test tube holders (adapters) for centrifuge	Sample Processing	FC
Water bottles for balance	Sample Processing	FC
Rubber bands for freezer boxes	Sample Shipping	FC

Ziplock plastic bags for freezer boxes	Sample Shipping	FC
Absorbent material (e.g., paper towels, absorbent pads)	Sample Shipping	UV
Packaging tape	Sample Shipping	FC
Dry ice (~15 - 20 pounds per shipping container)	Sample Shipping	FC
*Shipping labels (FedEx address labels)	Sample Shipping	UV
Category B labels (UN3373 “BIOLOGICAL SUBSTANCE, CATEGORY B”)	Sample Shipping	UV
Dry Ice labels (Dry Ice UN 1845, Class 9 - Miscellaneous)	Sample Shipping	UV
Styrofoam Shipping Containers (Polyfoam Packers or Thermosafe)	Sample Shipping	UV
-80°C Freezer	Equipment	FC
4°C Refrigerator	Equipment	FC
Refrigerated centrifuge with a horizontal (swing-out head) rotor – minimum 2000 g-force	Equipment	FC

*The University of Vermont will cover every other week shipping from Field Centers to the Central Biorepository.

Exam equipment & supplies provided by the MESA MIND Ancillary Study

Item	Provided by
Stopwatch (for cog testing and SPPB)	FC
CASI “kit” (pen, soft-lead pencil with eraser, five objects for naming and recall)	CC
Blank sheets of paper; piece of blank cardboard (for covering five objects during recall)	FC
CASI questionnaire	CC
Digit Symbol scoring template	CC
Digit Symbol answer sheet	CC
Two No. 2 graphite pencils without erasers	FC
Drawing of complex figure (UDS: Benson Complex Figure Test)	FC
Tape to mark areas for 4-meter walk and narrow walk (SPPB)	FC
Chair without arms for Chair Stand test. (SBBP)	FC
Bed or exam table (Arterial Stiffness)	FC
Sheets (Arterial Stiffness)	FC
Wedge pillow or rolled towels to reduce weight of arms or legs against bed surface (Arterial Stiffness)	FC
Electrodes (3 per participant) (Arterial Stiffness)	FC
USB drive for exporting data (Arterial Stiffness)	FC

Exam equipment & supplies provided by the MESA Sleep Ancillary Study

Item	Procedure	Provided by:
RIP belts, Nox cannula w/filter, Snap on electrodes (small size), Blue snap sensors, lead with attached electrode, NuPrep skin prepping gel, Ten20 Conductive EEG paste, Tensive Adhesive Gel	Polysomnography	Sleep AC
Tape Measure, 60”	Polysomnography	Sleep AC
Marking pencil for skin (marking electrode placement)	Polysomnography	Sleep AC
Nylon hair comb/hair clips	Polysomnography	Sleep AC
Medicine cups 1 oz.	Polysomnography	Sleep AC
Latex free gloves (small, medium, large sizes)	Polysomnography	FC
Cotton-tipped applicators 6”	Polysomnography	Sleep AC

Prep N' Stay skin preparation solution	Polysomnography	Sleep AC
Gauze squares, 1"x1", 4"x4", Single-ply 1" non-stretch gauze rolls	Polysomnography	Sleep AC
Tongue depressors, non-sterile 6"	Polysomnography	Sleep AC
PDI Sani-Cloth Disinfecting Wipes	Polysomnography	FC
PDI Sani-Cloth Disinfecting Wipes	Actigraphy	FC
PDI Sani-Cloth Disinfecting Wipes	ABPM	FC
Toothbrushes (for cleaning electrodes)	Polysomnography	Sleep AC
Bandage scissors	Polysomnography	Sleep AC
Under pads (blue chux for surface protection)	Polysomnography	FC
Transpore/Micropore tape, Cover Roll Stretch Adhesive Tape	Polysomnography	Sleep AC
Powerex MH-C801D battery chargers and NiMH rechargeable batteries	Polysomnography	Sleep AC
AAA alkaline batteries	Polysomnography	Sleep AC
Ziploc plastic bags	Polysomnography	Sleep AC
Computer (desktop or laptop) with Windows version 10 64-bit and Google Chrome	Polysomnography	FC

Exam equipment & supplies provided by the MESA Lung Ancillary Study

Item	Procedure	Provided by:
SensorMedics model 1022 dry-rolling seal volume spirometer is fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface	In clinic spirometry	Lung
Surface Pro with OMI spirometry software	In clinic spirometry	Lung
Calibration syringe, 3.0L, Han Rudolph Model #5530	In clinic spirometry	Lung
Spirometer hoses, 3 ft long	In clinic spirometry	Lung
Disposable, filtered mouthpieces	In clinic spirometry	Lung
Nose clips	In clinic spirometry	Lung
Albuterol metered dose inhaler (MDI)	In clinic spirometry	FC
Disposable spacers	In clinic spirometry	Lung
Metrizyme detergent	Spirometry	Lung
N95 masks	Spirometry/Nasal Brushing	Lung
Disposable gloves	Spirometry/Nasal Brushing/Hair	FC
Disposable gowns	Spirometry/Nasal Brushing	Lung
Eye protection (Face shield)	Spirometry/Nasal Brushing	Lung
EasyOne spirometer and cable	Home spirometry	Lung
Filtered spirettes	Home spirometry	Lung
Tablet PC	Home spirometry	Lung
Flocked Nasal Swab	Nasal Brushing	Lung
Patient labels for cryovials and Ziplock bags	Nasal Brushing/Hair	Lung
RNALater solution	Nasal Brushing	Lung
2 ml Cryovials	Nasal Brushing/Hair	Lung
Patient labels for cryovials and Ziplock bags	Nasal Brushing/Hair	Lung
Small Ziplock bags	Hair	Lung
Tweezers (optional)	Hair	Lung
Scissors	Hair	Lung

Exam equipment & supplies provided by the MESA 24H-ACT Ancillary Study

Item	Procedure	Provided by:
ActiGraph wGT3X-BT [30 monitors/FC]	Activity monitoring	24H-ACT
ActiGraph belts or belt clips [1/participant]*	Activity monitoring	24H-ACT
ActiLife 6 Lite License [1/FC]	Activity monitoring data download	24H-ACT
Neo Hub w/ 7 USB-NEO Cables [1/FC]	Activity monitoring	24H-ACT
1 additional 7cc tube/participant (collected as part of MESA-MIND protocol)	Blood collection	24H-ACT
PDI Sani-Cloth Disinfecting Wipes	Activity Monitoring	24H-ACT
Prepaid mailers for returning monitors (e.g., Amazon Basics Poly Bubble Mailer, 8.5" x 12")	Activity Monitoring	FC

Exam equipment & supplies provided by the MESA Stress Reactivity Ancillary Study

Item	Procedure	Provided by:
Cardiac monitors (Cardea SOLO patch)	Heart Monitor Patch	Stress Reactivity
Prepaid mailers for returning monitors	Heart Monitor Patch	Stress Reactivity
Participant guides	Heart Monitor Patch	Stress Reactivity
Disposable razors to be used as needed	Heart Monitor Patch	Stress Reactivity
Extra gauze pads to be used as needed	Heart Monitor Patch	Stress Reactivity
Extra alcohol wipes to be used as needed	Heart Monitor Patch	Stress Reactivity
Latex free gloves (small, medium, large sizes)	Heart Monitor Patch	Stress Reactivity

Exam equipment & supplies provided by the MESA Glucose Homeostasis Ancillary Study

Item	Procedure	Provided by:
Continuous glucose monitor sensors	Glucose Monitor	Glucose Homeostasis
Continuous glucose monitor readers	Glucose Monitor	Glucose Homeostasis
Adhesive patches	Glucose Monitor	Glucose Homeostasis
Prepaid mailers for returning sensors	Glucose Monitor	Glucose Homeostasis
Alcohol wipes	Glucose Monitor	FC

3 EXAM 7 Procedures

3.1 Purpose of Exam Components

Exam and Questionnaire Components

	Purpose	Main or Ancillary
Reception and Consent*	Greet the participant. Review eligibility. Explain the schedule. Determine adherence to the fasting requirement. Obtain informed consent.	Main
Change Clothes	Standardize and facilitate anthropometric and other measurements.	Main
Blood Pressures	Obtain measure of sitting blood pressure of the brachial artery, at rest.	Main
Pulse Oximetry	Measure resting oxygen saturation.	Main
Anthropometry	Measure weight, height, and neck, waist, and hip circumferences.	Main
Phlebotomy	Obtain blood samples for lipids, chemistry, hemostasis, and other laboratory tests and for storage.	Main/Ancillary
Urine Collection	Obtain specimen for measurement of microalbuminuria.	Main
Hair sample collection	RNA-sequencing and gene expression	Ancillary
Snack	Provide the participant with a snack.	Main
Arterial Stiffness Measures	Measurement of arterial pulse waves and pulse wave velocity	Ancillary
Medications	Obtain information on types and dosages of all prescribed and over the counter medications.	Main
Medical History*	Obtain relevant medical history.	Main
Personal History/Demographics*	Obtain standard measures of education, income, wealth, occupation, smoking, and alcohol intake.	Main
Neighborhood Questionnaire	Obtain information on social and environmental factors in neighborhoods	Ancillary
Health & Life*	Obtain information about social/emotional factors	Main
Environmental Exposures Questionnaire*	Evaluate participant exposure to pollution	Ancillary
Sleep Questionnaire*	Obtain information about sleep quality	Ancillary
Family History*	Collect family history of dementia and stroke/TIA	Ancillary
Cognitive Function Tests**	Obtain measures of cognition function (CASI, Digit Symbol Coding, Digit Span Test) and expanded cognitive testing (UDS and PACC) to permit adjudication of MCI and dementia.	Ancillary
Clinician Physical Exam	Evaluate neurological status	Ancillary
Short Physical Performance Battery	Assess lower extremity functioning	Ancillary
Quick Dementia Rating Scale (QDRS)	Characterize change in cognitive and functional abilities. This test, along with the NACC Functional Assessment and Neuropsychiatric Inventory Questionnaires, is also administered to the participant's proxy.	Ancillary
Spirometry	Measure lung function (including post-bronchodilator spirometry in a subset)	Ancillary
Nasal Brushing	RNA-sequencing and gene expression	Ancillary

Exit Interview	Explain next steps and answer questions and solicit comments about the exam. Discuss referrals. Obtain tracking information. Schedule second visit if needed. Thank participant.	Main
----------------	--	------

*Consent and Questionnaires can be completed by phone, web survey, or in clinic.

**Cognitive function testing can be completed by video, or if necessary, by phone.

Monitoring / Measuring Devices and associated questionnaires

(Applied at Exam 7 clinic visit or at a later home visit)

Heart monitor patch	Worn for 7 days; mailed back to clinic or collected by technician at home visit	Ancillary
Daily Stress questionnaire	Complete each day the heart monitor patch is worn	Ancillary
Continuous Glucose monitor	Worn for up to 14 days; mailed back to clinic or collected by technician at home visit	Ancillary
Participant Diary	Record waking, sleeping, and mealtimes each day that monitors are worn	Ancillary
Wrist sleep actigraphy device	Determine sleep duration and quality. Worn for 8 days; mailed back to clinic or collected by technician at home visit	Ancillary
ActiGraph hip activity monitor	Detect waking behaviors. Worn for 8 days; mailed back to clinic or collected by technician at home visit	Ancillary
24-hour blood pressure monitor	Overlap with one night of wrist sleep monitoring but not with the PSG	Ancillary
Polysomnography device	Apply sensors at home visit; if not possible, a modified device will be mailed or distributed at Exam 7 visit.	Ancillary
Sleep PSG Questionnaire	Obtain information about sleep patterns and quality	Ancillary

Imaging Components

	Purpose	Main or Ancillary
Non-contrast Lung CT	Obtain lung CT scan to study the structure of the lungs.	Ancillary
Brain MRI	Measure brain structure and activity	Ancillary
Brain Amyloid PET Imaging	An optional test that quantifies β -amyloid deposition in the brain. Occurs within 2 weeks of the Exam 7 visit	Ancillary

3.2 Exam 7 Components Descriptions by Ancillary Study:

All participants will undergo the following:

Blood Pressure: Resting blood pressure will be measured in the right arm after five minutes in the seated position. An automated oscillometric method (Dinamap) and appropriate cuff size will be used. Three readings will be taken; the second and third readings will be averaged to obtain the blood pressure levels used in analyses.

Anthropometry: Height and weight will be measured to the nearest 0.1 cm and 0.5 kg respectively. Body mass index (kg/m²) will be used a measure of overall obesity. Girths (neck at about one inch above where the neck meets the shoulders, waist at the umbilicus, and hips at the maximal circumference of buttocks) will be measured to the nearest 0.1 cm using a steel measuring tape (standard 4 oz. tension).

Pulse Oximetry: Resting oxygen saturation will be measured in the seated position. A pulse oximeter with a finger probe will be used. Nail-polish will be removed, if necessary. Oximetry will be measured off supplement

oxygen, if used. For participants who use supplement oxygen, supplement oxygen will be restarted immediately if they are short of breath, or their oxygen saturation drops below 82%.

Laboratory Measurements: Up to 70ml of blood and spot urine will be collected. Core measurements will include a lipid profile, glucose, creatinine, insulin, and HbA1C. White cells may also be cryo-preserved for future generation of cell-lines and isolation of DNA needed for genetic studies.

Questionnaires: Standard questionnaires will be used to collect information about demographics, socioeconomic and psychosocial status, physical function, medical and family history, medication use, dietary and alcohol intake, and smoking.

UDS physical exam and SPPB: Physical exam will assess basic neurological signs and symptoms of stroke and Parkinsonism. The Short Physical Performance Battery will be used to assess lower extremity function.

Arterial Stiffness Measures: Assessment of arterial pulse waves and pulse wave velocity will be performed using a brachial and leg cuff-based approach (with simultaneous, automated recording of the cuff blood pressure) using a Fukuda VaSera and/or SphygmoCor XCEL device.

Cognitive Function Testing: Cognitive testing (CASI, Digit Span, Digit Symbol, UDS v. 3 and PACC) will be performed at Exam 7.

Participants who are enrolled in the MESA Lung Ancillary Study will undergo the following:

Spirometry: Spirometry consists of participants inhaling and exhaling as hard and as fast as they can through the mouth. Participants will also be asked to breathe in and out slowly through the mouth. These actions will be repeated at least three times to ensure valid readings. For in-person clinic visits, a SensorMedics model 1022 rolling-barrel spirometer will be used for all readings, and the procedure will follow American Thoracic Society guidelines. Home visits will use a portable pocket spirometer device. A new mouthpiece will be used for each volunteer. Participants with airflow limitation (prebronchodilator FEV1/FVC ratio <0.70 or <LLN) will receive two inhalations of 90 mcg albuterol via MDI and spacer and will then repeat the spirometry test (“post-bronchodilator spirometry”) for up to an additional 5 minutes. Post-bronchodilator spirometry will only be performed at in-person clinic visits.

Lung function measured by spirometry is a specific, quantifiable marker of obstructive lung disease. It strongly predicts both pulmonary and cardiac events, including incident heart failure. Post-bronchodilator spirometry is necessary to define chronic obstructive pulmonary disease (COPD), the third leading cause of death. Repeat measures over time, as we are doing in MESA Lung, define of progression of lung disease.

Non-contrast Full-Lung CT Scan: Lung density, bronchial wall thickness, and hyperinflation will be measured on non-contrast full-lung CT scan to assess pulmonary emphysema. Experienced and trained technologists will scan the lungs of each consenting subject to obtain an accurate and reproducible assessment of airway anatomy. The technologist will transmit the scans to the CT Reading Center.

Pulmonary emphysema on CT scan is a specific, quantifiable marker for the presence of anatomical pulmonary emphysema. Its presence on CT scan is the contemporary measure of emphysema. Quantitative measures of emphysema on CT scan predict pulmonary and possibly cardiac events and are strongly correlated with left ventricular filling in a pattern that resembles subclinical heart failure with preserved ejection fraction. Repeat measures over time provide a measure of progression of emphysema.

Environmental Exposures Questionnaire: Participants will be asked to complete a respiratory questionnaire in addition to items to ensure safety of spirometry and, if selected, administration of albuterol.

Hair follicle Collection: All participants will be selected for hair follicle collection for an additional 5 minutes. Ten hairs are plucked from the scalp, inserted in a 2ml vial, and frozen at -80C.

Nasal Brushing: All participants will be selected for nasal brushing for an additional 5-10 minutes. A polyester-tipped flexible soft brush is inserted into the participant's nostrils, then rotated 180 degrees and withdrawn. After swabbing, the brush is cut off, the swab is placed in a vial and frozen at -80C.

Participants who are enrolled in the MESA-Mind Ancillary Study will undergo the following:

Brain MRI: MRI data will be acquired in accordance with multisite protocols including ADNI2, and the NINDS Common Data Elements recommendations. All images will be acquired on 3T Siemens scanners with a high resolution 20-channel head/neck coil. Sequences include: T1 and T2 (for morphology), T2 FLAIR (to quantify white matter hyperintensities), DTI (to assess microstructural integrity of the white matter), BOLD/fMRI (for resting state brain connectivity), pseudo-continuous arterial spin labeling (pcASL, for quantification of cerebral blood flow), and susceptibility-weighted Images (SWI). The brain MRI protocol is consistent with the Atrial Fibrillation Study MRI protocol

Amyloid PET Imaging: The subset of study participants who agree to participate in the optional Brain Biomarker Sub study (40%, n=216) will receive amyloid imaging. Amyloid PET brain imaging procedure is similar to those used in Alzheimer's Disease Neuroimaging Initiative (ADNI) and several large multicenter clinical trials and observational studies. Participants will be injected with an intravenous bolus of up to 5-15mCi (370 MBq) (+/- 10%) of Pittsburgh compound B (PiB, over 5-10 seconds), followed by an uptake period of 40 minutes (+/- 10%) as it crosses the blood brain barrier and binds to fibrillar amyloid in the brain. Once the participant is positioned in the PET research scanner (GE 16-slice PET/CT Discovery ST Scanner), brain emission images will be acquired continuously for 30 minutes to quantify amyloid uptake analyzed in over 700 MRI-defined regions. The extent of A β deposition in the brain will be quantified by PiB uptake visualized by PET using standardized uptake volume ratio (SUVR) of 6 primary cortical areas (i.e., anterior cingulate, prefrontal cortex, lateral temporal cortex, posterior parietal cortex, precuneus cortex and anteroventral striatum) relative to the uptake in the cerebellum. The total radiation exposure of the PET scan is 0.347 rems, which includes exposure associated with the head CT completed prior to the PET. Participants will be monitored from the time of tracer injection until after the imaging session is complete for signs of rare adverse events. Participants will also be contacted 24-72 hours after the procedure by telephone to inquire about adverse events.

3.3 Data Collection Forms

All forms will be administered using the REDCap Data Collection system using a tablet PC, unless otherwise noted below.

Form	Form completed by:		Location			Administration			
	Study Staff with participant	Participant without study staff	Clinic Visit	Home Visit	Remote Visit	Study Staff in-person / REDCap	Study Staff by Phone / REDCap	Participant Web Survey	Participant Paper form
<i>Study Tracking Forms</i>									
Clinic Reception*	X		X	X		X			
Participant Tracking	X		X	X		X	X		
Exam 7 Form Completion	X		X	X	X	X			
Exit Report	X		X	X	X	X			
<i>Exam Component Forms</i>									
Anthropometry	X		X	X		X			
Seated BP & Pulse Oximetry	X		X	X		X			
Biosample Collection	X		X	X		X			
Medications	X		X	X		X	X		
Arterial Stiffness	X		X			X			
UDS Physical Exam	X		X			X			
Short Physical Performance Battery	X		X			X			
Cognitive Function Testing Completion	X		X	X	X	X	X		
Neighborhood Questionnaire Completion	X		X	X	X	X	X		
<i>Participant Forms</i>									
Medical History	X	X	X	X	X	X	X	X	X
Personal History	(X)	X	X	X	X	X	(X)	X	X
Neighborhood Questionnaire	X	X	X	X	X	X	X	X	X
Health & Life	(X)	X	X	X	X	X	(X)	X	X
Physical Activity	X	X	X	X	X	X	X	X	X
Sleep Questionnaire	X	(X)	X	X	X	X	X	X	X
Family History	X	X	X	X	X	X	X	X	X
Sleep Study PSG Questionnaire	X	(X)		X		X		X	X
Environmental Exposures	X	X	X	X	X	X	X	X	X
Daily Stress Questionnaire	X	X		X	X		X	X	X
Participant Diary		X		X	X			X	X
Daily Stress Survey		X		X	X		X (or automated phone survey)		
<i>Reading Center and Monitoring Exclusion & Completion Forms</i>									
Spirometry Completion	X		X	X		X	X		

Form	Form completed by:		Location			Administration			
	Study Staff with participant	Participant without study staff	Clinic Visit	Home Visit	Remote Visit	Study Staff in-person / REDCap	Study Staff by Phone / REDCap	Participant Web Survey	Participant Paper form
Brain PET Exclusion	X		X			X			
Brain PET Acquisition	X		X			X			
Brain MRI Exclusion	X		X			X			
Brain MRI Acquisition	X		X			X			
Lung CT Completion	X		X			X			
CGM Completion	X		X	X	X	X	X		
Hip and Wrist Activity Monitors Completion	X		X	X	X	X	X		
Stress Reactivity Study Completion Form	X		X	X	X	X	X		
24H ABPM Home Tracking	X		X	X	X	X	X		
Sleep PSG Tracking	X			X		X			

(x) denotes allowable but less desirable options.

* Procedures performed by clinic staff in preparation for participant visit

Reading Center Investigators completed the following REDCap forms to report alerts and data quality.

- Sleep PSG Quality Summary
- Sleep ABMP Quality Summary
- Sleep Wrist Activity Quality Summary
- Heart Monitor Alerts
- Lung CT Alerts
- MRI Alerts

3.4 Order of Exam Components

The complete examination, including CT and MRI will require between 6-7 hours and can be performed in a single or multiple clinic, phone, and/or remote visits. Every effort should be made to perform all the components of the examination within a *four-week period*. Clinics may vary the exam sequence if needed.

Guidelines for clinic order are listed below. Many elements are left to the discretion of the individual field center.

1. Consent and participant questionnaires may be completed prior to the in-person clinic visit by phone, video visit, or using web surveys or mailed paper forms.
2. Anthropometry, blood pressure, and urine collection are completed while the participant is fasting, immediately following the greeting and informed consent, and before the blood draw.
3. Resting blood pressures should be collected before the blood draw and after the participant has been in the seated position for at least five minutes.
4. The blood draw should be done after an 8-hour fast and before 12:00 noon. Venipuncture should be performed in the fasting state after blood pressure measurement. If a participant comes to the clinic non-fasting, perform exam components that do not require fasting, and schedule the participant for another clinic visit for fasting blood collection.
5. Questionnaires and other exam procedures may be administered at any time during the clinic visit. During the interviews, make every effort to avoid distractions, ensure privacy, and maintain confidentiality for the participant. Do not conduct interviews during the snack or in the waiting area

in the clinic.

6. CT, MRI, and PET imaging are generally scheduled after the clinic exam and questionnaires. Heart Monitor patches, glucose monitors, and actigraphy devices cannot be worn during CT or MRI. CT, MRI, PET, spirometry, and questionnaires do not require fasting.

3.5 Exam Component Selection Requirements and Prioritization

Participants will be scheduled and received in the clinic with the expectation that they will undergo ALL procedures and complete ALL questionnaires for which they are selected. However, for those few participants who are unable to participate fully, the following guidelines should be followed.

Core Exam procedures (blood pressure, anthropometry, medications, phlebotomy) are prioritized above all ancillary study procedures.

MESA Lung components: Participants can complete either spirometry or Lung CT without agreeing to the other.

MESA MIND components: All participants are selected for arterial stiffness measures, SPPB, cognitive function testing, brain MRI, and collection of blood for plasmid biomarkers. None of these procedures require that they were completed at MESA MIND visit A. Those who complete cognitive function testing are eligible for the clinician's physical exam, Family History questionnaire, and informant interview. PET imaging requires either visit A or Exam 7 brain MRI imaging, and it occurs only one time (at either visit A or Exam 7). Completion of past procedures is noted in the Exam 7 REDCap Participant Information Form. Participants with a clinical or research diagnosis of dementia are not selected for PET imaging.

MESA Sleep components: Participants are encouraged to complete the home sleep study, activity monitors, and 24-hour blood pressure monitor. None are requirements for completing other MESA Sleep components.

MESA 24H-ACT components: The hip and wrist activity monitors must be worn together over the same time period.

MESA Stress Reactivity: Participants must agree to complete both the heart monitor patch and the daily stress questionnaire.

MESA Glucose Homeostasis: Participants must agree to complete both the continuous glucose monitor and the participant diary.

4 PREPARING FOR THE EXAM 7 VISIT

4.1 Scheduling

MESA Exam 7 will be scheduled over an 18-month period, beginning May 2022. Participants should be contacted to schedule an Exam 7 visit according to the visit window provided in the Participant Information Form. It may be convenient to schedule the Exam 7 visit during a Follow-up 23 or 24 phone call. Completing the follow-up call prior to the exam visit ensures that we have the most current information on the participant's health status and medical events. In some cases, the exam appointment may be scheduled outside of the follow-up call.

Prepare for the exam visit by reviewing the **Participant Contact History** (a summary of data from the participant's Exam 1–6 visits) and the Exam 7 REDCap Participant Information Form. The Contact History Sheet is available at <https://www.mesa-nhlbi.org/MESAE5Reports/default.aspx>.

Recruitment script:

As you may have learned from the winter newsletter, MESA is doing another exam: number 7! Your long-standing commitment to MESA is invaluable and we are excited to invite you to come back and see us.

The full exam could take up to about 6 hours, but you can choose to do as much or as little of the exam as you want. The exam involves a number of familiar elements like a review of your medical history and medications, measuring your blood pressure, height, and weigh, and a blood draw. You will also have the opportunity to participate in some new research involving small “wearable” devices that measure health and functioning across the entire day.

This exam will continue your wonderful contribution to science and medical research. When would it be most convenient to schedule your visit? [DATE: __/__/____ TIME: __:__ am/pm]

- *If participant indicates unwillingness to schedule a visit right now:* When would be a good time for me to call you back to schedule your visit? [DATE: __/__/____ TIME: __:__ am/pm]
- *If participant indicates inability to travel to clinic:* I understand that it would be hard for you to come to the clinic. If, in the future, we are able to come do portions of the exam at your home, would you be interested? [Y / N]

If participant should be using a legally authorized representative: Because this study visit includes questions about thinking and memory, we are sometimes required by the study's local Institutional Review Board to ensure your understanding of the study and what is expected of you. In some instances, when understanding is not complete, we are required to have a legally authorized representative for the participant sign the consent. Therefore, we request that you identify a friend or family member who you trust and bring them with you to your visit. The person could be a spouse, close relative, best friend, or someone who knows you very well.

Who is this person for you?

Study Informant /LAR Name: _____

Telephone number: _____

Relationship to you: _____

Can they come to the visit with you? _____

Thank you so much for talking with me today. We greatly appreciate your participation in MESA. If you have any questions, please feel free to call us at the clinic at (*clinic telephone number*)

4.2 Optional verbal consent for Exam 7 Questionnaires

Once the exam visit is scheduled, and the participant does not require a LAR for consent (based on MESA MIND Cognitive adjudication or events reporting), participants may give verbal consent to complete questionnaires either by phone, mailed paper forms, or emailed REDCap survey links ahead of their Exam 7 visit. Verbal consent is allowed because the questionnaires are minimal risk and non-invasive. Do not use the verbal consent process if the participant lacks decision-making capacity. The following script must be followed for verbal consent:

Just like the previous MESA Exams that you have completed, Exam 7 includes about one hour of questionnaires about your health and lifestyle, and your home and neighborhood environment. Some of the questions ask about sensitive topics like drug or alcohol use. If you would like to reduce the amount of time that you spend in clinic for your exam, you can choose to complete these questionnaires before you come to the clinic.

The questions can take up to one hour, and you can choose to complete as many or as few as you like. We can complete them over the phone, or I can send you paper forms to complete at home and bring to your clinic visit. I can also send you a web link to complete them on your own using a computer or tablet.

When you come to the clinic for your MESA exam, we will provide additional details and consent information about all Exam 7 procedures. There are a few things I'd like to explain now, before [we start the questionnaires/I send you the questionnaires].

We will keep your MESA record with the records from all of the people who join MESA. We will store all of these records securely. Your address will be 'geocoded' to allow it to be mapped in order to describe your neighborhood. This includes describing stores, hospitals, pollution, nature, and how easy it is to get around in your neighborhood.

Your MESA record does not have your name. We replace your name with a code. We limit who has the key that links codes to names. We will put a copy of your MESA record in databases managed by the NIH. Researchers use these databases to make discoveries about health. The NIH will store your MESA records securely. The NIH only allows the data to be used for health and medical research purposes.

Participating in MESA may be a risk to your privacy. If there is a data breach, someone could see or use your MESA record without permission. There is a chance they could figure out who you are. They could use information from your MESA record against you. It could impact your employment, insurance, or family relationships. Your privacy is very important to us. We will take great care to protect it. We believe the risk to your privacy is low, but it is not zero.

Your decision to completion these questionnaires ahead of the clinic visit does not affect your status as a MESA participant. If you have questions later about the research, or if think you have been harmed by participating in this study, you can contact the [ENTER CONTACT INFORMATION HERE].

Do you voluntarily agree to complete the Exam 7 participant questionnaires before your Exam 7 visit?

Record participant's response: Yes No

Participant name

Typed name of person obtaining consent

Date

MESA Tech/Interviewer ID

If no -> Thank you for your time. We appreciate your participation in MESA! [END]

If Yes Great! *Proceed with questionnaires by phone, or mailing/emailing them to the participant.*

Thank you so much for talking with me today. We greatly appreciate your participation in MESA and we look forward to seeing you at the MESA Clinic. If you have any questions, please feel free to call us at the clinic at (clinic telephone number)

In the Clinic Reception Forms, indicate Yes for “Verbal Consent for Exam 7 Questionnaires.” Complete Personal History, Medical History, Health & Life, Environmental Exposures, Neighborhood Questionnaire, Sleep Questionnaire, COVID-19 Questionnaire.

4.3 ALTERNATIVE VISITS

Some participants may not wish or be unable to come to the clinic for an Exam visit. In this case you can offer a couple of options for Exam 7:

- Home Visit
- Remote Visit
- Phone Visit

Home Visit: A home visit option allows participation for those who are unable or unwilling to come to the clinic. Home visits improve retention rates and provide an additional way to help keep participants connected to MESA. See the Home Visit MOP for specifics.

Remote Visit: The MESA Exam 7 Protocol includes a remote visit option to allow participation for those who are unable or unwilling to come to the clinic and do not want field center technicians to come to their home. Remote visits improve retention rates and provide an additional way to help keep participants connected to MESA. In general, it may take more than one remote visit to complete the examination. See the Remote Visit MOP for specifics.

Phone Visit: If a participant is unable or unwilling to complete a home or remote visit a phone visit may be an option. A phone visit only includes completion of the following:

- Environmental Exposures Questionnaire
- Medical History
- Personal History
- Neighborhood Questionnaire (and Neighborhood Questionnaire Completion form)
- Health and Life
- Sleep Questionnaire

In the Clinic Reception form select Phone Visit. This will activate the appropriate questionnaires. All questions are read to the participant over the phone and data is entered directly into REDCap. If the participant expresses interest in completing more of the Exam then a Clinic, Home or Remote visit can be scheduled.

4.4 COVID-19 screening policy

All participants should be screened for flu-like symptoms and a positive COVID test at:

- the time of scheduling
- the reminder phone call on the day before the visit
- the beginning of the visit.

If they screen positive, visits should be delayed until 14 days after a positive test or the beginning of symptoms, whichever is later, and until they are feeling in their normal health.

This screening is not a substitute for institutionally mandated screenings.

4.5 Pre-visit Reports and Forms

The clinic manager should review the clinic visits scheduled for the following day and check that the necessary materials and equipment are in place and that staff who speak the participants' language are available.

For each participant scheduled for the following day, print the **Contact History Sheet** and have their most recent Follow-up Phone Call forms available.

The Contact Cover Sheet, Contact History Sheet and other relevant documents are created as reports on the MESA website at <https://www.mesa-nhlbi.org/MESA5Reports/default.aspx>. Site-specific usernames and passwords are available from the Coordinating Center at jerryw@uw.edu. Follow-up 23/Exam 7 documents are available under the “Follow-up Reports” section.



After selecting any of “Contact List”, “Tracking”, “Participant Contact History”, or “Contact Log” reports, a screen will open that will allow selection of individual ID numbers or all ID numbers.



Telephone Follow-Up 23: Contact List

[Back to MESA Reports](#)

List follow-up not done only

Click here to enter an expected Followup Date Range

Click here to select individual ID number

Start date:



End date:



The **Contact List** report displays name, IDNO, contact window, FU23 and Exam 7 contact date, phone number, email, and language.

The **Tracking Report** displays everything from the Contact List, plus acoustic, address, secondary contact, and health care providers.

The **Participant Contact History** displays contact information plus the dates and status of all follow-up calls and exams, and brief participant notes.

These reports should be run frequently to ensure that calls are made within their target window and that no participants are missed due to “gaps” between designated “end date” of the previous time the report was run and the designated “start date” for the current run.

Participant that are identified as living in the same residence will have the same contact window assigned.

4.5.1 Administration of Forms

The MESA Exam 7 REDCap Program provides electronic forms that can be completed on a tablet, laptop, or desktop computer. Back-up forms are available as paper Adobe portable document format (PDF) files. The REDCap program is the primary data collection source and printing paper forms in advance of a visit should not be necessary. If the REDCap program or data collection tablet is unavailable, a PDF of the forms is available to print on the MESA website. Data should be directly entered in the REDCap Program and not on paper forms. If an internet connection is not available at the time of the interview, paper forms may be used, but answers will need to be entered into the Exam 7 REDCap program when available. Recording answers on paper forms misses the quality control measures that are programmed in the software (skip patterns, range checks, etc.).

Any patient-specific forms that must be printed should not be printed more than three days in advance to capture changes in eligibility for study components. For each participant, gather all the forms required for a visit, including the informed consent and medical release, and place into the participant’s binder. Make sure their ID matches the binder.

Data entry cannot proceed in the REDCap program without an internet connection. Ensure there is a strong internet connection prior to contacting a participant.

Formatted paper forms are available on the internal MESA website at <https://www.mesa-nhlbi.org/MesaInternal/ClinicForms.aspx>. Do not print forms directly from REDCap as they do not indicate skip patterns and they are not formatted for participant use.

All questions must be answered (all fields completed), as specified on the forms. Be concise, however, avoid using abbreviations and symbols. Indicate “refused” for any questions unanswered. When the participant is not sure of an answer, they should use a “best estimate” rather than not answer the question.

Study staff are responsible for reviewing all the completed forms at the respective visits when recording data.

At the time of data entry, the study staff username will be automatically recorded for each form in the REDCap program. Review all forms for accuracy and completeness as they are entered in the REDCap program. If errors are found while reviewing the forms, the error should be updated directly in the REDCap program.

See section 11 for instructions on using the Exam 7 REDCap Data Collection Program.

4.5.2 Call Log Form

Use the Call log form to track the outcome of attempts to schedule the Exam 7 visit. Each time a call attempt is made, enter the date and call status in the Call Log Form. If unable to reach the participant, use the “Unable reason” drop down menu to select a reason.

The Call log displays a warning at the top of the screen if the participant requires a legally authorized representative for consent.

Call Log

Data Access Group: **9 Test**

Editing existing MESA ID **9900005**.

MESA ID 9900005

Interviewer ID * must provide value

Requires LAR for Consent

Preferred language English Spanish Chinese reset

Interested in Home Visit Yes No reset

Call Date:	Call Status:	Unable Reason:
1) <input type="text" value="06-25-2022 14:21"/> <small>Now M-D-Y H:M</small>	<input type="text" value="Scheduled exam"/>	
2) <input type="text"/> <small>Now M-D-Y H:M</small>	<input type="text" value="Refused exam"/>	
3) <input type="text"/> <small>Now M-D-Y H:M</small>	<input type="text" value="Scheduled exam"/>	
4) <input type="text"/> <small>Now M-D-Y H:M</small>	<input type="text" value="Arranged a call back time"/>	
5) <input type="text"/>	<input type="text" value="Left a message"/>	
6) <input type="text"/>	<input type="text" value="No answer"/>	
7) <input type="text"/>	<input type="text" value="Deceased"/>	
8) <input type="text"/>	<input type="text" value="Unable"/>	
9) <input type="text"/>	<input type="text" value="Participant returned call"/>	
10) <input type="text"/>	<input type="text" value="Cancelled Exam"/>	

Exam 7 scheduled date: M-D-Y

Exam 7 scheduled time: H:M

Select “Now” to enter a timestamp of the current day and time. You can also select the date and time by clicking on the calendar and clock icons.

Editing existing MESA ID 9900002

MESA ID

Interviewer ID
* must provide value

Call Date:

1) 01-29-2021 13:24 [Now] M-D-Y H:M

2) [Now] M-D-Y H:M

3) [Now] M-D-Y H:M

Editing existing MESA ID 9900002

MESA ID

Interviewer ID
* must provide value

Call Date:

1) [Now] M-D-Y H:M

2) Jan 2021 [Now] M

3) [Calendar view showing date selection]

For [Time picker: 13:21]

Cor [Time picker: 13:21]

Hour [Slider]

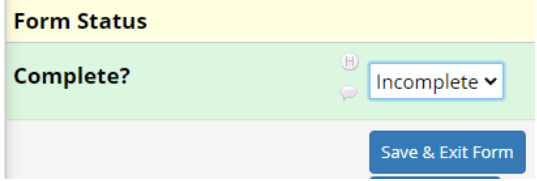
Minute [Slider]

[Now] [Done]

If the participant is unable or unwilling to come to the clinic for an exam, ask if they would be willing to have a home or remote exam instead. Record the response in the Call Log.

For each call attempt, select the outcome or “Call Status.”

<u>Final Call Status Codes</u>	<u>Form Status</u>
<p>Refused exam: Use this option as a final outcome when the participant refuses to complete Exam 7. If they cannot complete it now but would be willing to in the future, select “Arranged a call back time.”</p>	<p>After coding the call status, select “Complete” for the form status and then save and exit the form. The record status dashboard will display the form as green for “complete,” indicating that no further action is needed.</p>
<p>Scheduled exam: Use this option when a visit date has been set. Note that more than one exam can be scheduled in the log.</p>	
<p>Unable: Select the reason for unable to complete exam from the drop down list.</p>	
<p>Deceased: If deceased, update the participant status code in the MESA Participant Management EDC programs.</p>	
Attempted Call Status Codes	Form Status

<p>Arranged a call-back time: Use this option if the participant cannot schedule the exam now and they are willing to do so in the future.</p>	<p>After coding the call status, select “Incomplete” for the form status and then save and exit the form. The record status dashboard will display the form as red for “Incomplete,” offering a visual cue that additional action is needed.</p>
<p>Left a message</p>	
<p>No answer</p>	 <p>The screenshot shows a 'Form Status' section with a dropdown menu labeled 'Complete?' where 'Incomplete' is selected. Below it is a blue button labeled 'Save & Exit Form'.</p>

4.5.3 Participant Information Form

The information in this form is prefilled from data entered in the CC MESA database. It is for reference only. If edits are needed, contact the MESA CC.

Review the Participant Information Form. It will include participant ID, name, acrostic, birth date, QC ID, language spoken, Exam 7 visit window, and any procedures for which the participant has been excluded.

The data used to inform skip patterns in the Exam 7 Forms and notes from previous exams are also displayed here. Information cannot be edited within this form.

4.5.4 Exam 7 Notes Form

Enter notes from Exam 7 in this form. This text will be available in the Participant Information Form for the next follow-up phone call or exam.

4.6 Instruction to Participants before the Clinic Visit

Mail instructions to the participant 7–10 days before the clinic visit. Make a reminder call to the participant the day before the clinic visit and reiterate the instructions. If the participant is acutely ill (e.g., fever, COVID, “flu” bronchitis, etc.) or has had a positive COVID test when you make the reminder call, tell them not to come to the clinic. If they screen positive for COVID, visits should be delayed until 14 days after a positive test or the beginning of symptoms, whichever is later, and until they are feeling in their normal health. Locally institutions may have additional screening requirements for COVID.

Before the examination, make sure the participants understand the following instructions.

7. Participants must fast (except water) for at least 8 hours before the examination. Instruct them to have dinner at least 8 hours before their scheduled exam, and take their medications as prescribed in the morning. Please see note about diabetes medications in section 4.6.
8. Only water and prescription medications are permitted for 8 hours before the start of the exam. Participants should avoid heavy exercise for 12 hours before the visit.
9. Participants should not smoke on the morning of the visit.
10. Participants should remove nail polish or acrylic nails for pulse oximetry, and not have any metal in their hair (hair clips, hair pins) for brain MRI.
11. Participants should bring all current medications, both prescription and over the counter, including vitamin preparations, dietary supplements, injectable medicines such as insulin, inhalers, patches, and herbal remedies to the clinic. If the participant forgets to bring the medications, schedule another clinic visit to obtain this information or collect the information when the participant returns for imaging procedures.

12. Participants should bring the name and complete address of their health care providers, particularly if they wish to have examination results sent to that provider. They should also bring the current contact information for their Study Informant and alternative contacts.

4.7 Set up Participant Supplies

Set up vacutainer and aliquoting tubes for the basic Exam 7 on the racks and attach the pre-printed labels to the tubes. Place any additional pre-printed labels near the racks to be affixed the next day once consent for the related procedures has been obtained. Place all phlebotomy supplies on the blood drawing table (21g needle, luer adaptor, vacutainer barrel, tourniquet, alcohol pad, gauze 2x2, surgical tape, Band-Aid).

Make sure that the examination rooms are clean and have clean linen.

Prepare the participants' gowns (or scrubs) and slippers.

Prepare the examination room for seated blood pressure, anthropometry measurement, etc. Check all instruments that will be used for the examination.

Make sure a snack will be available for the participants.

Prepare information packets and return mailers for home monitors. Ensure that monitors are charged and ready for deployment.

4.8 Staffing

Prepare staff assignment sheets and make sure everyone knows their responsibilities. This is particularly important if you schedule several participants on a given day. Ensure that staff who speak the participants' language are available. The Participant Information Form in the Exam 7 REDCap Program includes the participant's language preference.

If participants have been scheduled for CT, MRI, or PET make sure that the respective technicians have the participant schedule and forms, and that the scanning centers are ready to receive the participants.

4.9 Guidelines for Examination of Diabetic Participants

Diet-controlled diabetics must fast overnight and are treated the same as non-diabetics.

Diabetics taking oral hypoglycemic medications or insulin must fast after midnight (unless a bedtime snack was prescribed by their physician) and come to the clinic without taking their hypoglycemic medication. They should bring their morning medication dose with them to the clinic. Schedule all known diabetics taking oral hypoglycemic medications or insulin for examination as early as possible (before 9 a.m.). Draw fasting blood samples promptly on arrival at the clinic (after measuring blood pressure). Immediately following venipuncture, serve breakfast and instruct participants to take hypoglycemic medication as prescribed.

5 Participant Reception and Consent

The Check-In and Reception process is the first thing the participant experiences upon arrival and sets the tone for the entire visit. The clinic reception process is important in setting the participant's frame of mind for the rest of the exam day. Greet each participant warmly as soon as they arrive at the clinic.

If a participant arrives at the clinic acutely ill (e.g., COVID-19, "flu" or bronchitis), do not continue with the clinic examination. Plan to contact them to reschedule the appointment after they have recovered.

5.1 Consent Procedures

The informed consent process is the cornerstone of ensuring safe and ethical implementation of the MESA. Informed consent is the primary process through which MESA procedures, risks, and benefits will be fully disclosed to potential participants and through which potential participants will choose whether to take part in the MESA Exam 7. This process will involve exchanges of information between participants, study staff, investigators, and other trusted advisors (such as a family member or legally authorized representative (LAR)), in the participant's language of choice (English, Spanish, or Chinese). Throughout the process, participants will be encouraged to ask questions of study staff and investigators.

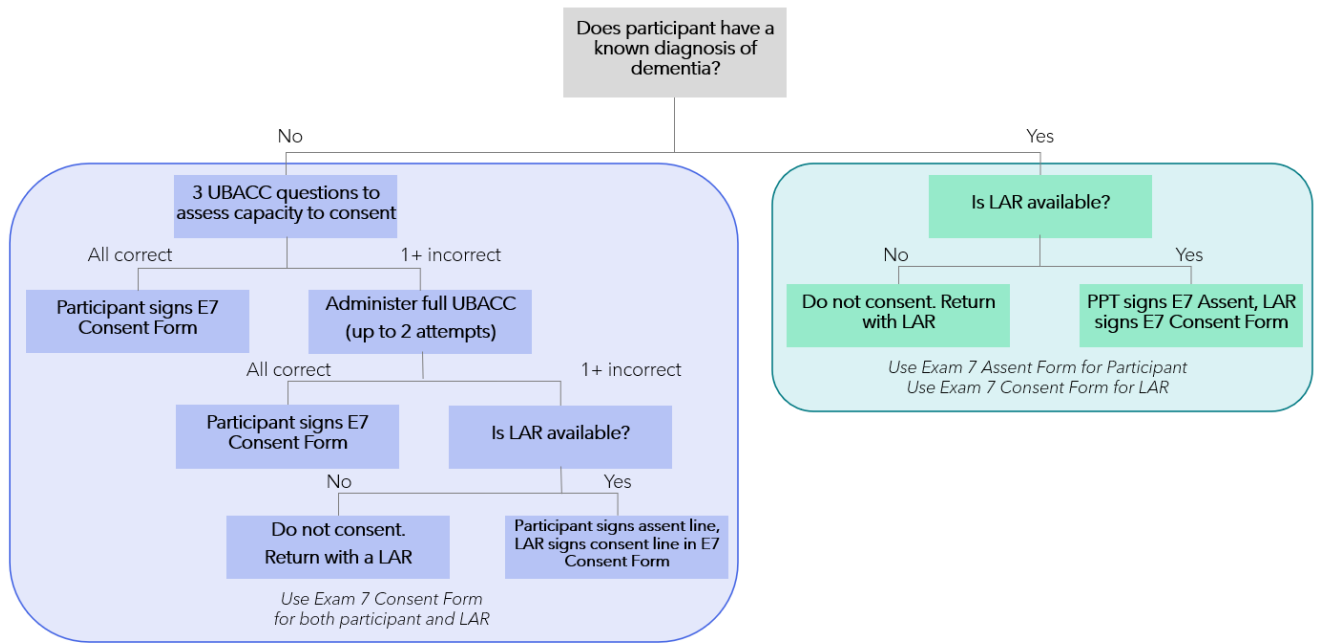
A trained Study Coordinator will be primarily responsible for providing a complete overview of the MESA Exam 7 protocol. This overview will include all elements of the protocol relevant to the individual participant including a general description of the exam procedures, the general risks and benefits associated with exam procedures, data and biosample collection, collection and use of genetic information, plans for continued long-term follow-up, and overall study risks and benefits. As part of this process, the Study Coordinator will review the entire written informed consent form with the participant and if applicable, their LAR.

The consent process can occur either in-person or via phone or video chat. The signed consent form must be received (via secure email, fax, regular mail, or any HIPAA-compliant procedure) by the RS before any study procedures, including questionnaires, can begin. IRB-approved, written informed consent will be required of all MESA study participants. Spanish and Chinese-speaking participants must review and sign an IRB-approved translated consent form. Participants and if applicable, their LAR will sign and date the consent form indicating their understanding and willingness to participate. Study activities will commence only after written informed consent is obtained. Documentation of consent process activities and participant's understanding is recorded in the Exam 7 REDCap Program.

The participant should be given a copy of the informed consent forms after they are signed and dated. Even though participants are free to withdraw from the study at any time, the consent form spells out our obligations to the participant and the participant's obligations to the study while they are a subject. Participants should be encouraged to keep the consent/assent forms. The consent forms contain useful information about the study, which participants may want to review from time to time. After the participant has signed the consent form, forward the consent form to the Principal Investigator for their signature.

The informed consent process should occur in a private setting where participants can freely ask questions without being overheard by others in the clinic. If extraneous parties (other than the participant's Legally Authorized Representative [LAR], if present) can hear the conversation, participants may be reluctant to ask appropriate questions. To avoid pressuring the participant, only one person associated with the study should be present when the participant reviews the informed consent form (ICF). If a second witness is required, they should be as unobtrusive and non-committal as the situation permits.

The following figure describes the steps for choosing the appropriate consent/assent process for the participant.



5.1.1 Consent for Participants without cognitive impairment

Forms: Exam 7 Consent Form, UBACC Questionnaire

Instruct the participant to read the ICF carefully. Ask the participant if they have any questions. After answering all questions, assess the participant’s capacity to consent by administering the first 3 questions from the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC) form (See section 6.2).

The University of California, San Diego Brief Assessment of Capacity to Consent form is a way for staff to identify those individuals who may be having some cognitive issues or individuals with diminished mental capacity. When administering the UBACC, it is acceptable for the participant to refer to the ICF.

If the participant answers the first 3 the items correctly, finish completing the consent form. If the answers any of the first 3 questions incorrectly, wait for a moment and re-administer the questions the participant missed (up to a total of three administrations at one sitting). If the response to any of these three questions is unacceptable, continue administering the full set of UBACC questions. If the participant answers all questions correctly, obtain consent from the participant using the Exam 7 Consent form. If any of the UBACC questions are not answered correctly, collect consent from a legally authorized representative (LAR) **and** assent from the participant, with both signatures collected on the Exam 7 Consent Form (do not use the separate Exam 7 Assent Form). If they fail the full UBACC and do not have an LAR present, they are sent home and asked to return with an LAR.

The outcome of UBACC screening is recorded in the Clinic Reception Form.

The Field Center PI may select which questions are to be asked. If Field Center staff feel that the participant’s ability to consent may be impaired, obtain consent from a legally authorized representative (LAR) **and** assent from the participant using the Exam 7 Consent form.

5.1.2 Consent for Participants with known cognitive impairment

Forms: Exam 7 Consent Form, Exam 7 Assent Form

Participants with a known cognitive impairment must bring an LAR to the MESA clinic visit. These participants will review and sign the MESA Assent Form and their LAR will review and sign the MESA Exam 7 Consent Form. Do not administer the UBACC questions to these participants.

Lack of capacity to consent is defined as:

- 1) Had to have an LAR at MESA Mind Visit A

- 2) Were adjudicated with probable dementia at Visit A (2-3% of cohort)
- 3) Have a clinical diagnosis of dementia

This information will be provided in the Contact History Report on the MESA website and in the Participant Information Form in the MESA Exam 7 REDCap program as “LAR required for consent.” Do not tell participants that they have a diagnosis of dementia. That label is not used in the cognitive adjudication results letters, and it could be upsetting to participants.

For LAR consent, the study team is required to go section by section reviewing the entire consent. Ask questions to ensure the LAR understands what was discussed and ask them to return the information (to confirm they understand); Encourage the LAR to ask any and as many questions as they have about the study and process.

A Legally Authorized Representative is legally allowed to consent for a patient when the patient temporarily or permanently lacks the capacity to consent on their own. Check with the IRB for acceptable definitions of LAR in your state.

5.2 Clinic Reception

PURPOSE

The Clinic Reception process is the means by which important information is collected as soon as the participant arrives. The participant’s consent status must be recorded in REDCap before any procedures can be performed.

DEFINITIONS

- Exclusion criteria: A list of medical conditions, procedures, events, and medications that exclude participation in the study or specific exam components.
- Acrostic: A code used instead of the name for confidentiality reasons. It is composed of the first four letters of the last name, the first two letters of the first name, and gender indicator (F/M).

METHODS

General Instructions

Once the participant and LAR (if necessary) have completed, signed and dated the informed consent and/or assent form, the specific consent components are entered in the Clinic Reception Form (this can be done while participant changes clothes). Following this, the procedures to be performed will be appropriately selected in REDCap and the clinic visit will begin.

After you have answered any questions, give the participant a gown (or robe) and slippers and take them to a dressing room to change. Provide a locker or other safe place for the participant’s clothing and any other items that need to be stored.

Specific Instructions

The Clinic Reception Form will first ask if the visit is “In Clinic”, “Home”, “Remote” or “Phone”. Selection of the appropriate type of visit will make the relevant REDCap forms available for this participant.

Ask the participant when they last ate or drank. Record the information in military (24:00 hours) time. Record the time, again in military time, when this form is being completed. The computer will calculate and display the amount of time elapsed since the participant last ate or drank.

Ask if the participant has been ill in the last seven days (e.g., cold, flu, fever, vomiting.) If the participant responds “Yes,” inform the participant that the clinic exam cannot be completed at this time, thank them and reschedule another visit.

The Visit Date and check in time will automatically be filled with the current date and time; if the actual visit took place on a different date, this field may be changed. If applicable, a second appointment date for Exam 7 should be entered in the screen. If the second appointment cannot be scheduled at this time, a clinic staff person should go back and enter the second appointment date as soon as the information is available.

The outcome of UBACC capacity to consent screening questions are recorded to determine the procedures to follow for consent, as described in section 5.1.

Associated permissions (HIPAA consent, medical records release, etc.) should be completed on this screen.

Note about the HIPAA Release Form: HIPAA forms are needed for making medical records requests (during clinical events surveillance and ascertainment). Hospital records departments require a copy of the form (the more recent the better) before they will provide the requested medical records. Because a recent HIPAA form is best when requesting medical records, Field Centers often request a new one each time the participant comes into clinic.

HIPAA consent applies only to medical records release (as a requirement of the hospital providing the medical records) and does not limit or otherwise inform concerning participation in any other aspect of MESA. Participants sign the consent form (specific to a study exam) prior to each clinic exam. When they sign that consent form, they are agreeing to participate in the study as defined in that document. That document is necessary and sufficient for participation in the activities it describes and no other document (or failure to sign some other document) would be allowed to supersede the consent (including the HIPAA consent form).

Complete the information about Exam 7 Consent. Once the participant has signed the consent, click “Yes” and additional items will be displayed on the screen.

Indicate participant consent for any ancillary study components for which they have been selected. On this form, also indicate other permissions related to sharing of data and samples.

In the Local Medial/Hospital Identification Number field, record the participant’s local hospital or medical record number (if any). This number is not required, however.

Once all consent responses have been entered, the remaining forms for the visit forms will be available. Note that forms in REDCap are displayed based on the type of visit (Clinic, Home, Remote, Phone) and the consent responses entered in the Clinic Reception form. For example if the response to brain MRI consent is “no” in the Clinic Reception form, the brain MRI Exclusion and Acquisition forms cannot be completed.

For participants selected to have CT, and/or MRI and/or PET in Exam 7, schedule the additional visits and prepare appointment reminders to give to the participant on exit. Record the date and time for the appointment(s) in the appropriate field on the form.

Specific Instructions

1. Print the Phlebotomy sheet and give/send to phlebotomist immediately.
2. To enter the data for a given procedure, click on that procedure on the Check-off screen; the selected computer form will open and will be ready for data entry.
3. Visit day progress order should be as shown on the screen for the first five steps/procedures. The remainder of the procedures could be performed in any order, but any home monitors must be applied after any scans performed that day.

5.3 REDCap Record Status Dashboard

This dashboard displays the forms and form completion status for all participants. You can select an individual form to complete or select the ID number to go to the Record Home Page. The Record Status Dashboard is the means to ensure that all parts of Exam 7 are completed.

Displaying: Instrument status only | [Lock status only](#) | [All status types](#)

MESA ID	Participant Information	Study Group Assignment	Exam 7 Notes	Call Log	Clinic Reception	Anthropometry	Environmental Exposures Questionnaire	Medical History	Personal History	Ne
3900001	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900002	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900003	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900004	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900005	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900006	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900007	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3900008	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

All Exam 7 forms for which the participant was selected and gave consent, will be displayed on this screen to allow for the tracking of the participant’s progress through Exam 7.

5.4 Post Exam Activities

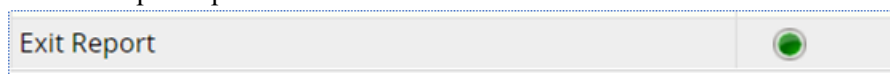
When the participant has finished the exam, check the list of forms to be sure all are complete. If there are forms or procedures remaining, schedule a second visit to complete the exam.

Make sure to schedule dates for the participant’s CT, PET, and/or MRI, examinations, if appropriate.

For participants selected to have CT, and/or MRI and/or PET in Exam 7, schedule the additional visits and prepare appointment reminders to give to the participant on exit.

5.4.1 Print and provide the Exit Report.

Exit reports are printed from the Exam 7 REDCap program at the end of the clinic visit. The letter is generated from data entered in the Anthropometry and Seated Blood Pressure Forms. You can access the form “Exit Report” from a participant’s list of instruments/forms. It will be the last item listed on a participant’s list of forms:



Open “Exit Report”

From the web browser, print the Exit Report for the participant.

Ask the participant if they have any questions at exam exit time. After you have answered any questions, thank the participant.

This concludes the clinic visit day for the participant.

6 PARTICIPANT QUESTIONNAIRES

6.1 Guidelines and Techniques for Successful Interviews

MESA exams are conducted at six Field Centers located throughout the United States, in three languages. In

order to produce data that can be analyzed across exams and compared with other studies, MESA has designed standardized approaches to train interviewers and collect information about participants. Standardization is achieved by creating centralized training procedures, participant scripts, accessing interviewer certification, and observing interviewers in the field.

Good interview technique aims to prevent interviewer bias, the preference or inclination that creates a systematic difference between responses obtained by different interviewers. It can be affected by either the interviewer or participant perception of each other, and their reactions to that perception.

Interviewers should start by reading the sections in this manual for the questionnaires they will be administering.

When completing the participant interview forms, clarify any participant responses that are unclear or incomplete. Ask the participant to elaborate or reconsider an incomplete or inappropriate answer without leading the participant or influencing the content of the answer to avoid creating a biased response.

Some questions addressed in the forms are personal and may be considered sensitive by the participant. When a participant shows reluctance in answering a question, reassure the participant regarding the confidentiality of the response and explain the importance of the question.

Skills for Successful Interviews

- Ask questions at using a clear, even pace and a conversational tone.
- Develop a thorough knowledge of the questions and response categories (this will keep the interview flowing smoothly).
- Understand how and when to use probes to clarify unclear responses.
- Think as an interviewer and temporarily put aside other roles (e.g., researcher, health care provider).
- Maintain a friendly but professional atmosphere.
- Keep the interview focused and on task.
- Accurately record responses directly into the Exam 7 REDCap program

The following procedures are recommended for a successful interview:

1. Prior to the visit prepare all materials necessary for the interview (e.g., appropriate reports, stamped self-addressed envelopes, response card flipbooks).
2. Find an area where both you and the participant can talk and use the computer comfortably with minimal distractions.
3. Make sure that the participant understands the questions and that you are interpreting the responses accurately. Do this by restating what you think the participant is telling you. At the same time, be careful not to impose your interpretations on the interview questions or the participant's comments.
4. Convey your interest in the participant's thoughts and feelings but do your best to keep them focused on the interview questions. When the participant strays from a question, try to use what they are saying to redirect the conversation back to the interview questions. Give positive reinforcement for direct answers. If necessary, set time limits at the outset of the interview to encourage the participant to stay on track.
5. Participants may try to convince you to answer certain questions for them. Let the participants know that you are interested in their answers.
6. Be aware of any hearing and vision impairments and their effects on the participant's understanding of the interview questions. If necessary, read the interview questions to participants who have visual impairments or limited reading ability.

7. Encourage, but do not force, participants to answer all questions.
8. If non-participants are present during the visit, address the participant directly and do not encourage conversation with other parties. If necessary, ask that you and the participant be left alone for a brief time to complete the questionnaire.
9. Be able to adapt to interruptions. Let the participant know that you are willing to continue the interview after the interruptions are completed.
10. Make the interview a positive experience for the participant. React favorably to answers and give compliments when appropriate.

6.2 University of California, San Diego Brief Assessment of Capacity to Consent (UBACC)

Purpose

The University of California, San Diego Brief Assessment of Capacity to Consent Questionnaire is a way for staff to identify individuals who may be having some cognitive issues or individuals with diminished mental capacity. The UBACC serves 2 purposes: (1) documenting for each participant that they manifested at least a basic level of comprehension of the study protocol prior to consent, and (2) screening for participants who may lack adequate capacity to consent.

Methods

This assessment of participants' capacity is administered verbally prior to obtaining consent signatures. Administer questions 1, 2, and 3 to all participants who do not have a known dementia diagnosis. If the response to any of these three questions is unacceptable, continue with administering the full set of UBACC questions. If the participant does not receive a perfect score on the full set, the incorrect questions may be re-administered for a total of 3 trials at one sitting. The participant is allowed to refer to the consent form. If the participant does not pass the UBACC, obtain consent from a legally authorized representative (LAR) and assent from the participant, both within the Exam 7 Consent Form. Do not use the separate Exam 7 Assent Form. If they have no LAR with them, participants are sent home but can try again at a later date.

When administering the UBACC, it is acceptable for the participant to refer to the ICF. Do not administer the UBACC to a participant with a known cognitive impairment, including:

1. Participants who had a LAR at MIND Visit A
2. Those with adjudicated probably dementia at Visit A
3. Those with a clinical diagnosis of dementia.

General Instructions

Instruct the participant to read the ICF carefully. Ask the participant if they have any questions. After answering all questions, assess the participant's capacity to consent by administering the first 3 questions from the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC) form.

If the participant answers the first 3 the items correctly, finish completing the consent form. If the answers any of the first 3 questions incorrectly, wait for a moment and re-administer the questions the participant missed (up to a total of three administrations at one sitting). If the response to any of these three questions is unacceptable, continue administering the full set of UBACC questions. If the participant answers all questions correctly, obtain consent from the participant using the Exam 7 Consent form. If any of the UBACC questions are not answered correctly, collect consent from a legally authorized representative (LAR) **and** assent from the participant, with both signatures collected on the Exam 7 Consent Form (do not use the separate Exam 7 Assent Form). If they fail the full UBACC and do not have a LAR present, they are sent home and asked to return with an LAR.

If Field Center staff feel that the participant's ability to consent may be impaired, obtain consent from a legally authorized representative (LAR) **and** assent from the participant using the Exam 7 Consent form.

After the participant has reviewed the consent form in detail, the explains that you will ask a few brief questions about the study. Participants should have a copy of the Exam 7 Consent Form that they can refer to when answering the UBACC questions. At the same time, comprehension is not synonymous with the ability to read the words on a consent form. Therefore, it is important that the participants be encouraged to explain the information relevant to each item in their own words to ensure that their responses reflect genuine comprehension, not merely an ability to read or repeat the consent text.

A low score on the UBACC should indicate difficulty with understanding, appreciation, or reasoning about information related to a study protocol and not difficulty understanding the questions on the UBACC itself. When a participant seems to be having difficulty understanding the wording of a UBACC question, attempt to rephrase the question in language appropriate to the individual (if a participant requires frequent rephrasing, this should be noted on the UBACC form).

Scoring

Each item is scored as 0 or 1 point, with 0 reflecting an incapable response and 1 indicating a clearly capable response. Total scores can thus range from 0 to 8. Participants who receive a score of less than 8 require a LAR to sign the Exam 7 consent form. Research staff should be familiar with the study protocol and with the UBACC scoring before they administer the scale. In the event of uncertainty in scoring, probe the participant to collect as much information as possible and discuss these items with the principal investigator for an appropriate score.

Specific Instructions

All participants without known cognitive impairment will complete the first three questions of the UBACC. The participant can review the Exam 7 Informed Consent Form as they provide answers.

1. **What is the purpose of MESA Exam 7 that was just described to you?** Score 1 point if the participant provides an appropriate answer, or 0 points if they do not.
2. **Do you have to participate in this exam if you don't want to?** Score 1 point if the participant responds "No" and 0 points if they respond "Yes."
3. **Please describe 2 things that will happen in this exam.** Score 1 point if the participant provides an appropriate answer, or 0 points if they do not.

If 3 points are scored, the UBACC Questionnaire is complete, and the participant may sign the Exam 7 Informed Consent Form.

If the response to any of these three questions is unacceptable, continue with administering the full set of UBACC questions.

4. **Is this study designed to improve your health?** Score 1 point if the participant responds "No" and 0 points if they respond "Yes."
5. **Please describe 2 risks or discomforts that people may experience if they participate in this exam.** Score 1 point if the participant provides an appropriate answer, or 0 points if they do not.
6. **Is it possible that participating in this exam won't have any benefit to you?** Score 1 point if the participant responds "Yes" and 0 points if they respond "No."
7. **Who will pay for your medical care if you are injured as a direct result of participating in this exam?** Score 1 point if the participant responds, "the institution or the hospital" and 0 points if they provide a different response.
8. **Where can people find the phone numbers of the people to contact if they have questions?** Score 1 point if the participant responds, "in the consent form" and 0 points if they provide a different response.

If the participant does not receive a perfect score on any question, the incorrect questions may be re-administered for a total of 3 trials at one sitting. The participant is allowed to refer to the consent form to find the correct answer. The outcome of UBACC screening is recorded in the Clinic Reception Form.

If the participant does not pass the UBACC, obtain consent from a legally authorized representative (LAR) and assent from the participant. If they have no LAR with them, participants are sent home but can try again later.

6.3 Participant Tracking

PURPOSE

The Participant Tracking Form used to review and update the participant's contact information, including the name, address, telephone number, and email address) on the participant, their health care provider(s), and any proxies or contacts they may designate. At Exam 7, this information will be reviewed and updated with any changes since the most recent follow-up contact.

Participant tracking is typically administered as part of the follow-up interview process. It should also be reviewed during the clinic exam.

MATERIALS

The participant's personal address book or contact list, a phone book, will all be useful in helping participants find and record the information asked for during this process.

DEFINITIONS

Proxy. A person designated by the participant who can answer health-related questions about the participant, if they are unable to answer. A proxy may, but does not have to, live with the participant and should be familiar with the status of the participant's health.

Contact. A person designated by the participant who can provide contact information if the participant does not respond MESA calls or letters. A contact does not live with the participant but knows how to get in touch with them.

METHODS

General instructions

The participant's current contact information is pre-populated in the Participant Tracking Form.

Current information is essential for maintaining contact with participants and for communicating with their contacts and health care providers. Verify that the information is correct or update the record with any changes reported by the participant. Emphasize to the participants that the tracking form needs to be updated as completely and accurately as possible. Encourage participants to designate as proxies *only* those people familiar with their health status, because the proxy will be asked to answer health-related questions if the participant is unable to.

Verify that this information is correct or update the record with any changes reported by the participant. This information will be used to update the MESA study database for future clinic visits and/or follow-up contacts. The participant should not use a nickname in place of a full, legal name. Boxes/spaces for items of information that are not applicable should be left blank. Obtain missing information over the phone.

Specific Instructions:

Start by entering the Participant Tracking Date

6.3.1 Section A: Participant Information:

Begin with, *Please VERIFY your name, address, telephone number(s), and email address (if you have one)*. Note any changes in the text fields in the electronic form.

Read the provided home address and update as necessary. If a new address is given, record the month and year of the move.

If the MESA CC has sent mail to this address previously and it was returned as invalid, "MESA mail returned Verify address" will be marked as "Verify." Make a special attempt to update these addresses.

Verify if the address is a street address (when the residence is physically located) or a mailing address (an address where they receive mail but not where they physically reside). If the given address is both a primary and street address, mark it as the street address. A separate mailing address is only added if it differs from the street address.

Indicate if the primary mailing address is outside the United States.

May we contact you by email or text? Inquire if the participant would like to receive text or email messages from MESA coordinators for visit or phone call reminders. Check all that apply.

6.3.2 Section B: Secondary Residence:

Do you have a secondary residence?

Record the address of any secondary residence where a participant spends more than 4 weeks per year. The 4 weeks do not need to be consecutive. Then record the month and year that the participant began using their secondary residence.

6.3.3 Section C: Contacts Information:

You previously provided us with information about friends or relatives who you are likely to keep in touch with, but who do not live with you, and who are not planning to move any time soon. Can you please tell me if the following information is still correct?

Read Contact names, relationship to participant, address, phone numbers, e-mail address from “Item C” of the form. If less than 3 secondary contacts are provided, ask for a minimum of 3.

Any new contacts can be added to the data entry fields at the end of section C.

Relationship to Participant		<input type="text"/>
Contact phone numbers:		
Home	<input type="text"/>	
Work	<input type="text"/>	
Cell	<input type="text"/>	
Email	<input type="text"/>	
Address	<input type="text"/>	
City	<input type="text"/>	
State	<input type="text"/>	
Zip	<input type="text"/>	

The participant should provide as much information as possible. Assist them, if necessary, in obtaining information. Record any changes regarding ‘contacts’ in the lines to the right of that particular ‘contact’.

If a ‘contact’ was used to obtain the information on this form, the interviewer should check the appropriate box under the name of the ‘contact’ person.

If the ‘contact’ used to obtain the information on this form is not listed among the current contacts, ask the ‘contact’ for their name, relationship to the participant, complete address, and telephone number. Fill the information in the spaces provided at the end of section B.

Encourage the participant to list contacts that do not all live at one address to obtain at least one contact that might be available if an entire family/household moves away.

If the participant consented to Cognitive Function Testing, use this script to collect contact information for the MESA MIND Study Informant:

In the previous exam, you were asked to identify one or two people who know you well (spouse, children, other relative, or friend), referred to as a “Study Informant,” who is willing to either (1) attend the visit with you or (2) receive a phone call from our team. Your “Study Informant” will talk with us about recent changes in your health status and answer questions about your memory, thinking, and functional abilities. The “Study Informant” phone call will take 15 minutes to complete.

Which of your MESA Contacts would you like us to contact as your Study Informant?

If they are not already listed, add them as a MESA Contact.

Select the chosen contact as the MESA MIND Study informant, or if the participant refuses to allow MESA to contact a study informant, select “Do not speak to my contacts about my health status.”

6.3.4 Section D: Health Care Providers Information:

You previously provided us with information about your personal physician or health care provider. Can you please tell me if the following information is still correct?

Read participant's health care provider name, business address, and telephone numbers on the form.

New Health care provider	
Do you have any new health care provider that you would like to add?	
Health care provider first name	<input type="text"/>
Health care provider last name	<input type="text"/>
Health care provider title (MD, PA, etc.)	<input type="text"/>
Health care provider place of business (name of clinic or hospital)	<input type="text"/>
Address	<input type="text"/>
City	<input type="text"/>
State	<input type="text"/> <input type="button" value="v"/>
Zip	<input type="text"/>
Health care provider phone	<input type="text"/>
Send participant's results to this person	<input type="radio"/> Yes <input type="radio"/> No

reset

If information is not correct, type any changes on the right side of the page.

When finished, update the Form Status to “Complete.” Click “Save & Go to Next Form” or return to the Record Home Page by selecting “Save & Exit Form.”

If the participant does not have a health care provider, the form is complete. Thank the participant.

Form Status	
Complete?	<input type="text" value="Complete"/>
<input type="button" value="Save & Exit Form"/>	<input type="button" value="Save & ..."/>
<input type="button" value="-- Cancel --"/>	<ul style="list-style-type: none">Save & StaySave & Go To Next FormSave & Exit RecordSave & Go To Next Record

6.4 Medications

BACKGROUND AND RATIONALE

The Medications Form is designed to enable collection of data on participants' use of all types of medications, both prescription and non-prescription, including supplements. Information about participants' use of medications is collected at the initial (baseline) clinic visit and at follow-up visits. The participant is asked to bring to the clinic containers for all medications used during the two weeks prior to the visit. The interviewer then transcribes the name of each medication, its strength, and for prescription medications, frequency of administration from the containers onto the data collection form. As the information is transcribed, the interviewer queries the participant about actual usage of each medication.

Collecting this information will allow us to describe medication use and any changing patterns of use over time and may help us ascertain the effect of medications on the progression of atherosclerosis in this study population. It will be important to know what medications each participant is taking, to assess and perhaps attempt to explain subsequent participant events and any change in the degree of disease detected at follow-up visits.

MATERIALS AND EQUIPMENT

Current version of the Physician's Desk Reference (PDR)

Printed list of participant's previous medications, collected at most recent prior visit.

DEFINITIONS

Time frame: All prescription and over-the-counter medications and supplements used during the *two weeks prior* to the clinic visit should be included.

Prescription medication: Medication for which a prescription was written by a physician or physician assistant and dispensed by a pharmacist or a physician.

Non-prescription or over-the-counter medication: Medication or supplements purchased without a prescription.

It should be noted that occasionally a physician would write a prescription for a non-prescription medication. In that case, the medication should be recorded as prescription. If, however, the physician *recommends* a medication, rather than actually writing a prescription for it, it should be recorded as non-prescription.

METHODS

This is an **interviewer-administered questionnaire**. Questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

Obtaining medication containers. A letter is sent to the participant before the clinic visit that includes instructions regarding medication containers. The participant is asked to bring to the clinic containers for all supplements, prescription, non-prescription medications and herbal medicines taken during the two weeks prior to the clinic visit.

Medication use interview. Prior to beginning the interview, place all medications in front of the participant. You will have a list of medications the participant reported at the previous exam. Check each medication brought in by the participant against this list. For each one that appears on the list, check the "Keep?" box at the left of that medication. ***IMPORTANT NOTE: You can only mark a medication to keep if the name and strength are identical to what appears on the list.*** Any other medications must be recorded as new medications, either in the spaces provided at the bottom of the list or on the standard Medications form.

When asking the participant about a particular medication, show the container to the participant, keeping the other medications in view. Always conclude the interview by asking the participant if any other medications have been taken during the previous two weeks. If the participant remembers other medications, record the name, strength and frequency administered for each one in as much detail as possible. *If you are unsure about the accuracy of the participant's responses, schedule a telephone interview to verify the prescription label*

information. At the end of the visit, make sure to return all medications and other personal belongings to the participant. Guidelines for completing the Medications Form follow:

6.4.1 Section A: Medication Reception

As you know, the Multi-Ethnic Study of Atherosclerosis will be describing all medications its participants are using, both prescription and over the counter. These include pills, liquid medications, skin patches, eye drops, creams, salves, inhalers and injections, as well as cold or allergy medications, vitamins, herbal remedies and other supplements. The letter you received about this appointment included a plastic medications bag for all your current medications and asked you to bring them to the clinic. Have you brought this bag with you? Are these all the medications that you have taken in the past two weeks?

If “yes”, ask “May I see them?” and record the information in the boxes in Section B of the form or in the appropriate area at the bottom of the list.

If “no”, make arrangements to obtain medications at another time but record any available information as described above as best possible by interviewing the participant for the information.

If participant brought the medication bag with their medications, but forgot one or more medications, record as “no”, record information in the boxes in Sections B, C and D and note in the Comments Section which medications were forgotten. If at all possible, probe participant for any information they may recall about those forgotten medications and enter as much information as possible.

If “refused”, record reason for refusal in Comments Section.

If “took no medicines”, form is complete.

Medication containers may be unavailable to the interviewer for a variety of reasons. Regardless of the reason, however, the interviewer should try to obtain the information necessary to complete the medication form.

If the participant forgets to bring medication(s) to the clinic, the interviewer is responsible for obtaining the necessary information at a second visit or by telephone interview.

If the participant remembers additional medication(s) taken during the previous two weeks, the interviewer should record as much information about the medication as possible at the time of the visit and then follow up with a telephone interview to check for accuracy and completeness.

If the medication containers are unavailable because the participant refuses to bring them to the clinic, the interviewer should document the reason for refusal in the Comment Section. The interviewer should then attempt to obtain the participant’s cooperation in obtaining the data, either by a second visit or by telephone.

If the participant brings a list of medications, instead of the medication containers, record all pertinent information from the list and note this in the Comments Section. If the interviewer has any doubt about the accuracy of the list, a follow-up telephone call should be scheduled to confirm what has been recorded.

Whenever medication information is collected by phone or from a list brought in by the participant instead of from the prescription container, try to verify the spelling of the name and the strength prescribed by referring to the PDR or some other source of accurate medicine listings.

6.4.2 Section B: Prescription Medications

The interviewer transcribes the name and dosage information from each medication container onto the Medications Form using the following guidelines:

Medication name. Print complete medication name using block capital letters. Record all characters and numbers referring to strength as well as the units. The name of each medication should be recorded *exactly* as it is written

on the container. Medication names that are misspelled or otherwise recorded incorrectly will cause data entry and analysis problems because they will not match the drug database. Do not record flavors of products or whether the preparations are sugar-free or sodium-free. If the medication name is longer than the 20 spaces available on the form, transcribe as much as possible and then record the complete medication name in the Comments Section. If it is not possible to transcribe the medication name, insert an asterisk (*) and explain in the Comments Section.

Combination Medications contain two or more drugs. Some combination medicines, such as Dyazide, come in only one fixed combination (hydrochlorothiazide 25mg and triamterene 50mg). These combination medicines do not usually list strength. Record the name in the “Medication Name” space and leave the “Strength” column blank.

Other combination medications are available in more than one fixed dose combination. For example, Inderide, which is a combination of propranolol and hydrochlorothiazide, is available as propranolol 40mg and hydrochlorothiazide 25mg, or propranolol 80mg and hydrochlorothiazide 25mg. These combination medications usually list the strength as in “Inderide 40/25” or “Inderide 80/25.” For these medications, record the name in the “Medication Name” space and the strength combination (e.g., 40/25) in the “Strength” space.

Strength.

- Record the strength of each medication in milligrams (mg) whenever possible, beginning with the first space on the left in the “Strength” column.
- When strength is in milligrams, *do not* record the abbreviation “mg;” record *only* the amount of drug (e.g., if the strength is “250 mg,” record only “250”).
- When strength is not recorded as milligrams, record *all* numbers, digits, and characters used to denote strength, including:
 - milliliter (ml)
 - per milliliter (/ml)
 - milliequivalent (mEq)
 - hour (hr)
 - per hour (/hr)
 - percent (%)
- When strength is separated by a “/” (e.g., 40/25, as in combination medications), record them in this section.
- When strength is given in grains (gr), convert to milligrams using the following formula: (number of grains) x 65 = number of milligrams. (1 gr = 65 mg.)
- When strength is given in micrograms (mcg or µg), convert to milligrams using the following formula: (number of micrograms) ÷ 1000 = number of milligrams. (1000 mcg = 1 mg.)
- When strength is given in milligrams per milliliter (mg/ml), as is often the case with liquid medicine, record as in the following example: Ampicillin 125 mg / 5 ml is recorded as “125/5 ml.” (Note omission of “mg.”)
- When strength is given as a percentage (%), record as such.
- When strength is given in units (U) or units/milliliter (U/ml), as is often the case with Insulin, record as in the following examples: “100/ml” or “100U/ml.”

- When it is not possible to record the strength, such as when it is not recorded on the medication label, record an asterisk (*) and explain in the Comments Section.
- Note: Do not record in the “Strength” column the number or quantity of medication items (e.g., number of tablets or tablespoons). See “Number Prescribed,” below.

Number Prescribed. This column is designed to capture information on the number of pills (or milliliters, drops, units, etc.) *prescribed* as opposed to the number actually taken. Information on the number prescribed should be taken from the medication labels.

- Record the total number of medication items (e.g., “tablets”) prescribed per the given time period (e.g., day, week, or month). Circle the appropriate letter in the “Number Prescribed” column to show whether the prescribed number is per day (D), per week (W), or per month (M).
- If the instructions include a range in the number of medication items and/or times/day (or week or month) they are to be taken, record the lowest number of each. For example, if the label says, “take 1–2 tablets 3–4 times per day,” record as “3 tablets/day” (i.e., 1 tablet 3 times/day = 3 tablets/day); or, if the label says, “take 1–2 tablets every 4 hours while awake,” record as “5 tablets/day” (i.e., 1 tablet every 4 hours from 7 a.m. to 11 p.m.).
- When it is not possible to record the number of medication items prescribed per day, record an asterisk (*) and explain in the Comments Section.
- When instructions read “take as directed,” record “1” as the number prescribed per day.
- When dosing instructions are complex (e.g., “take 1 pill every other day, alternating with 2 pills every other day”), record the *average* number per day (or week or month).

Number Prescribed: Specific Medications.

Pill/Tablets/Capsules: Record the total number prescribed per day (or week or month).

Solutions: Record the total number of milliliters prescribed per day (or week or month). Use the following conversions:

- 1 teaspoon = 5 ml
- 1 tablespoon = 15 ml
- 1 ounce = 30 ml

Eye Drops: Record the total number of drops prescribed per day (or week or month). For example, “two drops in right eye, three times a day” = 6 drops, or “one drop in each eye, twice a day” = 4 drops.

Inhalers (puffers): Record the total number of sprays or puffs prescribed per day (or week or month).

Insulin: Record the total number of units injected per day (or week or month).

Creams/Lotions/Ointments: Record the total number of applications prescribed per day (or week or month).

Patches: Record the total number to be applied to the skin per day (or week or month).

Nitroglycerin Ointment: Record the total number of inches to be applied to the skin per day (or week or month).

PRN (“as needed”) Medication is generally used for allergy, pain, or sleep; sublingual nitroglycerin is also used PRN.

- Use the “PRN Medicine?” column to indicate whether the medication is prescribed to be taken on an “as needed” basis.
- Circle “Y” only when the prescription instructions state “as needed,” “when needed,” “if needed,” etc.
- Circle “N” when the prescription instructions do *not* use the words “as needed,” “when needed,” “if needed,” etc.
- The words “as directed” do not mean the same as “as needed.”

Number Taken. This column is designed to capture information on the number of pills (or milliliters, drops, units, etc.) *actually taken* as opposed to the number prescribed. Information on the number *actually taken* should come directly from the participant. People do not always take their medications as prescribed. It is important to record information about both the number prescribed and the number actually taken as accurately as possible.

- Ask the participant, “**On the average during the last two weeks, how many of these did you take a day/week/month?**”
- Record the average number of pills (or other medication items) taken per day (or week or month) during the last two weeks.
- Code “0” if none of the medication items was taken during the previous two weeks. This includes instances in which a prescription was filled but none of the medication was taken during the past 2 weeks.
- When the number taken cannot be determined, record two asterisks (**) and explain in the Comments Section.
- Circle the appropriate letter (D, W, M) to show whether the prescribed medication was taken per day, per week, or per month.

6.4.3 Section C: Over-the-Counter Medications

Complete this section following instructions for Section B, above, but disregarding the instructions pertaining to “Number Prescribed” and “PRN Medication.”

6.4.4 Section D: Vitamins and Supplements

Whenever possible, *in the comment section*, record traditional medicine use in the same fashion as with other medicine i.e., name, dosage, frequency. If this is not possible, record the *purpose* of the medicine.

6.5 Medical History

PURPOSE

The Medical History identifies the participant's medical conditions and provides other information that may:

- be used to adjust for co-morbidity
- characterize the participant's access to medical care

METHODS

General instructions:

This is an **interviewer or self-administered** questionnaire. Questions should be read to the participant exactly as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read exactly as written.

For most questions, possible responses are “Yes”, “No,” or “Don’t Know”. A few other questions have choices as indicated. The interviewer should read all choices to the participant and have the participant choose the appropriate response/s for each question.

Do not probe to make interpretations about a participant’s specific symptoms. Ask questions as written and record answers as given by the participant.

Specific instructions:

Begin the questionnaire by reading to the participant the following introduction:

The following are some questions about your medical history. Please answer to the best of your knowledge.

Questions 1-18 pertain to conditions the participant has been told they have by a health care provider. The participant should choose “Yes” or “No” if they are fairly sure about the diagnosis and “Don't Know” if they believe they might have been told about the diagnosis but is not sure. If the person is cared for primarily by a health care provider other than a physician, such as a nurse practitioner, try to determine that the diagnosis was made in a medical setting and, if so, include the response. Any conditions that have been previously reported will be skipped.

Has a doctor ever told you that you have any of the following conditions?

1. *Kidney failure requiring dialysis or transplantation*

Choose Yes, No, or Don’t know.

2. *Diabetes*

Choose Yes, No, or Don’t know.

3. *Hypertension (high blood pressure)*

Choose Yes, No, or Don’t know.

4. *Hypercholesterolemia (high cholesterol)*

Choose Yes, No, or Don’t know.

5. *B12 deficiency*

Choose Yes, No, or Don’t know.

6. *Atrial Fibrillation*

Choose Yes, No, or Don’t know.

7. Emphysema or Chronic Obstructive Pulmonary Disease (COPD)

Choose Yes, No, or Don't know.

8. Asthma

Choose Yes, No, or Don't know.

9. Dyslexia

Choose Yes, No, or Don't know.

10. Parkinson's disease (PD)

Choose Yes, No, or Don't know.

If Yes, ask the following: *In what year was PD diagnosed?*

Enter year of diagnosis as best as can be recalled.

11. Post-traumatic stress disorder (PTSD)

Choose Yes, No, or Don't know.

12. Bipolar disorder

Choose Yes, No, or Don't know.

13. Schizophrenia

Choose Yes, No, or Don't know.

14. Depression

Choose Yes, No, or Don't know.

If Yes, continue to 14a

If No, skip to Q15

14a. Was depression diagnosed within the past 2 years?

Choose Yes, diagnosed within the past 2 years
or
No, diagnosed more than 2 years ago

15. Anxiety

Choose Yes, No, or Don't know.

16. Obsessive-compulsive disorder (OCD)

Choose Yes, No, or Don't know.

17. Any other psychiatric disorders not mentioned?

Choose Yes, No, or Don't know.

If Yes, continue to 17a and 17b

If No, skip to Q18

17a. What was the psychiatric disorder diagnosis?

Participant should specify diagnosis to the best of their ability.

17b. Was it diagnosed within the past 2 years?

Choose Yes, diagnosed within the past 2 years
or
No, diagnosed more than 2 years ago

18. Traumatic brain injury (TBI)

Choose Yes, No, or Don't know.

If Yes, answer Q18a – 18d

If No, skip to Q19

18a. Have you had a TBI with brief loss of consciousness, less than 5 minutes?

Choose No, Single, repeated / multiple, or Don't know.

18b. Have you had TBI with extended loss of consciousness, 5 or more minutes?

Choose No, Single, repeated / multiple, or Don't know.

18c. Have you had TBI without loss of consciousness, which might result from military detonations or sports injuries?

Choose No, Single, repeated / multiple, or Don't know.

18d. In what year was your most recent TBI?

Enter year of most recent TBI as best as can be recalled.

1. Do you usually have a cough on most days for 3 or more months during the year?

Choose Yes or No.

If Yes, ask the following: ***“For how many years have you had this cough?”***

Record and go to question 20.

2. Do you usually bring up phlegm from your chest on most days for 3 or more months during the year?

Choose Yes, No.

If Yes, ask the following: ***“For how many years have brought up phlegm from your chest like this?”***

Record and go to question 21.

3. In the last 12 months, have you had wheezing or whistling in your chest?

Select Yes or No. **If No, skip to question 22.**

21a. In the last 12 months, how often have you had this wheezing or whistling? (Read the options) Choose the most appropriate response.

21b. In the last 12 months, have you had an attack of wheezing or whistling in the chest that has made you feel short of breath? Select Yes or No.

4. Are you unable to walk due to a condition other than shortness of breath?

Choose Yes, No, or Don't know. **If No, skip to End.**

5. Do you get short of breath when hurrying on level ground or walking up a slight hill?

Choose Yes, No, or Don't know.

6. Do you walk slower than people of the same age on level ground because of breathlessness or have to stop for breath when walking at your own pace on level ground?

Choose Yes, No, or Don't know.

7. Do you stop for breath after walking about 100 yards or after a few minutes on level ground?

Choose Yes, No, or Don't know.

8. Are you too breathless to leave the house or breathless when dressing?

Choose Yes, No, or Don't know.

9. ***In the past 12 months, have you had a period when you had breathing problems that got so bad that they interfered with your usual daily activities or cause you to miss work?***

Select Yes or No.

If Yes, ask the following:

27a. “How many such episodes had you had in the past 12 months?”

Enter number of episodes

27b. “For how many of these episodes did you need to see a doctor or other healthcare provider in the past 12 months?”

Enter number of episodes

27c. “For how many of these episodes were you hospitalized overnight in the past 12 months?”

Enter number of episodes

27d. Altogether, for how many total days were you hospitalized overnight for breathing problems in the past 12 months?

Enter number of episodes

6.6 Personal History

PURPOSE

The Personal History questionnaire is used to collect information on socio-economic status (SES) and smoking and drinking habits, all of which are related to an individual's risk of cardiovascular disease.

METHODS

General instructions:

This is a **self-administered questionnaire**. Open the questionnaire on the data collection tablet for the participant and give brief instructions for completion. If the participant is unable to self-administer the questionnaire, then a MESA staff member will administer the questionnaire.

Ask the participant to try to answer all questions, unless instructed to skip the question. Remind them to request assistance from a staff member if anything is unclear. Most participants should be able to complete the questionnaire on their own. However, if the participant expresses or appears to have difficulty reading or comprehending the questions, offer to help and make arrangements for an interviewer administered version in the appropriate language.

Specific instructions:

- Instruct the participant to read the questions and their instructions carefully then fill out all questions, except those they are instructed to skip because of their response to a specific question.
- If they are unsure about an exact answer (e.g., for “average number of drinks per week”), tell them to give a best estimate.
- In questions where the participant is asked about number of times used, instruct them to fill in “00,” if use is less than one.

The participant will begin the questionnaire with the introduction below:

This form collects information about your background and lifestyle which may impact your risk of cardiovascular disease. Please complete all items except those which you are specifically instructed to skip. If you are unsure about the answer to a specific question, please estimate the answer to the best of your ability. If you have a question about a particular item, ask a staff member for clarification.

10. At your last MESA exam, you described your current *occupation* as [current occupation]. Has your employment status changed?

Participant should choose Yes or No.

If no, participant should skip to question #2.

If yes, participant should continue with 1a.

1a. Choose one of the following that best describes your current occupation:

Participant should select the most appropriate option.

11. What is the highest degree or level of school you have completed? Participant should select the appropriate option.

- If the response is “Completed high school (12th grade) or GED”, participant should select the GED box.
- If participant selects “Some college but no degree”, they should indicate how many years of college.
- If the response is “Graduate degree”, participant should specify the appropriate degree choice.
- If the response is “Some graduate school but no degree”, participant should indicate how many years of graduate study.

12. What language is generally spoken in your home?

Fill in the appropriate box or boxes. If “other,” specify the language.”

13. What is your current marital status?

Participant should choose the appropriate option.

The following questions have to do with family finances. We know from other research that financial strain is common and very important to consider in understanding people’s health. The following questions will be used to help give us a picture of the various financial situations experienced by persons participating in the MESA study. Any information you provide is strictly confidential and will be used for research purposes only.

14. Below is a list of income groups. Please choose which group best represents your total combined family income for the past 12 months. This includes the total income before taxes earned in the past year by all family members living with you. Please include money from jobs, net income from business, farm, or rent, pensions, dividends, welfare, social security payments and any other money received by you or any other family member living with you.

Participant should select the most appropriate option.

5a Including yourself, how many people are supported by the income listed in the previous question?

Participant should enter a number in the space provided.

5b How many of these are:

- Children under 18?
- Adults 65 and over?

Participant should enter a number in each space.

Participant should enter 00 if no one in that age category is supported by the given income.

15. Where do you usually go for medical care?

Participant should select (or write in) the place they go most often for medical care. Participant should select “other” only if the response clearly does not fit one of the given responses.

16. To help pay for your medical care, do you have:

Participant should select (or write in) all applicable options.

If “Other” is selected, participant should indicate what other option they have.

17. This question is about the house or apartment that you live in. Do you:

Participant should select the most appropriate option.

18. Do you or your family have investments such as stocks, bonds, mutual funds, retirement investments, or other investments?

Participant should select the appropriate response. If the participant does stocks or investments and their family does, and they receive no benefits from their family having these things, the participant should respond “no.”

19. Do you or your family own any land/business/property/apartments/houses other than the one in which you now live?

Participant should select the appropriate response. If the participant does not own land or property and their family does, and they receive no benefits from their family having these things, the participant should respond “no.”

20. Do you or your family own a car?

Participant should select the appropriate response.

21. What is your current living situation?

Participant should select the most appropriate option.

22. What type of residence do you live in?

Participant should select the appropriate option.

23. The next questions ask about what you often do on your own and what you need help from others to accomplish.

For each activity listed, participant should select “Yes”, “No”, or “Unwilling to answer”.

24. In general, would you say your health is:

Participant should select the most appropriate response.

The following two questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

For each activity listed, participant should select the most appropriate response.

25. MODERATE Activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

26. Climbing SEVERAL flights of stairs

During the PAST 4 WEEKS, have you had any of the following problems with your work or other regular activities AS A RESULT OF YOUR PHYSICAL HEALTH?

For questions 18 & 19, participant should select Yes or No.

27. ACCOMPLISHED LESS than you would like

28. Were limited in the KIND of work or other activities

During the PAST 4 WEEKS, were you limited in the kind of work you do or other regular activities AS A RESULT OF ANY EMOTIONAL PROBLEMS (such as feeling depressed or anxious)?

For questions 20 & 21, participant should select Yes or No.

29. ACCOMPLISHED LESS than you would like

30. Didn't do work or other activities as CAREFULLY as usual

31. During the PAST 4 WEEKS, how much did PAIN interfere with your normal work (including both work outside the home and housework)?

Participant should select the appropriate response.

The next three questions are about how you feel and how things have been DURING THE PAST 4 WEEKS. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the PAST 4 WEEKS -

For questions 23-26, participant should select the amount of time they felt that way

32. Have you felt calm and peaceful?

33. Did you have a lot of energy?

34. Have you felt downhearted and blue?

- 35. During the PAST 4 WEEKS, how much of the time has your PHYSICAL HEALTH OR EMOTIONAL PROBLEMS interfered with your social activities (like visiting with friends, relatives, etc.)?**

The next set of questions ask about alcohol, tobacco, and drug use.

All participants should answer questions 27, 33, 34, 35, and 40. Those who drink alcohol should complete questions 28–32; former tobacco smokers should complete question 38; current tobacco smokers should complete question 39; current non-smokers should complete question 41. If the participant feels uncomfortable with these questions, please reassure them that all collected information is strictly confidential.

- 36. Have you consumed any alcoholic beverages in the last three months?**

Participant should select Yes or No

If no, skip to question #33.

- 37. During the past three months, how often did you have at least one drink of any alcoholic beverage?**

Participant should select the most appropriate option.

For questions 29-32, participant should enter the number of servings they had per week.

- 38. How many glasses of red wine do you usually have per week?**

(1 serving = 3.5 oz glass, 1 bottle = 750ml = 8 glasses)

Participant should provide the average number of drinks per week. Record “00” if less than one glass of red wine per week.

- 39. How many glasses of white wine do you usually have per week?**

(1 serving = 3.5 oz glass, 1 bottle = 750ml = 8 glasses)

Participant should provide the average number of drinks per week. Record “00” if less than one glass of white wine per week.

- 40. How many cans, bottles, or glasses of beer do you usually have per week?**

(1 serving = 12 oz glass, 1 bottle = 355ml = 1 glass)

Participant should provide the average number of 12-ounce drinks per week. Record “00” if less than one serving of beer per week.

- 41. How many drinks of liquor or mixed drinks do you usually have per week?**

(1 serving of liquor = 1.5-ounce shot-glass, or one mixed drink)

Participant should provide the average number of drinks per week. Record “00” if less than one drink of liquor per week.

- 42. Has alcohol use EVER impaired your ability to work, drive, or interact in social situations?**

If Yes, participant should continue with 33a.

For any other response, participant should skip to question #34.

- 33a. In the past year, has alcohol use impaired your ability to work, drive, or interact in social situations?**

Participant should select the most appropriate option.

- 43. Has the use of drugs or other substances EVER impaired your ability to work, drive, or interact in**

social situations?

If Yes, participant should continue with 34a and 34b.

For any other response, participant should skip to question 35.

34a. Can you specify the drug or substance used?

Participant should enter the specific drug or substance used.

34b. In the past year, has the use of drugs or other substances impaired your ability to work, drive, or interact in social situations?

Participant should select the most appropriate option.

44. Which of the following best describes your current smoking status?

Participant should select the appropriate response.

If never smoked, participant should skip to questions 40 and 41.

These questions refer to cigarette smoking only. Vaping or e-cigarettes should not be included.

45. Have you smoked in the last 30 days?

Participant should select the appropriate response.

46. For how many years did you smoke / have you smoked?

Participant should enter best estimate of number of years smoked.

For the next two questions, the participant should record 00 if the average number of cigarettes per day is less than one. Make sure participants record the number of *cigarettes* per day. If a participant answers in number of packs per day, recalculate into number of cigarettes per day (1 pack = 20 cigarettes).

47. If former smoker: On average, how many cigarettes did you smoke per day?

Participant should provide the number of cigarettes smoked per day and then skip to question 40.

48. If current smoker: On average, how many cigarettes do you smoke per day?

Participant should provide the number of cigarettes smoked per day.

49. Did your mother smoke cigarettes when she was pregnant with you before you were born?

Participant should select the appropriate response.

50. Current non-smokers only: During the past year, about how many hours per week were you in close contact with people when they were smoking? (e.g., In your home, in a car, at work or other close quarters)

The goal of the question is to obtain information on passive exposure to *cigarette* smoke (excluding cigars, pipes, etc.) in any type of close quarters during the past 12 months. Participant should record the number of hours in a *typical* week; do not include isolated or atypical situations, such as holiday gatherings or short-term house guests who smoke. If participants do not remember the exact amount of time, ask them to give their best estimate. Record 00 if participant was exposed to less than 1 hour of cigarette smoke per week.

At this point, the participant has completed the questionnaire. MESA staff will review the questionnaire for completeness, clarify any questions that were not answered.

6.7 Health & Life (Social Determinants of Health)

PURPOSE

This questionnaire includes several instruments designed to measure psychosocial characteristics that may be important in understanding the causes of cardiovascular disease. These psychosocial factors may themselves lead to increased risk of cardiovascular disease or may interact with other traditional risk factors, such as diet or sedentary lifestyle. The areas assessed as part of this questionnaire include anger, anxiety, depression, chronic burden (stress), and emotional social support. A section on perceptions of unfair treatment or discrimination is also included, because the perception of discrimination may be an important source of stress for some groups.

MATERIALS/EQUIPMENT

This is a **self-administered** form. Provide the participant with either the data collection tablet or paper form and a pencil and give brief instructions for completion. If the participant is unable to self-administer the questionnaire, then a MESA staff member will administer the questionnaire.

DEFINITIONS

The terms used in the questionnaire should require no explanation, because they are used in the way they tend to be used by most people in everyday life.

METHODS

General Instructions

It is important that the participant have some private time in a quiet area to complete the form. The participant should be led to a quiet location with a table, handed the data collection tablet or paper form and a pencil for completion and told to answer each question by darkening the circle of the appropriate response. Review the top section of the form with the participant before starting. Emphasize that there are no right or wrong answers and that we are interested in their feelings and opinions about things. Also emphasize that they should not spend too much time on any one question. Show them that additional instructions are provided at the beginning of each section.

The participant should be asked to try to respond to all questions, unless instructed to skip the question. Remind them to request assistance from a staff member if anything is unclear. Most participants should be able to complete the questionnaire on their own. However, if the participant expresses or appears to have difficulty reading or comprehending the questions, offer to help and make arrangements for an interviewer-administered version in the appropriate language.

Important points for interviewers and participants to consider:

- If the topic should arise, remind participants that all information is strictly confidential and will only be used for research purposes. Explain that things about people's lives, including the stressful situations they go through, may be important to their health. Knowing about these things may help us understand the causes of heart disease better. Also emphasize that it is important to get complete data so that the study results will be valid. However, if a participant is upset by the questions or does not want to answer, they should feel free to skip the question or section. Refusal to answer the questions will not jeopardize their participation in the study.
- The measurement of these dimensions is complex. Generally, they are measured using scales or collections of questions that attempt to get at the same underlying concept in different ways. For this reason, some of the questions may seem repetitive. If questions on this arise, acknowledge that some questions may seem similar, but ask participants to respond to each one separately as best they can.
- The terms used should be understood by most people. If the participant asks about the meaning of any item or tries to qualify a statement, please re-read the statement (or question) to them. Obtain a copy of a

translated form if necessary. Do not attempt to explain the question or provide synonyms (unless specified in the specific instructions below), because this may create problems for some of the scales.

Specific Instructions

The next set of questions ask about situations where you might feel that you have been treated unfairly, and how you cope in those situations.

1a. If you feel like you've been treated unfairly, do you usually:

Participant should select the most appropriate answer

1b. And if you feel you've been treated unfairly, do you usually:

Participant should select the most appropriate answer

2. Think about the times that you have experienced discrimination in your lifetime:

What did you do?

Participant should select Yes or No for each action.

For each action, if yes, participant should answer ***Did you do that a lot, some, or a little?***

Questions 3–8 are intended to assess perceptions of having been treated unfairly. The perception of unfair treatment (as a result for example of discrimination) may be an important source of stress and could be related to health and cardiovascular disease. (Gender can be clarified as sex. Sexual orientation can be clarified as “whether you are gay, lesbian or straight.”). Possible answers for 3–8 are “yes” or “no.” Answers are selected by filling in the appropriate circle.

3. Do you think you have ever been unfairly fired or denied a promotion?

If no, go to question 4

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

4. For unfair reasons, do you think you have ever not been hired for a job?

If no, go to question 5

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

5. *Have you ever been unfairly stopped, searched, questioned, physically threatened or abused by the police?*

If no, go to question 6

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

6. *Have you ever been unfairly discouraged by an advisor or teacher from continuing your education?*

If no, go to question 7

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

7. *Have you ever been unfairly prevented from moving into a neighborhood because the landlord or a realtor refused to sell or rent you a house or apartment?*

If no, go to question 8

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

8. *Have you ever moved into a neighborhood where neighbors made life difficult for you or your family?*

If no, go to question 9

If yes, answer the following:

What was the main reason? (select one)

- Race or ethnicity
- Gender
- Age
- Religion
- Physical appearance
- Sexual orientation
- Income level or social class
- Other

Did this happen in the last 12 months?

Participant should select yes or no.

9. In your day-to-day life how often have any of the following things happened to you?

- a. You are treated with less courtesy than other people
- b. You are treated with less respect than other people
- c. You receive poorer service than other people at restaurants or stores
- d. People act as if they think you are not smart
- e. People act as if they are afraid of you
- f. People act as if they think you are dishonest
- g. People act as if they're better than you
- h. You are called names or insulted
- i. You are threatened or harassed

Possible answers for question 9 are "Almost every day," "At least once a week," "A few times a month," "A few times a year," "Less than once a year," or "Never." Answers are selected by filling in the appropriate circle.

6.8 Physical Activity

PURPOSE

The MESA Typical Week Physical Activity Survey (TWPAS) is designed to identify the time and frequency spent in various physical activities during a typical week in the past month. It is a Self-Administered or Interviewer-Administered form for participants who agree to wear the 24H-ACT hip monitor. The rationale for the selected time frame of a typical week in the past month is the intention to capture typical activity patterns in one's daily life.

The survey has 28 question items in categories of household chores, lawn/yard/garden/farm, care of children/adults, transportation, walking (not at work), dancing and sport activities, conditioning activities, leisure activities, occupational activities and volunteer activities.

METHODS

1. General Instructions

1.1 This survey is either **self-administered** or interviewer-administered. If self-administered, provide the participant with a laptop computer with the Physical Activity Survey screen already open and give brief instructions for completion. Ask the participant to try to answer all questions. Remind him/her to request assistance from a staff member if anything is unclear. Most participants should be able to complete the survey on their own.

1.2 Instruct participant to give the laptop back to the interviewer when the form is completed.

1.3 If the participant expresses or appears to have difficulty reading or comprehending the questions, or if he or she has difficulty using the computer, offer to help and make arrangements for an interviewer administered version in the appropriate language. If interviewer administered, questions should be read to the participant verbatim as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read verbatim.

1.4 For the majority of the questions, response choices are "Yes" or "No". Record the response given by the participant. If "Yes", ask for the number of days per week, amount of time in hours and/or minutes per day the participant spent doing the particular activity.

2. Specific Instructions

Items to be completed by the interviewer:

Enter Technician ID and Date.

ID# will be pre-filled. Please verify that the ID is a match to the participant.

- Instruct the participant to read each question and its instructions carefully then enter his or her response.
- Show the participant how to click on choices or enter responses.
- Explain that the computer will help by automatically skipping the questions that don't need to be answered because of a prior response.
- Explain that not checking a number is interpreted the same as 0 (e.g. for 15 minutes only the hours would remain unchecked while the minutes would be recorded as 15).
- Explain that if the participant would like to change an answer to one of the questions, that the question response should first be checked "No" (which will reset the days, hours, and minutes all to unchecked). Then if the participant would like to record a different amount of time indicate "Yes" and then proceed with responding with the corrected number of days, hours, and minutes.
- If he/she is unsure about an exact answer (e.g., for number of days per week of an activity), tell him/her to give a best estimate.

Begin the questionnaire by reading the following instructions to the participant:

Think about the types of activities you did in a typical week in the past month. Please indicate whether you did or did not perform each of the following activities in a typical week. For each item that you respond ‘yes’, you will be asked for the number of days in a typical week you did these activities and the average amount of time per day in hours and minutes.

Define intensity levels for the participant:

Most of the survey questions ask about light, moderate, and heavy intensity activities.

Light intensity refers to activities that require little effort and are easy to do.

Moderate intensity refers to an effort that is harder than light intensity but is not an all-out effort.

Heavy intensity is a very hard activity and requires all-out effort.

Questions people might ask about completing the Physical Activity Questionnaire, and some sample responses:

What if every week in the past month was different?

Think about the week that was most typical of your activity patterns for that activity in other times of the year and fill in the circle for the number of days and hours per day and or minutes per day.

What if the length of time is different each day?

Think about the average in all the days that reflects your typical time for the activity in a typical week.

I was on vacation in the past month when I went on a 2-week bicycle trip. Should I include this in the estimates?

In this case, think about a typical week in the past couple of months that reflects your usual activity patterns. We are trying to identify the activity patterns you do on a usual basis, so if your vacation was not typical, do not include it.

It is possible that a person will spend more time doing activities on one day or another (e.g., weekends). If this is the case, ask him/her to estimate the usual time during each event in a typical week, averaging in the longer and shorter days.

For example, if the participant engages in an activity for 30 minutes/day 5 days/week and 1.5 hours/day 1 day/week, ask him/her to add about 15 minutes extra to each day (45 minutes/day 5 days a week), to take into account a single day that has a prolonged bout of activity compared to the usual.

Item-by-Item Clarification

Household chores

“In a typical week in the past month, did you do: (light effort / moderate or heavy effort household chores).” The examples should be read to the participant for clarification.

If no, record no and you will be skipped ahead to the next question.

If yes, then ask, “About how many days per week?” Record the number of days. Then ask, “About how many hours or minutes per day?” Record the number of hours and/or minutes (e.g. for a response of 1hr and 15 mins, record 1 under hours and 15 under minutes). This series of questions should be applied to similar types of questions in the questionnaire.

1. **Light Effort Household Chores:** These activities are light intensity, routine, usually daily activities that people do during the care and maintenance of a household. Examples include cooking and cleaning after cooking, straightening up the house, grocery and household shopping and putting things away, changing the bed, doing the laundry, ironing. Housecleaning in a structured, organized way should not be included here, as that would involve more moderate intensity chores.

2. Moderate or Heavy Effort Household Chores: These activities are more structured and might not occur on a daily basis. Examples include heavy cleaning (washing windows, moving furniture to clean), vacuuming, scrubbing the floors or walls, mopping—either standing up or on hands and knees—repairing home appliances or lawn and garden tools, washing the car.

Lawn/Yard/Garden/Farm

“In a typical week in the past month, did you do: (moderate/heavy effort lawn/yard etc.)”

3. Moderate Effort Lawn/Yard/Garden/Farm Activities: These activities refer to outside chores involved in caring for a house, farm, or ranch. They may involve yard work, cleaning out the garage, raking the leaves, sweeping the porch or sidewalk, or other moderate effort chores. Encourage the participant to think of activities done in a typical week in the past month. This category may include seasonal activities; if so, the activities reported should be typical of the past month.
4. Heavy Effort Lawn/Yard/Garden/Farm Activities: These activities require heavy effort and may be seasonal. Examples include digging dirt, shoveling snow or using a snow blower, chipping ice, tilling a garden, mending fences, chopping and hauling wood, and removing trees.

Care of Children/Adults

“In a typical week in the past month, did you do: (light/moderate effort child/adult care)”

5. Light Effort Care of Children/Adults: These activities require physical movement by the respondent and include bathing, feeding, changing diapers, playing with a child, or other similar activities. Do not count time sitting with a child (as in babysitting) without active engagement in physical activities. Include only the time spent involved in physical activities.
6. Moderate Effort Care of Children/Adults: These are intentional activities that require moderate effort to complete and may include activities of lifting and carrying dependent others or pushing a wheelchair or stroller. Include only the time spent moving.

Transportation

“In a typical week in the past month, did you do: (use transportation)”

7. Drive or ride in car, ride the bus/subway, including travel to work: These are all light activities and do not include walking. Have the respondent include all time spent in transportation where they are sitting in any vehicle above.

Walking (not at work)

“In a typical week in the past month, did you do: (walking to get to places, etc.)”

8. Walking to get places: In general, walking is underreported in the time estimates. This would include walking for transportation, walking to and from work, walking to the store or from the car into the store and back, walking to get the mail, etc.
9. Walking for exercise, pleasure, social reasons, walking during work breaks, walking the dog: These are classified as intentional walking and are different in intention than those in item #8. The walking may be for exercise or part of a daily routine that is done with family members, animals, or for personal reasons. Walking for transportation should be included in item 8.

Dancing/Sport Activities

“In a typical week in the past month, did you do: (dancing in church / team sport / dual sports)”

10. Dancing in church, ceremonies or for pleasure: Remind the participant to think of a typical week in the past month to estimate usual dancing behaviors. Some may dance only occasionally—a few times a year. This would not be included as a “yes” response to this category unless it was typical of the past month. Ceremonial or religious dancing would need to be done regularly enough to represent a typical week in the past month.
11. Team sports: The purpose of including team sports activities is to group exercise activities that are done with others. These are probably seasonal activities that are done in leagues or other organized settings. Remind the participant to think of a typical week in the past month and to stay within that framework when responding.
12. Dual sports: These activities involve mostly racket sports or other one-on-one sports activities. They could include fencing, ping-pong, or other activities done with another person.
13. Individual activities: These may be sports activities, such as golf and bowling, or more individual relaxation/meditation activities, such as yoga or Tai Chi. Remind respondents to think of days and time spent during a typical week in the past month only.

Conditioning Activities

“In a typical week in the past month, did you do: (moderate/heavy effort conditioning)”

14. Moderate Effort Conditioning Activities. Conditioning activities are those that can be done alone or with others. They are different from sports, because the intention is to gain an element of fitness rather than have a contest or win a game. Moderate effort activities are not for competition, nor are they all-out effort. Intensity of exercise should be moderate enough that respondents should be able to talk with others while they are performing the activities. Examples are low impact aerobics, recreational (slow) bicycling, rowing on a rowing machine or in a lake, swimming in a pool or lake, or using weight lifting or conditioning machines at a health club.
15. Heavy Effort Conditioning Activities. These are very intense activities done for maximum fitness levels and include high impact aerobics (e.g., Tai-bo, kick boxing), competitive or maximum effort running, bicycling, swimming, and work on health club machines. Exercise at this intensity would be very hard and the respondent would have difficulty carrying on a conversation during the performance.

Leisure Activities.

“In a typical week in the past month, did you do: (these leisure activities, watching TV)”

16. Sit or recline and watch TV: This is a sedentary, leisure-time pursuit. Do not include the time watching TV while doing other things. The question is to be used as a marker of sitting or reclining and watching TV as a single pursuit.
17. Read, knit, sew, visit, do nothing, non-work recreational computer: These are markers of sedentary activities that exclude watching TV. If people report knitting while watching TV, make sure they select one category or the other and avoid duplicate category reporting.

Occupational Activities

18. ***Do you work to earn money?***
If “no”, skip to question 24.
If “yes”, continue to question 19.
Respondents should report activities only if they work to earn money. Volunteer activities will be asked about in question 24. Unpaid household activities and caring for others were included in questions 1–6.

19. ***How many days per week and hours per day do you work in all jobs?***

Record the number of days/week and hours/day. If the respondent works at more than one job, record the total days worked per week in all jobs. To estimate the average hours worked per week, ask the respondent to consider the hours they work in the second job (or third, if applicable) and then add them to the average time they work per day. See the example about averaging time per day when activities are done longer on some days of the week than on others.

Respondent should fill in the circles for the time spent in each activity at work. The hours per day for all activities should equal the total hours per day worked. Recommend that the respondent keep a cumulative total of the hours recorded doing occupational activities, in order to avoid estimating more time in occupational tasks than time they work on an average day. They can also subtract the hours from the total time worked per day as they identify how the time is spent in different types of activities.

“At work, did you do:”

20. Light Effort/Sitting Activities: For most respondents, this will be the most hours in the work day.
21. Light Effort/Standing Activities: These are likely intermittent activities that would be done in a clerical setting (e.g., office work related to filing, using a copy machine) or sustained activities done in a labor setting (e.g., checkout clerk in a store, assembly line worker assembling parts, medical field examining patients). Teaching in a classroom falls into this category.
22. Moderate Effort/Standing or Walking Activities: For some occupations (office work, clerical, professional), these may be more intermittent, as in walking down the hall, walking between office buildings, and delivering items. For labor settings, this could relate to jobs such as delivery person (overnight express delivery, food delivery, mail delivery) or jobs that require mostly walking and standing (nurse, custodian, physical education teacher, coach, firefighter, police officer, physical therapist).
23. Heavy Effort/Manual Labor: These occupations require manual effort that involves substantial movement and labor. Types of activities may include digging ditches, ranch or farm labor, delivering furniture, loading and unloading trucks, seasonal farm work.

Volunteer Activities

24. ***Do you work as a volunteer and/or at church in activities you have not yet mentioned on this survey?***

If “no”, skip to question 28.

If “yes”, continue to question 25.

This question is designed to identify time spent in unpaid, work-like activities outside the home.

“Did your volunteer work include:”

25. Light Effort Activities: The respondent should identify light activities that required little effort and were done predominantly while sitting or standing (e.g., cooking at church banquet).
26. Moderate Effort Activities: The respondent should identify activities that required moderate effort and were done predominantly while standing and walking (e.g., participating in a neighborhood clean-up project).
27. Heavy Effort Activities: The respondent should identify activities that required heavy effort, such as pushing, lifting, carrying, and climbing (e.g., building a house for Habitat for Humanity).

Walking Pace

28. *When you walk outside of your home, what is your usual pace?*

Ask respondent to estimate the usual pace he/she walks most of the time. Consider all walking activities (e.g., at work, on the way to work, for exercise, in walking with children or others, or when running errands). Select the appropriate option.

Offer the following guidelines:

Casual strolling pace = up to 2 mph = 30 minutes per mile

Average or normal pace = 2-3 mph = 20-30 minutes per mile

Fairly brisk pace = 4-5 mph = 12-15 minutes per mile (very fast or almost a slow jog)

Brisk or striding pace = More than 5 mph = 10 minutes per mile (race-walking)

After completion of the interview, the interviewer should check to make sure all questions were answered then indicate that the survey is complete.

6.9 Family History Questionnaire

PURPOSE

The Family History form collects information on dementia and conditions which may have affected the participant's immediate family members.

METHODS

This is a detailed form, and participants may not have all the information for their family members. This is an interviewer-administered questionnaire, but questions may require more probing than in other standardized MESA interviews. Please collect as much information as the participant can and indicate where information is missing or unknown.

Specific Instructions

1. *Do you have any first-degree relatives (biological parents, full siblings, or biological children?) who have had cognitive impairment, dementia, or Alzheimer's disease (AD)?* Select yes or no.

If no, continue to question 2.

If yes, say, *Please provide details below for each affected first-degree relative, including parents, siblings, and children.*

Mother: ask if the participant's mother had dementia, Alzheimer's Disease, or cognitive function. Select the condition or none. If a condition is recorded, ask for the age of onset.

Father: ask if the participant's father had dementia, Alzheimer's Disease, or cognitive function. Select the condition or none. If a condition is recorded, ask for the age of onset.

Sibling: ask if the participant's sibling had dementia, Alzheimer's Disease, or cognitive function. Select the condition. If the participant does not have a sibling do not make a selection in the dropdown box and continue to the Child question. If a condition is recorded, ask for the age of onset and ask *Do you have another affected sibling?* If no, continue to child question . If yes, enter the information for each affected sibling.

Child: ask if the participant's child had dementia, Alzheimer's Disease, or cognitive function. Select the condition. If the participant does not have a child do not make a select in the dropdown box. If a condition is recorded, ask for the age of onset and ask *Do you have another affected child?* If no, continue to question 2. If yes, enter the information for each affected child.

2. 2. Do you have any first-degree relatives (biological parents, full siblings, or biological children?) who have had a stroke or transient ischemic attack (TIA)? Select yes or no.

If no, the form is complete.

If they are unsure, say, ***Transient Ischemic Attacks (TIA) are stroke-like symptoms that disappear within 24 hours. This is commonly referred to as a 'mini stroke. Please provide details below for each affected first-degree relative including parents, siblings, and children.***

Mother: ask if the participant's mother had a stroke or TIA. Select yes or no for each condition. If a condition is recorded, ask for the age of first TIA or first stroke.

Father: ask if the participant's father had a stroke or TIA. Select yes or no for each condition. If a condition is recorded, ask for the age of first TIA or first stroke.

Sibling: ask if the participant has a sibling who has had a stroke or TIA. Select yes or no for each condition. If the participant does not have a sibling skip the yes/no response for siblings and continue to the Child question. If a condition is recorded, ask for the age of first TIA or first stroke and ask ***Do you have another affected sibling?*** If no, continue to child question. If yes, enter the information for each affected sibling.

Child: ask if the participant has a child who has had a stroke or TIA. Select yes or no for each condition. If the participant does not have a child skip the yes/no response for the child. The form is complete. If a condition is recorded, ask for the age of first TIA or first stroke and ask ***Do you have another affected child?*** If no, the form is complete. If yes, enter the information for each affected child.

6.10 Environmental Exposures Questionnaire

PURPOSE

This questionnaire will help estimate changes in participants' exposure to air pollutants by gathering current information about the characteristics at their primary and secondary residences, lifestyle, daily travel, and to identify trace metals that might exist in the foods they eat.

METHODS

This is an **interviewer or self-administered** questionnaire. Questions should be read to the participant exactly as they appear on the form to ensure standardization. In addition, any introductory and transitional wording should be read exactly as written. The interviewer should read all response choices to the participant and ask the participant to choose the appropriate response/s for each question.

Do not probe to make interpretations about a participant's specific responses. Ask questions as written and record answers as given by the participant.

DEFINITIONS

Definitions of different types of housing:

Single-family or free-standing: A house in which one family lives. A group house with multiple un-related people and one kitchen would be in this category. The house would also generally have to have all four exterior walls exposed.

Manufactured home/mobile home: Similar in function to a single-family house but has generally been built off site and transported to that location. These are also known as single- or double-wides," "mobile homes," or "trailer homes," and are often situated in trailer parks.

Row house/townhouse/brownstone: This is generally a group of housing units set down side-by-side with adjacent walls. This would differ from a side-by-side triplex because it would have more than three units.

Duplex/triplex, free-standing: A single building split either vertically or horizontally into two or three separate dwellings. Generally, each will have a separate entrance that is "lockable."

High rise apartment/condo/co-op (4 floors or more): A building with multiple housing units on each floor and 4 or more floors.

Low rise apartment/condo/co-op (1-3 floors): A building with multiple housing units on each floor and 3 or fewer floors.

SPECIFIC INSTRUCTIONS

The participant will begin the questionnaire with the introduction below:

1. *What type of building do you live in?*

Single family or free-standing → If selected, skip to Question 3

Manufactured home/mobile home → If selected, skip to Question 3

Row house/townhouse/brownstone → If selected, skip to Question 2a

Duplex/triplex, free-standing → If selected, skip to Question 2a

High rise apartment/condo/co-op (4 floors or more) → If selected, skip to Question 2a

Low rise apartment/condo/co-op (1-3 floors) → If selected, skip to Question 2a

Other, please specify → Participant should describe type of building and continue to Question 3.

Note: Refer the participant to Cue Card #1 in the Questionnaire Response Card Flip Book for examples of these types of buildings.

1a. What floor do you live on?

Basement

Ground floor

Second floor

Third floor or higher → If selected, answer 2b. If other choice selected, skip to Question 3.

Note: Refer the participant to Cue Card #2 in the Questionnaire Response Card Flip Book for examples of these types of buildings.

1b. Which floor? Enter the floor number where participant lives.

2. Do you use air conditioning in your residence?

If no, go to question 3

If yes, answer the following:

2a. What type of air conditioning does your residence have?

Central A/C

Window unit(s) → If selected, ask

How many of them are there? Enter number of window units in residence

Other, please specify Participant should describe type of air conditioning.

2b. How often was the air conditioning used in the past July?

Not used at all

A few days a month

More than half of the days of the month, but less than daily

Almost daily (thermostat used also)

Other, please specify: → Participant should describe frequency of air conditioning use.

2c. How often was the air conditioning used in the past January?

Not used at all

A few days a month

More than half of the days of the month, but less than daily

Almost daily (thermostat used also)

Other, please specify: → Participant should describe frequency of air conditioning use.

3. Is an air cleaner/filter used in your residence (stand-alone or central)? Choices are Yes, No, and Don't know.

If no or don't know, go to question 4

If yes, continue with Questions 3a and 3b:

3a. What type of air cleaner/filter is used? (Please check all that apply)

HEPA filter

Electrostatic precipitator

Negative ion generator

Ozone generator

Regular or fiberglass furnace filter

Don't know

Other, please specify → Participant should describe type of air cleaner/filter, even if another type has been specified as well.

3b. How often is the air cleaner/filter used?

Never

A few days a month

More than half of the days of the month, but less than daily

Every day or nearly every day

Don't know

4. **What are the heating sources used in your residence? Please tell me of any that are used at least once a month.** Choices are Yes, No, or Don't know

Radiators (steam or hot water)

Forced air (vents)

Electric space heater

Baseboard heat

Gas space heater

Kerosene space heater

Wood burning stove

Fireplace

Open stove

Other, please specify → Participant should describe other heating source.

Note: Refer the participant to Cue Card #3 in the Questionnaire Response Card Flip Book for examples of these types of heaters.

If the participant still does not know which type of heating source they use, provide the participant with the following definitions:

Gas space heaters: include gas fireplaces and gas fireplace inserts

Wood burning stoves: include wood or pellet burning stoves

Fireplaces: wood burning fireplaces

Open stove: This category is used if you turn on your cooking stove and open it to heat the house or room

5. **In SUMMER, (Jun. – Aug.):**

5a. How many windows did you usually have open?

None → Skip to Question 6

All

Some

5b. How often did you open windows??

A few days a month

More than half of the days of the month, but less than daily

Almost daily

Other, please specify: → Participant should describe how often windows were open if not one of the choices above

6. **In WINTER, (Dec. – Feb.):**

6a. How many windows did you usually have open?

None → Skip to Question 8

All

Some

6b. How often did you open windows??

A few days a month

More than half of the days of the month, but less than daily

Almost daily

Other, please specify: → Participant should describe how often windows were open if not one of the choices above

7. **Do you spend more than four weeks per year living at another address (secondary residence)?**

If no, continue to Question 8

If yes, answer the following:

7a: How many weeks per season do you spend at your secondary residence.

Enter the number of weeks spent at the secondary residence for each season. Add up the total for all seasons and enter the number in the “Total” box. Do not read “Total” to the participant.

7b: For interviewer only: Is the total weeks for all four seasons spent at the secondary residence 8 weeks or more? (do not read to participant)

If yes, continue to Question 8.

If no, skip to Question 12.

This question will not be displayed in REDCap. A skip pattern is programmed based on the number of weeks reported in question 7a.

The next few questions will ask about the structure and characteristics of your secondary residence.

8. Do you use air conditioning in this residence?

If no, go to question 9

If yes, answer the following:

8a. What type of air conditioning does your residence have?

Central A/C

Window unit(s) → If selected, ask

How many of them are there? Enter number of window units in residence

Other, please specify Participant should describe type of air conditioning.

8b. How often was the air conditioning used in the past July?

Not used at all

A few days a month

More than half of the days of the month, but less than daily

Almost daily (thermostat used also)

Other, please specify: → Participant should describe frequency of air conditioning use.

8c. How often was the air conditioning used in the past January?

Not used at all

A few days a month

More than half of the days of the month, but less than daily

Almost daily (thermostat used also)

Other, please specify: → Participant should describe frequency of air conditioning use.

9. In SUMMER, (Jun. – Aug.): How many windows did you usually have open?

Choices are None, All, or Some

10. In WINTER, (Dec. – Feb.): How many windows did you usually have open?

Choices are None, All, or Some

11. Is an air cleaner/filter used in your residence? (stand-alone or central)?

If no or don't know, go to question 12

If yes, continue with Questions 11a and 11b:

11a. What type of air cleaner/filter is used? (Please check all that apply)

HEPA filter

Electrostatic precipitator

Negative ion generator

Ozone generator

Regular or fiberglass furnace filter

Don't know

Other, please specify → Participant should describe type of air cleaner/filter, even if another type has been specified as well.

11b. How often is the air cleaner/filter used?

Never

A few days a month

More than half of the days of the month, but less than daily
Every day or nearly every day
Don't know

12. *Do you commute, or otherwise travel, more than two days per week?*

If no, go to question 16

If yes, continue with Question 13:

13. *On average, how many hours each day do you spend doing the following during your travel time:*

Walking or biking

In a private car or taxi

On a bus

On a train or subway

Other → Participant should specify mode of transportation.

Record hours and minutes spent traveling by each mode of transportation each day. This includes BOTH commute time and recreational time using that mode of transportation.

If the participant does not use one of the modes of transportation, mark 00 in the appropriate boxes.

The overall goal is to determine how much time the participant spends traveling for work and leisure activities and the distribution of transportation types.

14. *On average, what percent of your travel time do you spend on or next to:*

Freeways, expressways, highways, toll roads, etc.

Other major, heavily traveled roads or streets

Residential or lightly traveled roads, streets, or paths

Percentages should add up to 100%. Record responses and check if they add up to 100%. If the participant has difficulty coming up with percentages, suggest the following:

Never - 0%

Almost never - 1-25% of the time

Sometimes - 26-50% of the time

Often - 51-75%

Always - 76-100% of the time

If the participant leave their home during a typical week but does not travel on any of the roads described, fill in all boxes with 0%.

15. *What traffic condition best describes the majority of your travel time during the day?*

Light traffic, moving at the speed limit

Heavy traffic, moving below the speed limit

Congested or 'stop and go'

Heavy traffic, moving at or above the speed limit

Be sure to differentiate between heavy traffic, moving below the speed limit and heavy traffic, moving at or above the speed limit.

16. *Do you usually spend 2 hours or more per day or 10 hours or more per week at a single location (working, school, volunteering, socializing, etc.) or doing a specific activity away from your household?*

If no, skip to question 19

If yes, continue with Question 17:

17. Is this an indoor location or an outdoor location?

Indoor location

Outdoor location → Skip to Question 19

18. What do you do at this location?

School

Work → Answer Questions 18a – 18c

Volunteer →

Hobby

Other

19a. Briefly describe the industry you work or volunteer in:

Participant should specify work or volunteer industry as briefly as possible

19b. Briefly describe your activities when you work or volunteer:

Participant should specify work or volunteer activities as briefly as possible

19c. Are you regularly exposed there to vapors, gases, dusts, or fumes?

Responses are Yes or No

19. Approximately what number of hours per day (or hours per week) do you spend outdoors in each of the following four seasons?

Winter (Dec. – Feb.):

Spring (Mar-May):

Summer (Jun-Aug):

Fall (Sep-Nov):

20. Do you engage in any of the following hobbies or interests?

Jewelry making or repair

Stained glass making

Soldering/welding

Pottery and ceramics

Make, cut, or set tile

Recycle or fix batteries

Motor vehicle repair

Hunt with guns, firearm practice and/or cast bullets

Responses for each item are Yes, No. or Don't know

21. Read the following introduction to the food frequency questions:

Now I'm going to ask you, on average, how often you've eaten certain foods during the past year. Your choices will be never, a few times a year, 2-3 times a month, once a week, twice a week, 3-4 times a week, 5-6 times a week, or every day.

Apple juice

Grape juice

Pear juice

White rice or dishes made with white rice

Brown rice or dishes made with brown rice

Rice milk

Rice syrup

Rice cereal

Liver

Kidney Meats

Spinach, lettuce, other green leafy vegetables

Participant should respond with one of the choices read by the interviewer.

This question is used to assess metal exposure from dietary sources. These are foods that can have trace amounts of metals in them, which is an environmental exposure.

6.11 Neighborhood Questionnaire

Alzheimer's Disease and related dementias (ADRD) pose a major and increasing public health challenge within the US and across the world. The prevalence of Alzheimer's Disease and related dementias (ADRD) in the U.S. is projected to more than double by 2060 due, in part, to the aging population. This rising burden necessitates research to identify points of intervention to slow cognitive decline.

The Neighborhood Ancillary Study's main objective is to identify unique patterns of neighborhood change related to the causes of prevalence and disparities in cognitive decline and dementia. The long-term goal is to find community-level strategies for stemming cognitive decline and ameliorating disparities in cognitive decline and dementia.

6.11.1 General Instructions

Review the top section of the form with the participant before starting. Emphasize that there are no right or wrong answers and that we are interested in their feelings and opinions about things. Also emphasize that they should not spend too much time on any one question. Show them that additional instructions are provided at the beginning of each section.

The participant should be asked to try to respond to all questions, unless instructed to skip the question. Remind them to request assistance from a staff member if anything is unclear. Most participants should be able to complete the questionnaire on their own. However, if the participant expresses or appears to have difficulty reading or comprehending the questions, offer to help and make arrangements for an interviewer administered version in the appropriate language.

Important points for interviewers and participants to consider:

- If the topic should arise, remind participants that all information is strictly confidential and will only be used for research purposes. Explain that things about people's lives, including stressful situations they go through, may be important to their health. Knowing about these things may help us understand the causes of heart disease better. Also emphasize that it is important to get complete data so that the study results will be valid. However, if a participant is upset by the questions or does not want to answer, they should feel free to skip the question or section. Refusal to answer the questions will not jeopardize their participation in the study.
- The measurement of these dimensions is complex. Generally, they are measured using scales or collections of questions that attempt to get at the same underlying concept in different ways. For this reason, some of the questions may seem repetitive. If questions on this should arise, acknowledge that some questions may seem similar, but ask participants to respond to each one separately as best they can.
- The terms used should be understood by most people. If the participant asks about the meaning of any item or tries to qualify a statement, please re-read the statement (or question) to them. Obtain a copy of a translated form if necessary. Do not attempt to explain the question or provide synonyms (unless specified in the specific instructions below), because this may create problems for some of the scales.

6.11.2 Neighborhood Questionnaire Completion Form

Record completion status and administration details for the MESA Neighborhood Questionnaire in the Exam 7 REDCap program using the **Neighborhood Completion Form**.

6.11.3 Specific Instructions

1. ***Right now, how likely are you to recommend this neighborhood as a good place to live?***

Question 1 asks about recommending the participant's neighborhood. Remember, their neighborhood should be the area within a 20-minute walk or about one mile from their homes. Possible answers are

Very likely

Somewhat likely
Somewhat unlikely
Very unlikely

2. ***On an average week about how much time would you say that you spend in your neighborhood? When thinking of the time you spend in your neighborhood include the time you spend in your home (including sleeping time) as well as the time you spend doing things in your neighborhood. Choose the best option for each of the time periods.***

Question 2 asks participants about how much time they spend in their neighborhoods based on specific time periods. Possible answers are:

All or almost all of the time
Most of the time
About half of the time
Some of the time
None or almost none of the time

Now I am going to ask you about times when you leave your home and neighborhood.

Questions 3-6 ask participants about how much they leave their homes and neighborhoods. Questions 4 and 6 are prefaced by a yes or no question. If they answer yes in questions 3 and 5, they can answer questions 4 and 6 respectively.

Possible answers for questions 3 and 5 are

Yes
No

Possible answers for questions 4 and 6 are

Less than once a week
1-3 times a week
4-6 times a week
Daily
Don't know
Refuse

3. ***During a typical week, do you leave your neighborhood?***
4. ***In a typical week, how often have you left the neighborhood?***
5. ***During a typical week, weather permitting, do you go outside the house?***
6. ***In a typical week, how often have you gone outside the house?***

For each of the statements, please choose the best option to indicate whether you agree. In answering these questions, please think of your neighborhood as the area within about a 20-minute walk (or about a mile) from your home.

Questions 7-45 ask participants about the qualities of their neighborhoods. The participant is asked to what extent they agree with the statements listed. The responses will be used to develop different indices of the participant's residential environment. The statements should be self-explanatory. If the participant has questions on the meaning of any of the statements, attempt to clarify by repeating the statement. Do not attempt to elaborate on the statement as this may create problems in the scales. The participant should not spend too much time on any one question. The responses are ordered from ***Strongly Agree*** to ***Strongly Disagree***. ***Neutral (neither agree nor disagree)*** is the middle option.

7. ***There is a lot of trash and litter on the street in my neighborhood***
8. ***There is a lot of noise in my neighborhood***
9. ***In my neighborhood, the buildings and homes are well-maintained***

10. *Buildings and homes in my neighborhood can be easily accessed by all people regardless of abilities*
11. *My neighborhood is attractive*
12. *My neighborhood is a great place for older adults*
13. *It is pleasant to walk in my neighborhood*
14. *There is a lot of grass, trees, and other vegetation in my neighborhood*
15. *The trees in my neighborhood provide enough shade*
16. *Green spaces and greenery in my neighborhood (e.g. parks, gardens, natural areas) are high quality and well maintained*
17. *My neighborhood has available and welcoming public spaces (e.g. parks, plazas, public gardens)*
18. *There are locations for me to gather with other people in my neighborhood (e.g. coffee shops, barbers, churches, libraries)*
19. *In my neighborhood, it is easy to walk to places*
20. *I often see other people walking in my neighborhood*
21. *Streets in my neighborhood are well lit at night*
22. *My neighborhood has lots of sidewalks and crosswalks*
23. *In my neighborhood, the streets and sidewalks are in good condition*
24. *Pedestrian signals in my neighborhood provide enough time to cross streets*
25. *Intersections in my neighborhood have curb cuts (a small ramp built into the curb of a sidewalk to make it easier for people to pass from the sidewalk into the road)*
26. *I frequently limit outdoor activities in my neighborhood to prevent a fall*
27. *I often see other people exercise in my neighborhood*
28. *In my neighborhood there are places for people to rest during walks (e.g. benches)*
29. *My neighborhood has heavy traffic*
30. *There are stores within walking distance of my home*
31. *I would be able to get where I need to go in my neighborhood even without a car*
32. *Places of interest in my neighborhood are well marked with visible signs (i.e. there are easy wayfinding signs)*
33. *There are publicly accessible restrooms/washrooms in my neighborhood*
34. *A large selection of fresh fruits and vegetables is available in my neighborhood*

35. *A large selection of low-fat foods is available in my neighborhood*
36. *There are many opportunities to purchase fast foods in my neighborhood*
37. *I feel safe walking in my neighborhood day or night*
38. *Violence is a problem in my neighborhood*
39. *My neighborhood is safe from crime*
40. *People around here are willing to help their neighbors*
41. *People in my neighborhood don't get along with each other*
42. *People in my neighborhood can be trusted*
43. *People in my neighborhood do not share the same values*
44. *There are opportunities for me to learn new skills and information in my neighborhood (e.g. university courses, library lectures, continuing education events)*
45. *My neighborhood has activities for older adults (e.g. those at community centers, senior center, libraries, or other places)*
46. *Please indicate if you regularly join in the activities of each type of organization with people in your neighborhood.*
47. *My neighborhood has a lot of public art (e.g. murals, sculptures, or other art installations).*

Question 47 a-l ask participants to answer yes or no questions about the activities they participate in. Possible answers are *Yes* and *No*. If participants ask what “regularly” means, please explain to them that it is acceptable if they answer however regularly means to them.

- a. *A neighborhood association like a block association, a homeowner or tenant association or a crime watch group*
- b. *Religious groups or charitable organizations*
- c. *Parent-teacher associations or other school support or service groups*
- d. *Youth organizations such as youth sports leagues or the scouts*
- e. *Clubs or associations for senior citizens or older people*
- f. *A labor union*
- g. *A professional, trade, farm, or business association*
- h. *Adult sports clubs or leagues or an outdoor activity club*
- i. *A literary, art, discussion or study group or a musical, dancing, or singing group*
- j. *Any other hobby club or society*
- k. *Ethnic, nationality, or civil rights organizations*
- l. *Other public interest groups, political groups, or party committees*

Now we will ask you some questions about the way your neighborhood might be changing. Thinking about changes in your neighborhood please identify the degree to which the following changes have happened. When answering these questions, think about the ways your neighborhood may have been changing in the past three to five years or the way it is currently changing.

Questions 48-55 ask participants about changes happening in their neighborhood. Possible responses for these questions are:

Not happening
Happening a little
Happening a lot
Don't know

48. New businesses are opening

49. Long-standing businesses are being replaced by different businesses

50. More expensive or fancier grocery stores are opening

51. The cost of housing has increased (i.e. renting or buying)

52. Construction of new buildings on vacant lots or to replace old buildings

53. Construction of new or improved resources, such as parks, bike lanes, transit, or sidewalks

54. People are “flipping” properties, buying and fixing them up to rent or sell

55. Changes are leading to tension or conflict between me and my neighbors

56. New people are moving into my neighborhood

Question 56 asks participants if new people are moving into their neighborhood. Possible responses are:

Not happening
Happening a little
Happening a lot
Don't know

If participants answers *Happening a little* or *Happening a lot*, they are asked to answer question 56.

57. In what ways are people who are moving into your neighborhood different than you? Check all options that apply

Possible responses to question 56 are:

Racial or ethnic background
Income or wealth
Job or employment
Education
They are students
Family structure
Age
Religion
Culture and values
The activities they enjoy
Other, please specify: _____
None; people moving into my neighborhood are the same as me

58. On a scale of 1-10 with 10 being the most and 1 being the least, overall how much has change has happened in your neighborhood during the last three to five years?

59. On a scale of 1-10 with 10 being the fastest and 1 being the slowest, how quickly have change been happening in your neighborhood during the last three to five years?

Questions 58 and 59 ask participants to respond to statements on a scale from 1-10. For question 58, a response of 1 means “Least change” and a response of 10 means “Most change”. For question 59, a response of 1 means “Slow” and a response of 10 means “Fast”. If administered verbally, ensure responses from participants are only given as whole numbers.

These questions will ask for your feelings about any changes happening within your neighborhood. Rate your agreement with each statement from 'strongly agree' to 'strongly disagree.'

Questions 60-69 ask participants about their feelings about changes happening in their neighborhood. The participant is asked to what extent they agree with the statements listed. The responses will be used to develop different indices of the participant's residential environment. The statements should be self-explanatory. If the participant has questions on the meaning of any of the statements, attempt to clarify by repeating the statement. Do not attempt to elaborate on the statement as this may create problems in the scales. The participant should not spend too much time on any one question. The responses are ordered from ***Strongly agree*** to ***Strongly disagree***. ***Neither*** is the middle option.

60. If I had to move right now, I could afford to move to a similar house or apartment within my neighborhood

61. I feel welcome in most new businesses in my neighborhood

62. I feel the personality of my neighborhood has changed

63. I trust people moving into my neighborhood

64. I feel good about the changes happening in my neighborhood

65. I am afraid of being pushed or forced out of my neighborhood

66. I would support changes to my neighborhood (e.g. new stores, sidewalks, parks) even if the changes make it more expensive for me to live here

67. Changes in my neighborhood are meant for people like me

68. Changes happening in my neighborhood make me feel unsure that I will stay here.

69. I feel I have a say in what changes occur in my neighborhood

Finally, we are going to ask you some questions about how you get around your neighborhood.

Questions 70 and 71 ask about neighborhood mobility.

70. Do you currently drive? Question 70 can be responded to with either ***Yes*** or ***No***.

71. Select the way you most often get around your neighborhood (select one).

Drive yourself

Have someone drive you

Use public transportation

Rideshare or taxi

Walk

Bike

Thank you for your time in answering these questions. Your responses help researchers to understand neighborhoods and their impacts on health.

6.12 Sleep Questionnaire

PURPOSE

This form is intended to collect information about MESA participant's sleep habits and behaviors to better understand the causes of cardiovascular disease and brain health. This questionnaire includes questions about sleep duration, sleep quality, snoring and discomfort in the legs that participant may know by herself/himself or what others have told her/him. It also asks about sleep disorders such as sleep apnea, insomnia, and restless legs that have been diagnosed by a health care professional.

DEFINITIONS

Most terms used in this questionnaire are from everyday life; therefore, terms do not need to be explained. The following guidelines should be used should participants require further explanation or not understand the original wording of the questionnaire. Otherwise, if the participant asks about the meaning of any item or tries to qualify a statement, re-read the question and ask the participant to answer as s/he best understands it.

METHODS

1. General Instructions

- 1) This is an **interviewer-administered questionnaire**. Have the participant choose the appropriate responses for each question. Ask the participant to estimate the answer to the best of her/him ability. Ask questions as written and record answers as given.
- 2) Remind the participant that we will use this information only for research purposes. Explain to the participant that some sleep habits and behaviors may be important to their health. Knowing about these things may help us understand the causes of heart disease and brain health better.
- 3) Carefully read to the participant the introduction of each section or group of questions (some questions may refer to things that happened 4 weeks ago whereas others may refer to things that happened in a different period).

2. Specific Instructions

For **questions 1**, respond the number of hours and or minutes. Use two digits for the hours and two digits for the minutes. Record a number in each box.

1. *How much sleep do you usually get each night (or over the longest time you are in bed)*

This refers to the total duration of sleep (in hours and minutes) s/he estimates s/he gets during each major sleep period (i.e., usually over the night; not including naps). If participants are unsure, ask them to estimate how long it usually may take, and reassure them that it is not uncommon to not be able to know exactly how long it takes to fall asleep

2. *Have you had problems falling asleep, staying asleep, or waking up too early that occurred three or more times per week and lasted 3 or months?*

Choices are "yes" or "no". Yes" should be answered if the participant had problems falling asleep, staying asleep, or waking up too early that occurred at least three times per week and happened for at least three months.

a. *If yes, when did these problems first start*

Choose one of the options:

- In the last year
- Between one and 5 years ago
- Between 5 and 10 years ago
- More than 10 years ago

b. *Do you currently have problems with falling asleep, staying asleep, or waking too early?*

Choose one of the options:

- Yes
- No

3. *Overall, how was your typical night's sleep during the past 4 weeks* (Note: this refers to overall sense of sleep quality and how much sleep felt restful or restorative).

Possible answers for question 3:

- Very sound or restful
- Sound and restful
- Average quality
- Restless
- Very restless

4. *Do you feel your sleep has changed over the past five years?*

Possible answers for question 4:

- Definitely much worse
- Somewhat worse
- A little worse
- About the same
- Somewhat better
- Definitely much better

5. *Over the past 4 weeks, how often have you snored?* Participant can report these symptoms based on his own perceptions or based on what others have told him.

Possible answers for question 5:

- Never
- Rarely (1-2 nights a week)
- Sometimes (3-5 nights a week)
- Always or almost always (6-7 nights a week)
- Don't know

6. *Over the past 4 weeks, how often have you had times when you stopped breathing during your sleep?* Stop breathing may include breathing pauses followed by snorting sounds

Possible answers for question 6:

- Never
- Rarely (1-2 nights a week)
- Sometimes (3-5 nights a week)

- Always or almost always (6-7 nights a week)
- Don't know

7. *Do you ever experience a desire to move your legs because of discomfort or disagreeable sensations in your legs?* Ask the participant whether he ever experiences a need to move his legs because of uncomfortable feelings in his calves like an irritating, creeping, crawling sensation.

Choices are “yes” or “no”. If “yes” ask:

a. *Do you sometimes feel the need to move to relieve the discomfort, for example by walking, or by rubbing your legs?*

Choose one of the options:

- Yes
- No
- Don't know

b. Are these symptoms worse when you are at rest, with at least temporary relief by activity?

Choose one of the options:

- Yes
- No
- Don't know

c. Are these symptoms worse later in the day or at night?

Choose one of the options:

- Yes
- No
- Don't know

8. *How likely are you to doze off or fall asleep during the daytime when you don't mean to?* Ask the participant to calculate her/his chances of dozing off (not just feeling tired).

Choose one of the options:

1. Never
2. Sometimes
3. Often
4. All of the time

9. *Many people are more alert in the mornings and consider themselves to be morning people. Others are most alert in the evenings and consider themselves to be evening people. What do you consider yourself to be?* Ask the participant whether s/he feels best (most alert and ready to be active) in the morning or evening, s/he should choose the “definitely” category, respectively. If s/he tends to feel better in the morning, but this is not a strong preference, s/he should pick “more a morning than an evening person”. If s/he tends to feel better in the evening, s/he should pick “more an evening than a morning person.” If s/he absolutely cannot decide whether s/he feels better in the morning or evening, s/he should choose “neither a “morning” nor an “evening” type”.

Choose one of the options:

- Definitely a morning person
- More a morning than an evening person
- More an evening than a morning person
- Definitely an evening person
- Neither a "morning" nor an "evening" type

The following questions ask about diagnosed sleep disorders.

Have you been told by a doctor or other health care provider that you have any of the following: Ask the participant whether a health care professional gave her/him the diagnosis for the following conditions.

10. *Sleep apnea (or obstructive sleep apnea, OSA)?*

Choices are “yes” or “no”. ” Yes” should be answered if the participant had been told by a health care provider that s/he has sleep apnea

If yes: Do you use any of the following for your sleep apnea?

A pressure machine such as CPAP, APAP, or BiLevel?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

A dental device during sleep (a device put in your mouth at night that moves the jaws open)?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

Oxygen during sleep?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

11. *Insomnia*

Choices are “yes” or “no”. ” Yes” should be answered if the participant had been told by a health care provider that s/he has insomnia

If yes: Do you use any of the following for your insomnia?

Over the counter medication?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

Over the counter medication?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

Prescription sleeping pills (such as trazadone, Ambien)?

Choices are “Yes” or “No”

If yes: About how many nights a week do you use this?

12. *Restless legs?*

Choices are “yes” or “no”. ” Yes” should be answered if the participant had been told by a health care provider that s/he has restless legs

13. *Which of the following best describes your usual work schedule?* Participant should indicate their most usual work schedule. Typical times for shifts are: Day: 8 to 4 or 5 to 9; Afternoon: 4 to midnight; Night: 11 to 7AM; Split: Usually within one day, 24 hour periods separated by an unpaid block of time (as in

food industry workers working from 10 am to 2 PM and then 5 to 9 PM); Irregular: Following no pattern, erratic and changing as work needs change; Rotating: a schedule of alternating day/afternoon/evening shifts (any combination; period of rotation may be every day(s) or over days.). Participants who don't work outside of the home or if working in the home, do not get paid for defined work, should answer "don't work."

Choose one of the options:

- Day shift
- Afternoon shift
- Night shift
- Split shift
- Irregular shift / On-call
- Rotating shifts
- Don't work

6.13 Sleep Study PSG Questionnaire

PURPOSE

This form is intended to collect information about MESA participant's sleep habits and behaviors to better understand the causes of cardiovascular disease and brain health. The sleep characteristics assessed as part of this questionnaire include sleep duration, sleep quality, insomnia, sleepiness, naps, and dreams, which are measured by a set of questions or a scale.

DEFINITIONS

Most terms used in this questionnaire are from everyday life; therefore, terms do not need to be explained. The following guidelines should be used should participants require further explanation or not understand the original wording of the questionnaire. Otherwise, if the participant asks about the meaning of any item or tries to qualify a statement, re-read the question, and ask the participant to answer as s/he best understands it.

METHODS

This is an **interviewer-administered questionnaire**. Have the participant choose the appropriate responses for each question. Ask the participant to estimate the answer to the best of her/him ability. Ask questions as written and record answers as given.

3. General Instructions

- 4) Remind the participant that we will use this information only for research purposes. Explain to the participant that some sleep habits and behaviors may be important to their health. Knowing about these things may help us understand the causes of heart disease and brain health better.
- 5) Ask the participant to respond to the questions to be best of her/his ability even if s/he is unsure about the answer to a specific question. Emphasize that it is important to get complete data so that the study results will be valid. Emphasize that there are no right or wrong answers and that we are only interested in the feelings and opinions about sleep.
- 6) Read carefully to the participant the introduction of each section or group of questions (some questions may refer to things that happened 2 weeks ago whereas others may refer to things that happened in a different period).
- 7) In questions that ask about time, enter the time in hours and minutes and check whether it is am or pm. Remember that times at and after noon until before midnight are PM and midnight and times until noon are AM. Use two digits for the hours and two digits for the minutes, i.e., if the participant usually goes to bed at 8.30 pm, you should enter in the form 08:30 and click pm.
- 8) In questions that ask about number of hours and minutes, enter "00," in hours if it is less than one hour and also enter minutes with two digits, i.e., 5 minutes will be "05".
- 9) For questions regarding sleep times on weekdays and weekends, the intention is to understand possible differences on work or "off" days (if the participant has a regular working schedule); otherwise, it is to understand differences between times that participant goes to sleep on Friday and Saturday and wakes up on Saturday and Sunday.

Specific Instructions

Questions 1- 6 ask about participant typical sleep patterns. Ask the participant what time s/he goes to

bed, gets out of bed, time takes to fall sleep and how much time s/he sleeps on weekdays and weekends separately.

For **questions 1 and 2**, record the TIME in the space for each question. Enter the time in hours and minutes using a 12-hour clock time frame and check AM or PM. The participant should provide the times relative to their usual longest period in bed (i.e., not including naps) on their average weekday and weekend. The time should reflect times from “lights off” to arising from bed. For example, if they read in bed, or watch TV in bed before sleep, they should report the times they turn off the light and close their eyes to sleep. If they lay in bed awake in the morning, they should report the times they get out of bed. Check to make sure that the times for awakening occur after the times reported for falling asleep and AM and PM are reported correctly.

1. *What time do you usually go to bed (try to fall asleep):*
 - a. *On weekdays or work days?*
 - b. *On weekends (Saturday, Sunday) or days off?*
2. *What time do you usually get out of bed:*
 - a. *On weekdays or work days?*
 - b. *On weekends (Saturday, Sunday) or days off?*

For **questions 3-6**, ask participant for the number of hours and or minutes. Use two digits for the hours and two digits for the minutes. Write a number in each box.

3. *How long does it usually take you to fall asleep at bedtime?* Question refers to time participant estimates it takes to fall sleep after turning the lights off. If participants are unsure, ask them to estimate how long it usually may take, and reassure them that it is not uncommon to not to be able to know exactly how long it takes to fall asleep- that is why we are using actigraphy and PSG to also measure sleep.
4. *After waking up, how long do you usually stay in bed before getting out of bed?* Question refers to time participant takes to get out of the bed, once s/he wakes up. Some people wake up and fall asleep multiple times over the night; “after waking up” refers to the “last” sleep before getting out of bed with the intention of “starting their day.”
5. *How much sleep do you usually get each night (or over the longest time you are in bed)*
This refers to the total duration of sleep (in hours and minutes) s/he estimates s/he gets during each major sleep period (i.e., usually over the night; not including naps). Weekdays refer to sleeping Sunday through Thursday and Weekends Friday and Saturday nights (unless the participant works and works on a schedule that is not a typical M-F work week).
 - a. *On weekdays or work days?*
 - b. *On weekends (Saturday, Sunday) or days off?*

6. *During a usual week, how many times do you nap for 15 minutes or more?*

Ask the participant to estimate the number of naps s/he has during a usual week. Some people plan naps while other people fall asleep unintentionally. Here a nap is defined as any period outside of their typical sleep period (usually overnight) that is at least 15 minutes long, whether they intended or didn't intend to sleep. Part b asks the participant to estimate whether all of the naps reported were planned, unplanned, or a mixture. If the participant does not know they can answer “don't know”). If participant do not nap, s/he should enter “00” and skip to the following question (to Q#7). A nap is defined as any period of sleep lasting aside from the major sleep period.

If you usually nap 1 or more times per week:

- a. *On average, how long is your typical nap?*
- b. *In general, were these naps planned, or did you fall asleep without meaning to?*

Choose one of the options:

- Naps planned
- Fell asleep without planning to
- Both (some planned, some not)
- Don't know

Questions 7-14 ask about the quality of sleep

Below is a list of questions that ask about the quality of participant's sleep DURING THE PAST TWO WEEKS.

7. *In the past two weeks, have you had problems falling asleep, staying asleep, or waking up too early?*

Choices are “yes” or “no”. Yes” should be answered if the participant perceives any problems in any of these areas. **If no, skip to question 15**

When asking the participant to answer the next set of questions, remind them that the choices are none, mild, moderate, severe, or very severe. If needed, repeat the choices after each question. If the participant has difficulty understanding what each adjective means, remind them to choose the word that seems to reflect how severe the problem felt to them.

Possible answers for questions 8-10 if “yes” to Question 7:

- None
- Mild
- Moderate
- Severe
- Very severe

8. *Please rate the current SEVERITY of your difficulty falling asleep.* Question refers to the severity of the participant's difficulty getting to sleep after turning off the lights for their longest sleep period.
9. *Please rate the current SEVERITY of your difficulty staying asleep.* This refers to problems staying asleep due to waking up too much.
10. *Please rate the current SEVERITY of your problem of waking up too early.* This refers to waking up very early and not being able to fall back to sleep.
11. *To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, ability to function at work/ daily chores, concentration, memory, mood, etc.)?* Here, remind the participant of the new choice of responses and read these out. “Sleep problem” refers to any of the problems in falling asleep, staying asleep or waking up too early mentioned earlier.

Possible answers for question 11:

- Not at all interfering
- A little
- Somewhat
- Much
- Very much interfering

12. How *NOTICEABLE* to others do you think your sleeping problem is in terms of impairing the quality of your life? Here, remind the participant of the new choice of responses and read these out. If the participant reports that there is no one in a position to notice the impact of their sleep on their quality of life, they should answer “not at all noticeable”. “Sleep problem” refers to any of the problems in falling asleep, staying asleep or waking up too early mentioned earlier.

Possible answers for question 12:

- Not at all noticeable
- Barely
- Somewhat
- Much
- Very much noticeable

13. How *WORRIED/ distressed* are you about your current sleep problem? “Sleep problem” refers to any of the problems in falling asleep, staying asleep or waking up too early mentioned earlier.

Possible answers for question 13

- Not at all
- A little
- Somewhat
- Much
- Very much

14. How *SATISFIED/ dissatisfied* are you about your current sleep pattern? Question refers to the participant’s overall sleep pattern—i.e., their patterns of sleeping and waking.

Possible answers for question 14

- Very satisfied
- Satisfied
- Neither Satisfied nor Dissatisfied
- Dissatisfied
- Very Dissatisfied

Questions 15-22 ask about participants sleep over the last month. Let the participant know that some of these questions may sound similar to those they just asked, but these focus on how often s/he experienced the situation in **THE PAST FOUR WEEKS**. If symptoms have varied over this period, the participant should estimate how often the symptom has occurred on average over this time. Please state the new responses, repeating these responses with each question, as needed.

Possible answers for questions 15-21:

- No, not in the past 4 weeks
- Yes, less than once a week

- Yes, 1 or 2 times a week
- Yes, 3 or 4 times a week
- Yes, 5 or more times a week

15. *Did you have trouble falling asleep?*

16. *Did you wake up several times a night?* (Note: assumes the participant's long sleep is during the night. If a shift worker or otherwise gets their longest sleep in the day, that should be referenced).

17. *Did you wake up earlier than you planned to?* (Note: this refers to their "final awakening").

18. *Did you have trouble getting back to sleep after you woke up too early?*

19. *Did you take sleeping pills to help you sleep?* (Note: this refers to over-the counter (OTC) or prescribed medications for sleep).

20. *Did you have sleep difficulties that made you very irritable?* (Note: this refers to the participant's perception that sleep caused them to feel irritable).

21. *Did you feel overly sleepy during the day?* (Note: this refers to feeling sleepy- fighting the urge to go to sleep or have trouble staying awake).

22. *Overall, was your typical night's sleep during the past 4 weeks:* (Note: this refers to overall sense of sleep quality and how much sleep felt restful or restorative).

Possible answers for question 22:

- Very sound or restful
- Sound and restful
- Average quality
- Restless
- Very restless

Questions 23-25 ask about use of medications and caffeinated drinks that may influence sleep.

The following questions ask about use of medications and caffeinated drinks DURING THE PAST FOUR WEEKS.

Possible answers for questions 23-25:

- No, not in the past 4 weeks
- Yes, less than once a week
- Yes, 1 or 2 times a week
- Yes, 3 or 4 times a week
- Yes, 5 or more times a week

23. *Do you ever use an over-the-counter medicine (like Benadryl or Tylenol PM) to help you sleep?* (Note: this can include other similar OTC medications)

24. *Do you ever use a prescription medicine (like trazodone or Ambien) to help you sleep?*

25. Do you ever use caffeinated drinks (coffee, soda, energy drinks, etc.) to help you stay awake?

Questions 26-33 ask about behavior related to feeling sleepy or alert DURING THE PAST WEEK.

The following questions ask about feeling sleepy or alert during the day in the last 7 days

Possible answers for questions 26-32:

- Not at all
- A little bit
- Somewhat
- Quite a bit
- Very much

26. I had a hard time getting things done because I was sleepy.

27. I felt alert when I woke up.

28. I felt tired.

29. I had problems during the day because of poor sleep.

30. I had a hard time concentrating because of poor sleep.

31. I felt irritable because of poor sleep.

32. I was sleepy during the daytime.

33. I had trouble staying awake during the day

Question 34 is used to determine a person's level of daytime sleepiness (in contrast to feeling tired)

34. What is the chance that you would doze off or fall asleep (not just "feel tired") in each of the following situations? If you are never or rarely in the situation, please give your best guess for what would happen.

Possible answers for each item of question 34:

- Not a chance
 - Slight chance
 - Moderate chance
 - High chance
-
- a. Sitting and reading
 - b. Watching TV
 - c. Sitting inactive in a public place (such as a theater or meeting)
 - d. Riding as a passenger in a car for an hour without a break
 - e. Lying down to rest in the afternoon when circumstances permit
 - f. Sitting and talking to someone
 - g. Sitting quietly after a lunch without alcohol

- h. *In a car, while stopped for a few minutes in traffic*

Question 35 and 36 refer to questions about sleepiness and driving that may have happened in the LAST TWO YEARS.

In the last two years, have you had any times when you:

35. *Nearly fell asleep while driving?* (Note: this refers to feeling as though you were dozing off but did not actually fall asleep.)

Choices are “yes” or “no”. If yes,

- a. *How many times?*

36. *Fell asleep while driving?* (Note: this refers to having fallen asleep while you were driving a vehicle, regardless of how short that was.)

Choices are “yes” or “no”. If yes,

- a. *How many times?*
b. *Did this result in a car crash?*

Choices are “yes” or “no”

37. *At what time in the evening do you feel most tired and, as a result, most in need of sleep?* (Note: this does not refer to the actual times you go to sleep but the time you feel so tired you could go to sleep.)

Choose one answer

- 8:00 PM-9:00 PM
- 9:00 PM-10:15 PM
- 10:15 PM-12:45 AM
- 12:45 AM- 2:00 AM
- 2:00 AM- 3:00 AM

Questions 38-40 asks about things that may influence your sleep:

38. a. *When in bed, before going to sleep, do you usually* (Note: usually means more often than not)

Choices are “yes” or “no” for each of the following items:

- a. Watch TV
- b. Read books, magazines, etc (paper format)
- c. Read on an electronic device (Kindle, phone, etc)
- d. Talk or text using a phone
- e. Have a light on
- f. Listen to music

38.b. *In the two hours before you go to bed, do you usually:*

- a. Smoke cigarettes, pipes or cigars
- b. Drink alcohol (this may be right before going to bed)
- c. Drink caffeinated beverages (coffee, etc.) (this may be right before going to bed)

39. Do you usually: (choose one answer)

- Have a bedpartner (Note: someone you usually share a bed with)
- Sleep in a room with another person, but don't share a bed
- Sleep by yourself (Note: there is usually no one else in your bedroom)
- Prefer not to answer

40. Do any of the following make it difficult to sleep?

Possible answers for the following items are:

- Never
 - Sometimes
 - Usually
 - Always
-
- a. Noise in the house
 - b. Noise outside
 - c. Temperature too hot or cold
 - d. Too much light
 - e. Worry or stress
 - f. Body pain (joints, legs, back)
 - g. Chest pain
 - h. Headache
 - i. Acid reflux/heartburn
 - j. Shortness of breath or problems breathing

Questions 41-43 ask about dream experiences

41. How often do you remember your dreams? (Choose one option): (Note: this refers to remembering your dreams you had after waking in the morning; it does not mean fully remembering them but having a memory of a dream and a sense of what it was about).

- Never → if selected “never” skip to Question 43
- Less than once per month
- About once or twice per month
- About once or twice per week
- More than 3 times a week but not every night
- Most nights

If response to Q41 was not “Never”.

42. When you do remember a dream, do you tend to recall it quite clearly?

Choices are “yes”, “no”, or “not sure”

For all participants:

43. Have you ever been told, or suspected yourself, that you seem to ‘act out your dreams’ while asleep (for example, punching, flailing your arms in the air, making running movements, etc.)?

Choices are “yes”, “no”, or “not sure”

7 EXAMINATION PROCEDURES

7.1 Anthropometry

PURPOSE

Anthropometry was obtained in each of the previous MESA exams. The purpose is the same as for previous exams.

MATERIALS AND EQUIPMENT

- Stadiometer (Accu-Hite Measure Device with level bubble) (height ruler with triangle level is used at some centers)
- Detecto Platform Balance Scale in lbs/kg
- Gulick II 150 cm anthropometric tape
- Full length mirror
- Four 50-pound weights (certified prior to first MESA visit) to calibrate scale

METHODS

Methods for completing the Anthropometry portion of Exam 7 are the same as in Exam 1. Some important points are reiterated here.

General Instructions:

For all measurements, participants should wear light clothing but no shoes (thin socks or “pillow slippers” OK). Have participants completely empty their pockets and remove excessive amounts of jewelry that could affect the weight measurement. Provide lockers with locks for valuables.

Specific Instructions:

7.1.1 Standing Body Height

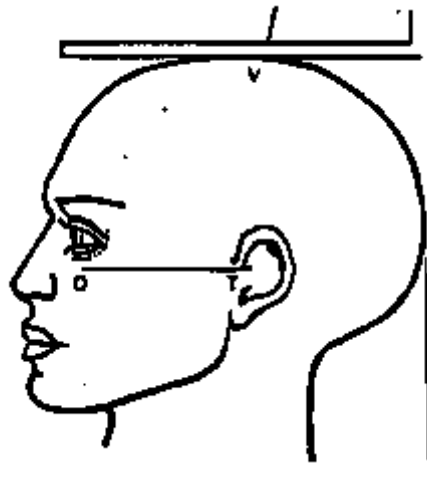
Equipment

- Stadiometer (Accu-Hite Measure Device with level bubble) (height ruler with triangle level used at some centers is adequate)

Before measuring height, make sure the floor is level, the wall is at a 90-degree angle to the floor, the wall is straight, and the Stadiometer is mounted perpendicular to the floor.

Record the results, to the nearest tenth (0.1) of a cm, in Box 1a on the Anthropometry Form.

For accurate measurement of height, the participant must be standing in a vertical plane. To achieve this position, have the participant stand erect on the floor or horizontal platform, with back against the vertical Stadiometer, heels against the wall, and feet or knees together—whichever come together first. Have the participant look straight ahead, with head in the Frankfort horizontal plane (Figure 1, below).



The Frankfort Plane includes the lower margin of the bony orbit (the bony socket containing the eye) and the most forward point in the supratragal notch (the notch just above the anterior cartilaginous projections of the external ear)—also referred to as the upper margin of the external auditory meatus (the hole in the ear).

Figure 1. Frankfort Plane for Measuring Body Height

Place the headboard over the crown of the head, with the headboard forming a right angle to the scale. The headboard should touch the scalp lightly.

Ask the participant to step out from under the headboard. Record the participant's height to the nearest 0.1 centimeter in Box 1a of the Anthropometry Form.

If you are unable to measure the actual height of the participant because the headboard does not rest directly over the scalp, estimate height to the nearest 0.1 cm, record in Box 1a of the Anthropometry Form and answer "yes" to the question, "Was there a modification in protocol?"

If any modification was made to obtain height, bubble in "yes" to the question, "Was there a modification in protocol?"

7.1.2 Body Weight

Equipment

- Detecto Platform Balance Scale in lbs/kg

Always balance the scale so that the indicator is at zero when no weight is on the scale. The scale should be on a firm, level surface. Instruct the participant to stand in the middle of the platform of the balance scale, with head erect and eyes looking straight ahead. Adjust the weight on the indicator until it is balanced. *Record the results, to the nearest 0.5lbs, in Box 2a.*

If the participant is too obese to stand securely on the scale's platform when looking straight ahead, they may stand sideways on the scale to take the weight measurement; facing to the side rather than the front will provide the participant a wider base and more stability.

If a participant has a prosthetic limb or breast prosthesis, measure weight with the limb on.

If a participant is frail or unsteady, measure weight while participant is lightly steadied by you or an assistant.

If a participant is unable to stand on the scale for a weight measurement, do not attempt a weight measurement. Answer “yes” to the question, “Was there a modification in protocol?”

If any modification were made to obtain weight, bubble in “yes” to the question, “Was there a modification in protocol?”

7.1.3 Girth Measurements

Equipment

- Gulick II 150 cm anthropometric tape
- Full length mirror

Technique

- Do *not* take abdominal and hip girth measurements over loose clothing. It is ok if taken over light well-fitted clothes.
- If a participant is very large, you may have them hold one end of the tape while walking the tape around to obtain the measurement. If any circumference exceeds 150 cm, use the 250 cm tape measure. (Take care not to offend the person being measured and change to the larger tape as discretely as possible.)

Abdominal Girth

Apply a Gulick II anthropometric tape horizontally at the level of the umbilicus and instruct the participant to breathe normally. Move to the participant’s right side to take the measurement; do not take this measurement from the front. Be sure to keep the tape horizontal while making the measurement; use the wall-mounted mirror to assure horizontal placement on all sides.

Round abdominal girth measurement to the nearest 0.1cm and record in Box 3a.

*If the circumference exceeds 150 cm, record “yes” for the question, “**Was there a modification in protocol?**”*

Hip Girth

Take the hip girth measurement from the participant’s right side; do not take this measurement from the front. Instruct the participant to stand with their feet together. Measure hip girth at the maximum circumference of the buttocks. Check to see that the tape is level in front and back.

Round hip girth measurement to the nearest 0.1cm and record in Box 3b.

*If the circumference exceeds 150 cm, record “yes” for the question, “**Was there a modification in protocol?**”*

Comments/Modifications to the Protocol

If you have comments or if there have been modifications to the protocol as described above, answer “yes” to question 4 on the Anthropometry Form and record comments in the space provided. If there are no comments or modifications, answer NO to question 4.

Quality Control ~ Calibration Check of Scales and Equipment Check

Equipment:

- Four 50-pound weights (certified prior to first MESA visit) to calibrate scale
- Gulick II anthropometric tapes

Check scales for accuracy monthly.

Place two weights on the scale and record the numeric value obtained in the “Light Poise” column of the “Scale Calibration Checklist.” Add two more weights and record the numeric value obtained in the “Heavy Poise” column.

The values obtained should be within ± 1.0 pound of the expected weight. If either value exceeds this limit, the scale must be calibrated by the manufacturer or by the appropriate institution personnel.

When the scale is not in use, keep it balanced at 300 pounds. This keeps the tension off the internal spring mechanism.

Examine anthropometry tape measures on a weekly basis for sign of wear.

7.1.4 Neck Circumference Measurement

Objective and Purpose

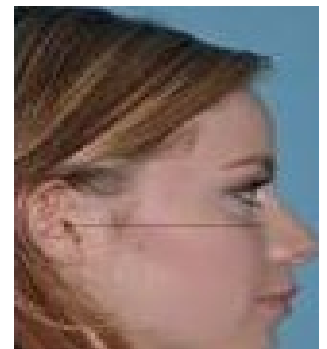
To describe the process for obtaining a neck circumference measurement. Neck circumference provides an anthropometric measurement that provides information on risk for heart disease and sleep apnea. Obtaining consistent measurements of neck circumference may aid in understanding risk factors for health outcomes in MESA.

Materials and Equipment

- Non-elastic measuring tape

Definitions

Head in the Frankfort Horizontal Plane. The head is in the Frankfort plane when the horizontal line from the ear canal (auditory meatus) to the lower border of the orbit of the eye is parallel to the floor. This is usually achieved by having the participant look forward, in a natural head position (i.e., head not pointing to the ceiling or floor).



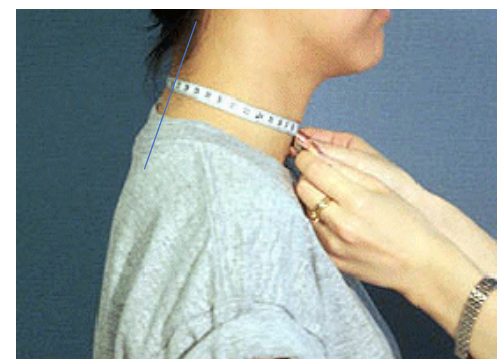
Method

General Instructions for Neck Measurement:

- Participants should wear light clothing on the upper part of their body
- The measurement should be taken over bare skin, ensuring that hair is not under the tape measure.

Technique

1. Participant must stand or sit with the head in the Frankfort horizontal plane. Having the participant looking straight ahead at a distant mark, gently tilt the head up or down to achieve the proper alignment if needed.
2. Apply the measuring tape around the neck at the point below the thyroid prominence, keeping the tape perpendicular to the longitudinal axis of the neck. The zero end of the tape should be below the end from which you are recording. This should be a smooth downward sloping measurement (Figure).
3. If the thyroid prominence cannot be located, ask the participant to swallow and feel for the “nob” that bobs up and down.
4. In women, the thyroid prominence may not be felt; use a point midway along the neck, from the point.
5. Take the neck circumference three times and record each.
6. Record the participant’s neck circumference to the nearest 0.1 centimeter



References

1. Lohman, Timothy G., Roche, Alex F., Martorell, Reynaldo, ed. Anthropometric Standardization Reference Manual. Human Kinetics Books. Champaign, IL: 1988
2. **NHANES Anthropometry Procedure Manual.**
www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf

7.2 Seated Blood Pressure

PURPOSE

Blood pressure (BP) level is a major risk factor for coronary heart disease, congestive heart failure, and stroke. Heart rate reflects autonomic nervous system function and cardiovascular fitness. The measured BP level is subject to biological and observer variability. The purpose of a specific measurement protocol, or training and certifications of technicians, and of ongoing quality control is to minimize variability due to known exogenous factors and to reduce imprecision and biases in measurement.

The Dinamap® automated device will be used in Exam 7 for in-clinic exam for consistency with data collection from previous MESA Exams. If the Dinamap is unavailable, an OMRON 10 Series Upper Arm blood pressure monitor be used.

MATERIALS AND EQUIPMENT

- Measuring tape (for arm circumference).
- Watch or stopwatch (to time five-minute rest and resting heart rate).
- Hand calculator (to average 2nd and 3rd BP readings).
- Blood Pressure Device (Use Dinamap for in-clinic visits, use OMRON Series 10 for at-home visits or as a backup for the Dinamap).

Dinamap® automated blood pressure device (Dinamap Monitor Pro 100®, which includes printer paper, power cable, and power converter.)

- Blood pressure cuffs in a variety of sizes (Dura-cuf Adult Assortment Pack® [#2699]).
- Copy of Critikon® chart for choosing correct BP cuff size (see Table 2).

OMRON 10 Series Wireless Bluetooth Upper Arm blood pressure monitor

DEFINITIONS

Sphygmomanometry: Measurement of blood pressure.

Oscillometric device: Method for measuring blood pressure that relies on the oscillation or fluctuation in arterial pressure generated by the cardiac cycle and transmitted to an inflated blood pressure cuff overlying an artery. This method differs from the auscultatory method, which relies on audible changes over an artery during deflation of an inflated cuff.

7.2.1 Blood Pressure Classification

The 2017 American College of Cardiologists/American Heart Association Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults defines categories of blood pressure according to the following criteria:

Table 1. Classification of BP in Adults Aged 18 Years or Older*.

BP Category	SBP (mm Hg)		DPB (mm)
Normal	Less than 120	and	Less than 80
Elevated*	120-129	and	Less than 80
Hypertension**			
Stage 1	130–139	or	80–89
Stage 2	140 or more	or	90 or more

BP indicates blood pressure (based on an average of ≥ 2 careful readings obtained on ≥ 2 occasions); DBP, diastolic blood pressure; and SBP, systolic blood pressure.

* Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

Alert levels requiring **immediate referral** (send participant directly to a physician or hospital) for MESA participants are:

- **Systolic BP >210 mm Hg**
- **Diastolic BP >120 mm Hg**
- **Pulse >130 beats per minute**

Alert levels requiring **urgent referral** (*within one week*) are:

- *Systolic BP 180–210 mm Hg*
- *Diastolic BP 110–120 mm Hg*

Alert levels requiring follow-up within two months' time, and, therefore, we recommend physician notification for systolic or diastolic BP above these levels.

- BP >140/90 mm Hg

Guidelines state that blood pressure classifications and referral recommendations are based on the average of two or more readings on two or more occasions. In MESA uses the average of the 2nd and 3rd blood pressure readings (see below) to reduce the impact of reactivity (higher first reading) on the estimate of the value of the underlying blood pressure. Thus, the average of the 2nd and 3rd readings should be used in deciding whether a participant meets criteria for an alert level. This will require on-the-spot arithmetical manipulation of the systolic and diastolic values. A hand calculator may be useful. The data forms include fields for these averaged values and for documenting any actions taken.

7.2.2 Preparation

Record the date of the procedure, blood pressure device type and device number on the Seated Blood Pressure Form during the five-minute rest period.

Before the BP measurement procedure, explain to the participant what to expect and how long the procedure will take. The following script is suggested:

This part of the exam involves taking your resting blood pressure. It will take about 10 minutes. We would like you to sit with both feet on the floor and your arm supported on the table. We will have you sit quietly for five minutes. Then we will take your blood pressure three times, one minute apart (2 minutes apart for the OMRON device), using an automated device. We will give you your blood pressure readings and some material to help you interpret them at the end.

Rest Period

The participant should rest for five minutes (timed using a watch or stopwatch) prior to the heart rate and blood pressure measurement.

When the five-minute rest period is over, but before the first blood pressure measurement is started, *record the time of day on the Seated Blood Pressure Form* (examples: 04:25 P [p.m.] or 11:38 A [a.m.]).

Positioning the Participant

The workstation should be free of excessive noise or distractions.

The participant should be seated and relaxed in a comfortable chair, to ensure that:

- They are sitting up (not slouched).
- Both feet are on the floor (legs/ankles not crossed).
- Right forearm is supported resting on the table.

The participant should not talk, eat, or drink during the procedure.

Ideally, the blood pressure device output will not be visible to the participant during the measurement, as this may cause anxiety.

7.2.3 Dinamap Methods

Cuff Size Selection

Use the proper cuff size to avoid under- or over-estimation of the correct blood pressure. Selection of the proper sized cuff is based on the guideline that the length of the inflatable bladder in the cuff should be at least 40% of the arm circumference. Measurement of the bladder length in the Critikon® cuffs confirms that the chart in Table 3 conforms to this guideline. A copy of this chart should be available during the BP measurement procedure for easy reference. *Selection of cuff size should be based on the Critikon® chart in Table 2, and only Critikon® cuffs should be used.* If the participant’s arm size falls in a range in which there is overlap of two Critikon® cuff sizes, use the *larger* cuff.

Measure the right arm circumference as follows:

- Ask the participant to bare the upper arm.
- Ask the participant to sit or stand holding forearm horizontal, i.e., parallel to the floor.
- Measure arm length from the acromion (bony extremity of the shoulder girdle) to the olecranon (tip of the elbow) using a metric tape.
- Mark the midpoint on the dorsal (back) surface of the arm.
- Ask participant to relax arm alongside of the body.
- Draw the measuring tape snugly around the arm at the midpoint mark, keeping the tape horizontal. Only pull the tape snug enough so that the first red-bead marker can be seen. Tape should not indent the skin. If you can see both beads, the tape is too tight. *Record the arm circumference measured to the closest (0.1) cm in Field 1 on the Seated Blood Pressure Form.*
- Use the criteria in Table 2, below, to determine cuff size. *Check the cuff size used in Field 2 on the Blood Pressure Form by filling in the appropriate circle.*

Table 2. Cuff Size Indicated by Measured Arm Circumference

Arm Circumference*	Cuff Name**	Bladder Length (cm)
12-19	Child	8
19.1-25	Small Adult	10
25.1-33	Adult	13
33.1-40	Large Adult	17
40.1-50	Thigh	

* These circumferences are printed on the corresponding cuff for verification.

** Critikon Dura-cuf® nomenclature is also printed on the cuff.

Setting up the Dinamap® BP Machine

Load the printer paper by opening the flap on the side of the device. There is a diagram showing how to thread the paper on the inside of the door. There is a gray plastic wheel to the left of the roller. Just to the right of the gray wheel is a *gray plastic lever*. Gently flip this lever up. This releases the roller so that you can use the gray plastic wheel to turn the roller to thread the paper. Flip the gray lever down when finished.

To turn on the Dinamap[®] device, push the "Off/On" button on the front control panel (lower left).

After five seconds an initial message will appear on the LCD screen. It will consist of a WARNING and the instruction, "PUSH A FRONT PANEL KEY TO START."

In the main menu select PRINT using the gray toggle knob. In the next menu, select AUTO and then push the toggle knob. This will program the device to print the blood pressure measurements.

Do not touch the monitor again until you have completed steps 4–6, below, and you are ready to proceed with blood pressure measurement.

Application of the Blood Pressure Cuff

Place the appropriate cuff around the upper right arm so that the mid-height of the cuff is at heart level. Palpate the patient's brachial artery and place cuff so that the artery is aligned with the cuff arrow marked "artery."

Place the lower edge of the cuff, with its tubing connections, two centimeters above the natural crease across the inner aspect of the elbow.

Wrap the cuff snugly around the arm, with the palm of the participant's hand turned upward.

Secure the wrapped cuff firmly by applying pressure to the locking fabric fastener over the area where it is applied to the cuff.

Do not wrap the cuff too tightly around the arm. You should be able to insert the first joint of two fingers under the cuff. The cuff should be snug but not tight.

Be sure all air is squeezed out of the cuff before each inflation.

Blood Pressure Measurement

To begin the blood pressure procedure, access the Main Menu on the Dinamap[®] by pushing the "Start/Stop" button at the lower right of the monitor. (Please note that the gray knob located at the upper right of the monitor allows you to change selections in the monitor screen, in a manner similar to a computer mouse or pointing device. Rotate the knob to move from one item to another in the monitor screen and push it to select the desired option.)

Use the knob to select the set bp option from the menu and then press the knob (equivalent to clicking a mouse) to implement the selection. The next menu appears automatically.

Use the knob to select AUTO BP and then press the knob.

Immediately after you select AUTO BP the monitor will start the first blood pressure measurement. However, during this first inflation, select the window that has appeared to the right of AUTO BP and push the knob, so that there is a black number against a clear background in the window. Rotate the knob to select "1." This will select one minute as the interval between sequential blood pressure measurements. Push the knob again (colors in window will reverse) to implement the selection. (The device will retain this setting, even after it is turned off, so you will not have to repeat this step again.)

Palpate the radial pulse during inflation. The radial pulse should not be palpable at peak inflation pressure. If the participant's radial pressure remains palpable when the device begins to deflate, the device will complete its deflation procedure and then should automatically reset itself for a higher inflation pressure and repeat the measurement. In the unlikely event that this does not occur, manually reset the inflation pressure:

Rotate the knob until the window to the right of TGT PRESSURE is highlighted, push the knob and rotate it again until it reaches 210, and push it again to select. Repeat the blood pressure measurement.

It is not necessary to repeat or prolong the five-minute rest period, if this happens, but explain the change in the procedure to the participant (e.g., “I think we need to use a higher inflation pressure—I'm just going to reset the machine”).

If a higher maximal inflation pressure is needed, reset this parameter at 260 mm Hg, and, if necessary, at 300 mm Hg. Check carefully to be sure that the cuff is properly positioned on the participant's arm with the arrow at the brachial artery.

When the radial pulse is obliterated at maximal inflation, the first blood pressure measurement will be obtained. The device will automatically obtain the 2nd and 3rd measurements, at two-minute intervals.

Record the three sequential blood pressure readings in the Seated Blood Pressure Form.

After the 3rd measurement is obtained, return to the main menu and select TREND and then PRINT ALL. When printout is obtained and verified, proceed to TREND and then CLEAR. When the monitor requests confirmation, select YES. Paste or staple the printout in the ad-hoc page.

To keep the machine from continuing with further automatic blood pressure measurements go to the main menu, select SET BP and then MANUAL. There is no need to turn off the machine if another participant is ready. If for any reason the machine automatically starts an unnecessary inflation, push the “Start/Stop” button at the lower right-hand corner of the monitor and then select MANUAL, as explained above. Remove the blood pressure cuff from the participant's arm and thank the participant for their time.

Quality Assurance/Quality Control Procedures for Dinamap Pro 100

Once a week each device should be used simultaneously with a paired device to simultaneously measure the blood pressure in each arm of a non-smoker under the age of 50, in whom there is no reason to suspect that the blood pressure in the two arms should differ. Repeat the measurement three times.

If the paired blood pressure measurements agree within 4 mm Hg or less, for both systolic and diastolic BP, the devices are considered in calibration.

Investigate any systematic divergence, even if less than 4 mm Hg (e.g., by switching arms and/or pairing the devices with a third device).

If the two devices differ by more than 4 mm Hg, calibration must be done. It should be recognized that, if the cuff deflation rate is 2 mm Hg/sec and the heart rate is 60 bpm, divergences of 2–4 mm Hg would be expected, even if the device is in perfect calibration.

7.2.4 OMRON 10 Series Methods

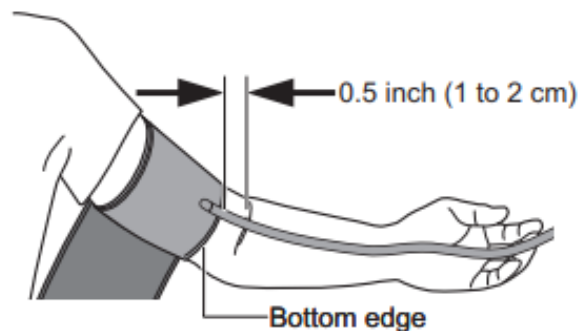
Application of the Blood Pressure Cuff

Plug the arm cuff into the monitor by inserting the air plug into the air jack securely until it clicks.

Place the cuff around the upper left arm so that the mid-height of the cuff is at heart level, with the arm resting comfortably on a table. The bottom edge of the cuff should be 0.5 inch (or 1 – 2 cm) above the inside elbow and the air tube should be on the inside of the arm, aligned with the middle finger.

Wrap the cuff securely around the arm.

If applying the cuff to the right arm, place the cuff around the upper right arm. The air tube should instead run along the side of the elbow, along the bottom of the arm. Avoid having the arm rest on the air tube.



Blood Pressure Measurement

To begin the blood pressure procedure, press the “Start/Stop” button on the lower right of the monitor. All symbols on the screen display will appear before starting a measurement.

Use the guest mode to take a single measurement by pressing and holding the “Start/Stop” button for more than 3 seconds. No readings will be stored in memory in this mode.

Release the “Start/Stop” button when the user ID and date/time display on the top right corner of the screen turn off. The arm cuff will automatically start to inflate.

To stop the measurement at any point, press the [START/STOP] button once to deflate the arm cuff.

Once the monitor detects the participant’s blood pressure and pulse rate, the cuff automatically deflates. *Record the first blood pressure reading in the Seated Blood Pressure Form.*

Wait 2-3 minutes before pressing and holding the “Start/Stop” button for more than 3 seconds again, entering into guest mode. Releasing the “Start/Stop” button after the user ID and date/time display turn off will initiate another reading. *Record the second blood pressure reading in the Seated Blood Pressure Form.*

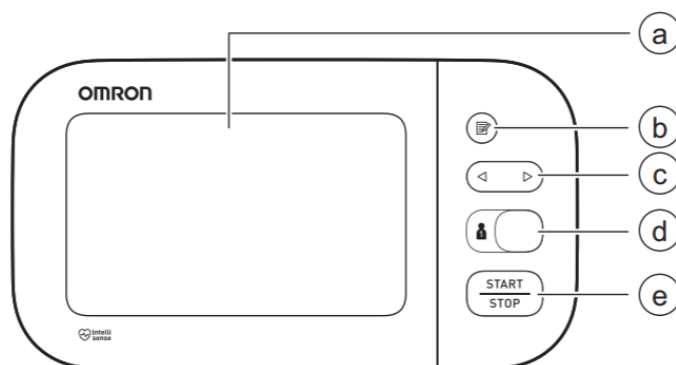
Repeat waiting 2-3 minutes and pressing, holding, then releasing the “Start/Stop” button to take a third measurement. *Record the third blood pressure reading in the Seated Blood Pressure Form.*

The monitor will automatically turn off after 3 minutes.

Optionally, the OMRON 10 monitor can take and automatically record measurements for 2 people using the “User ID selection” switch above the “Start/Stop” button. The monitor can store up to 100 readings per user. User 1 is designated by moving the switch to the right-most position. User 2 is designated by moving the switch to the left-most position.

After selecting a User ID, press the “Start/Stop” button once. Once the monitor detects the participant’s blood pressure and pulse rate, the cuff automatically deflates. The blood pressure and pulse rate are displayed with the previous reading.

Front of the monitor



- (a) Display
- (b) [Memory] button
- (c) [Forward/Backward] buttons
- (d) [User ID selection] switch
- (e) [START/STOP] button

Wait 2-3 minutes before proceeding with a second reading using the same User ID, pressing the “Start/Stop” button only once.

Wait another 2-3 minutes before finishing with a third reading using the same User ID.

To view the three consecutive readings stored in memory on the device, press the circular “Memory” button on the top right corner of the device, above the left and right arrow buttons, with the User ID selected.

A memory number will appear on the bottom left corner of the screen. After the memory number appears, the latest reading will appear on the right side of the screen, along with a past reading on the left for comparison.

Press the left or right arrow buttons to scroll through the previous readings stored in memory. The left directional arrow indicates older readings. The right directional arrow indicates more recent readings.

To view the average reading based on the 3 readings taken in the most recent 10-minute timeframe, start with the monitor turned off and the User ID selected. Press and hold the circular “Memory” button for more than 3 seconds. An “AVG” symbol will flash on the top of the screen, above a calculated average reading on the right side of the screen.

Once the three consecutive blood readings are recorded in the Seated Blood Pressure Form, click on the “Memory” button again just once with the User ID selected. Wait until the latest reading along with a past reading appears on the display. While holding the “Memory” button down, press and hold the “Start/Stop” button for more than 3 seconds. The display should start flashing.

When the display stops flashing, all readings for the designated User ID are deleted. Turn off the monitor by pressing the “Start/Stop” button once or waiting 3 minutes.

New readings for the selected User ID can be taken the next time the monitor is turned on.

Storing and Cleaning the OMRON 10 Series Monitor

After using the monitor, unplug the air plug by pulling on the plastic air plug at the base of the tube, not the tube itself.

Gently fold the air tube into the arm cuff, avoiding bending or creasing the tube excessively.

Avoid storing the monitor and its components:

- If wet.
- In locations exposed to extreme temperatures, humidity, direct sunlight, dust or corrosive vapors such as bleach.
- In locations exposed to vibrations or shocks.

To clean the monitor, use a soft dry cloth or a soft cloth moistened with mild (neutral) detergent only. Then wipe with a dry cloth. Do not use any abrasive or volatile cleaners, including gasoline, thinners, or similar solvents. Do not immerse the monitor and its components in water.

7.2.5 BP Measurement Instructions for Participants With Short, Thick Arms

Occasionally there will be a participant whose upper arm is too thick and short for the thigh cuff or on whom the thigh cuff pops open on inflation. The alternative procedure in this case is to obtain the resting blood pressure in the right *forearm*.

Measure the forearm circumference at the midpoint between the olecranon (elbow) and the ulnar styloid (wrist)

bone on pinkie side). Select the proper size cuff based on the forearm measurement. The blood pressure procedure is otherwise the same.

Document on the Seated Blood Pressure Form that you have measured the *forearm blood pressure*.

7.2.6 Reporting Blood Pressure Results to Participants

The technician may verbally provide the participant with the blood pressure reading (the average of the last two pressures), *if asked*, after the procedure has been completed.

Alternatively, if the blood pressure is normal (<140/90), the technician may say that it is normal, particularly if asked.

If the blood pressure is not normal (>140/90) but not at an alert level (>210 mm Hg), the technician should exercise the standard option of not discussing the interpretation or stating that it does appear to be high (or “somewhat elevated”) but that, again, it will be discussed later.

If an alert level is identified, the technician should calmly notify the clinic coordinator when the procedure has been completed. (If symptoms of severe hypertension are present, the technician should notify the clinic coordinator immediately.)

7.3 Pulse Oximetry

PURPOSE

The rationale for measuring oxygen saturation is to assess cardiopulmonary function.

MATERIALS AND EQUIPMENT

Pulse Oximeter: Devon Medical Handheld Pulse Oximeter PC-66

METHODS

Preparation

1. Resting oxygen saturation will be measured while the participant is resting for blood pressure measurement.
2. Explain the procedure to the patient
3. Verify that the probe is clean, dry and in good condition before applying it to the participant
4. Ask the participant to remove nail polish or acrylic nails that may impair the effective transmission of light (have some nail varnish remover on hand just in case).
5. The pulse oximeter is placed on the hand of the opposite arm that the blood pressure cuff is applied.

Positioning the Participant

1. The workstation should be free of excessive noise or distractions
2. The participant should be seated and relaxed in a comfortable chair
3. The participant should not talk, eat, or drink during the procedure

Reading the pulse oximeter

1. Place oximeter on participant's finger during the beginning of the resting period prior to blood pressure measurements.
2. Verify that the probe is well positioned
3. Record the apparent median value obtained while observing the monitor over a one-minute observation period in Q9 of the Seated Blood Pressures Form.
4. In Q10 of the Seated Blood Pressure Form, record if the participant is using supplemental oxygen. If yes, record the flow rate in liters per minute.

For participants using oxygen

If the subject is using oxygen, the pulse oximeter should be placed on the participant's finger first. Next, the participant's oxygen should be discontinued while monitoring the oximeter for a period of five minutes. If the pulse oximeter reading falls to 82% or less, oxygen will be replaced and a reading of 82% will be recorded as the participant's oximetry. The apparent median value obtained while observing the monitor over a one-minute observation period should be recorded.

Quality Assurance/Quality Control Procedures for Oximeter

1. Clean sensor/probe as per manufacturers' guidelines in between each patient use.
2. Calibration as per manufactures instructions
3. Daily quality control check on self

4. Carry spare alkaline batteries
5. To avoid any leakage from the batteries, remove them if the pulse oximeter is not in regular use
6. Report immediately to the Clinic Coordinator if the pulse oximeter appears to be malfunctioning

Certification requires five documented, correctly performed pulse oximetry measurements, following the MESA certification form

7.4 Biosample Collection

PURPOSE

The purpose of the Biosample Collection Form is to record information related to the blood draw, spot urine, and hair follicle collection. The Sample Processing Form tracks sample aliquots issues that may affect processing for the central laboratory.

MATERIALS/EQUIPMENT

See separate Exam 7 Laboratory MOP for specific materials.

METHODS

General instructions

There are two possible blood draw configurations depending on the Field Center from which the participant is enrolled.

Data entry software will create the appropriate Phlebotomy form automatically.

The process of labeling of tubes and cryovials for a given participant will be dictated by the specific version of the Phlebotomy form for that person.

Copies of the Biosample form and the Processing form are included with the shipment of samples to the Central Laboratory.

The Exam 7 Laboratory MOP includes the details about the blood draw and processing.

Specific Instructions:

Biosample Collection Form

Print the participant's Biosample form immediately after they sign the informed consent and the responses have been recorded in the Consent Form.

Give the form to the phlebotomist or lab tech as soon as possible to inform them how to complete the setup of the sample tubes and cryovials, or if the prepared MESA setup is all that is needed.

Indicate whether the blood, urine and hair collection were completed.

If blood, urine, or hair were not collected, select the reason why not

Indicate whether the participant is selected as a QC subject.

After the blood draw has been completed, retrieve the completed Biosample Form and enter the information in the appropriate fields on the REDCap Data Collection Program.

7.5 Clinician's Physical Examination

The physical examination in MESA-MIND is a neurological examination that is essential to classification of cognition by MESA-MIND adjudicators. The examination is designed to be conducted by a clinician with experience in physical examination of patients or participants for signs of Parkinson's disease or stroke. The physical examination focuses on signs of Parkinson's and stroke which may confound the diagnosis of Alzheimer's disease and related dementias. Each component is designed to be deemed as clearly present or not. Marginal evidence of each sign (e.g. +/-) is not a requested ascertainment. The entire examination is estimated to take 10-15 minutes, depending on experience of the examiner and the age, mobility and cognitive state of the participant. For each section, the question numbers refer to the MESA-MIND Clinician's Physical Exam Form.

Training Process:

Training videos will be available on the MESA website that demonstrate each of the desired components. There will be a webinar close to study start-up for clinicians to ask questions and get any clarification needed.

Cognition: (*all are tests for cortical cognitive deficits caused by stroke/CVD [re: question 3a]*)

Aphasia:

1. Spontaneous speech (assess during informal interview)
2. Comprehension (overall assessment of the ability to correctly respond to commands during the exam)
3. Repetition (ask the participant to repeat, "The caring grandmother baked cookies for everyone")

Apraxia:

1. Ask the participant to "Pretend to use a hammer"
2. Ask the participant to "Pretend to strike a match and blow it out"

Neglect:

1. Visual extinction to double simultaneous stimulation - Ask the participant to look forward at the examiner's face, then have the participant count the examiner's fingers presented simultaneously in both right and left visual fields.
2. Tactile extinction to double simultaneous stimulation - Have the participant close their eyes, then have the participant identify whether they can feel light touch applied simultaneously to both sides of their body.

Cranial Nerves:

Cranial nerve II:

- Visual fields (*tests for cortical visual field loss caused by stroke/CVD [re: 3d]*) - Ask the participant to look forward at the examiner's face. Then have the participant count the examiner's fingers presented singly in both right and left visual fields.

Cranial nerves III, IV, and VI:

- Cardinal positions of gaze (*tests for focal finding consistent with SIVD [re: 3b]*) - Ask the participant to move their eyes and follow the examiner's finger into all cardinal positions of gaze.

Cranial nerve V:

- Facial sensation: light touch (*tests for focal finding consistent with SIVD [re: 3b]*) - Ask the participant identify light touch applied to areas V1, V2, and V3 on both sides of their face.

Cranial nerve VII:

- Facial movement: (*tests for motor findings consistent with stroke/CVD [re: 3c] and PD [re: 2d]*) - Ask the participant to wrinkle forehead then smile big.

Cranial nerve XII:

- Tongue protrusion and atrophy (*tests for motor findings consistent with stroke/CVD [re: 3c]*) - Ask the participant to stick their tongue out as far as possible.

Motor:

1. Atrophy [re: 4] - Ask the participant to relax, then inspect all limbs for muscle atrophy
2. Tone - Ask the participant to relax, then inspect all limbs for muscle tone:
 - (1) all extremities (*spasticity=stroke [re: 3c]; rigidity/cogwheeling=PD [re: 2c]*)
 - (2) axial, i.e., neck/spine (*rigidity=PD [re 2c]*)

3. Strength (*tests for motor findings consistent with stroke/CVD [re: 3c]*) - Inspect all major muscle groups for strength by having the participant exert force against the examiner's resistance:
 - graded: normal = normal power against resistance or abnormal = weak against resistance
 - check arm abduction; elbow flexion/extension; wrist flexion/extension; finger flexion/extension
 - check hip flexion; knee flexion/extension; ankle flexion/extension; toe flexion/extension
4. Resting arm tremor (*PD [re: 2a]*)

Sensation:

1. Light touch all limbs (*tests for focal finding consistent with SIVD [re: 3b]*) - Ask the participant to identify light touch applied to the distal and proximal aspects of all limbs

Coordination:

1. Finger-nose-finger and heel-to-shin (*tests for motor findings consistent with stroke/CVD [re: 3c] and PD [re: 2d]*) - Ask the participant to repeatedly touch the examiner's finger and then their nose; the examiner is to move their finger to a different site during testing. Ask the participant to drag their heel up and down their shin, testing both legs.
2. Rapid movements hands and feet (*tests for motor findings consistent with stroke/CVD [re: 3c] and PD [re: 2b]*) - Ask the participant quickly move their fingers, quickly pronate/supinate the forearms, and quickly make a fist and open the fingers bilaterally. Ask the participant to move their heels up and down as quickly as possible.

Reflexes:

1. DTR's at ankle, knee, elbow (biceps only) (*tests for motor findings consistent with stroke/CVD [re: 3c]*) - Test for DTRs using a reflex hammer. Test plantar response using a blunt object such as a tongue depressor, etc.
2. Plantar response (*tests for motor findings consistent with stroke/CVD [re: 3c]*)

Gait and Balance:

1. Routine and tandem stance and gait (PD [re: 2d and e]; CVD [re 3c]; apractic [re: 5]) - Ask the participant to ambulate in a normal fashion for 10 to 20 feet. Ask the participant to ambulate with the feet falling on a line for about 10 feet.
2. Pull test (PD (re: 2f)) - Ask the participant to stand in front of the examiner. Ask the participant to try to keep their balance as the examiner lightly to moderately pulls the patient backwards at their shoulders.

7.6 Short Physical Performance Battery

7.6.1 Introduction

Expanded Short Physical Performance Battery (SPPB): The SPPB consists of tests of balance, gait speed, and chair stand, performed in this order, and is administered at Visit A and Visit B. If a specific maneuver is not attempted, the reason for this is selected from one of the options on the form. It is critical, but very difficult, to distinguish between someone who is unable, and therefore unwilling, to try a test versus someone who simply refuses to do the test because they are not interested in participating. This is a judgment that rests with the examiner. If someone refuses to participate in any of these tests, “refused” will be marked on the form unless it is quite clear that they are refusing because they are unable or afraid to attempt it. Refusals are considered missing data.

7.6.2 Equipment

The following equipment is required for the expanded SPPB: digital stopwatch, masking tape, measuring tape, script, and a straight-backed armless chair with a hard seat. The chair seat is between 17 and 18 inches high, and the depth of the seat is between 18 and 19 inches.

To eliminate the effect of different footwear on test performance, these tests are performed in tennis shoes or comfortable walking shoes with minimal or no heels. The participant may perform the tests in stocking or bare feet if appropriate footwear is not available. Women wearing high heels should change into another pair of shoes or go without shoes to perform the tests.

7.6.3 Balance Tests

The tests of balance provide an assessment of the participant’s ability to hold four basic standing positions with the eyes open. The four positions (shown below) are side-by-side stand, semi-tandem stand, full tandem stand (or heel-to-toe), and one leg stand and are performed in this order. Participants taking this test must be able to stand unassisted without using a cane and those using a cane will be asked, if they are willing, to try the test without it. If they say yes, they will be assisted to assume the correct position for testing.

For each position, the examiner first describes and then demonstrates the appropriate stand. Place the participants close enough to a wall where they can reach out to it if needed, especially for the harder tests (full tandem and one leg stand). The participants then assume the correct foot position while supported by the examiner. Many people will need little support to help them into position but others will need strong support until they are in position and steady. Wait until they feel steady before moving on to the next step. If they cannot be steadied in the correct position with support, the maneuver will not be attempted and will be coded as “Not attempted, you felt unsafe.” This applies to all four balance tests.

Once the participant is steady, ask if they are ready. When they say yes, the examiner relinquishes support, says “Ready, begin,” and starts timing. The stopwatch should be ready to begin timing as soon as the arm is released. Timing is continued until the participants move their feet, grasp the examiner or wall for support, or until 10 (side-by-side and Tandem Stand Short) or 30 (semi-tandem, Tandem Stand Long, and one-leg stand) seconds have elapsed. Any time less than 10 or 30 seconds will be recorded to the nearest hundredth of a second. *No encouragement is given during the balance tests* (e.g., just state: “You only have 10 seconds to go”).

The examiner should stand next to the participants as they get into position and then step back a half step as they perform the test. It is important not to crowd the participant so much that they have trouble using their arms to keep their balance. On the other hand, the examiner should be close enough to grab their arm or let them grab your arm if they lose their balance. Based on prior experience, most participants simply step out of position if they lose balance.

7.6.4 Side-by-Side Stand

The first position is the *side-by-side stand*. In this balance test, participants are requested to stand for 10 seconds with their feet together in a side-by-side position as shown. Participants unable to hold the side-by-side stand for 10 seconds do not proceed further with the balance tests. Participants who successfully complete the side-by-side test proceed to the semi-tandem position. If a participant does not attempt this test, the reason will be marked on the form, and balance testing is discontinued.



It is not important to stop the stopwatch and the test at exactly 10 seconds. The time does not have to be measured exactly if the participant holds the position for more than 10 seconds. The examiner should not watch the stopwatch continuously during the test, but should watch the participant and be prepared to stop the watch if the participant steps out of position or grabs the examiner's arm.

7.6.5 Semi-Tandem Stand

In the *semi-tandem balance test*, participants start with the heel of one foot placed to the side of the big toe of the other foot. Either foot can be placed in the forward position. Participants are requested to stand for 30 seconds. Those who successfully hold the semi-tandem position for 30 seconds proceed to the third balance test, the TANDEM STAND LONG. Those who hold the position for greater than 10 but less than 30 seconds proceed to the TANDEM STAND SHORT. Those who fail to hold the position for 10 seconds do not perform the remainder of the balance tests. If a participant does not attempt this test, the reason will be marked on the form, and balance testing is discontinued.



7.6.6 Tandem Stand – Short and Long

The third position evaluated is the *tandem position*. To assume the tandem position, the heel of one foot is placed directly in front of the toes of the other foot. Either foot can be placed in the forward position. Participants are asked to hold this position for 10 seconds for the Tandem Stand Short test. If doing the Short test, this will be the last balance test administered. If a participant does not attempt this test, the reason will be marked on the form, and balance testing is discontinued.



Participants who maintain the semi-tandem balance for more than 30 seconds will attempt to hold the tandem position for 30 seconds (Tandem Stand Long). Only participants who hold this position for 30 seconds continue on to the one-leg stand (see below). Those who hold the position for 1 to 29.99 seconds are given one additional chance to complete the test. If they are unable to hold the position for 30 seconds within 2 trials, the testing ends. If the participants hold the tandem position for less than 1 second, the balance testing will end without a second attempt. If a participant does not attempt this test, the reason will be marked on the form, and testing is discontinued.

7.6.7 One Leg Stand

The final position evaluated in the balance tests is the *one-leg position*. Participants who progress to this stage of the balance testing will attempt to stand on one leg for 30 seconds. They may stand on either leg, whichever is more comfortable. The one-leg stand is demonstrated by lifting one leg so that the toes are about 2 inches off the floor, with the knee flexed. Once the participant puts their foot on the floor, timing should be stopped. Participants who hold this position for 30 seconds continue on to the gait speed test. Those who hold the position for 1 to 29.99 seconds are given one additional chance to complete the test. Holding the position for less than 1 second results in ending the test and moving on to the gait speed test. They do not get a second chance to complete this test if they hold the position for less than 1 second. If a

participant does not attempt this test, the reason will be marked on the form, and balance testing is discontinued.

7.6.8 Gate Speed Tests

For this test, the participant's ability to walk 4 meters is assessed. A stopwatch and a marked walking course are needed. Detailed instructions for laying out the course are provided in **Figure 1**. Participants are instructed to start with their toes touching the start line and when instructed to begin, walk at their usual speed. Timing is started when the participants lift their foot to begin walking (this is when the foot starts to move across the starting line). Wait until the participants actually begin to move before starting the watch rather than when the "begin" command is given. Timing is stopped when the heel of the first foot completely crosses the 4-meter mark, not when the heel strikes the ground.

A cane may be used during the walk, but if participants with canes can walk short distances without them, they should be encouraged to do so. Many people with assistive devices use them only when they walk outdoors or for long distances indoors. Doing the test without the device provides a much more accurate assessment of the functional limitations of the participant. Ask the participants if they ever walk at home without the device. Then ask if they think they can walk a short distance without the device for the test. Participants who normally use assistive devices should be watched particularly closely during the test to prevent falling.

The position of the examiner is critical for the walk. If too close, the examiner will set the pace. If too far behind, the examiner will not be in a good position if the participant falls. The best position to maintain during the walk is to the side and slightly behind, outside of the participant's visual field. Record the time when the heel of the participant's first foot crosses the 4-meter line. If the foot lands on the line but doesn't cross it, this is not the end of the test. The examiner will need to anticipate when the first foot will fully cross the line and be ready to stop the watch as it crosses the line. The examiner should imagine a plane of glass at the finish line that the foot breaks when it crosses. This is the time to stop the watch. The time to the nearest hundredth will be recorded on the form.

If the examiner has trouble with the stopwatch or the timing was not accurate, the gait speed test should be repeated. If the walk was not attempted or not completed, select a reason from the options on the data sheet.

7.6.9 Narrow Walk Test

In this test, the participant's ability to walk 4 meters within a narrow space is assessed. The examiner will need a stopwatch and a marked walking course. Using the course diagram laid out above for the 4-meter gait speed test, place two lines of tape that go from the start to the finish line that are 20 cm apart. The 20 cm should be measured between the inside edges of the tape— the edges that face each other.

Participants are instructed to start with their toes touching the start line and when instructed to begin, walk at their usual speed, but staying in between the two lines. Timing is started when the participants lift their foot to begin walking (this is when the foot starts to move across the starting line). Timing is stopped when the heel of the first foot completely crosses the 4-meter mark, not when the heel strikes the ground. As above, a cane may be used during this walk test.

The examiner should be sure the participant stays within the lines. "Not staying within the lines" is defined as stepping on, or going outside of, the colored tape two or more times. Up to 3 trials to obtain 2 valid times are performed.

7.6.10 Chair Stand Test

The final test of the SPPB is the chair stand test. To perform this test a stopwatch, the script, and a straight-backed chair with a hard seat are needed. A standard chair should be placed on a nonslip surface (hard surface or low pile carpeting) with the back of the chair against a wall for stability.

In this test, participants are first instructed to fold their arms across their chest and to try to stand up one time from an armless chair placed against a wall. If the participant is successful rising from the chair once, they are then asked to stand up and sit down 5 times as quickly as possible. Timing begins as soon as the command to stand is given and continues until the participant straightens at the end of the fifth stand.

To ensure safety, the examiner should stand in front of the participants and be prepared to catch them if they fall forward. However, do not stand so close that the participants feel hemmed in and slow their pace during the chair stands. For the first portion of the test, record whether the participants were able to rise from the chair without the use of their arms. If the participant is unsuccessful, the examiner should ask them to try to stand using their arms. Inability to complete the single chair stand with arms folded or being able to do it only with use of the arms ends the chair stand test.

For the second portion of the test (multiple chair stands), instruct the participants to stand up straight as quickly as they can five times without stopping in between. After standing up each time, the participants must sit down and then stand up again, keeping their arms folded across their chest. Emphasize the word “quickly” and perform the demonstration quickly to further reinforce this point. **The gait speed test is done at normal speed but the chair stand test should be done as quickly as possible.** Count the stand number only after the participant has straightened up. Do not pace the test with the counting. If the participants do not stand up or sit down completely, stop the test and demonstrate again.

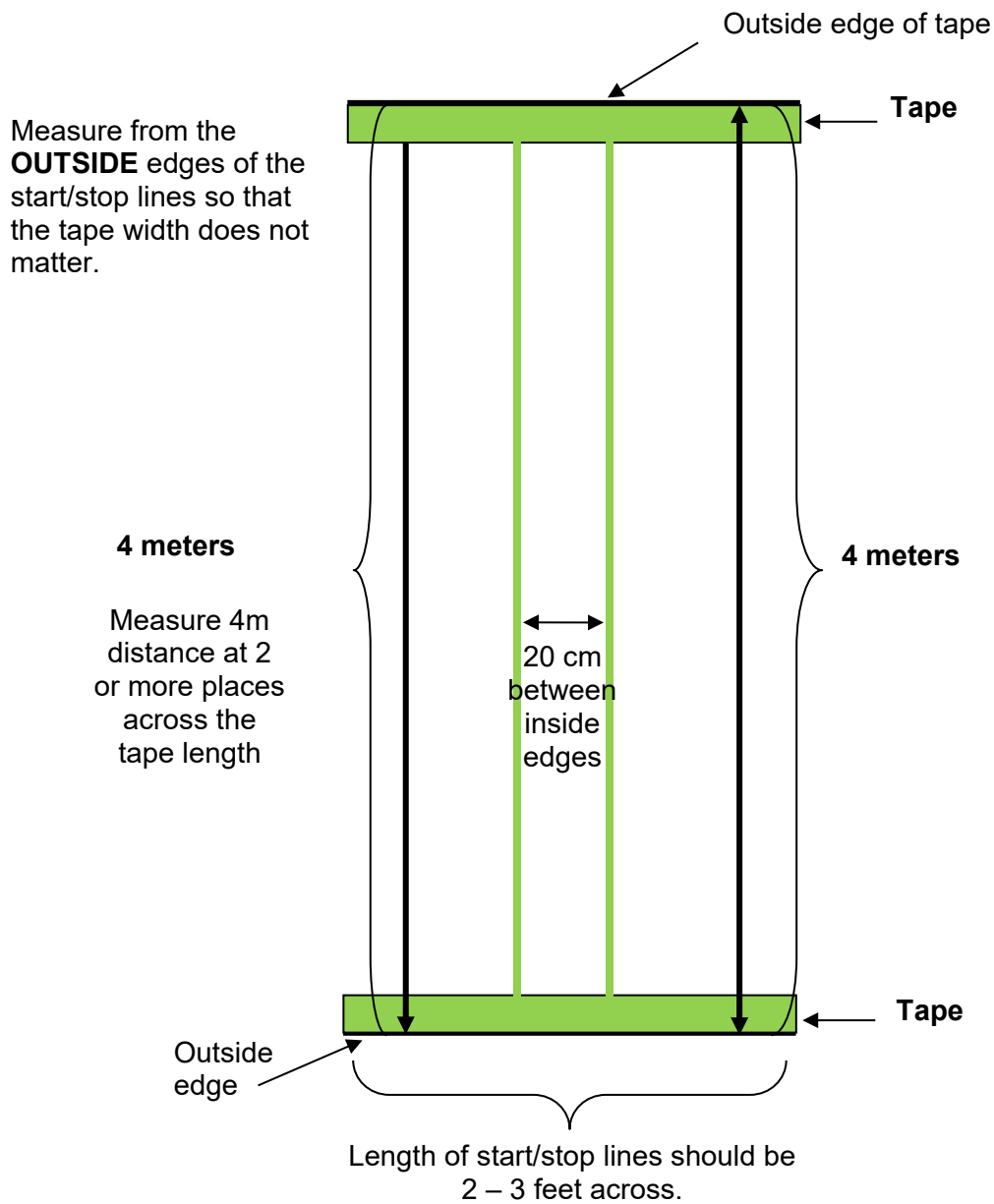
Timing begins when the command to stand is given and continues until the participant straightens their body at the end of the fifth rise. This contrasts with the gait speed test where timing begins only when the participants begin to move. During the test, count out loud as the participants rise from the chair up to five times. Do not coach or encourage the participants during the test. Watch the participants closely and stop the test if the participants are tired or short of breath during the repeated chair stands. The test should be stopped if the participant must use their arms to rise at any time, or if they have not completed the five chair rises after one minute. The examiner should also stop the test if, for any reason, they are concerned about the participant’s safety. If the participants stop before completing the five rises, ask them if they can continue. If the participant says yes, continue timing. If the participant says no, stop the test.

7.6.11 Video Certification

Certification to administer the extended SPPB will be done with a volunteer who is not a study participant, either by video call with Michelle Gordon (Wake Forest, migordon@wakehealth.edu) or the administration can be video recorded and uploaded to the MESA-MIND OneDrive folder.

If the video file size is too large to be uploaded to the OneDrive folder, it can be uploaded to the NextCloud folder. Uploading to these folders requires a UW NetID. If you upload to the NextCloud folder, please also **send an email to mesamind@uw.edu**, notifying us of the upload. Issues with or questions about file uploading can be sent to mesamind@uw.edu.

Figure 1: Course Layout for the Gait Speed Test and Narrow Walk Test



7.7 Cognitive Function Testing

Cognitive Testing Forms are recorded in the Wake Forest University data collection software. See separate Cognitive Assessment and Informant Interview (QDRS) MOPs (Module C) at <https://www.mesa-nhlbi.org/MESAMind/Account/MESAMindInternal/Documents>.

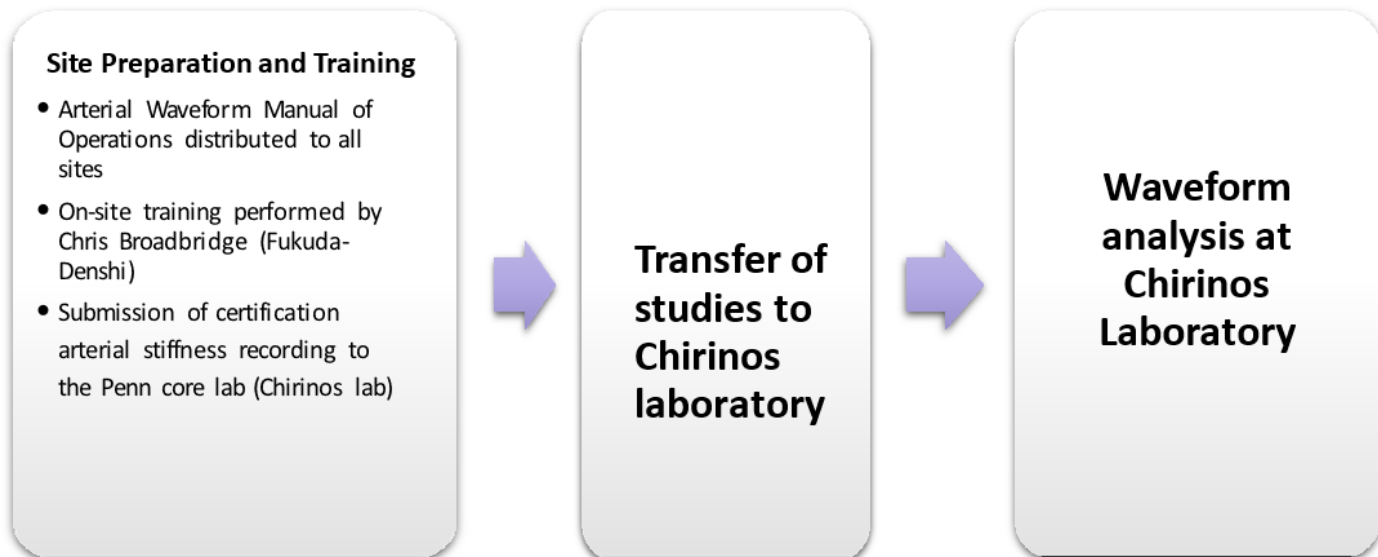
Record completion status and date of cognitive function testing and informant interview in the Exam 7 REDCap program using the **Cognitive Function Testing Completion Form**.

The Cognitive Function Testing Completion form will be disabled in REDCap when a participant's cognitive testing result from MESA MIND visit A is adjudicated as 'probable dementia'. If a participant does not have a previous MESA MIND Visit A adjudication of 'probable dementia' and they fail the UBACC screening questions, proceed with Cognitive Function Testing after consenting with a LAR.

7.8 Arterial Stiffness Measures

7.8.1 Introduction

The MESA 6 exam included a measurement of arterial stiffness using the VaSera device. The Multi-Ethnic Study of Atherosclerosis (MESA) MESA MIND exam will also include such as measurement. zStudy-wide Process Overview



7.8.2 Technician Certification

All sites must be certified by the Penn CL to ensure the performance of the highest quality arterial stiffness recordings and to maintain consistency in how these recordings are performed study wide. Any technician who will be performing arterial stiffness recordings must submit one certification study performed using the protocol contained in this manual and transferred electronically to the Penn CL for review and certification. Studies will be evaluated for adherence to protocol and image quality. Feedback and suggestions from the Penn CL will be provided for each certification study submitted. If the certification study is deemed inadequate, site technicians will have the opportunity to re-submit a new study. Upon submission of an adequate sample study, the technicians will be officially certified.

A general outline of the process is outlined below:

1. Participate in on-site training
2. Read and review the Arterial Pulse Wave Manual of Operations, and contact the Penn CL with any questions before performing the certification arterial stiffness recording
3. Perform the certification recording on a non-study subject, making sure to include all required information
4. Copy the study directly from the VaSera device to the Penn Box MESA MIND folder (each site will receive a site-specific link).
5. Wait for confirmation of certification from the Penn CL before submitting any arterial stiffness recordings performed on study subjects

7.8.3 Guidelines for Acquisition of Arterial Stiffness Recordings

Background Information

The VaSera VS-2000 device uses sensitive brachial cuffs, ankle cuffs, and thigh cuffs to obtain oscillometric blood pressure measurements and arterial pulse waveforms and a phonocardiograph on the chest to record heart sounds (**Figure 1**). Five waveforms are generated during the test: a phonocardiograph recording, and 4 arterial pulse wave recordings (**Figure 2**). Two test runs per subject will be performed: one using ankle cuffs, and one using thigh cuffs.



Figure 1: Appropriate set up of the VaSera device

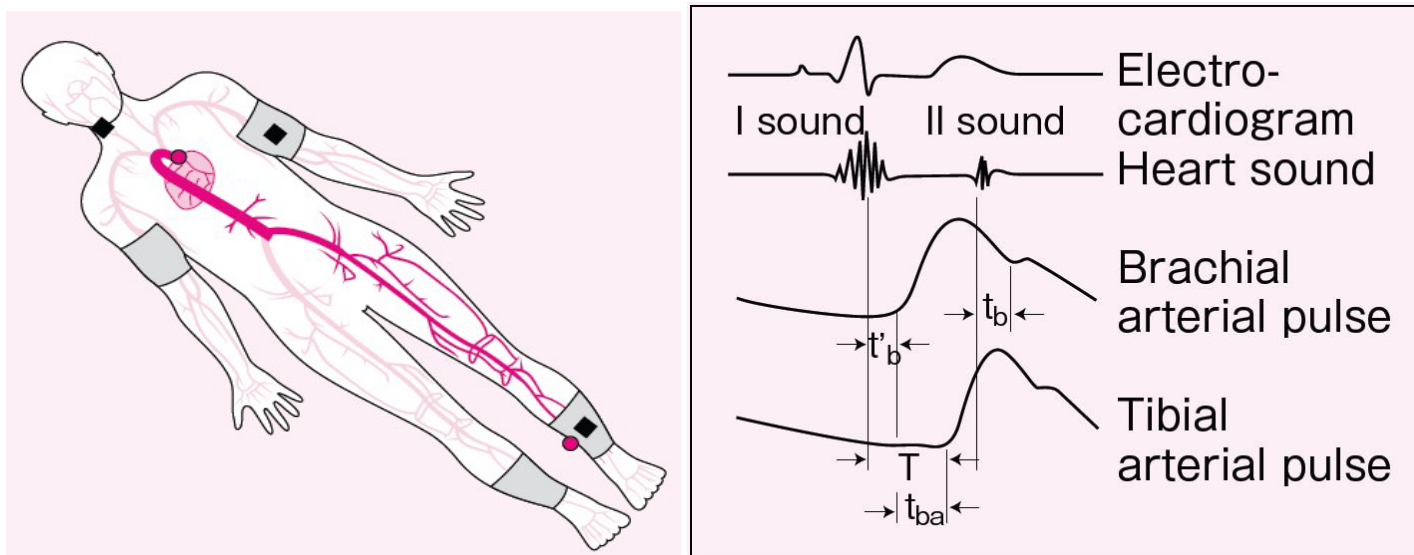


Figure 2: Proper placement of brachial and arterial cuffs (left) and the four distinct waveforms acquired by the VaSera device (right)

The arterial waveforms and phonocardiogram obtained by the VaSera device form the basis for estimation of arterial stiffness and blood pressure measurements.

Conditions Before Measurement

Before beginning the arterial stiffness measurement, ensure the following:

- Room temperature: The temperature of the testing room should not be too cold; above 72 degrees is ideal.
- Bed/exam table size: Subjects should be put to lie horizontal (head pillow allowed) on a bed/exam table that is wide enough to allow for arms resting comfortably supported at sides, without effort, and long enough that heels are supported by the bed surface.
- Subject's clothing: light, loose fitting clothing is optimal; cuffs should be wrapped against bare skin, but if clothing needs to be pushed or rolled up, avoid situations where this affects blood flow (no constriction). Shoes and socks should be removed.
- Rest before measurements: Pre-measurement rest is critical to test accuracy. Subjects should be comfortably supine for five minutes prior to beginning the measurement.
- Subject must be motionless, silent & Relaxed during the test: Ensure that the subject does not move or speak during the measurement and has some time to relax before the measurements are initiated.
- No sleep: Do not allow subjects to fall asleep during the measurement period.
- Reduction of weight of legs and arms against bed surface: Rolled towels or the gray VaSera limb cushions can be used to raise the ankles and arms from the bed to prevent extra compression of the cuffs during measurements.

Selecting the Appropriate Cuff Size

It is **critical** that the cuffs used for the examination fit the arms and ankles of the subject appropriately. If the cuffs are the right size, the INDEX mark falls within the RANGE zone when the cuffs are wrapped over the arm or ankle (refer to the table below for detailed information on cuff sizes). If the cuff used is too small, blood pressure measurement will be artificially elevated, and the arterial stiffness value cannot be measured accurately.

Cuff Type	Range of Limb Circumference
Brachial – Small	17-22 cm
Brachial – Medium	22-30 cm
Brachial – Large	30-39 cm
Ankle – Medium	20-30 cm
Ankle – Large	30-42 cm
Thigh – Large (150LL)	120 cm (maximum)
Thigh – Medium (150M)	80 cm (maximum)

Wrapping Cuffs Properly

Wrapping the Brachial (Arm) Cuffs

- Ensure that the air hose outlet of the cuff is lined up with the center of the brachial artery on the inside of the upper arm.
- The bottom part of the cuff should be immediately above the elbow, but not over the elbow joint.
- Wrap the cuff firmly, but make sure that it is not so tight that it constricts the brachial artery.

Wrapping the Ankle Cuffs

- Ensure that the air outlet hose extends upward from the medial ankle bone – if the cuff is wrapped correctly, the arrow on the label points to the apex (peak) of the ankle bone (malleolus).
- The lower edge of the cuff should be approximately 1 cm above the ankle bone.
- The ankle cuffs may be easier to wrap if the subject bends their knees
- Wrap the cuff firmly, so there are no gaps at the cuff’s upper and lower edges, and ensure that it does not constrict the ankle.
 - If the circumference of the ankle is smaller than the calf, wrap the cuff in a slightly spiral shape so that uniform pressure is applied to the top and bottom of the cuff and no gaps are present between the cuff and the ankle.

Wrapping the Thigh Cuffs

- Wrap the cuff firmly around the upper thigh, with its upper edge **as high on the thigh as possible** (as close to the femoral pulsation point as possible). When wrapped **the air hose connections for the thigh cuffs should be pointing down towards the feet.**
- For obese subjects, use the extra-large size thigh cuff.

7.8.4 Attachment of the Heart Sound Microphone (Phonocardiogram)

The heart sound microphone transmits the heart sound to the sensor via bone conduction. Firmly attach the heart sound microphone using double-sided tape (provided) just left of the sternum, between the second and third ribs.

Key points:

- Attach the microphone directly over the bone, avoiding areas of thick hair and/or body fat (both of which can interfere with sound detection)
 - For subjects who are obese, position the microphone over the sternum at a slightly higher

- location
 - For subjects who have thick body hair, use surgical tape or a beanbag to keep the microphone close to the body
- Make sure that the cord of the heart sound microphone does not have any tension and is clear from snagging.
- The heart sound microphone is highly sensitive to ambient sound, so keep the room quiet during testing.
- Always attach the PCG sensor last before testing and take it off first at the end of the test! This helps to ensure safe handling.

CAUTION! Be careful not to drop the heart microphone (phonocardiograph); it can break internally with shock, and under this situation, will no longer measure clear heart sounds.

7.8.5 Performing the Examination

Power on the VaSera device.

Ensure that the Vasera USB files-storage media stick is properly inserted into the front of the base-unit of the VaSera.

Have the subject lie flat in a comfortable and well-supported position, so that they can relax and remain still.

Attach both ankle cuffs, both thigh cuffs, and the phonocardiograph sensor (PCG sensor) to the subject, as previously described. The lower-body air hoses should first be connected to the ankle cuffs for the heart-to-ankle stiffness (CAVI) measurement and for the ankle brachial index (ABI) blood pressure measurement.

At the rightmost top of the screen, touch the section for “ID and name”, and fill in the demographic information:

- Subject ID number (ex. 4099901). **Please double check that the ID number has been entered correctly.**
- Name: please leave blank or retype the ID number
- Fill in the age in years, gender, height in centimeters. **Height is very important, since it is used to compute the heart to ankle distance.**

Explain the examination to the subject in detail to avoid unnecessary stress. Ensure that the room is quiet, that the cuffs are correctly wrapped and positioned, and that the subject is silent, still, and relaxed. During the examination itself, avoid doing anything that may interrupt the subject’s state of relaxation, stillness, and silence. The slightest movement from the subject during testing may adversely affect the quality of the pulse waveform collected.

Performing the first test (using the ankle cuffs):

- Select the “PW/BP Exam” from the “EXAM” test selection menu (top-right of the screen). From the options that appear, select, “PW/BP Exam”. The test takes approximately 8 minutes per run. One run will be performed using the ankle cuffs. One run will be performed using the thigh cuffs. A two-minute rest period between runs, per subject, is required.
- During the measurement of arterial stiffness, a weak cuff inflation pressure (50 mmHg) is applied to cuffs on all four limbs (whether measuring heart-to-ankle or heart-to-thigh arterial stiffness), and the ankle and brachial blood pressures are measured bilaterally. Thigh blood pressures are not measured. Brachial blood pressure accuracy is important, since it is applied to the calculation of arterial stiffness.
- Observe, carefully, the pulse and heart-sound waveforms being displayed on the screen. Ensure clean signals free of movement or other artifacts. When satisfied with the signal quality and the detection marks being displayed on them, **PRESS THE START GREEN BUTTON TO BEGIN RECORDING.**
- Immediately after pressing the start button and completing the recording, check the waveforms. Confirm that each type of waveform is being accurately recorded on the screen. The key point is to

confirm that the heart sound, brachial notch, and rise of the pulse wave are detected without any problems:

NOTE: some signal samples shown in this document include ECG signals. These ECG signals are not produced by the current VaSera model (VS-2000), but were produced by a prior model (VS-1500AU)

- Heart sound waveform: Check that there is a primary radical wave in the second heart sound (signal shows a distinct first and second “sound” with a consistent beat-to-beat pattern).
- Brachial pulse wave: Check that the pulse wave rises smoothly and that there is a notch on the downward slope (“dicrotic notch”). Make sure that the baseline is stable and not contaminated by subject motion.
- Ankle pulse wave: Check that the pulse wave rises smoothly and that there is a clearly defined starting point to each pulse, and this shape occurs consistently from heart-beat to heart-beat; there should be no notch on the ankle wave form. Make sure that the baseline is stable and not contaminated by subject motion.
- Thigh pulse wave: Check that the pulse wave rises smoothly and that there is a clearly defined starting point to each pulse, and this shape occurs consistently from heart-beat to heart-beat; (there should be no notch on the thigh wave form). Make sure that the baseline is stable and not contaminated by subject motion.

Performing the second test (using the thigh cuffs):

- A two-minute rest period between runs, per subject, is required.
- Select the “PW/BP Exam” from the “EXAM” test selection menu (top-right of the screen). From the options that appear, select, “**Thigh Exam**”. During the “thigh exam”, which requires the thigh cuffs, you must switch the air-hose attachments from the ankle cuffs to the thigh cuffs, keeping the connection sides consistent. The thigh cuffs should be wrapped snugly around both thighs—one thigh per cuff. **Each wrapped cuff should be about 20mm shorter than the thigh circumference on the proximal portion of the thigh.** Disconnect the air-hoses to the ankle cuffs and use the freed hoses to attach the right and left thigh cuffs, keeping the sides of attachment consistent.
- Next, press the START button to call up the distance entry window; Select “ENTER AF”. Next, enter the pulse-transit distances, **AF, L2, and L3** into the VaSera system in the on-screen pop-up form. These distances should be obtained using the measuring tape, in centimeters on the body surface, as follows:
 - a. AF: Measured distance between the point just left of the sternum, at the second intercostal space, and the femoral pulsation point of the right leg.
 - b. L1: Estimated (calculated by the device, and not entered) arterial pulse transit distance between the aortic valve and the femoral pulsation point of the right leg (=1.3 x “AF” distance).
 - c. L2: Measured distance between the femoral pulsation point of the right leg and center of thigh cuff on the right leg.
 - d. L3: Measured distance between the center of thigh-cuff on the right leg and the center of the ankle-cuff on the right leg.
 - e. L: Estimated (calculated by the device, and not entered) arterial pulse transit distance between aortic valve and the ankle pulsation point (= L1 + L2 + L3)

IMPORTANT: Please note that the diagram shown on the distance input window does not exactly match the descriptions above, but please follow the steps above; they are modified distances suitable for thigh-cuff use.

- Push the Start button to inflate the thigh cuffs. Results are automatically calculated.
- The test is completed with the measurement of a brachial blood pressure, which is carried out automatically, and used by VaSera to calculate arterial stiffness.

NOTE: The whole exam takes approximately 8-11 minutes. One run will be performed using the ankle cuffs. During the measurement of arterial stiffness, a weak cuff inflation pressure (50 mmHg) is applied to cuffs on all four limbs (whether measuring heart-to-ankle or heart-to-thigh arterial stiffness), and the ankle and brachial blood pressures are measured bilaterally. Thigh blood pressures are not measured. Brachial blood pressure accuracy is important, since it is applied to the calculation of arterial stiffness.

FINAL STEP: The site technician should also fill a "VaSera Transmittal Form" for every test performed to be sent to the Penn CL ([Appendix 1](#)). This form is used to record basic physiologic information about each subject and also gives the site technician the opportunity to comment on any problems with waveform acquisition. All forms should be saved into the Penn+box subfolder called "VaSera Transmittal Forms".

7.8.6 Assessing the Quality of the Signals

The following figures include some sample signals from the VaSera device, which can be used to judge the signal quality. **Please review these examples carefully.**

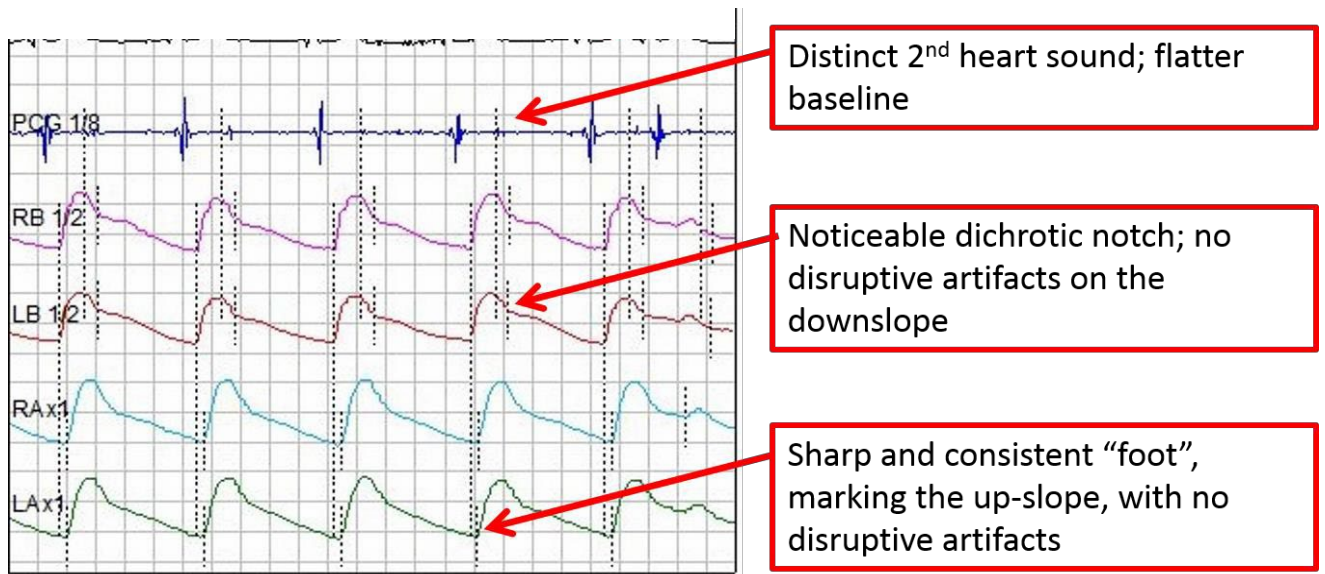


Figure 3: The four types of waveforms recorded during the examination and the appropriate appearance of each.

Always check the phonocardiograph signal; if you can't distinguish the second heart sound, the VaSera device probably can't either.

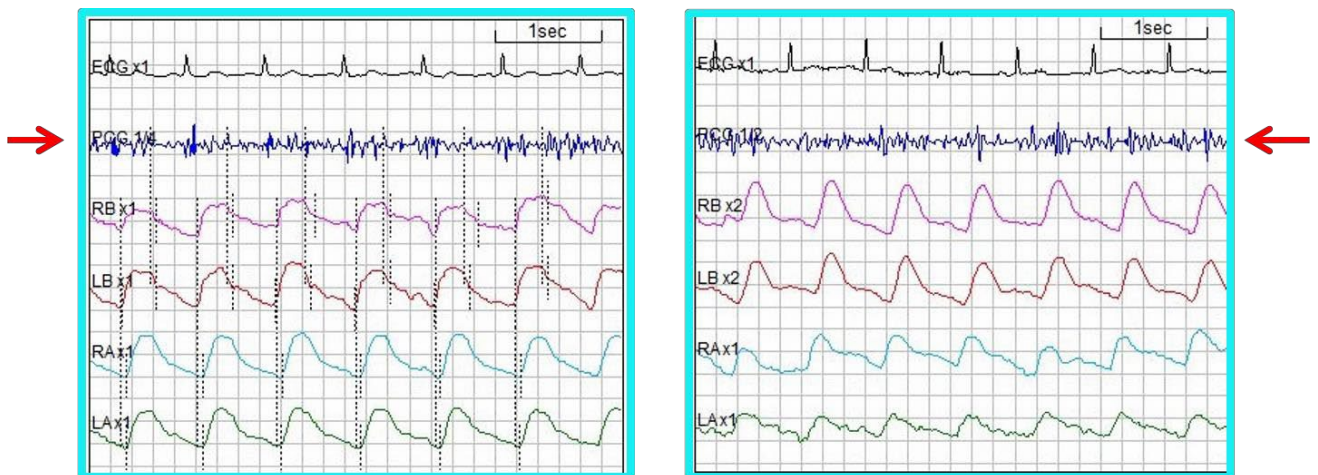


Figure 4 demonstrates some examples of PCGs of high, borderline and low quality.

Figure 4A. Good quality PCG:

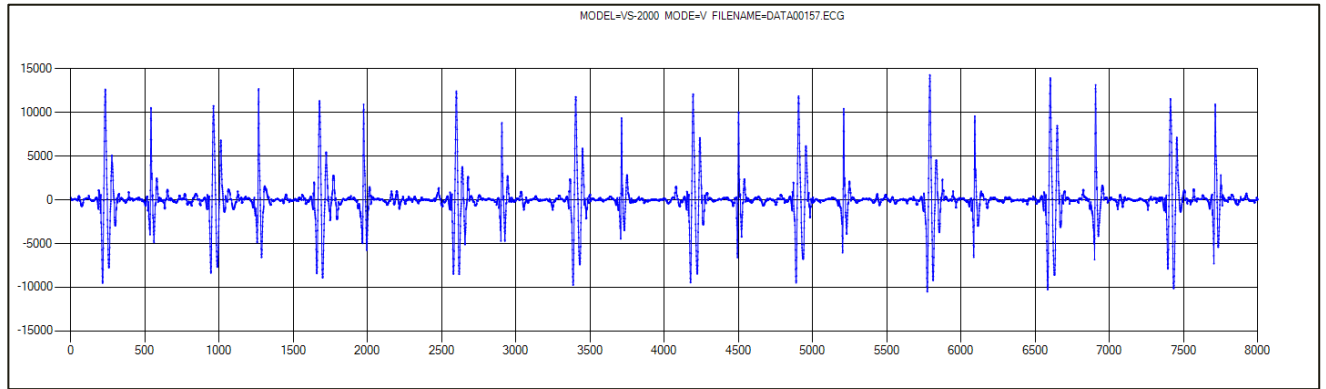


Figure 4B. Borderline quality PCG:

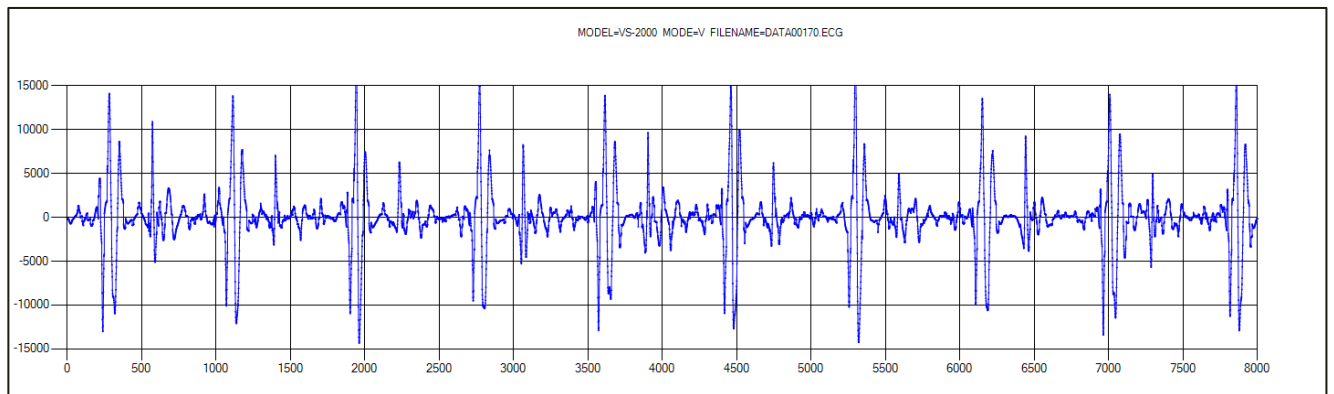
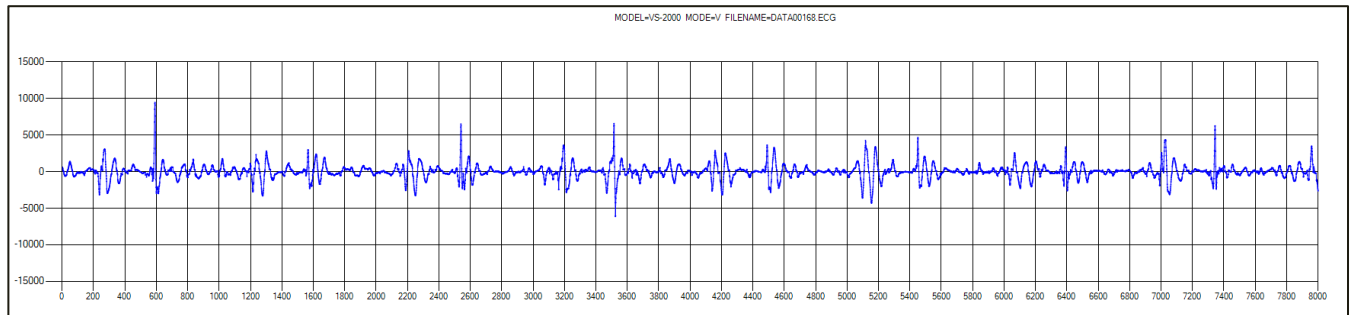


Figure 4C. Poor quality PCG:



Check the brachial waveforms: is the dicotic notch clearly visible and easily distinguishable? Similarly, are the ankle waveforms clear, consistent from beat to beat and free of wandering of the baseline?

Figure 5 shows several examples of high-quality waveforms with a clearly distinguishable dicotic notch (the brachial waveform is shown in red, the ankle waveform is shown in green)

Figure 5. Examples of high-quality waveforms

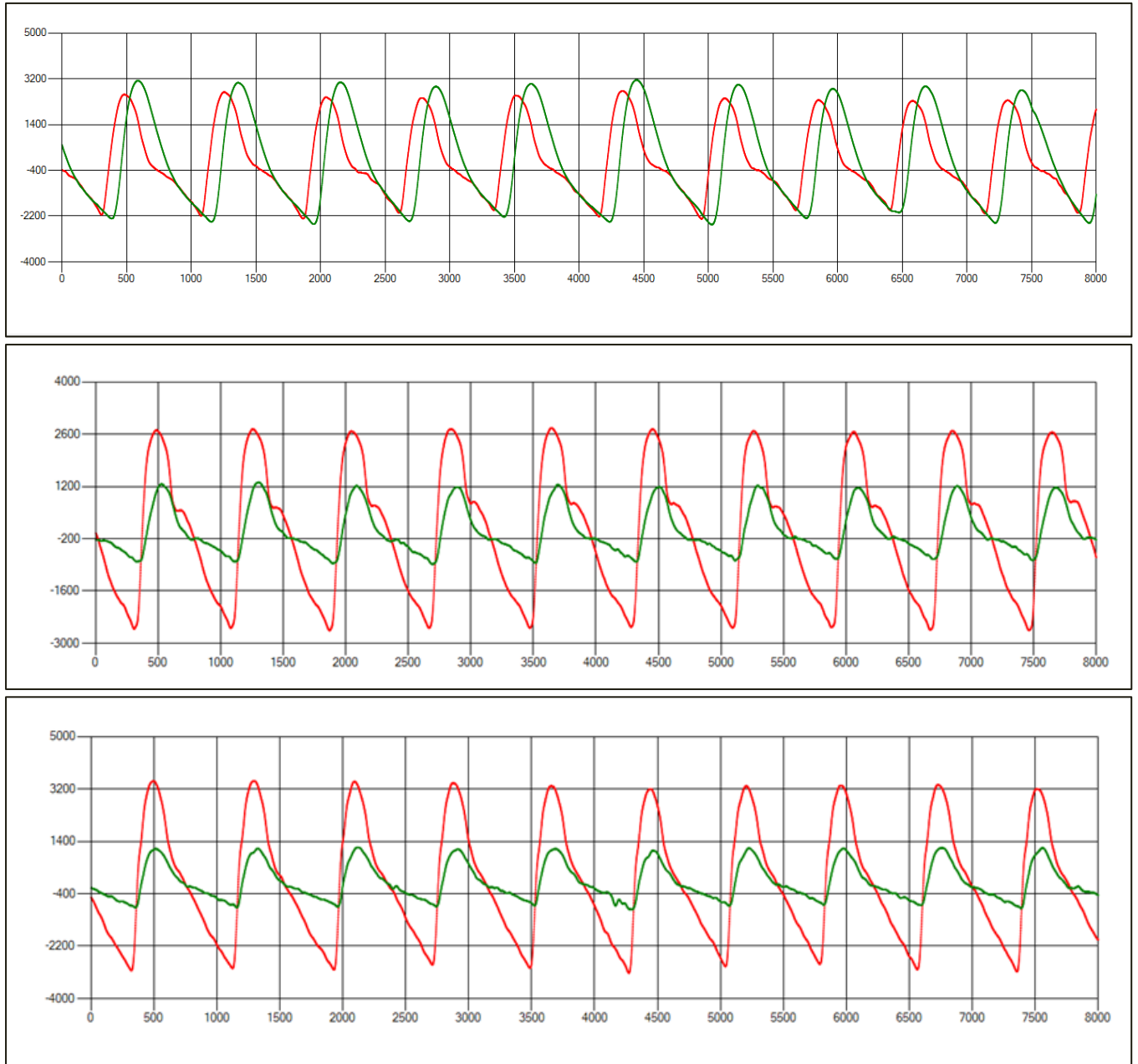
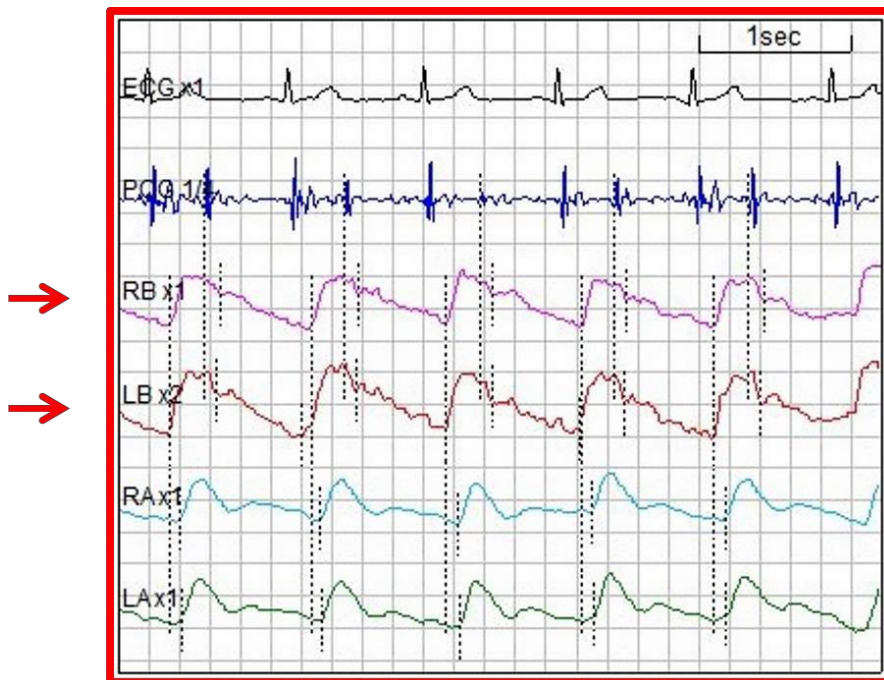


Figure 6: Example demonstrating the right and left brachial waveforms. Although a dirotic notch is visible, note that there is noise in both brachial signals, particularly on the left (LB). This can usually be resolved by asking the subject to remain completely still.



Check the ankle signal. Are the troughs or “feet” of the ankle waveforms at the ends of consistent and regular up-slopes? NOTE: there is no dirotic notch expected on the arterial waveform measured at the ankle.



Figure 7: Figure demonstrating a noisy right ankle waveform. The left ankle waveform is clear, with well-defined “feet” and regular up-slopes. Ensure that the waveforms are free of artifact. Any movement from the subject, beyond relaxed breaths, can disrupt the signals.

Figure 8: Figure demonstrating artifact in the phonocardiograph signal. There is also pronounced noise in the right and left brachial recordings. The left ankle waveform also demonstrates pronounced noise.



Figures 9-11 show some more examples of noisy waveforms.

Figure 9. Example of noisy ankle waveform (green)

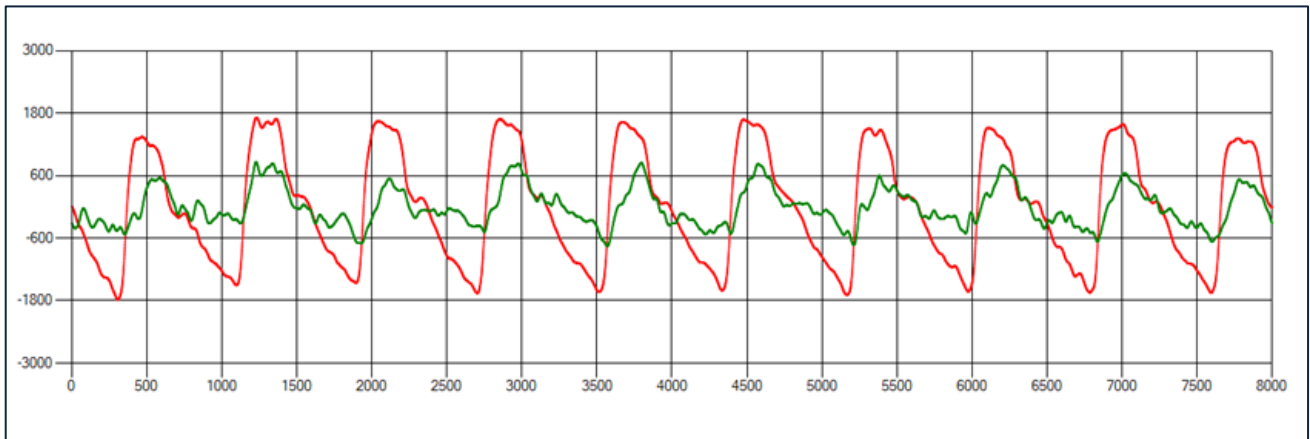


Figure 10. Example of noisy ankle waveform (green)

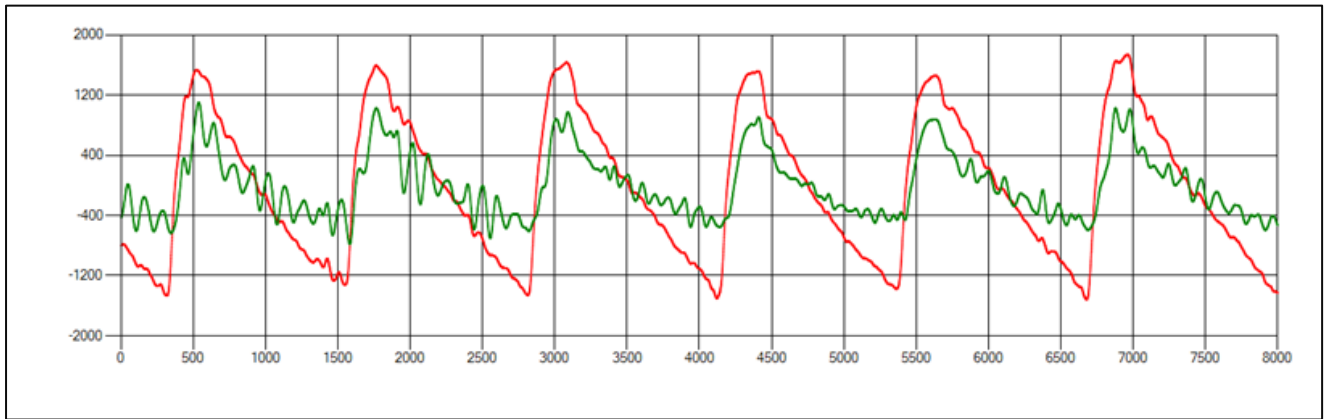


Figure 11. Example of noisy waveforms. There is noise superimposed on the beats, with variable morphology from beat to beat.

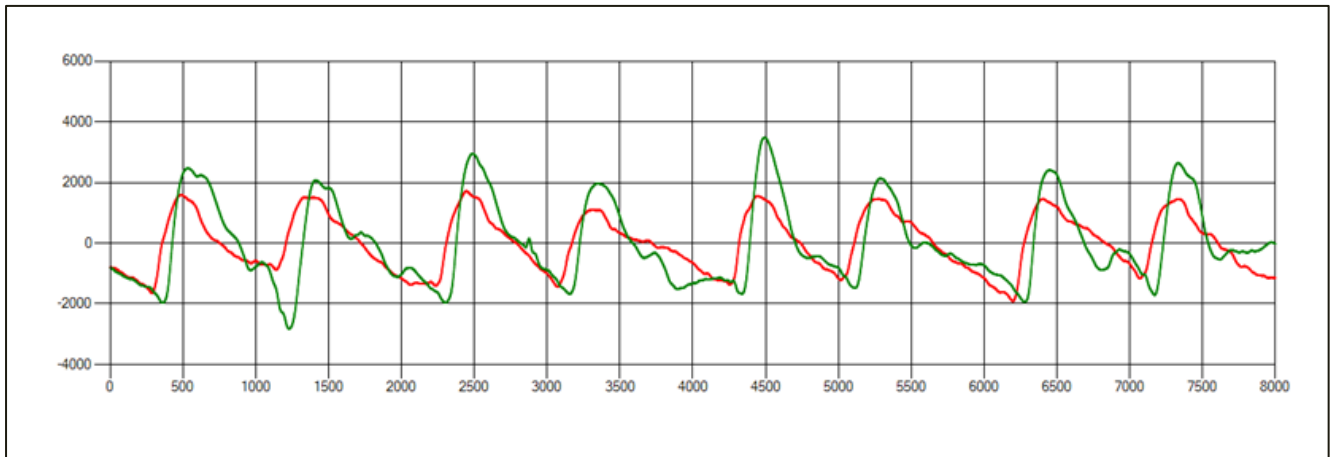
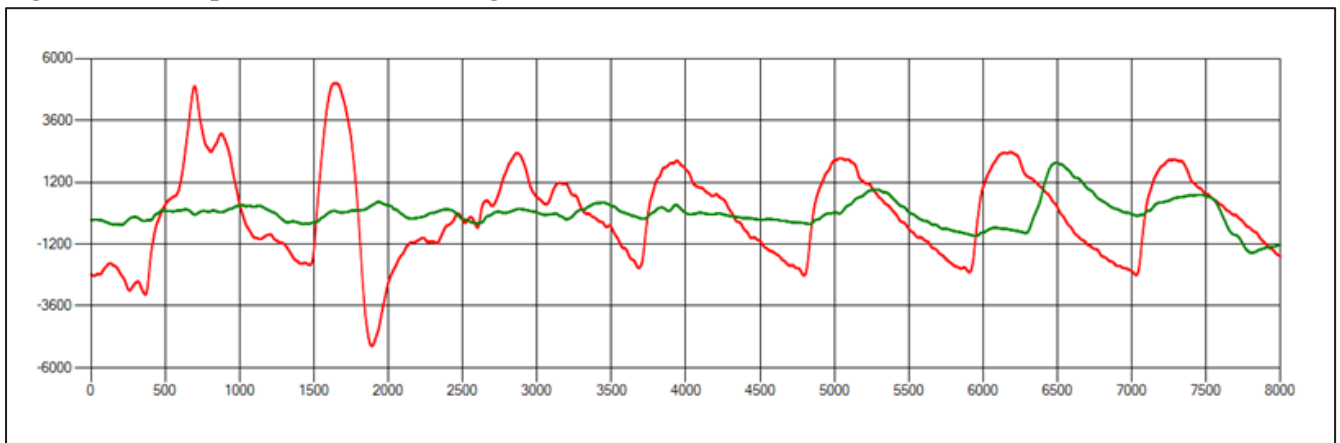
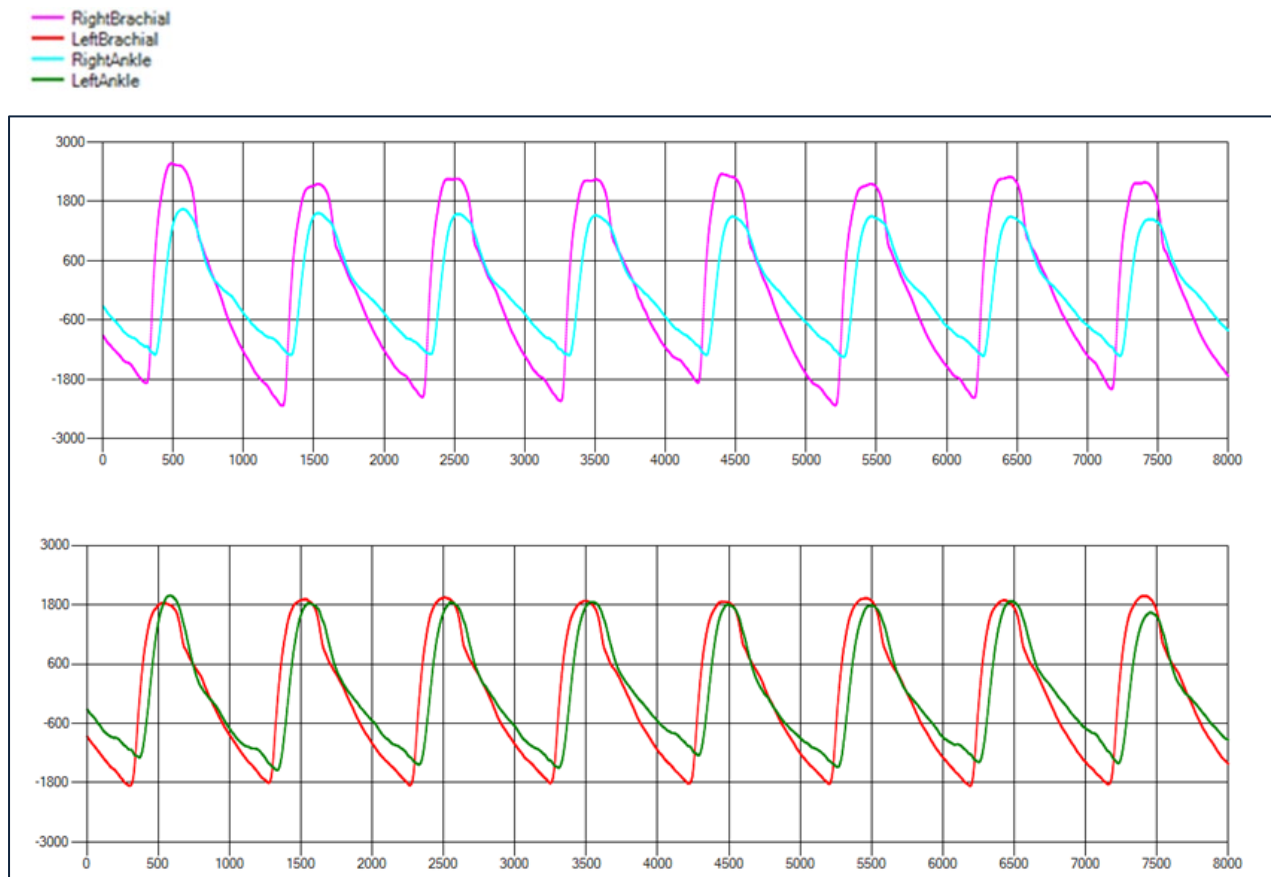


Figure 12. Example of useless recording. No consistent beats are identified



Again, we are aiming for high-quality recordings, as in the following example

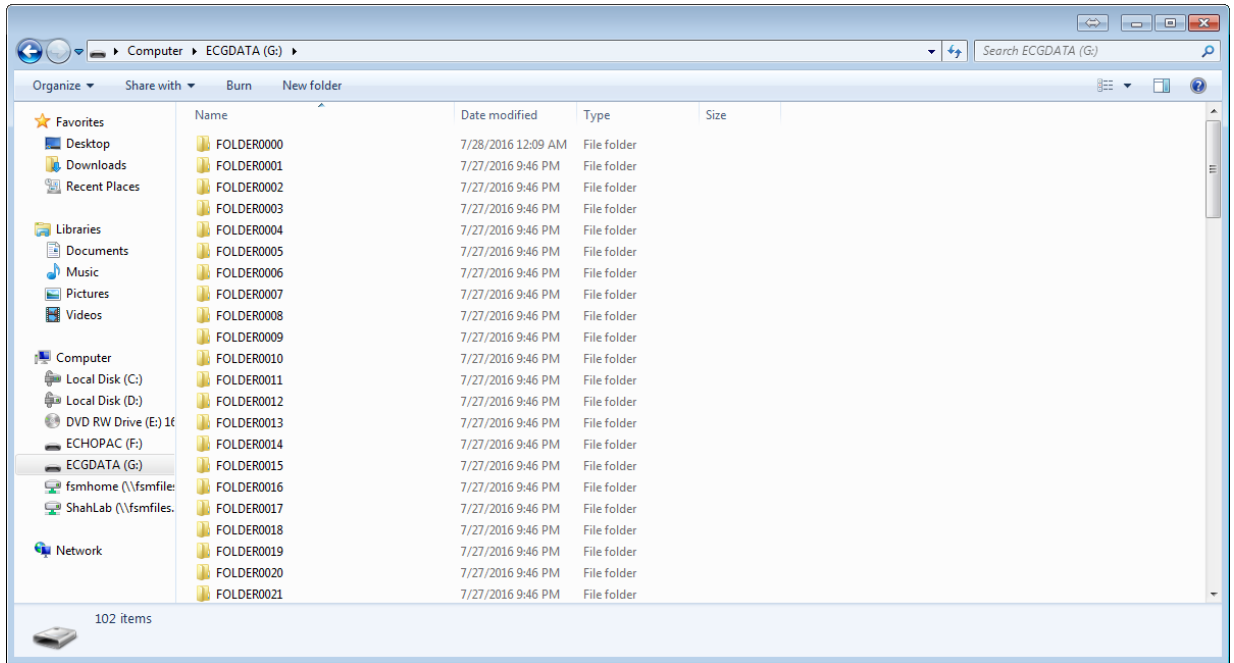
Figure 13. High-quality recording. All 4 waveforms (right and left arm and ankle are of high quality and noise-free).



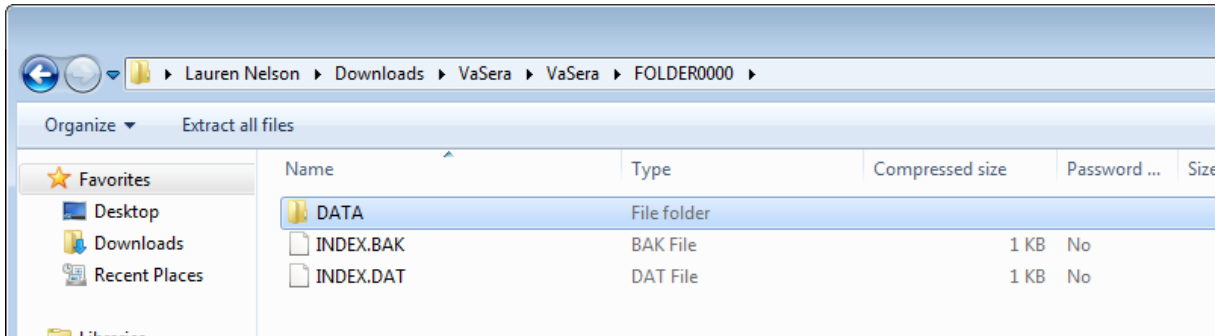
Once you are satisfied with the quality of all three waveforms, confirm that the test-check condition is good; this is represented by a double concentric circle symbol (◎). If the test-check condition is poor, this is represented by triangles; if you encounter this problem, confirm that cuffs and heart sound microphone are attached correctly, and repeat the measurement. Poor quality test data should not be submitted to the Penn CL. Please be familiar with recognizing a good-quality versus a poor-quality test result.

7.8.7 Instructions for Electronic Transfer of Arterial Stiffness Waveforms to the Local PC and to the Penn CL

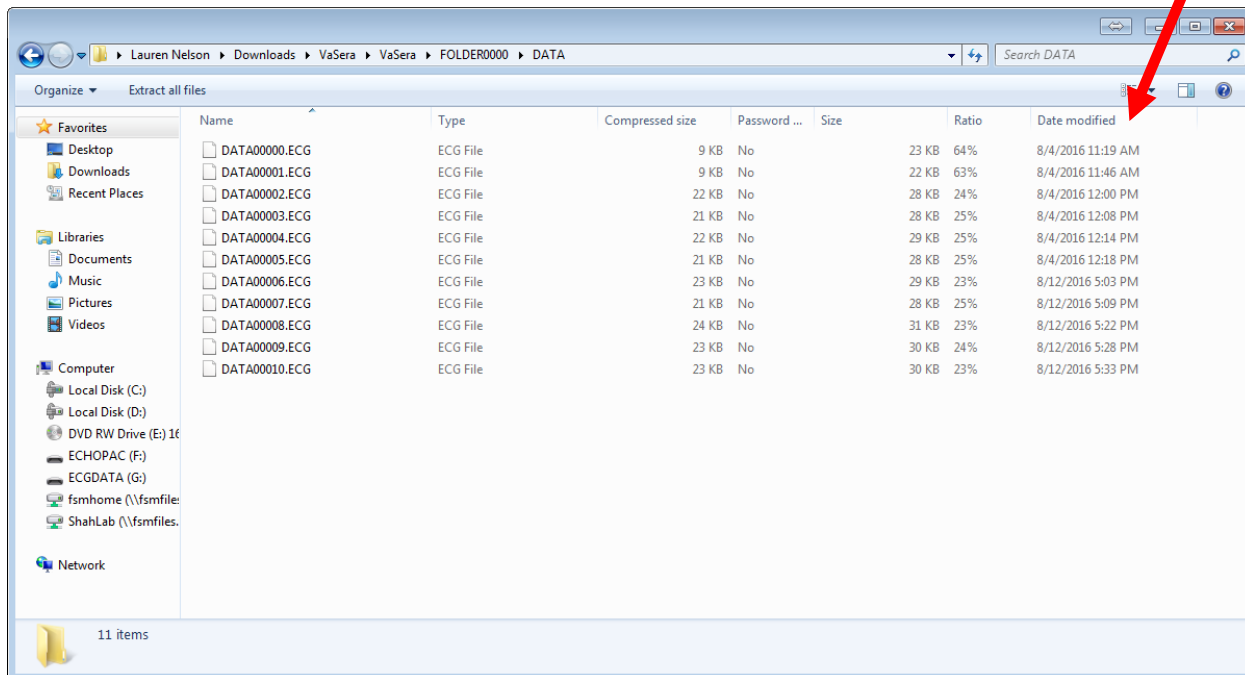
1. All data is automatically stored to the data storage USB media attached to the VaSera device. At the end of the examination, remove the USB media from the VaSera device; then, insert it into the PC (non-Macintosh computer).
2. Create a folder on your local PC called “MESA VaSera”; this will be your main folder for raw data storage.
3. Remove the USB from the VaSera device and plug it into your computer. Open the drive (it should be labeled ‘ECGDATA’). This is what the drive will look like:



4. Locate the data in question. There should be a series of folders on the drive, labeled sequentially (FOLDER0000, FOLDER0001, FOLDER0002, etc.). Data will be saved in FOLDER0000 first. When that folder fills up, the data will be saved in FOLDER0001, then FOLDER0002, etc. To find your data, click on this folder:

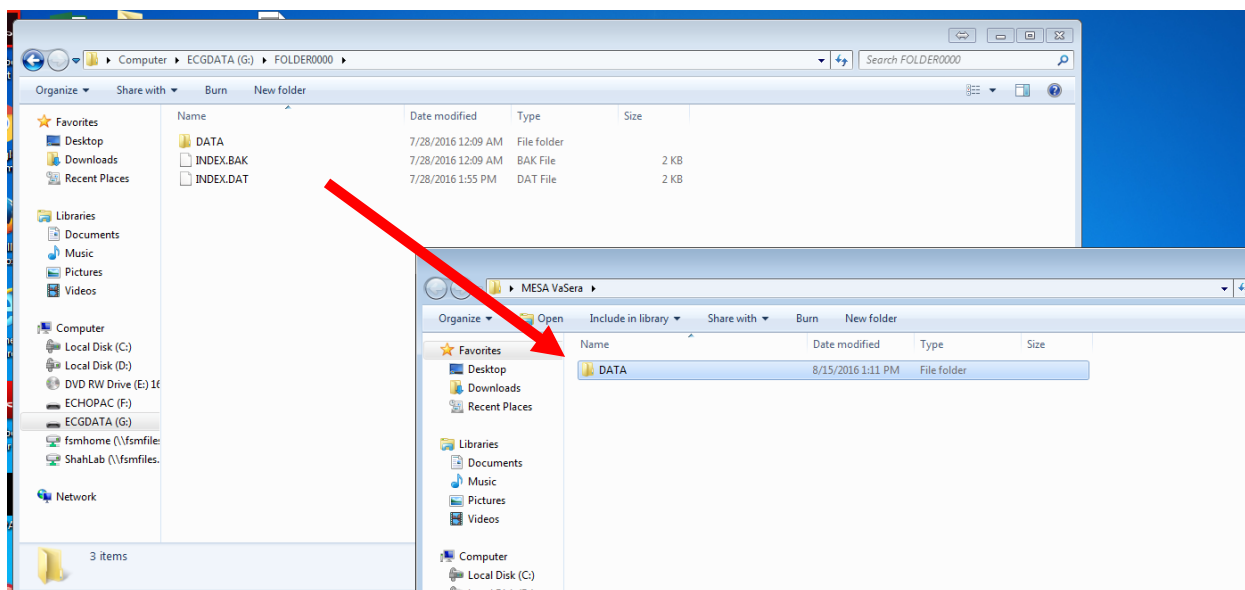


Next, open the 'Data' folder. There you should see a list of all files stored within that folder. Instead of patient names, the files are labeled 'DATA0000, DATA0001, DATA0002, etc. Check the date and time of the studies listed to confirm that you are in the correct folder.

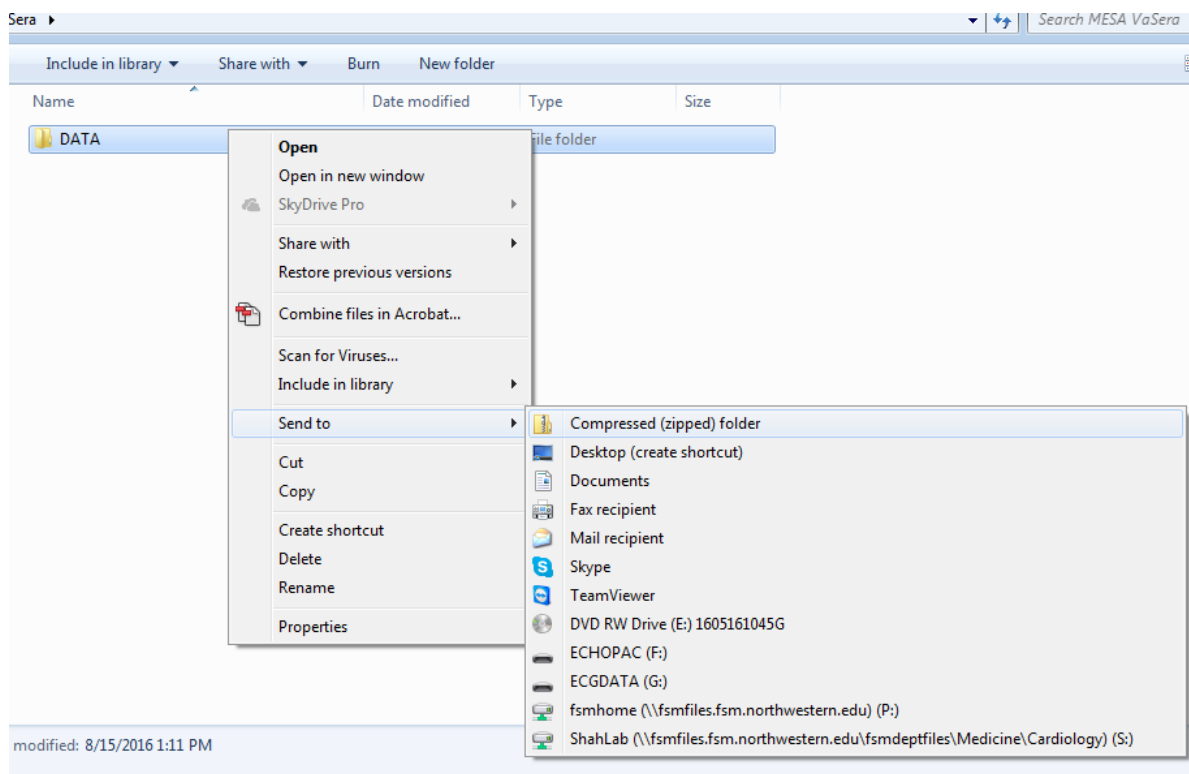


* Note: With the number of tests we will be doing in MESA MIND, it is unlikely that you will ever fill up the first folder (FOLDER0000), but it's always good to make sure that FOLDER0001 is empty (if you ever find contents in FOLDER0001, please communicate with the core lab for further instructions).

5. Once you have determined the location of your files, copy the **entire** 'DATA' folder and paste it into your local assigned computer's data storage location for the VaSera arterial stiffness data, "MESA MIND Study VaSera Data" folder that that you should have set up on your computer (important: do not cut or delete original files and folders from the USB memory stick; only copy them).

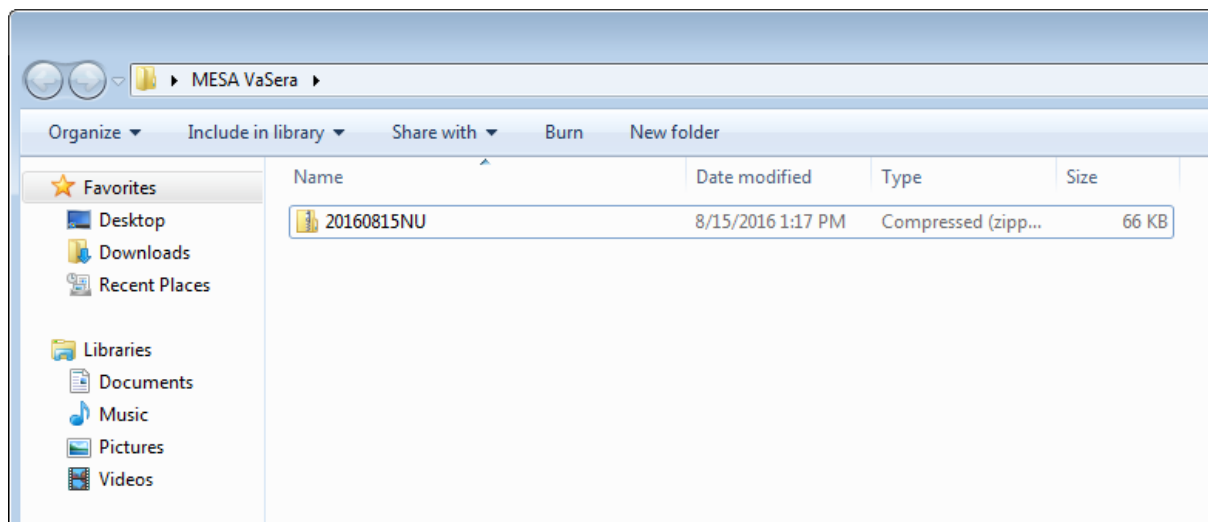


6. Once the folder has been given a new name, carry out the following easy steps to compress or “zip” it: Right click on the folder, and select ”Send to compressed (zipped) folder”. The compressed/zipped folder will appear in addition, and will be available for transfer to the Box system.



7. Rename your zipped file based on the current date and institution initials in the following format: InstitutionInitials_yyyymmdd. Examples of possible zipped folder names for each of the six MESA sites transferred on December 1st 2020 would be:
 - 20201201WF
 - 20201201UM
 - 20201201NU
 - 20201201LA
 - 20201201JH
 - 20201201CU

If you always use the same system for naming your zipped data folder, they will sort nicely and chronologically in a list—this makes them easier to manage!



8. To transfer the data, log in to Box and open the Box folder specific to your institution that the Penn core lab has established. Simply drag and drop the re-named zipped file on your computer into Penn+Box. Remember to return the USB memory stick to the VaSera device and insert it into the “USB-3” slot before the next set of arterial stiffness testing begins!

NOTE: Specific sites that are unable to utilize Penn+Box will transfer data using customized processes provided by the University of Washington DCC as per mutual agreement with the Penn VaSera Core Lab. As of Dec 15, 2020, these are DatAnywhere at Columbia and UW OneDrive at Johns Hopkins.

7.8.8 Core Lab Quality Review

Upon receipt of each arterial stiffness recording, all waveforms will be evaluated for quality and adherence to protocol. Feedback will be provided to the site technicians upon receipt of waveforms at regular intervals (every 2 months). More frequent review and feedback will take place ad hoc when problems are identified with specific sites.

7.8.9 References

- Fukuda Denshi Co., LTD. A guideline for using VaSera more effectively: what to do and check when taking measurements. Japan: ME Times, 2

7.8.10 Contact Information

Julio A. Chirinos, MD, PhD, FAHA, FESC
Director, Arterial Hemodynamics Core Lab
University of Pennsylvania Perelman School of Medicine
South Tower, Rm. 11-138. Perelman Center for Advanced Medicine.
3400 Civic Center Blvd. Philadelphia, PA. 19104.
Phone: 2152007779
Email: julio.chirinos@uphs.upenn.edu


Caroline A. Margo
Staff member, Arterial Hemodynamics Core Lab
University of Pennsylvania Perelman School of Medicine

South Tower, E27. Perelman Center for Advanced Medicine
 3400 Civic Center Blvd. Philadelphia, PA 19104
 Phone: 571-888-0931
 Email: Caroline.Margo@Pennmedicine.upenn.edu

Christopher Broadbridge
 Sales & Marketing Manager, Vascular
 Products Fukuda Denshi USA, Inc.
 Phone: 425-241-7396
 Email: Cbroadbridge@fukudaamerica.com

7.8.11 VaSera Arterial Stiffness Transmittal Form

The current version of the Arterial Stiffness Transmittal Form is posted on the MESA website at <https://www.mesa-nhlbi.org/MesaInternal/ClinicFormsSection.aspx#exam7forms>



Exam 7
Arterial Stiffness

Participant ID #:

Acrostic:

Technician ID:

Date: / /
Month Day Year

Transcribe from participant visit records:

Age

Height

Weight

cm

lbs

Male
 Female

Heart Rate: bpm

Blood Pressure: Systolic / Diastolic

Results of the arterial pulse wave exam:

Complete →

Quality of waveform: Good Fair Poor

Were multiple recordings performed? Yes No

Incomplete →

Reason exam incomplete or not done:

- Poor arterial waveform
- Undetectable arterial waveform
- Equipment malfunction
- Time/staff/room constraints
- Examinee refused or uncooperative
- Examinee physically unable
- Other: _____

Comments: _____

Sonographer ID #: _____

MESA Exam 7 | Arterial Stiffness | Interviewer-administered | v1

11/9/2021

Page 1 of 1

7.9 Spirometry

7.9.1 Background

7.9.1.1 The MESA Lung Study IV

The MESA Lung Study IV is measuring spirometry among all MESA participants who participate in MESA Exam 7 and agree to spirometry. Spirometry is measured in the MESA Lung Study IV to define COPD, to assess obstructive and restrictive lung disease, and to measure decline in lung function over MESA Exams 3, 4, 5, 6 and 7. COPD is now the third-leading cause of death globally; however, few preventative strategies are available for COPD besides smoking cessation and avoidance and MESA Lung is the longest and largest multi-ethnic study of lung function.

We will perform spirometry in the clinic using the same equipment and protocol as for MESA Exams 3, 4, 5, and 6. Given the age of MESA participants, they will have the option of having spirometry measured at home, if they are unable to come to the clinic, using a small portable spirometer. An update to this MOP will include those details.

In addition to spirometry, the MESA Lung IV includes the following components:

1. Hair follicles are collected for all MESA participants who agree to the collection. We will measure gene expression in hair follicle cells, which have some similarities to cells in the lung. The MOP for the hair follicle collection is in the phlebotomy section as it occurs right after phlebotomy.
2. Nasal brushing is performed for all MESA participants who agree to the brushing. We will measure gene expression in nasal cells, which have substantial similarities to cells in the lung. Nasal brushing will be performed right after spirometry. The MOP for the nasal brushing is attached separately.
3. Chest CT scan is acquired for those who consent to the CT scan to measure emphysema in the lungs. The details of the lung CT scan are included in the MESA CT Manual of Operations. The additional procedures are summarized in the table on the following page. It will usually be performed on a separate date for scheduling reasons.

7.9.1.2 Spirometry

Spirometry is the simplest, most precise, and least expensive test for the assessment of pulmonary function. Low lung function is a major independent predictor of morbidity and mortality from cardiovascular, pulmonary and all causes.

The important spirometry measurements are the forced vital capacity (FVC), which is greatest forced volume of air exhaled from a maximal inspiration to a complete exhalation; the forced expiration volume in one second (FEV₁), which is the volume of air exhaled in the first second of the FVC maneuver; and the ratio between these two values: FEV₁/FVC. A low FVC defines restrictive lung disease whereas a low FEV₁/FVC ratio defines obstructive lung disease. These measurements were made in MESA Exam 3, 4, 5, and 6. In MESA Lung IV, we shall perform these measurements at Exam 7 following the same protocol.

Participants with airflow obstruction in the MESA Lung IV Study will receive a bronchodilator, after which “post-bronchodilator” spirometry will be performed. The bronchodilator is very helpful in differentiating the two main types of obstructive lung disease. Asthma is characterized by airflow obstruction which is intermittent and which is generally reversible with a bronchodilator; COPD is characterized by airflow obstruction which is chronic and does not fully reverse with a bronchodilator.

Two professional societies publish widely recognized spirometry guidelines: the American Thoracic Society (ATS) and the European Thoracic Society (ERS), and a combined ATS + ERS spirometry guideline was

published in 2005 with an update in 2017. The original authors of this manual were members of the spirometry guidelines committee. The instruments and methods in this manual conform to these guidelines and exceed their accuracy and repeatability recommendations.

The spirometers, software, and quality assurance program are the same as in the original MESA Lung Study, the 4th National Health and Nutrition Examination (NHANES IV), and the Hispanic Community Health Study (HCHS)/SOL. This standardization of methods makes the results of these large government-funded studies directly comparable.

Spirometry results are very dependent on an adequate effort by the participant performing the test. The participant must be instructed to completely inhale and forcefully exhale throughout the entire expiratory maneuver. If the participant does not produce an adequate effort, the results are not valid. It is therefore **essential** that you explain, demonstrate, and evaluate each maneuver to coach the best possible effort from the participant.

Although the OMI software provides technical feedback to the technician, the technician still must instruct and demonstrate the test procedures to the participant. In addition, the technician must observe the results (flow-volume curves, volume-time curves, test values, and computer quality assessments) to determine the best coaching instructions to provide to the participants. This requires that the technician be familiar with what constitutes a valid test including unacceptable maneuvers as well as provide appropriate coaching instruction. There is no substitute for a well-motivated and well-trained technician.

The testing room is quiet and private, without distractions. No other tests are conducted in the room during spirometry testing. The ambient temperature in the testing room is maintained between 65-78°F. Ask for air conditioning if the room becomes uncomfortable due to high humidity or high temperatures.

7.9.2 Equipment and Supplies

- SensorMedics model 1022 dry-rolling seal volume spirometer is fitted by OMI with a digital volume encoder, temperature sensor, and RS232 serial computer interface (you should have from Exam 3/4/5/6).
- OMI spirometry software is installed on a notebook computer with Windows.
- Calibration syringe, 3.00 liters, Han Rudolph model # 5530 (you should have from Exam 3/4/5/6).
- Spirometer hoses, 3 feet long
- Disposable, filtered mouth pieces
- Nose clips
- Albuterol metered-dose inhalers (MDIs) **Field center to provide
- Disposable spacers
- Personal protective gear: n95, disposable gown, face shields,
- Gloves **Field center to provide
- Metrizyme detergent

Note: Although this spirometry system is much larger than spirometers commonly used for clinical practice (office spirometers), it is more accurate. The volume accuracy of this system is better than 1.5 percent, which exceeds the ATS-ERS recommendation (accuracy within 3.5%).

7.9.2.1 Advantages of the Sensor Medics Zero Return Spring

- The spirometer's piston is returned to the zero position at the end of each maneuver by the zero return spring, reducing the time required to test a participant.

- Any leak in the spirometer or between the participant and his/her mouthpiece is easily detected because of the obvious loss in volume as a result of the positive pressure (0.4 cmH₂O) generated by the return spring
- There is a clear indication when the participant comes off the mouthpiece.
- The spirometer is always stored with minimal volume in the spirometer, which eliminates the development of a “blip” due to seal memory within the measuring volume.

7.9.2.2 Initial Equipment Setup

1. Set up the equipment and connect cables on a solid desk or table. Make sure that the rod on the rolling barrel (at back of unit) can slide backwards without hitting a wall or other object.
2. Connect the power cords to a grounded electrical socket.
3. Turn on the spirometer.
4. Power up the laptop computer.
5. Use the OMI Setup Program (desktop icon).
 - Double click on “OMISetup” windows icon.
 - The initial password to enter the setup program is ‘omisetup’
 - There are three screens showing user, spirometer and other information. Details are given in the appendix.

Setup Screen 1.

Hit F1 Key for Help

Registration Number: 12345

Register To: John Q. Public

Address: 1095 Willowdale Road
Anywhere, Texas 445566

Location: Medical Department

Spirometer Make: SensorMedics

Spirometer Model: 322

Spirometer Serial Number: 23459876

Computer ID: 3456098

Allow maintenance mode with system password

Change System Password

Proceed to Next Screen Cancel

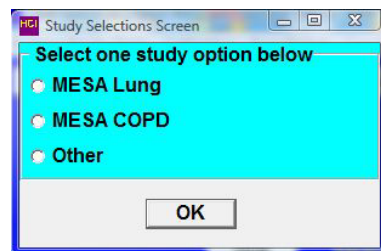
Setup Screen 2. Please don't change the settings on this screen, which have been standardized for this study.

Setup Screen 3. Do not change the setting (also standardized for this study):

7.9.2.3 Daily Leak and Calibration Checks

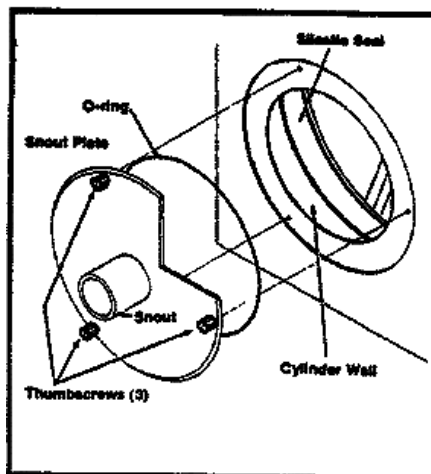
Perform a leak and calibration check before each day of testing.

1. Double click “OMIWSP.exe” windows icon.
2. Select “MESA Lung”
3. Enter your initials
4. Select “Calibration”
5. Select Leak Test from pull-down “Calibration” menu.
6. A leak test is performed by checking that the negator (return spring) is engaged and then adding 3 liters of air into the spirometer with the calibrating syringe.
7. Click on “Start Timing”. The computer then monitors the spirometer volume for 60 seconds and determines if the volume is maintained. A progress bar shows the time left until completion of the leak test.
8. The result of the leak test are written to a calibration/leak test log file, including the date and time of the test, by clicking on the “Save” button. A warning is displayed if a leak larger than the 20ml is observed.
9. Select “Perform Cal/Leak Check” button on the main screen or in the “Calibration” menu.
10. Check that the “Current Volume” is zero.
11. Fill the calibrating syringe and connect it securely to the spirometer hose.
12. Click on “OK” or type any key, inject the full 3-liters from the syringe into the spirometer, and then pull back on the syringe. (NOTE: When injecting air from the syringe, do not “slam” the syringe at the end of the injection by pushing the air out too vigorously as this may cause erroneous calibrations.)
13. The computer determines the volume injected. You then verify the calibrating syringe’s volume and the computer compares this volume with the volume measured by the spirometer. The computer displays the difference between the syringe and spirometer-determined volume in both absolute volume and as a % Error.
14. Detach the calibration syringe and store it near the spirometer.
15. View Calibrations: The “View Calibrations” menu item allows you to view all previous calibration results.



7.9.2.4 How to Clean the Spirometer

1. Clean the inside of the spirometer at the end of each day.
2. Wear gloves. Disassemble the spirometer for cleaning. Unplug the power cord. Remove the snout plate by rotating the three thumbscrews counterclockwise until the snout plate is free. It is not necessary to remove the blue adaptor from the snout for cleaning. Carefully reach inside the cylinder and slowly push back the piston.
3. Wipe the snout plate, O-ring and cylinder wall with a germicidal disposable cloth. Do not use alcohol, acetone, other volatile agents or abrasive cleaners on the rolling seal.
4. Allow the interior of the spirometer to dry thoroughly (perhaps overnight) before reattaching the snout plate.



5. Examine the O-ring for any irregularities. If damaged, replace it. Lubricate the O-ring lightly with stopcock grease. Fit the O-ring into the groove on the back of the snout plate.
6. Position the snout plate so that the three thumbscrews are aligned with the three holes on the spirometer housing. Tighten only “finger-tight”.

7.9.2.5 How to Clean the Hoses

Hoses should be cleaned and disinfected weekly.

1. Tubing will be cleaned and disinfected daily using a solution of metrizyme detergent and water according to the following protocol.
2. Add one ounce of metrizyme to every gallon of water (can be cold or warm but not hot) in the 5-gallon bucket.
3. Rinse hoses after use in this solution. Hoses that are not rinsed soon after use (i.e., saliva or mucous has dried) should be soaked in this solution for 10 minutes (IT'S ONLY NECESSARY TO SUBMERGE HOSES FOR 10 MINUTES IF THEY'VE DRIED (EG LEFT OVER THE WEEKEND WITHOUT CLEANING)).
4. Ideally, re-rinse hoses with water.
5. Hang hoses up to dry using clothes pegs.

7.9.3 How to Test Participants

You should first complete the first page for the Spirometry Completion Form. The spirometry exclusion criteria at the end of the manual should have already been applied to every participant.

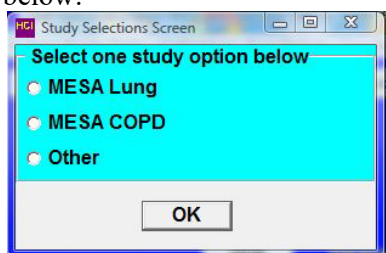
In addition, if the participant is selected for a post-bronchodilator test by the spirometry software, you will be prompted to ask some additional questions before a decision about administering the bronchodilator is rendered by the spirometry software. Anyone meeting spirometry exclusion criteria will not start spirometry. The albuterol exclusions (which you will be prompted to administer by spirometry software) must be checked before administering the bronchodilator (albuterol).

The accuracy of spirometry depends on your skills, which influence the effort exerted by the study participant. Consequently, it is crucial that the examination protocol be observed consistently. The participant must be carefully prepared and “coached.”

The spirometry program is started by clicking on the spirometry icon located on the desktop.



Before you can do any testing, you must first select the study into which the participant is selected (consent for spirometry is part of the main MESA consent, unlike in prior exams). Select the “MESA Lung” button. Selecting this box implies that the participant will be asked to receive albuterol only if they have airflow obstruction (MESA COPD is an older study in which all participants got albuterol). The Study Selection screen is shown below:

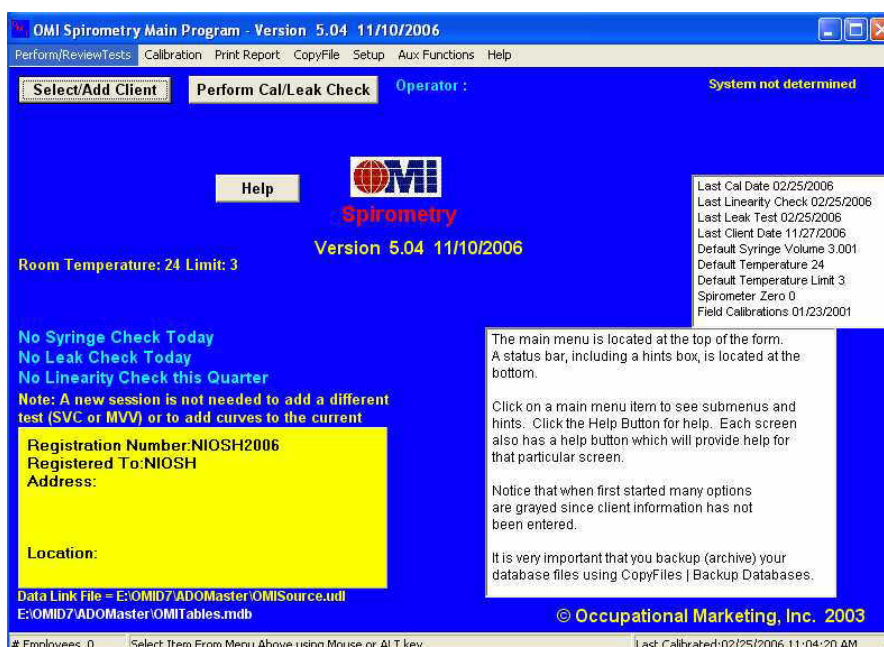


7.9.3.1 Spirometry Instructions, Preparation and the FVC Maneuver

Tight clothing, such as a tie, vest, belt, or body-shaping garment which might restrict maximal breathing efforts, should be loosened. Dentures, *if they are loose*, should be removed and placed in a clean denture cup, since they prevent a tight seal from being formed around the mouthpiece. If dentures are not loose, leave them in place.

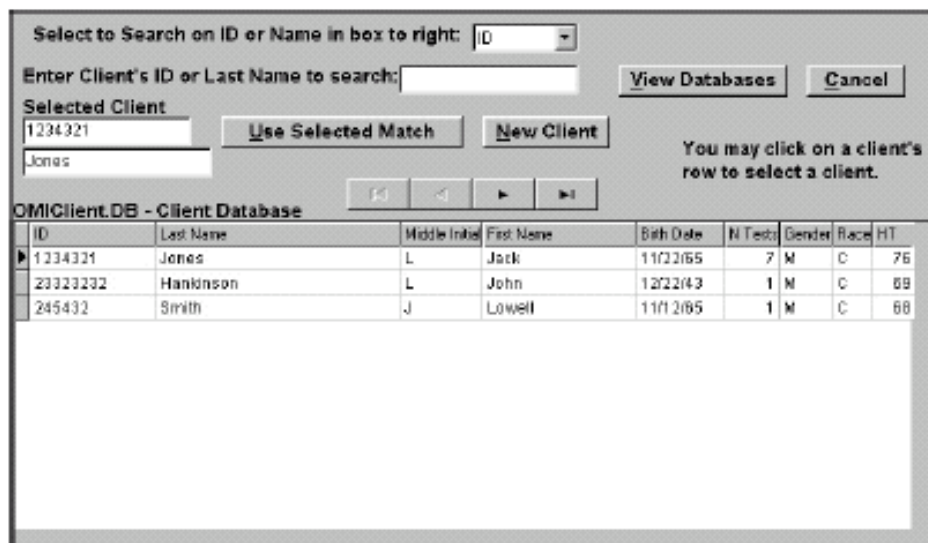
A note about SARS CoV2: Spirometry is considered a potentially aerosolizing procedure so all technicians are expected to wear FULL personal protective equipment (PPE) including a properly fitted n95 mask, disposable gown, eye protection, and disposable gloves when in the room in which spirometry is being performed.

1. Select “Perform/Review Test” main heading and/or “Select/Add Participant” button
2. Bring up Participant Screen

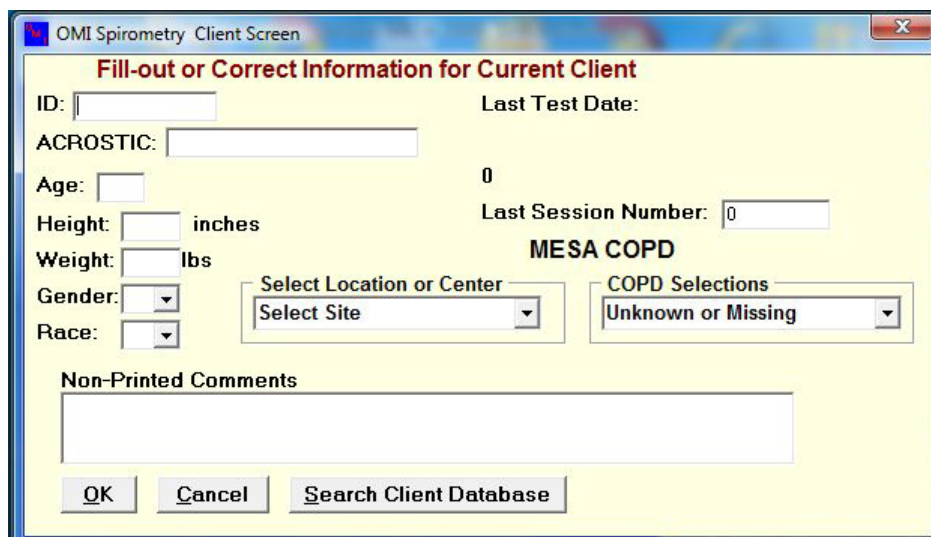


3. You should use the “Use Selected Match” function rather than having to choose to enter a “New Participant.” Information for almost all participants will be preloaded. To search for a participant, select to search on ID or ACROSTIC; then start typing the ID or ACROSTIC in the search field. The bottom grid will display the closest match to the partial ID or ACROSTIC as it is entered. If the ID is not there,

select “New Client.” Before any participant is tested, demographic information must be confirmed and edited if necessary.



4. Edit/Paste/Enter participant information. The participant’s information including ID, ACROSTIC, age, gender, race/ethnicity and height should be preloaded and appear in the screen. Verify that the information is correct (particularly age and height) and, if it is, click “OK.” Other information on the screen does not need to be entered. If the preloaded information is wrong, double-check ID and ACROSTIC match the participant then update the incorrect information. Please use the information as recorded on the Exam 7 Anthropometry form for height and weight. For a participant who is not preloaded into the software (which should be rare and only occur for those that have moved Field Center), enter ID, ACROSTIC, age, gender, race/ethnicity and height. For participants not preloaded in the software, you may also need to select your site or center.



5. Confirm you (and any other staff in the room) are wearing FULL PPE.
6. Attach a clean breathing hose to the spirometer, if not already on (since we using filtered mouthpieces in Exam 7, hoses can be reused and only need to be cleaned once per week).
7. Explain the purpose of the FVC and the need for extra effort from the participant to get maximal results. Say “I want to measure how much and how fast you can breathe out” and explain that you want the participant to take a very, very deep breath, blast out and then breathe out all the way out.

8. Explain to the participant the proper position of the mouthpiece. Ideally ask them to lower their mask, stick out their tongue, and show them appropriate mouthpiece positioning. Note that you cannot demonstrate on this on yourself as you need to wear the N95 mask at all times.
9. **Demonstrate a deep inspiration: exaggerate body language, eyes wide, shoulders back, on tiptoes. Blast out.**
10. Ask the participant to sit during the examination. Encourage them to sit up straight. If participant wants to stand during the examination, they may do so.
11. Place nose-clip on their nose. It may be removed between trials. If the nose-clip falls off or is uncomfortable, try another one, or the participant may hold his nose during each maneuver.
12. Have the participant do a trial deep breath in and blast out. The following instructions may be helpful:
 1. “Lower your mask.”
 2. “Take a great big breath of air as far as you can inhale.” (Phase I)
 3. “Put the mouthpiece into your mouth and seal your lips tightly around it.”
 4. “Blast your air into the tube as hard and fast as you can.” (Phase II; the exhalation should be made with the lips tight around the mouthpiece with maximal force and speed.)
 5. “Keep on blowing out the same breath of air, until I tell you to stop.” (Phase III; for the trial maneuver, stop the participant after a 1-2 seconds of Phase III rather than 6 or more seconds of the real maneuver).
 6. “Replace your mask.”

Review the procedure and correct any problems from the trial.

7.9.3.2 The FVC Maneuver

Click “Perform FVC Test”

The screenshot shows a software interface for configuring a spirometry test. At the top, it says "Please verify and complete information below then click appropriate button below". There are buttons for "Return to Main Screen", "Proceed with Testing", "Test Type" (with radio buttons for FVC, SVC, and MVV), "Change Operator", and "Help".

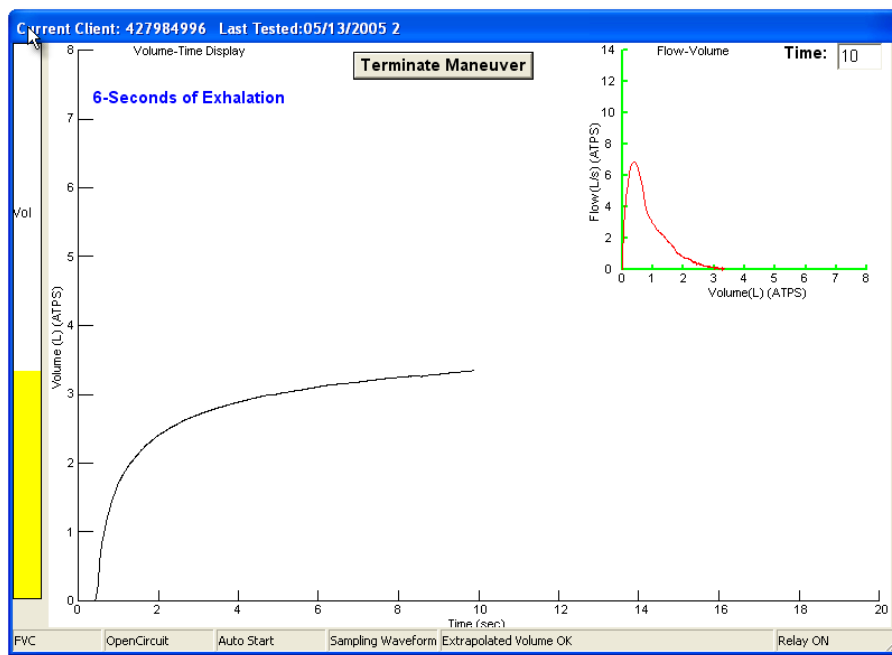
Below these are input fields for "Client ID" (12344455), "Last Name" (Jones), "Last Session Number" (18), "Session Number" (19), and "Spirometer Temperature" (0 C). There are also "Pre or Post Test" options (Pre-Test, Post-Test) and a "Bronchodilator" checkbox. A note states "Above items can be changed using Main Menu".

At the bottom, there is a table titled "OMISum.db" with the following data:

ID	Session	Test Date	Test Time	FVC	FEV1	EFV1	FEF	MVV	SVC	N FVC	N SVC	N MVV
12344455	13	03/10/98	6:44:48 PM	0	0	M	0			1	0	0
12344455	14	03/10/98								0	0	0
12344455	15	03/11/98	9:59:13 PM	4345	3258	M	4533			6	0	0
12344455	16	03/21/99	11:47:06	0	0	M	0			1	0	0
12344455	17	03/21/98	11:48:45	0	0	M	0			2	0	0
12344455	18	03/21/98	12:10:30	0	0		0			2	0	0
12344455	19											

Select “Proceed with Testing” and a “Volume-Time and Flow-Volume Graph” screen appears. A window prompts “Start Test?” When ready, click “OK.”

The message “Wait, Checking Spirometer” appears in red on the screen. AFTER THE MESSAGE DISAPPEARS, instruct the participant to take a deep breath, place the mouthpiece in his/her mouth, and **BLAST the air out!** Watch participant.

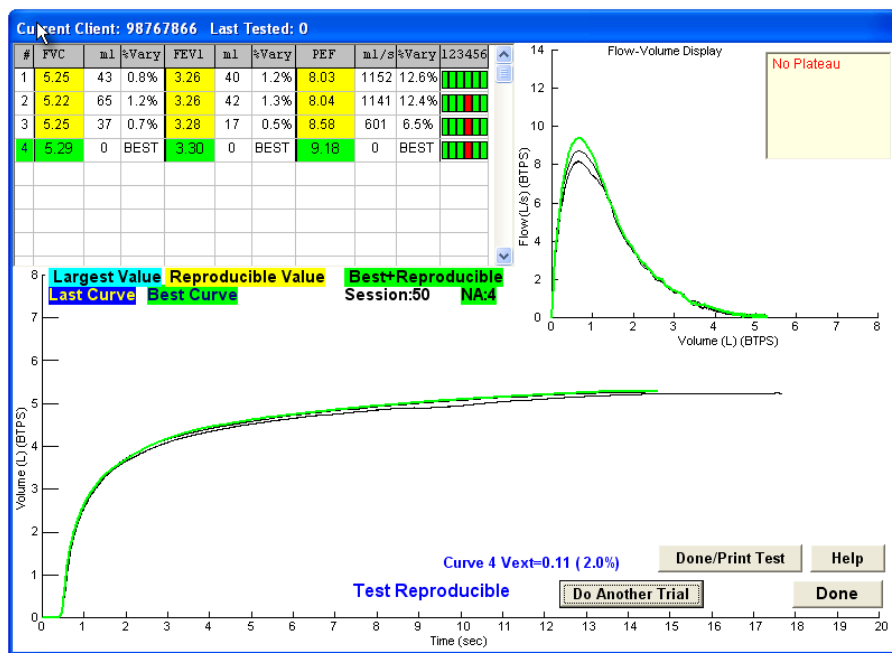


Quietly coach the participant to exhale until the “Plateau Achieved” message is displayed and the bar on the left side turns green. Just say, “Keep going...you are still getting more air out.” It is *not* helpful for them to “squeeze out the air.” Help the participant to move the mouthpiece away from their face (to reduce the risk of cross-contamination).

Indicate standing or sitting, and your impression of the participant’s effort.

Press “Calculate Curve”.

A result screen is then displayed, including Trial Number, FVC, FEV₁, and PEF (peak flow). After the second and successive trials, differences from the largest observed values and the 6-item acceptability code are displayed. All of the flow-volume and volume-time curves are also displayed superimposed. The last maneuver is highlighted in dark blue and the best curve is lime green. All of the remaining curves are black. Any deleted or unacceptable curves are red. The quality assessment information should be used to judge whether a curve should be accepted or rejected. Click on the quality code box for a description of the acceptability codes. A repeatability message is displayed.



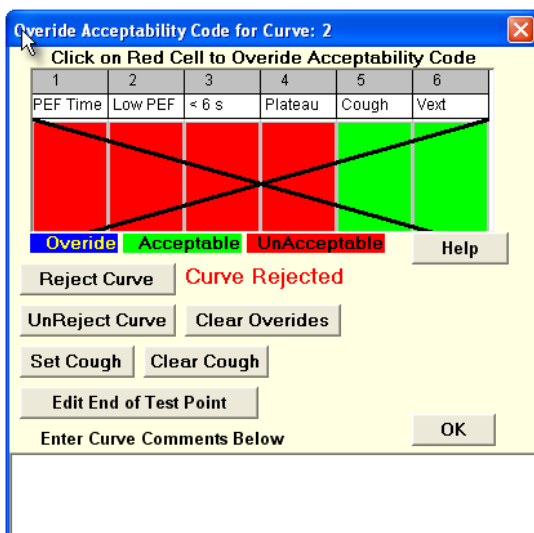
The Quality code box - A more detailed view of the maneuver values is shown below. The largest values for FVC, FEV₁, and PEF are indicated by “BEST” to the right of the value in the “%Vary” column. An important goal of testing is to match the largest and second largest FVC and FEV₁ within 150 ml of each other. This is called repeatability.

To obtain the best test session quality grade (an A), the FEV₁ and FVC must match within 100 ml. A scroll-bar on the right can be used to scroll up or down when more than 8 maneuvers have been done (but this will rarely be necessary).

#	FVC	ml	%Vary	FEV1	ml	%Vary	PEF	ml/s	%Vary	123456
1	5.25	43	0.8%	3.26	40	1.2%	8.03	1152	12.6%	
2	5.22	65	1.2%	3.26	42	1.3%	8.04	1141	12.4%	
3	5.25	37	0.7%	3.28	17	0.5%	8.58	601	6.5%	
4	5.29	0	BEST	3.30	0	BEST	9.18	0	BEST	

For experienced technologists ONLY:

How to over-ride the acceptability criteria: Click on the quality code box (extreme right column), and a popup window is displayed, allowing you to over-ride any acceptability code or reject a curve. The repeatability criteria are then re-applied and a message as to whether the test is reproducible is displayed. For acceptability codes, a red bar indicates the criterion is unacceptable. Click on the “Reject Curve” button if you wish to reject a curve, “Set Cough” button if you feel the computer did not correctly detect a cough, “Clear Cough” button if you feel the computer incorrectly label the curve as having a cough. Any code that is “over-riden” is colored in blue instead of red.

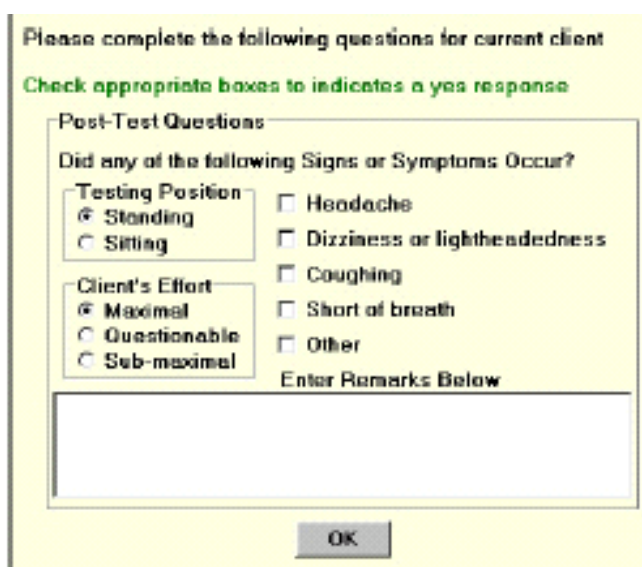


Criteria for an acceptable maneuver: no hesitation or false starts; the volume of back-extrapolation (Vext) less than 5% of the FVC or 0.15 L (whichever is greater). No coughing during the first second; no glottis closure, no mouthpiece obstruction by tongue or dentures. There should be a plateau at the end of the volume-time graph; and the maneuver should last at least 6 seconds.

Criteria for a repeatable test session: after three acceptable maneuvers, the two highest values for FVC and FEV₁, taken from acceptable forced expiratory maneuvers, must show minimal variability. The two largest FVC values should agree within 150 ml; the two largest FEV₁ values should agree within 150 ml. Testing should continue until three acceptable tests (all green in the code box) and repeatability criteria are met (yellow values), until a maximum of eight tests have been performed, or until the participant cannot or should not continue. To obtain the highest quality rating, the FEV₁ and FVC repeatability must be within 100 ml.

Proceed or Done: You decide to proceed to perform another maneuver (“Do Another Trial”), or to stop performing additional FVC maneuvers (“Done”).

Post Test Questionnaire: After test completion, the “Post Test Questionnaire” screen will appear. On this screen, indicate the testing position, participant (client) effort, and add comments, if you wish. Then click “OK.”

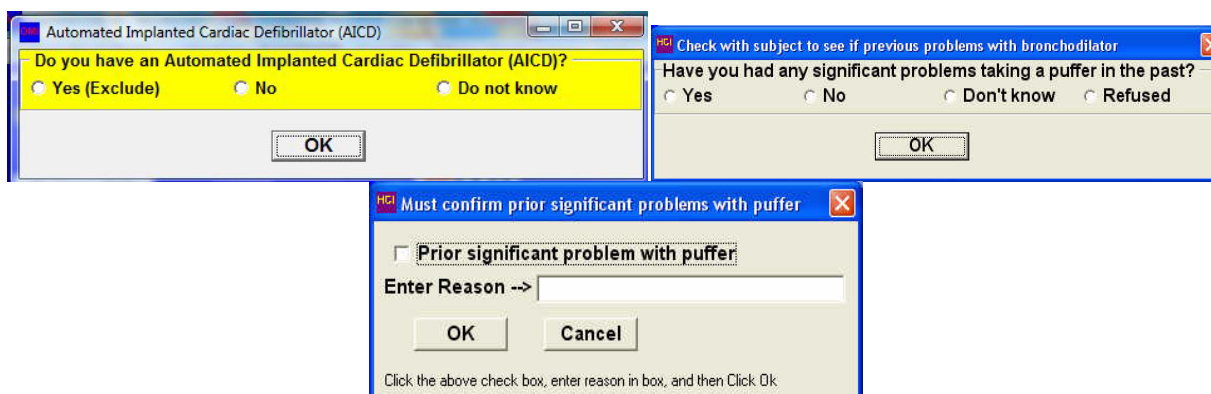


7.9.4 Post-Bronchodilator Testing

The MESA Lung IV participants who have airflow obstruction will be offered post-bronchodilator spirometry to determine if the airway obstruction is reversible (indicating that asthma is more likely than COPD). These participants will also undergo post-bronchodilator SVC testing. For this purpose, airway obstruction is defined as a FEV1/FVC below the Lower Limit of Normal (LLN) calculated using the NHANES III reference equations *or* FEV1/FVC below 0.70. Selected participants will receive albuterol if they have no contraindications to albuterol administration (see Spirometry and/or Albuterol Exclusions Section).

The following screen will appear if the participant is selected for post-bronchodilator spirometry and has no contraindication based on information collected earlier in the exam. These screens are to check to see if the subject has had an automated implanted cardiac defibrillator or any SIGNIFICANT problems with a bronchodilator puffer in the past. Ask the participant about “any SIGNIFICANT problems taking a puffer in the past” and show the puffer to the participant (this is much faster than trying to explain what a puffer is; the puffer is immediately recognizable to participants who have taken them in the past).

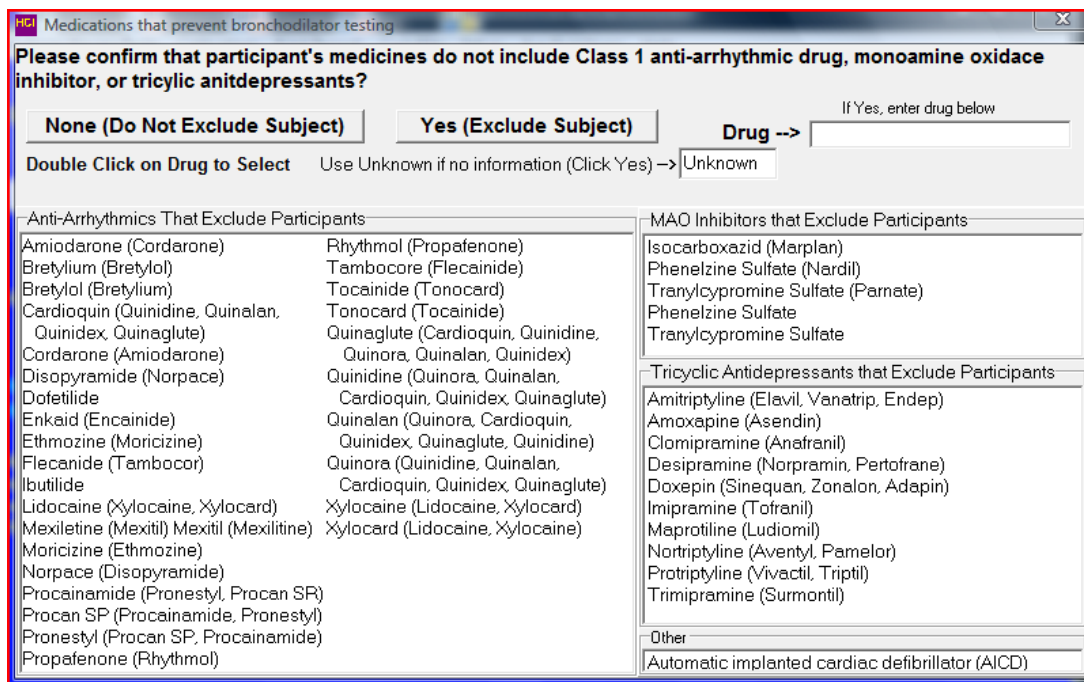
NOTE: Bronchodilators frequently cause a brief coughing spell. Cough is a normal response to a bronchodilator. Cough should NOT be considered a significant problem with a puffer. In other words, if a participant reports cough following bronchodilator administration, click “No” and proceed with bronchodilator testing.



The screen (above-left) will appear for anyone who meets the study criteria for a bronchodilator test. Note the participant can refuse the bronchodilator test at this point by selecting “Refused.” If you click “Yes”, you must verify your selection by clicking the “Prior significant problem with puffer” checkbox (above right) and by entering the prior significant problem in the text box. Doing so will abort the post-bronchodilator testing protocol.

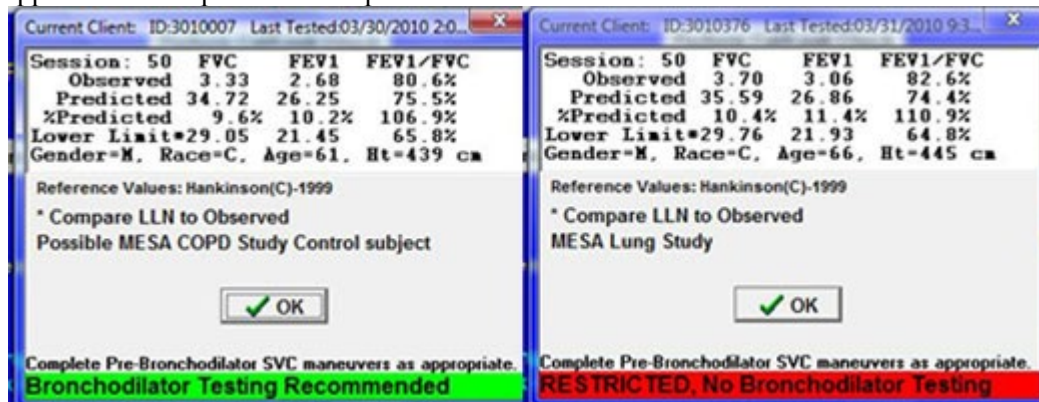
You will also be asked to check the participant’s medications to make sure that they are not taking one of the medications on the lists provided (see panel below).

NOTE: Although these lists are long, all of these medications are prescribed rarely – even in patients with cardiac disease and depression. Anti-arrhythmics are prescribed only for a few patients with or at risk for severely abnormal heart rhythms (i.e., NOT for the much more common “heart disease” [coronary heart disease] and generally not for atrial fibrillation). MAO inhibitors and tricyclic antidepressants are both older types of antidepressants that are rarely prescribed for depression these days. Tricyclic antidepressants (particularly amitriptyline [Elavil]) are still occasionally prescribed for chronic nerve pain.



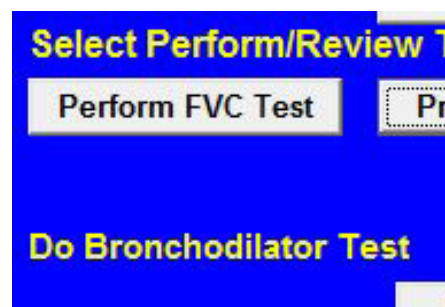
If you check “Yes (Exclude Subject)”, you should enter the “Drug” by typing it or double-clicking on a drug from the bottom panels. If the participant did not bring their medications AND does not know what medications they are taking AND has abnormal heart rhythm, depression or chronic pain, enter “Unknown” for the Drug and click “Yes (Exclude Subject).”

One of the two following panels will then appear. If a participant is selected for and has no contraindications to bronchodilator testing, the “Bronchodilator Testing Recommended” box (left) will appear and you should proceed with bronchodilator testing (Section 4.1). If a subject has a contraindication for a bronchodilator, the “RESTRICTED, No Bronchodilator Testing” message will appear instead (right). Note that the screens below appear after completion of the pre-bronchodilator FVC maneuver – see text at bottom of screens below.



Appendix B shows a flow chart for determining whether albuterol administered for a post-bronchodilator test. After administering albuterol, perform first the SVC Test and then the FVC Test as before. Notice that a message that you should be performing a bronchodilator test will appear on the main screen.

If you have any concerns about administration of albuterol in a given participant, if you believe the participant should not have selected for albuterol administration or if you have other questions or uncertainty about albuterol administration, then contact the either PI (Dr. Barr or Dr. Smith) for further assessment prior to proceeding.



is
post-
been

Wait 10 minutes after administration of the albuterol and then repeat the FVC maneuver as described in Section 3.2 above (3-8 more attempts).

Post Test Questionnaire: After test completion, the “Post Test Questionnaire” screen will appear. On this screen, indicate the testing position, participant (client) effort, and add comments, if you wish. Then click “OK.”

Please complete the following questions for current client

Check appropriate boxes to indicate a yes response

Post-Test Questions

Did any of the following Signs or Symptoms Occur?

Testing Position

Standing

Sitting

Client's Effort

Maximal

Questionable

Sub-maximal

Headache

Dizziness or lightheadedness

Coughing

Short of breath

Other

Enter Remarks Below

OK

7.9.4.1 How to Give Albuterol

1. Shake the metered dose inhaler (MDI) or puffer. Point it away from faces, and then activate it once to verify aerosol delivery.
2. Attach a clean disposal spacer (squeeze the edge of the flat cardboard spacer to open it for use following directions on the package). The spacer contains a one-way valve so that the participant can only breathe in through it, as intended.
3. Discharge the MDI into the spacer once by pressing on the top of it.
4. Hold the MDI and spacer in front of the participant's open mouth.
5. Ask the participant to exhale slowly.
6. Ask them participant to lower their mask.
7. Place the spacer in the participant's mouth and ask them to inhale *slowly*. Count to five slowly.
8. Ask the participant to hold their breath (ideally 15-30 seconds) during which they can replace their mask and then to exhale slowly.
9. Wait one minute and repeat above steps 3-8 to administer another puff of albuterol.
10. Wait 10 minutes and then repeat spirometry
11. Click on the main menu item “Perform/Review Test”
12. Click on “Add Post Bronchodilator Test”
13. Perform FVC test as previously described
14. Click on main menu item “Print Report”
15. Click on “Print Participant Report” menu item
16. Click “Print All”
17. Click on “Apply Selection” button
18. Click on check box “Print report to screen only” so that it is checked
19. Click “Print Report” button

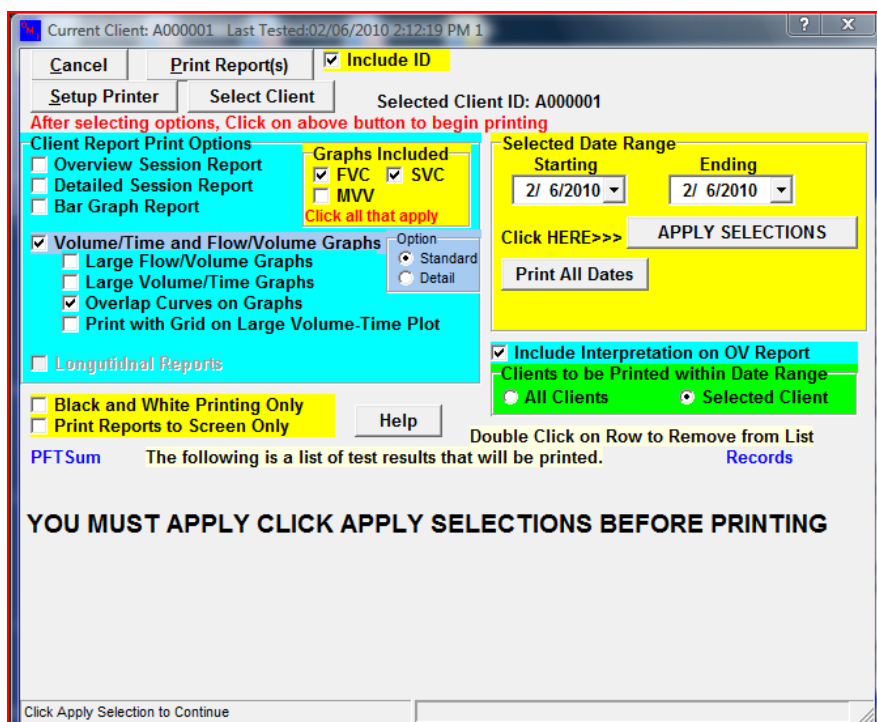


7.9.4.2 Possible Side-Effects of Albuterol

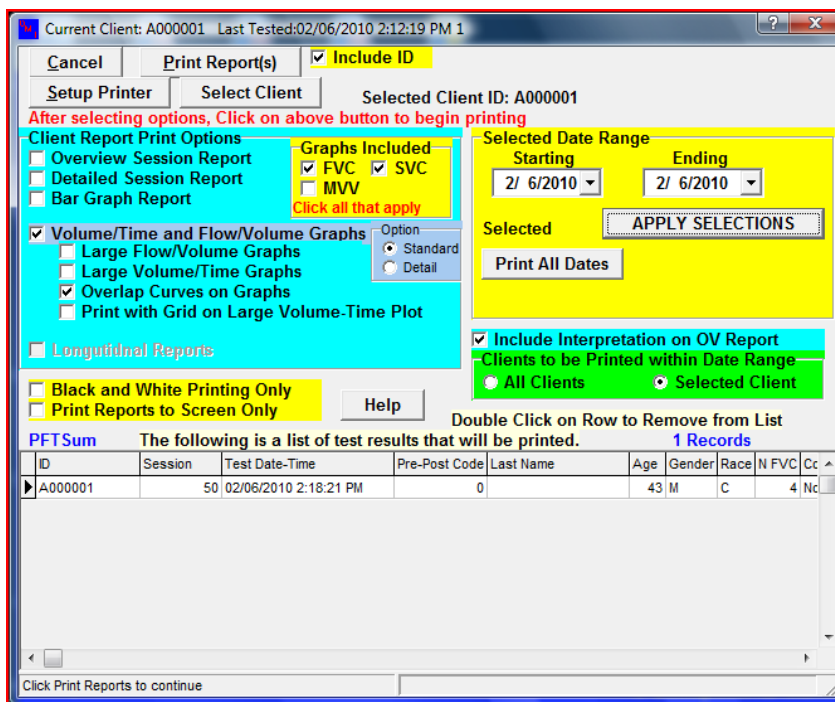
Albuterol is a mild stimulant, like caffeine, so some people (especially those who don't drink coffee or tea regularly), may experience mild nervousness, lightheadedness, a slight tremor, or a headache for up to an hour after inhaling albuterol. These are not worrisome symptoms and will subside before the end of the visit. Albuterol may also increase the heart rate, but does not cause arrhythmias, even in older people. Albuterol is used by tens of thousands of patients with asthma or COPD daily to relieve shortness of breath.

7.9.5 How to Print a Report

At the end of each test session, use the "Print Report" main menu item to print all test results. The "Print Current Test" menu item under "Perform/Review Test" is used, while participant information and results are still current in the computer. The right mouse button can also be clicked to display a popup menu with the "Print Current Test" menu item. Notice both the FVC and SVC check boxes are checked. You must click "Apply Selections" to complete the selection of tests to be printed.



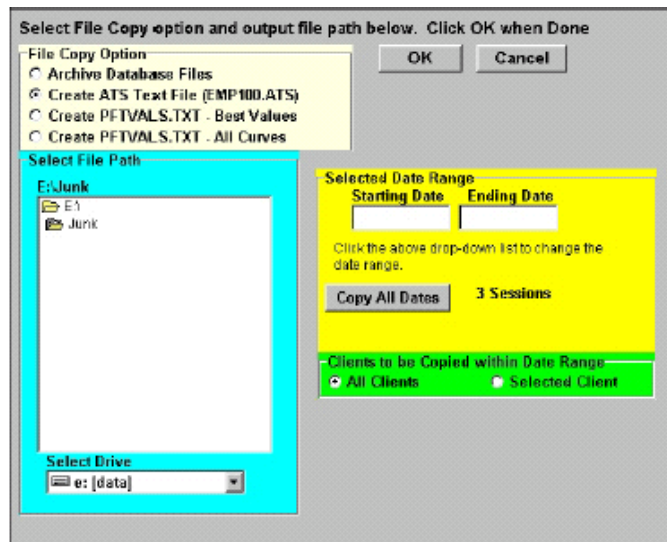
After Clicking "Apply Selections" the Test to be printed will appear in grid box. Select "Setup Printer" and choose, print to PDF. Click "Print Reports" to save the curves to your desktop. After the curves are saved to the desktop, you may print a paper copy, if required, by changing the printer in "Setup Printer" to your local or network printer and re-print. In the Spirometry Completion form, you will be asked to upload a copy of these reports in the appropriate section.



After the curves are saved to the desktop in PDF format, you may print a paper copy, if required, by changing the printer, again, in “Setup Printer” to your local or network printer and re-print.

7.9.5.1 Copy File

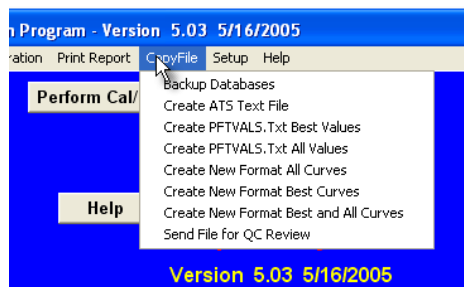
The “Copy File” main menu item provides you with a convenient means of backing up the data files. The sub-menu items under “Copy File” allow you to select several types of files to copy, some with selected date range limitations. You may select the output path using a file dialog box or use the default setting established in the setup program. The text files (EMP100.ATS and PFTVALS.TXT) can be limited by specified date range or for a selected participant. The backup files allow you to back up all the database files - compressed into one PKZIP compatible file. Again, the user can select the path for this file or the default path established in setup will be used. When you click the “OK” button, the list of database files is shown in the left list box, and as each individual file is placed in the backup zip file, it is listed in the right list box. Progress bars for both the individual files and for all files are shown. A default name of “OMIBackup.Zip” is used unless you specify another file name. The computer checks to see if the file already exists and prompts you to replace or update the file or exit and rename the backup file.



Copy Text File Screen

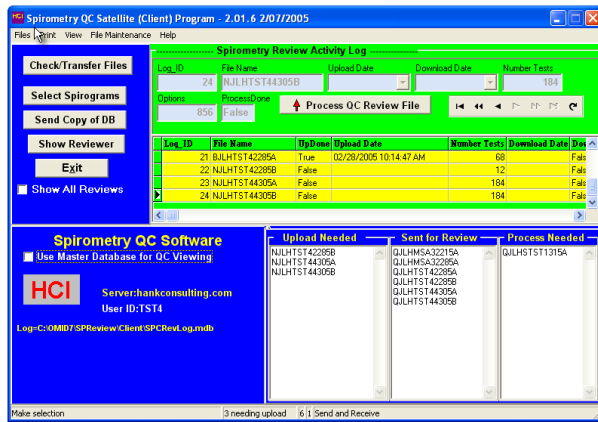
7.9.5.2 Send File for Review every Friday

The “Send File for Review” menu item, located under “Copy File” on the main screen is used to send data to the quality control center within the main spirometry program. Clicking on “Send File for QC Review” or the “SpRevParticipant” desktop icon runs the program which will select participant spirograms to be sent for review.



Copy File Menu - Send File for QC Review

Start Send File Program - Clicking on *Send File for QC Review* or desktop icon will execute the transfer program, see below. The yellow grid in the middle of the screen shows a list of files uploaded to the QC Reviewer and the transmission dates. Click on “*Send Copy of DB*” button to send a copy of the latest results to the QC Reviewer. The first time you run the program, you will be asked to select your field site (see figure on right).

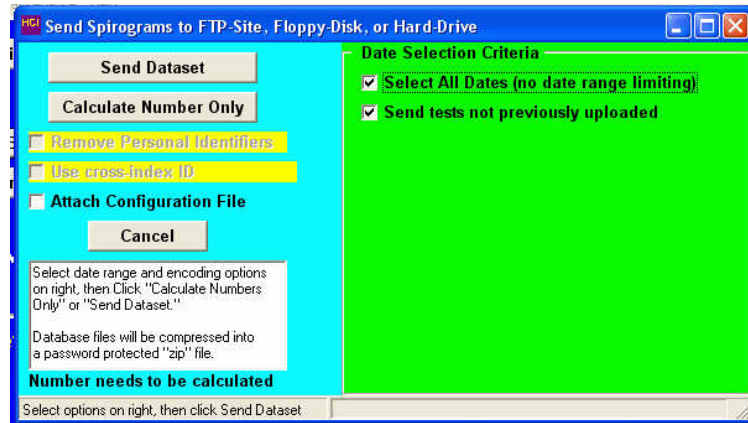


File Selection Program - Main Screen

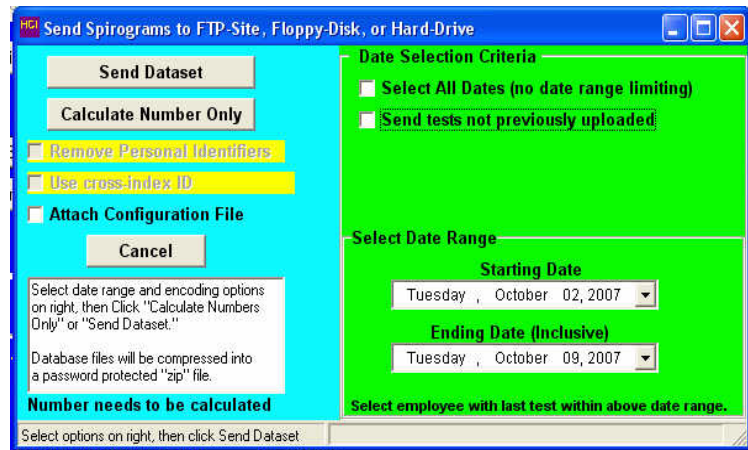


Select Site (User ID)

Selecting Date Range - The *Send Copy of DB* button will cause the *send spirometry selection screen* to appear. Use the Standard option below (both boxes on right checked). However, you may need to select the dates or date range of tests to include in the transmission if you need to resend some tests. The default starting date is the day after the date of your last transmission and the default ending date is the current date. The default settings of *Remove Personal Identifiers* and *Use cross-index ID* should remain checked.

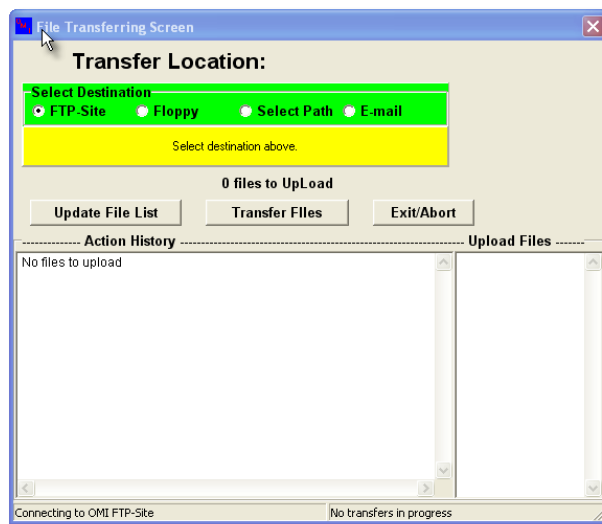


Send Spirograms Selection Screens (Standard)



Send Spirograms Selection Screen (by Date)

Transmitting Data - After verifying that the dates are correct, click the “Send Dataset” button to continue the transmission of the spirometry results. If you receive a warning message that you are about to a replacing an existing file, click OK as this file is no longer needed. The Transfer Location screen will appear where you can select where you want the file to be sent. You should copy the file to a USB memory stick via the “Select Path” option. Transfer the file on the USB memory stick to the MESA computer then email to the Spirometry Reading Center. The default is to use the Select Destination option shown in the screen below (FTP-site).



File Transfer Option Screen

After the file has been transmitted, you may exit the File Transfer Option Screen and the File Selection Program and return to the main spirometry screen.

7.9.6 Quality Assurance

Upon completion and review of each batch of incoming data, you will be notified quickly of any errors with calibration and procedures. Each month, statistics will be compiled for each technician summarizing the quality of the tests done and the results of calibration checks. The reports may indicate that you may need additional training.

7.9.6.1 Training

Technicians from each Field Center will be trained centrally. Training will also include completion of a web-based spirometry training course, including answering all the review questions. Chapter 5 (hand-measurements) is optional. Retraining may be done by an experienced on-site technician.

7.9.6.2 Certification

The examination includes a formal web training, 50 multiple choice questions (written exam), and a practical demonstration of skills including leak and calibration checks, cleaning, and testing of a naive participants. A passing score of at least 70 points is necessary for certification for the written exam. Only certified technicians will perform pulmonary function testing in this study. A web-training account can be obtained from john@hankconsulting.com.

In addition, the slides from the spirometry training are on the MESA Lung website, <http://www.uwchsc.org/MESALung/MesaLung2.aspx> under the link, “[Spirometry for MESA Lung Webinar - February 2010](#).” These should be reviewed, if not seen in Central Training, and provide a useful reference as the study goes on. The user name and password for the MESA Lung website are the same as for the main MESA website.

For staff previously certified spirometry, 5 valid tests must be completed, transmitted to the Spirometry Reading Center and graded. For staff without prior spirometry experience, 5 observed and 5 unobserved valid tests must be completed, transmitted to the Spirometry Reading Center and graded.

PF technicians should test at least one person (participant, another technician or staff member) per week between the training session and the start of recruitment. To retain certification, technicians must test at least ten participants each month.

7.9.6.3 Site Visits

The results of the first 50 spirometry test sessions performed by each technician will be closely examined by the QC Supervisor (John Hankinson). Copies of suboptimal quality test sessions with comments for improvements will be sent to you the same day as they are evaluated.

A site visit to each of the four clinical centers may be made during the first three months of recruitment. Complete calibration, leak, and linearity check, and spirometry testing of at least three participants by each technician will be observed. Copies of suboptimal quality test sessions will be reviewed. More efficient methods as well as protocol violations will be discussed during the site visits and later in a written report.

7.9.6.4 The Need for Spirometry QC

Examination of spirograms from the Framingham study revealed that more than 18% were of clearly unacceptable quality. Two more recent studies, with over 12,000 adults each, found that 40-50% of the spirometry maneuvers were of unacceptable quality. Manual measurements from spirograms are tedious and prone to error and deviations in test performances and lack of regular leak checking and calibration can result in loss of study data.

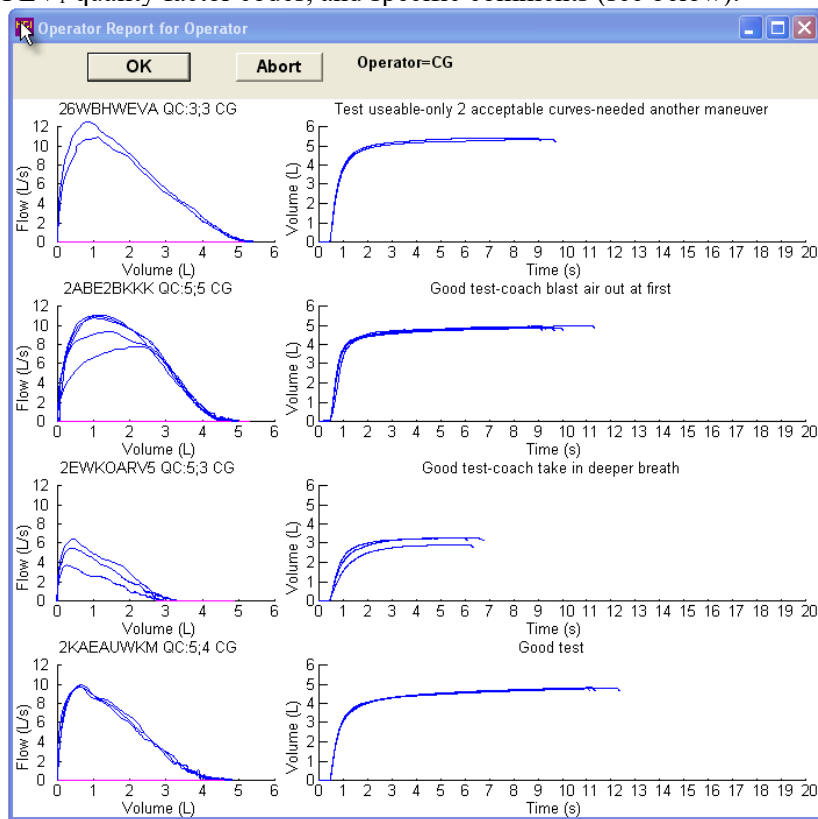
Evaluations of commercially available spirometers emphasize the importance of spirometry quality control procedures. Factors affecting spirometry quality include:

1. Participant
2. Maneuvers
3. Technician
4. Equipment
5. Analysis

7.9.6.5 Implementation of QC Procedures

There are five separate levels of quality control implemented for spirometry testing which address the five factors known to influence the results:

1. Daily spirometer leak and calibration checks using a 3.00 liter syringe as the “gold standard” check maneuver immediately after it is performed.
2. Eight computerized checks of FVC maneuver acceptability and repeatability check every maneuver immediately after it is performed.
3. The PF technician is trained to recognize the patterns of acceptable maneuvers, watching the participant during the performance, and reviewing the colorfully displayed flow-volume curves on the computer monitor.
4. The results of the leak and calibration checks and the best 3 FVC maneuvers are stored and sent to the PF Reading Center for review by the PF QC Supervisor. Monthly reports are compiled for each technician’s performance.
5. Results from all of the above are taken into account during the analysis of the data by the PF Reading Center. The calibration factors, PF tech’s impression of the participant and the maneuver quality, and the QC supervisor’s impression of test session quality are all integrated to obtain the final FEV₁ and FVC results reported to the Data Coordinating Center. An operator report will be sent by e-mail to each technician periodically and at a minimum at the completion of testing at a study site. The operator report (password protected “pdf” file) contains copies of all tests performed by a technician with flow-volume, volume-time curves, FVC and FEV₁ quality factor codes, and specific comments (see below).



7. The following statistics are reported each month by the quality supervisor:

- Average number of acceptable maneuvers, by technician.
- Percentage of participants with non-repeatable tests results, by technician.
- Percentage of participants with. less than 3 acceptable maneuvers, by technician
- Percentage of participant with less than 2-acceptable maneuvers, by technician.
- Average FVC quality score, by technician.
- Average FEV₁ quality score, by technician.

Quality grades (A-F) are computed for FEV₁ and for the FVC (quality codes) based in part on the number of acceptable maneuvers. An acceptable maneuver for FEV₁ quality purposes is no cough or large extrapolated volume. At least 6-seconds of exhalation and a plateau in the volume-time curve (30 ml in one second) are needed for an acceptable quality FVC. However, a maneuver that does not have a plateau but the exhalation is longer than 15-seconds is considered acceptable.

Test session QC grades are assigned as follows:

A = 3-acceptable curves, plus largest and second largest value within 100 ml

B = 2-acceptable curves, plus largest and second largest value within 150 ml

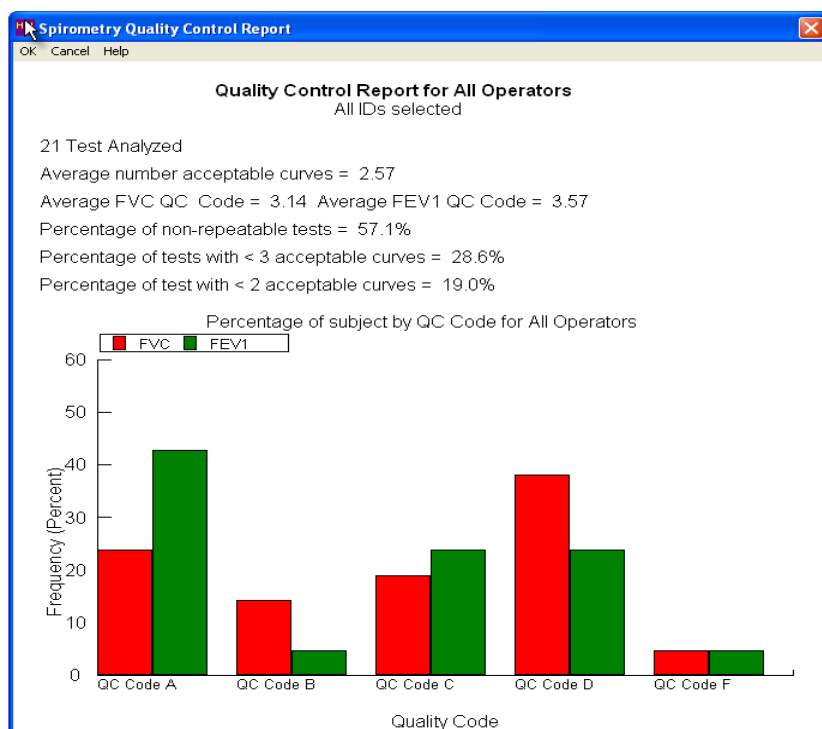
C = 2-acceptable curves, plus largest and second largest value within 200 ml

D = 1 acceptable curve plus no end of test requirement for FVC QF

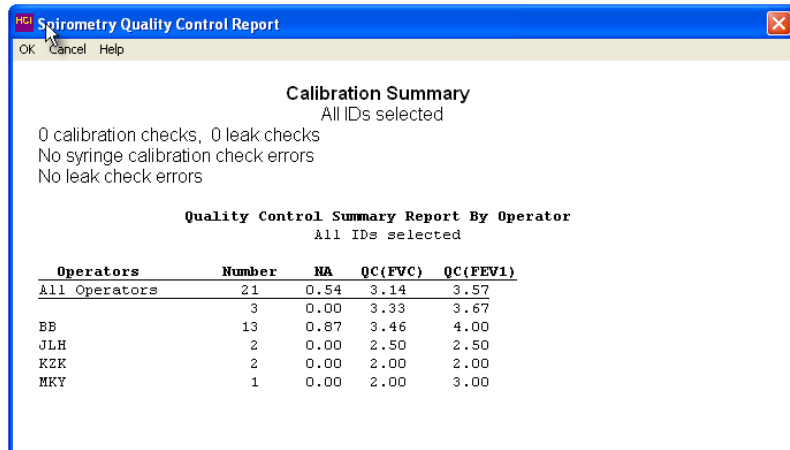
F = no acceptable curves

The QC supervisor may assign a slightly higher QC grade for participants with obvious airways obstruction where it is difficult to obtain a plateau or reproducible test. A lower grade may also be assigned if a curve is judged to be unacceptable because the FVC or FEV₁ cannot be accurately measured.

7. In addition to the quality control summary report, a calibration summary report is also provided. Trends of average FVC and FEV₁ quality scores will be monitored during the study to determine if quality issues need to be addressed. Sample quality control reports (individual technician reports are similar to the All Operators report) are shown below:



Quality Control Report - All Operators Combined

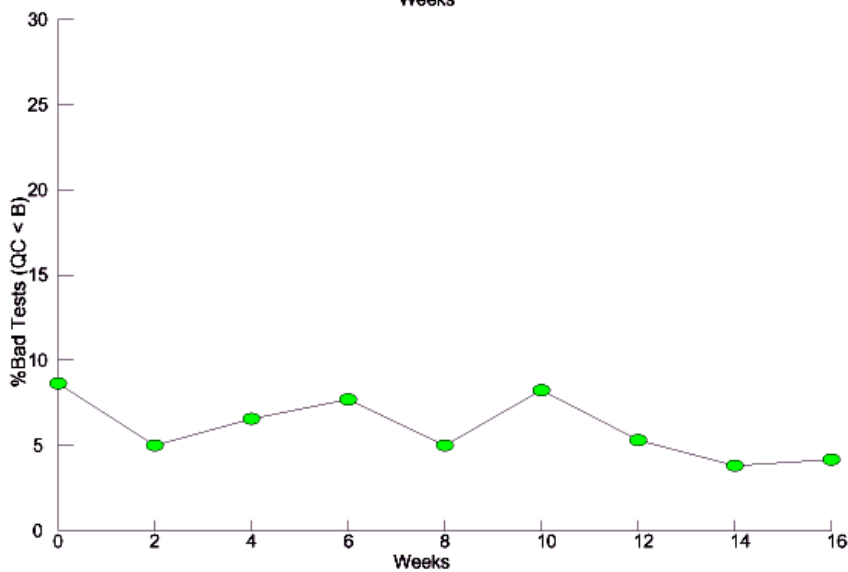
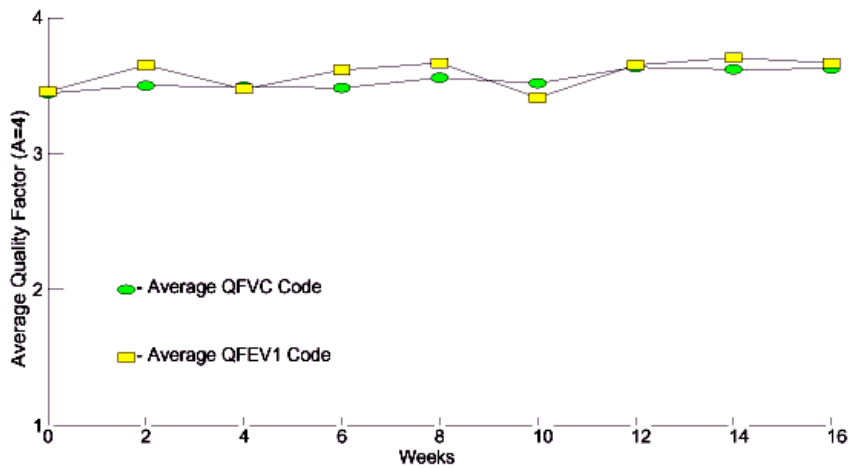


Calibration and Quality Control Summary Report

Trend Period 10/1/2003 to 2/15/2004 (18 weeks)

Week	N	QFVC	QFEV1	%Bad	Week	N	QFVC	QFEV1	%Bad	Week	N	QFVC	QFEV1	%Bad
0	81	3.44	3.46	8.6%	2	80	3.50	3.65	5.0%	4	61	3.49	3.48	6.6%
6	91	3.48	3.62	7.7%	8	120	3.56	3.67	5.0%	10	85	3.52	3.41	8.2%
12	132	3.64	3.65	5.3%	14	105	3.62	3.70	3.8%	16	24	3.63	3.67	4.2%

QC Code Trends for All Operators; 4=A, 3=B, 2=C, 1=D, 0=F



Quality Control Trend Analysis

7.9.7 Safety Procedures

All equipment must be plugged into a grounded electrical outlet.

To minimize cross-contamination:

- Use a clean hose for each participant
- Use disposable, filtered mouthpieces
- Keep the participant's mouth higher than the spirometer snout.
- Participants do not inhale from the spirometer.
- The spirometer and accessories will be cleaned and disinfected at regular intervals.
- Tubing will be cleaned and disinfected daily (see Section 2.5)
- Instruments will be cleaned at the end of each testing session (see Section 2.4)
- Seal will be inspected and cleaned at the same time.

Study technicians are expected to wear personal protective equipment for the entire spirometry procedure including a well-fitted n95, disposable gown, eye protection, and gloves. When not performing spirometry, participants are expected to wear a surgical mask covering their mouth and nose.

***COVID TESTING – mention that different sites have different policies for pre-spirometry covid testing??

For participants that do not understand English, Spanish Versions of the exam instructions will be provided.

In rare cases, a participant may hyperventilate and feel dizzy during the examination. Ammonia capsules are available in the event of a participant becoming faint. A participant who feels faint should be guided onto the chair with head down towards knees and encouraged to breathe slowly and deeply until recovered. A physician should be summoned whenever a participant fails to recover normal breathing, faints or reports feeling ill.

7.9.8 References

Banks DE, Wang ML, McCabe L, Billie M, Hankinson J. Improvement in lung function measurements using a flow spirometer that emphasizes computer assessment of test quality. *J Occup Environ Med.* 1996 Mar;38(3):279-83.

Enright PL, Beck KC, Sherrill DL. Repeatability of spirometry in 18,000 adult patients. *Am J Respir Crit Care Med.* 2004 Jan 15;169(2):235-8.

Enright PL, Johnson LR, Connett JE, Voelker H, Buist AS. Spirometry in the Lung Health Study. 1. Methods and quality control. *Am Rev Respir Dis.* 1991 Jun;143(6):1215-23.

Enright PL. How to make sure your spirometry tests are of good quality. *Respir Care.* 2003 Aug;48(8):773-6.

Hankinson JL, Viola JO. Dynamic BTPS correction factors for spirometric data. *J Appl Physiol: Respirat Environ Exercise Physiol* 1983; 55:1354-1360.

Hankinson JL, Castellan RM, Kinsley BS, Keimig DG. Effect of spirometer temperature on measurement of FEV₁ shift changes. *J Occupat Med* 1986; 28:1222-1225.

Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. *Am J Respir Crit Care Med* 1999; 159:179-187.

Hankinson JL, Bang KM. Acceptability and repeatability criteria of the American Thoracic Society as observed in a sample of the general population. *Am Rev Respir Dis.* 1991 Mar;143(3):516-21.

Hankinson JL. State of the art of spirometric instrumentation. *Chest.* 1990 Feb;97(2):258-9.

Hankinson JL. Pulmonary function testing in the screening of workers: guidelines for instrumentation, performance, and interpretation. *J Occup Med*. 1986 Oct;28(10):1081-92.

Johnson LR, Enright PL, Voelker HT, Tashkin DP. Volume spirometers need automated internal temperature sensors. *Am J Respir Crit Care Med*. 1994 Dec;150(6 Pt 1):1575-80.

Krowka MJ, Enright PL, Rodarte JR, Hyatt RE. Effect of effort on measurement of forced expiratory volume in one second. *Am Rev Respir Dis*. 1987 Oct;136(4):829-33.

Gjevre JA, Hurst TS, Taylor-Gjevre RM, Cockcroft DW. The American Thoracic Society's spirometric criteria alone is inadequate in asthma diagnosis. *Can Respir J*. 2006;13(8):433-7.

Li AM, Tsang T, Wong E, Chan D, Sung R, Ng PC. Bronchodilator effect of salbutamol from two different spacer devices. *Pediatr Pulmonol*. 2006 Apr;41(4):326-30.

Liistro G, Vanwelde C, Vincken W, Vandevoorde J, Verleden G, Buffels J; COPD Advisory Board. Technical and functional assessment of 10 office spirometers: A multicenter comparative study. *Chest*. 2006 Sep;130(3):657-65. \

Malmstrom K, Peszek I, Al Botto, Lu S, Enright PL, Reiss TF. Quality assurance of asthma clinical trials. *Control Clin Trials*. 2002 Apr;23(2):143-56.

Miller MR, Hankinson J, Brusasco V, et al for the ATS/ERS Task Force. Standardisation of spirometry. *Eur Respir J*. 2005 Aug;26(2):319-38.

Townsend MC, Morgan J, Durkin D, DuChene AG, Lamb S. Quality control aspects of pulmonary function testing in the Multiple Risk Factor Intervention Trial. *Control Clin Trials*. 1986 Sep;7(3 Suppl):179S-92S.

Townsend MC, DuChene AG, Fallat RJ. The effects of under-recorded forced expirations on spirometric lung function indices. *Am Rev Respir Dis* 1982; 126:734-737.

Townsend M. The effects of leaks in spirometers on measurements on pulmonary function. The implications for epidemiologic studies. *J Occupational Med* 1984; 26:835-841.

Townsend MC, Hankinson JL, Lindesmith LA, Slivka WA, Stiver G, Ayres GT. Is my lung function really that good? Flow-type spirometer problems that elevate test results. *Chest*. 2004 May;125(5):1902-9.

Wise RA, Connett J, Kurnow K, Grill J, Johnson L, Kanner R, Enright P. Selection of spirometric measurements in a clinical trial, the Lung Health Study. *Am J Respir Crit Care Med*. 1995 Mar;151(3 Pt 1):675-81.

7.9.9 Appendix A: The OMIWSP Setup Program

There are three configuration screens. It is important that these configurations are selected, otherwise the data needed for the study and subsequent analyses may not be stored.

Screen 1

Registration Information

Registration Number- set by OMI

Address: your address

Location: your location

Computer ID: take your pick

Maintenance Mode – Disabled

Spirometer Information

Spirometer make: SensorMedics

Spirometer Model: 1022

Spirometer Serial Number: to be entered

Screen 2

Report Header - (enter up to 4 lines)

Site Name

Site address

Phone #

Spirometry Report

Adjustable Parameters

Barometric Pressure - 760

Leak Volume – 20ml

Repeatability Criterion: 150ml

PEF Repeatability Percent - 20

Plateau Volume -40

Plateau Time - 1

Time Check Percent Allowed - 02.0

Extrapolated Volume Criteria - 150

MVV Test Time - 12

Communications Port - 1

Test Start Method - Auto

Starting Session Number - 50

Automated Interpretation - Yes

Interpretation Level - 95%

Interpreter Algorithm - MESA

Selected data path - C:\Program Files\OMI\Database

Use Program Dr. for Cal Path - No

Allow temporary database path change – No

Nomograms

Scale

Caucasian – Hankinson-1999 1.00

Black- Hankinson-1999 1.00

Asian- Caucasian 0.88

Hispanic – Hankinson-1999 1.00

Other 1 - Caucasian 1.00

Other 2 - Caucasian 1.00

Report options

Detailed Session Report - No

Overview of Session Report - No

Volume/Time & Flow Volume Graphs - No

Large Flow/Volume Graphs - No

Large Volume/Time Graphs - No

Overlap Curves on Graphs - Yes

Include Baseline Comparisons - No

Black & White Printer - No

Disable Box (yellow) if below LLN - No

Absolute Values Trend - Yes

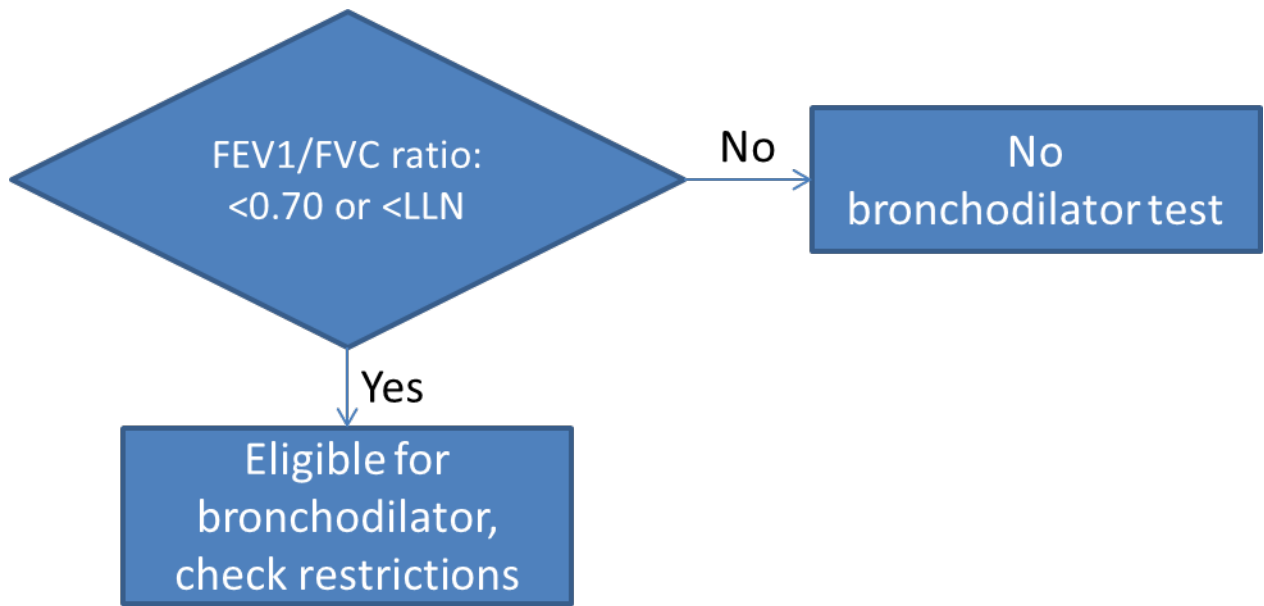
Percent Predicted Trend - No

Percent Deviation Trend - No

Screen 3

<u>Adjustable Parameters</u>	Backup File Path - C:\Program Files\OMI\OMI Spirometry	
Enter Manual Temperature - No		<u>Parameter Print List</u>
Save Raw Data - Yes		SVC – Yes
Enter Participant’s Testing Position - Yes		MVV – No
Save Results in Text File - Yes		FEV _{0.5} – No
Verify Height and Date - No		FEV ₃ – No
Save Results in Enhanced Text File - Yes		FEV ₆ - Yes
Perform SVC and/or MVV Tests -Yes		FEF _{25%} - No
Require Operator Password - No		FEF _{50%} - No
Require PEF Repeatability - No		FEF _{75%} - No
Use FET < 6s Criteria - Yes		PEF - Yes
Draw Inspiration – No		FEF _{25-75%} - No
Use Largest PEF - Yes		FEF _{0.1-1.2} - No
Use PEF Acceptability Criteria - Yes		FEV _{0.5} /FVC% - No
Check End of Test Plateau - Yes		FEV ₁ /SVC% - No
Use Cough Detector - Yes		FEV ₃ /FVC% - No
Use Time to PEF - Yes		FEV ₁ /FEV ₆ % - No
Enter Participant’s Test Effort - Yes		
Enter 4-Level Curve Assessment- No		
Enter Deviations from Test Criteria - No		<u>Exclusion Criteria</u>
Enter Pre-Test Questions - No		PEF Repeatability - No
Enter Post-Test Questions – Yes		Time to PEF - No
Edit Remarks after Test - Yes		<6-seconds - No
Use Open Circuit Method - Yes		No Plateau - No
Other Options		Large Vext - Yes
Best Test - ATS Criteria (Largest Value)		Cough - Yes
Date Format - mm/dd/yyyy		
Height Units - inches Weight -lbs.		
Force Confirmation of Ht & Wt. – No		

7.9.10 Appendix B: Flow Chart for Determination of Post-Bronchodilator Test



7.9.11 Contact Information

7.9.11.1 Personnel

R. Graham Barr, M.D., Dr.P.H. (MESA Lung PI)
622 W 168th St, PH9, East Rm 105
New York, NY 10032-3720
Phone: 212-305-4895
Email: rgb9@cumc.columbia.edu

Emilia Hermann, M.D., M.S.
622 W 168th St, PH9, East Rm 105
New York, NY 10032-3720
Email: eah2191@cumc.columbia.edu

John Hankinson, Ph.D. (Spirometry Reading Center co-I)
Suite 103, PMB 505
1860 Barnett Shoals Rd
Athens, GA 30605
Phone: (706) 742-8986
Email: john@occspiro.com

Spirometry Information and Installation Web Site: <http://occspiro.com/mesa>

User ID: mesa

Password: [FEV1ratio] be sure to include brackets

7.9.11.2 Equipment

SensorMedics / Viasys / CareFusion

(manufactures the dry-rolling seal spirometer)

22705 Savi Ranch Parkway
Yorba Linda, CA 92887-4645
phone (714) 283-1830 or (800) 520-4368

Occupational Marketing, Inc (OMI)

(OMI added the computer interface to the spirometer and provides software support)

11211 Kathy Freeway Ste, 420, Houston, Texas 77079
phone (800) 869-6783; 281-492-8250

Hans Rudolph, Inc. (makes the calibration syringe)

7200 Wyandotte, Kansas City, MO 64114
Phone (816) 363-5522

7.9.11.3 *Supplies*

The following items will be provided centrally. Specifications and contact details are provided for your information.

Nose Clips: “Snuffer” Alliance Tech Medical. Contact person Romney Fischer, 800-848-8923, Order number 555 0047, #100.

Hoses: # 1011-xx Clean-Bor Tubes 1-3/8" (35mm) ID, 34" (Box of 50 1011-34-BULK) Available at <http://www.vacumed.com/zcom/product/Product.do?compid=27&prodid=682>.

Detergent: Detergezyme (enzymatic presoak and cleaning solution). Metrex Corp. #10-4500, 1 gallon bottle. Cardinal Health

Stop-cock grease (if needed): Any silicone-based variety (available at local hardware stores). Do not use petroleum-based grease.

7.9.12 Definitions and Symbols

ATPS is the condition of air inside the spirometer - Ambient Temperature and Pressure, and Saturated with water vapor. The ambient temperature of the spirometer is usually lower than body temperature; this has the effect of cooling and contracting the volume of air exhaled into the spirometer.

ATS is short for American Thoracic Society, the scientific branch of the American Lung Association - the Easter Seal folks. The ATS promotes accurate spirometers by recommending spirometry standards.

BACK EXTRAPOLATION (V_{ext} , EV or BEV) is the standard method used to determine "time zero" when measuring the FEV₁. The amount of slowly exhaled volume at the start of the maneuver excluded from the FEV₁ by this technique is called the back extrapolated volume (BEV or EV). The BEV should be less than 5% of the vital capacity, otherwise the maneuver is considered to have started too slowly.

BD is bronchodilator. We are using the classic rapid-onset, short-acting bronchodilator: albuterol.

BTPS stands for Body Temperature (usually 37 degC) and Pressure, and Saturated with water vapor (100% humidity), which is the condition of air inside the lungs before it is exhaled into a spirometer. ATS standards require that volumes and flows be reported as if they were under these conditions.

CALIBRATION SYRINGE is a large metal cylinder with a rubber sealed piston used to check the volume accuracy of spirometers. The ATS recommends that it be 3.00 liters in size.

COPD stands for Chronic Obstructive Pulmonary Disease, a general term for lung disease caused by cigarette smoking - a mixture of emphysema, bronchitis, and hyperreactive airways.

DIAPHRAGM is the large, dome-shaped muscle between the lungs and the abdomen. Its strength is measured by the MIP test.

EV (see Back Extrapolation)

FET is short for Forced Exhalation Time. The FET should be at least ten seconds for the FVC maneuver to be considered acceptable, otherwise the FVC may be underestimated. Unfortunately, the FET cannot be seen on a flow-volume curve, and must be displayed separately.

FEV₁ is the most important spirometry variable, short for Forced Expiratory Volume in one second. It is convenient to think of it as the average flow rate during the first second of the FVC maneuver. It is reduced with airflow obstruction.

FEV₁/FVC RATIO is the most sensitive and specific index of airways obstruction measured by a spirometer. It is normally above 70%.

FLOW-VOLUME CURVE is the graph obtained from a forced exhalation maneuver plotted with flow on the vertical axis and volume on the horizontal axis. When compared with the traditional spirogram, it has the advantage of allowing easy recognition of unacceptable or poorly reproducible maneuvers and disease patterns.

FVC is the Forced Vital Capacity, the volume of air exhaled during the maneuver named after it. The participant takes as deep a breath as possible and then quickly exhales as much air as possible. The FVC is reduced with restrictive disorders.

OBSTRUCTION is a decrease in maximal airflow rates caused by airway narrowing. The FEV₁/FVC ratio and the FEV₁ are both decreased.

PEF stands for Peak Expiratory Flow, the highest flow measured during the FVC maneuver. It is a good index of effort used at the onset of the maneuver. It can be seen on a flow-volume curve but not on a spirogram.

PF (or PFT) is short for Pulmonary Function (lung tests).

Post-BD is short for spirometry done after albuterol.

PRED is short for the predicted value of a PF parameter. It is determined from the regression equation from a large population study of supposedly normal people.

RESTRICTION is a decrease in lung volumes. Scarring of lung tissue (fibrosis), heart failure, pneumonia, and simple obesity are some of many causes. The FVC is reduced while the FEV₁/FVC ratio is normal or increased.

SPIROGRAM is an older term for the volume-time graph produced by water-sealed spirometers.

VOLUME-TIME TRACING is the graph produced directly by volume-sensing spirometers. It is traced by a pen connected to the spirometer bell with volume on the vertical axis.

Vext (see Back extrapolation)

7.9.13 Methods Summary

Daily Procedures

Calibrate Instruments

- Power-up workstation
- Check spirometer water level
- Run leak and volume checks (CAL)

Identify each participant

- Select participant's ID number (STATIONS)
- Administer spirometry questionnaire
- Verify name, age, and height (NEW then INF)

Perform Spirometry Test (FVL)

- Demonstrate FVC maneuver
- Attach clean tube & mouthpiece
- Obtain 3 acceptable FVC maneuvers
- Review maneuver quality
- Obtain another 2-5 FVC maneuvers

When indicated, administer albuterol and perform post-BD spirometry

Add comments (FIN)

Clean Equipment

- Clean the breathing hoses
- Rinse and dry the hoses overnight

Weekly Procedures (Friday afternoon):

- Upload week of spirometry data to PF Reading Center via e-mail
- Clean the breathing hoses
- Check the spirometer for leaks
- Rinse and dry hoses over the weekend

7.9.14 Spirometry and/or Albuterol Exclusion Criteria

Questionnaire Exclusion Items on Completion Form:

1. Is systolic blood pressure >180 OR diastolic blood pressure >110 from Seated Blood Pressure?

- YES – STOP (do not perform spirometry or nasal swab)
NO - Proceed

2. Have you had a cold or the flu that started in the past 4 week, or have you had a positive COVID test in the past 4 weeks?

- YES – STOP and reschedule spirometry and nasal swab once participant is 4 weeks past infection
NO - Proceed

3. Have you had a heart attack, stroke, or eye, chest, or abdominal surgery in the last 3 months?

- Yes – STOP (Do not perform spirometry or administer albuterol) – OK to do nasal swab if no other exclusions
No – Proceed

4. Have you had any significant problems doing spirometry in the past?

- Yes (Do not perform spirometry or administer albuterol) – OK to do nasal swab if no other exclusions
No – Proceed

5. [FOR PTS SELECTED FOR BRONCHODILATOR ONLY] Do you have an implanted cardiac pacemaker or implanted cardioinverter-defibrillator (ICD)?

- Yes (OK to perform spirometry but do not administer albuterol)
No – Proceed

Automated Exclusion Item:

1. Systolic blood pressure \geq 200 mmHg or diastolic blood pressure \geq 110 mmHg – assessed earlier in Exam and leads to exclusion from all exam components, including spirometry and bronchodilator administration.

Other Albuterol Exclusions Items Assessed by Spirometry Software:

1. Report of use of Class 1 anti-arrhythmic drug, monoamine oxidase inhibitor, or tricyclic antidepressant (assessed on the Medication history form) leads to exclusion from bronchodilator administration. All of these drugs are very rarely prescribed and the risk of inhaling albuterol is theoretical. If any of the following prescribed medications are reported on the Medication form, **avoid giving albuterol:**

Anti-Arrhythmics:

Amiodarone (Cordarone)
Bretylum (Bretylol)
Bretylol (Bretylum)
Cardioquin (Quinidine, Quinalan, Quinidex, Quinaglute)
Cordarone (Amiodarone)
Disopyramide (Norpace)
Dofetilide
Enkaid (Encainide)
Ethmozine (Moricizine)
Flecainide (Tambocor)
Ibutilide
Lidocaine (Xylocaine, Xylocard)
Mexiletine (Mexitil) Mexitil (Mexilitine)
Moricizine (Ethmozine)

Norpace (Disopyramide)
Procainamide (Pronestyl, Procan SR)
Procan SP (Procainamide, Pronestyl)
Pronestyl (Procan SP, Procainamide)
Propafenone (Rhythmol)
Rhythmol (Propafenone)
Tambocore (Flecainide)
Tocainide (Tonocard)
Tonocard (Tocainide)
Quinaglute, Quinidine, Quinalan, or Quinora
Xylocaine (Lidocaine, Xylocard)
Xylocard (Lidocaine, Xylocaine)

MAO Inhibitors:

Isocarboxazid (Marplan)
Phenelzine Sulfate (Nardil)
Tranlycypromine Sulfate (Parnate)
Phenelzine Sulfate
Tranlycypromine Sulfate

Tricyclic Antidepressants:

Amitriptyline (Elavil, Vanatrip, Endep)
Amoxapine (Asendin)
Clomipramine (Anafranil)
Desipramine (Norpramin, Pertofrane)
Doxepin (Sinequan, Zonalon, Adapin)
Imipramine (Tofranil)
Maprotiline (Ludiomil)
Nortriptyline (Aventyl, Pamelor)
Protriptyline (Vivactil, Triptil)
Trimipramine (Surmontil)

2. Also avoid giving albuterol to patients with an automatic implanted cardiac defibrillator (AICD).
-

7.9.15 Spirometry and Nasal Swab Completion Form

Purpose

Page 1 of the Spirometry and Nasal Swab Collection Completion Form is designed to evaluate if subjects are medically able to perform spirometry (Questions 1 -5) to assess whether albuterol should be administered (Questions 7-8) and to document completion of spirometry (Questions 6 and 9). The second portion of this form is designed to capture information on eligibility for the nasal swab collection (Q10-13) and completion of the nasal swab (Q14).

Methods

This is an interviewer-administered form. Please administer questions before starting spirometry exam. The questions can be answered by filling in a bubble or a blank with a number or word. Most questions are self-explanatory. Specific instructions are given for some questions.

Specific instructions

Q.1. Are spirometry and nasal swab collection being performed in clinic or at a home visit?

- If the spirometry exam is being done at a home visit, only perform pre-bronchodilator spirometry and do not administer albuterol.

Q.2. Is systolic blood pressure >180 OR diastolic blood pressure >110 from Seated Blood Pressure?

- If the response to either of these is “yes” then do not perform spirometry or the nasal swab. Enter “Not Completed” in Q6 (Pre-bronchodilator spirometry was:” and Q14 (Was nasal swab completed”

Q.3. Have you had a cold or the flu that started in the past 4 week, or have you had a positive COVID test in the past 4 weeks?

- If the answer is yes, do not perform spirometry or the nasal swab. If there are no other exclusion criteria, reschedule the spirometry and nasal swab collection once participant is 4 weeks past infection.

Q4. Have you been told that you had a heart attack, stroke, or eye, chest or abdominal surgery in the last 3 months?

- If the participant answers “yes” that they have been told that he/she had a heart attack or stroke in the LAST 3 MONTHS or surgery on the EYE, CHEST or ABDOMEN in the LAST 3 MONTHS, fill in the bubble next to “Yes” and DO NOT PROCEED with spirometry. Answer Questions 5 and 8 only, and fill in your Technician ID number at the bottom of page 2. If the participant reports a transient ischemic attack (TIA) in the last 3 months, follow the same procedure and do not perform pulmonary function testing. If the participant had a more remote heart attack/stroke/TIA or more remote eye/chest or abdominal surgery, in general it is fine to proceed with spirometry. We presume that participants will complete spirometry sometime in their clinic visit after blood pressure measurement. Participants with very high blood pressure (>210/120 mmHg) will therefore be excluded by the MESA protocol from performing pulmonary function testing. If not sure, consult MESA-Lung Principal Investigator Dr. Barr or Spirometry Consultants Drs. Enright and Hankinson before performing the test.
- If the participant has NOT been told that he/she had a heart attack or stroke in the last 3 months, proceed to Question 2.

Q.5. Have you had any significant problems doing spirometry in the past?

Ask if the participant has had any significant problems doing spirometry in the past. If the participant has never done spirometry in the past, answer ‘no.’ If the participant has done spirometry in the past and did have a significant problem, then answer ‘yes’ and describe the problem in the comments box. If the problem was indeed significant and likely to recur with retesting, DO NOT PROCEED with spirometry. Complete Questions 5, stating the reason that spirometry were not performed. If you are uncertain if the problem is significant and/or likely to recur, consult with the Project Coordinator, Field Center Principal Investigator, and/or MESA-Lung Principal Investigator (Dr. Barr), and/or MESA Lung Co- Investigator (Dr. Hermann), or Spirometry Consultant (Dr. Hankinson) before performing the test.

Q.6. Pre-Bronchodilator Spirometry was:

- If pre-bronchodilator spirometry was completed, fill in the bubble next to “**Completed,**” and record the time at completion (hours AND minutes, AND fill in a bubble next to am or pm). FOR THE PURPOSE OF THE COMPLETION FORM ONLY, COMPLETED IS DEFINED AS THE PARTICIPANT COMPLETING AT LEAST ONE CURVE (MANEUVER).
note that we do not based the definition of “complete” on whether or not the curves are reproducible
Upload a copy of the PDF of the spirometry curves into the E7 REDCap Spirometry Completion Form. See section 7.9.5, above, for details on how to print the curves to PDF and save on the spirometry tablet’s desktop.
- If pre-bronchodilator spirometry was not completed, fill in the bubble next to “**Not completed. If not completed,**” specify the reason(s) why the spirometry was not completed. Select one or more from the provided options “refused” “physically unable” “cognitive unable” “equipment problem”. For other reasons the spirometry was not completed, check “Other” and specify in the provided blank.

Continue with Page 2 on the **Spirometry Completion Form** on the following page.

NOTE: If this is a hone visit, skip to Nasal Brushing section (Q10)

Q.7. Do you have an implanted cardiac pacemaker or implanted cardioverter-defibrillator (ICD)?

- **If yes, and participant is selected for post-bronchodilator spirometry, do not continue with post-BD spirometry. Skip to Q9 and note that post-BD spirometry was not completed.**

Q.8. If selected for albuterol?

- Participants may be selected for albuterol by the spirometry software if they have airflow limitation. See Appendix B for details.
- Administer 2 puffs of albuterol as per Section 4 above and record the time. After 10-15 minutes, proceed with post-bronchodilator spirometry as per Section 4 above and complete Item 7 on completion of post-bronchodilator spirometry.
- If the spirometry software does not select the participant for albuterol, check off the “**No**” box, do not administer albuterol and skip to end.

Q.9. Participants Selected for Albuterol and Post-Bronchodilator Spirometry:

If post-bronchodilator spirometry was completed, fill in the bubble next to “**Completed,**” and record the time at completion (hours AND minutes, AND fill in a bubble next to am or pm). “Completed” is defined as in Item 5 above. Upload a copy of the PDF of the spirometry curves into the E7 REDCap Spirometry Completion Form. See section 7.9.5, above, for details on how to print the curves to PDF and save on the spirometry tablet’s desktop.

- If post-bronchodilator spirometry was not completed, fill in the bubble next to “**Not completed. If not completed,**” specify the reason(s) why the spirometry was not completed. Select one or more from the provided options “refused” “physically unable” “cognitive unable” “equipment problem”. For other reasons the spirometry was not completed, check “Other” and specify in the provided blank.

Nasal Swab Collection – For details on the collection method, see section 7.11 of the MESA Exam 7 MOP, below. Questions 10-13 are exclusion criteria for the nasal brushing. It is important to ask all of these questions prior to the nasal swab collection.

Q.10. Are you currently taking an anticoagulant such as warfarin, low molecular weight heparin, or newer oral direct acting anticoagulants?

- If Yes, do not perform nasal swab. Select NO for question 14.

Q.11. Are you currently taking aspirin, clopidogrel or other anti-platelet medication?

- If Yes, do not perform nasal swab. Select NO for question 14.

Q.12. Have you had recent nasal trauma or surgery?

- If Yes, do not perform nasal swab. Select NO for question 14.

Q.13. Do you have a history of severe nose bleeds?

- If Yes, do not perform nasal swab. Select NO for question 14.

Q14. Was nasal swab completed?

- If the nasal swab was completed, fill in the bubble next to the appropriate number of nares swabbed (1 or 2) and then enter in the time it was completed: hour, minutes, and whether it was performed in the AM or PM.
- If the nasal swab was not completed, full in the bubble next to the “No” and then provide a reason not completed in the sub question. If ineligible, mark “Other, please specify” and enter ineligible in the text box.

7.10 Hair Sample Collection

Why are we collecting hair?

For the first time in MESA, we will be collecting hair samples from participants in Exam 7. We are collecting the hair from the scalp to look at the cells on the end of the hair (called the hair follicle). When hair is plucked, these cells come off the scalp with the hair (see picture below). We will look genomic material in these cells to investigate links between key genes and emphysema and potentially cardiovascular disease.

MATERIALS:

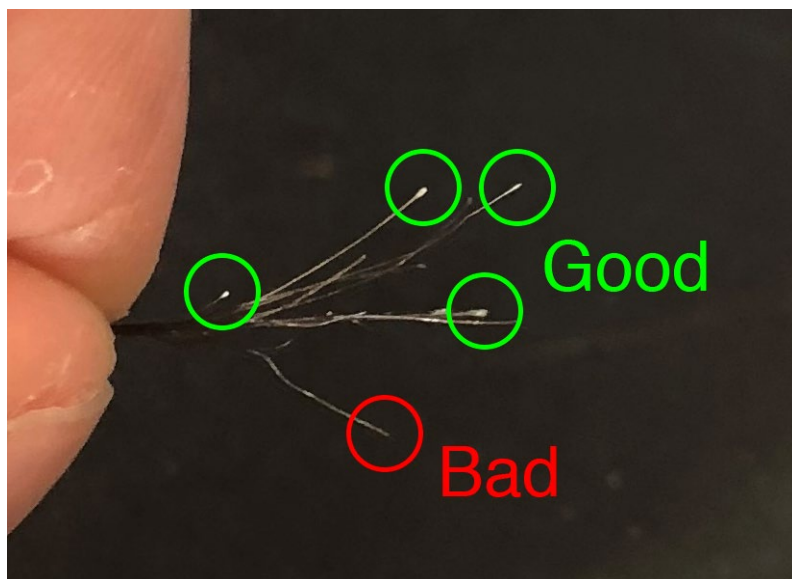
- 2mL cryovial tube
- Gloves
- Tweezers (optional)
- Scissors
- Small zip lock bag
- Participant ID labels (two labels per participant)
- -80C freezer

SET-UP:

- Label 2mL cryovial and zip lock bag.
- Clean tweezers/scissors with ethanol.
- Put on gloves

PROCEDURE:

1. Wearing gloves, pull a few hairs from the participant's **scalp** (using tweezers or your hand). For each hair, inspect the follicle side to ensure that there is tissue attached (see image). **10 hairs with follicle attached** are needed in total. Do not collect from a location if it causes excessive irritation or pain. We are not collecting hair from elsewhere on the body.
2. Place each hair, follicle side down, into a 2mL cryovial tube. For long hair, cut the extra hair strand with scissors approximately 1 inch from the hair follicle. Avoid touching the follicle.
3. Remaining hair strands should be placed into a labeled zip lock bag.
4. Freeze the cryovial at -80C within 5 minutes of collection. Record: collection date/time and -80C freeze time.
5. Hair strands stored in zip lock bags can be stored and transported at room temperature.
6. Wash or wipe scissors (and tweezers) with ethanol in between subjects.



TIPS AND TRICKS

- There are ~3 outcomes from pulling a hair: 1. a broken strand, 2. flakes of tissue attached to the end of the hair strand, or 3. a chunk of tissue which is very apparently an entire hair follicle. Outcome 2 is most often seen with fine hair. As long as tissue is attached (outcomes 2 or 3), it is acceptable. Broken strands (outcome 1) should be discarded and do not count towards the collection.

- Use tweezers or your hand to pull hairs, whichever method you find easier. For both strategies, wear gloves. Using a quality set of tweezers and pulling one hair at a time tends to be easiest.
- Some subject's follicles extract more easily from the top of their head, and for some the sides or back of the head is best. A good strategy is to establish a nice part in the hair for yourself, and if the follicle comes nicely with the hair, stay in that spot and collect 3-4 hairs. Repeat that process 3-4 times to collect the 10 hair follicles. (The only reason you move around the scalp is to prevent participant discomfort).
- When placing the hair follicles into the tube, stick them as far into the tube as possible (this will help prevent them from falling out as you add more hairs). Cover the opening of the tube with a gloved finger while collecting more hairs. For subjects with long hair, it tends to be easiest to add 3-4 hairs (they will be held in by your finger covering the opening and pressing on the strands), then cut the excess hair strands together, then proceed to collect more and repeat this process until 10 hair follicles are collected.
- Be careful when adding more hairs/uncovering the opening/closing the tube – the hair can and will come out of the tube. The follicles can stick to each other/etc.
- You may have to use different plucking strategies depending on the person. Often fine hairs come more easily if pulled slowly and close to the root so the hair strand does not break, and coarse hairs are more robust to any speed, but this can vary across individuals and the inverse can be true. Try multiple strategies if a collection is challenging.
- Be patient, be confident, and be thorough. It is pointless to subject someone to hair pulling if the follicle is not collected and if the minimum number is not collected because then the sample itself will be of lower quality and has a high chance of yielding zero data. It can be helpful to distract them with conversation, their phone, another exam relevant task, etc., especially if the collection is difficult.

7.10.1 Hair Collection Completion Form

The Hair Collection procedure is performed in conjunction with Biosample Collection. Completion of the Hair Collection should be documented on the Biosample Collection Form.

There are no exclusions for hair collection.

After the hair sample is collected, complete Q14 on the Biosamples Completion form.

Q14. Was hair collection completed?

If completed, mark "Yes" and then enter the number of follicles (1-10) collected and number of shafts (1-10) collected. Please also note the appropriate location of the hair collection. If hair is collected from multiple locations, choose the location where the most follicles and shafts were collected.

7.11 Nasal Brushing Sample Collection

Nasal brushing

We are performing a gentle nasal brushing of both nostrils in order to collect epithelial cells from inside the nose. This involves inserting a soft, short brush into the nose and twirling it, which feels tickly for the participant but should not cause any pain. The brush brushes off some epithelial cells from inside the nose, which we then collect in a cryovial. These cells from the nose are very similar to epithelial cells in the lung and react to insults (like cigarette smoking and ozone) in the same way as epithelial cells in the lung. This allows us to understand lung biology in an unprecedented way.

MATERIALS:

- -20C enzyme mini cooler FOR HOME VISITS ONLY
- 1 x 2mL cryovial tubes containing 700uL of RNALater solution
- Gloves
- Flocked nasal swab
- Larger cooler/container for transport FOR HOME VISITS ONLY

SET-UP:

- FOR HOME VISITS ONLY, store enzyme cooler in -20C for at least 24hrs before use. Store in -20C in between collections.
- Label 2mL cryovials.
- Place approximately 700 ul of RNALater in the cryovials, if not already done.

SAFETY:

- Nasal brushing must be done in full PPE as it can't be performed with the participant wearing a mask over the nose and mouth.
- The participant should wear a mask over the nose and mouth at all times except it should be lowered to uncover the nose during the brief procedure. Re-cover the nose after the procedure.
- We recommend doing the nasal brushing after spirometry in the spirometry room when you are still in full PPE.

PROCEDURE:

1. Complete the Spirometry and Nasal Brushing exclusion criteria questions on the Spirometry/Nasal Brushing questionnaire form. Do not perform the nasal brushing if the participant has an exclusion criteria. If they do not have any exclusion criteria, proceed.

Nasal brushing exclusions include:

- Systolic blood pressure >180 OR diastolic blood pressure >110 from Seated Blood Pressure.
- A cold or the flu that started in the past 4 weeks, or a positive COVID test in the past 4 weeks.
- Currently taking an anticoagulant such as warfarin, low molecular weight heparin, or newer oral direct-acting anticoagulants.
- Currently taking aspirin (any dose, including “baby aspirin”), clopidogrel or other anti-platelet medication in the past seven days.
- Recent nasal trauma or surgery.
- A history of severe nose bleeds.

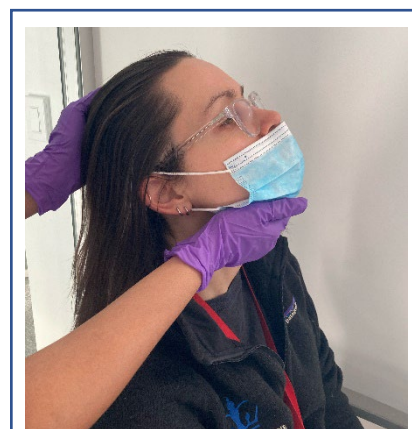
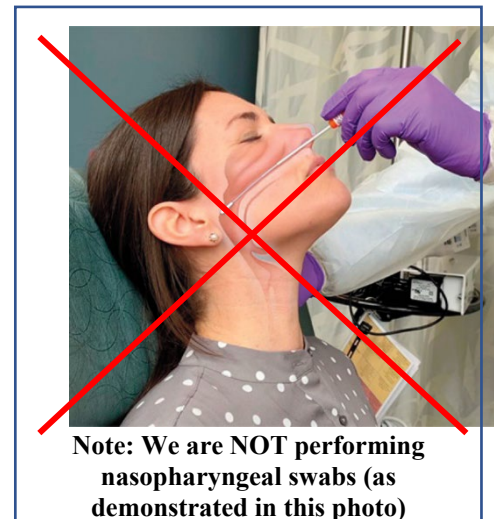
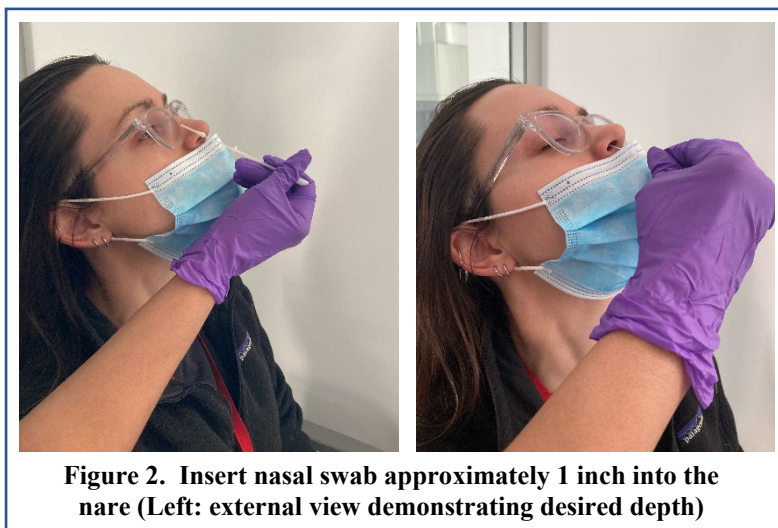


Figure 1. Lower participant's mask below the nose but covering the mouth. Tilt the participant's head back slightly.

2. Put on full PPE (N95 mask, gown, eye protection, gloves), if you have not already.
3. Participants should sit upright in a straight-backed chair.
4. Ask them to thoroughly blow their nose prior to the brushing in order to remove excess mucus (provide a tissue). Note that this can't be done with a mask over their nose.
5. Hold their head as shown and tilt it as far back as is comfortable for the participant.
6. Gently insert a new Flocked Swab approximately 1 inch into the right nare, parallel to the direction of the nose. It should go straight in with minimal resistance. If you encounter resistance, try a slightly different angle. If you can't get it in without encountering resistance, try the other nares.
7. Once inserted, rotate the flocked swab 270 to 360 degrees three consecutive times.
8. Repeat the process for the left nare using the same flocked swab.
9. Remove the flocked swab from the nose and placed it in a 2mL cryovial containing 700 ul of RNAlater. The participant should put their mask over their nose again.
10. Rigorously jiggle the swab up and down in the cryovial for 10 seconds and then scrape the edges of the swab on the vial to ensure collection of all available epithelium and infiltrating leukocytes.
11. Discard the flocked swab.
12. Place the cryovial containing the cells in the -80C on-site freezer, ideally within 5 minutes of collection. IF PERFORMING AT HOME, please the cryovial in -20C enzyme cooler for transportation to on-site freezer -80°C within a few hours. Do not allow sample to thaw. The cryovial must be stored long-term at -80°C.
13. Record the collection date/time and -80C freeze time.



CERTIFICATION:

1. Read the MOP
2. View the central training video (or attend the training)
3. Complete and video record nasal brushing for two 'participants' and submit for certification.

7.11.1 Nasal Swab Collection Completion Form

Please see section 7.9.15 for instructions on how to complete the Nasal Swab Collection portion of the Spirometry and Nasal Swab Collection Completion Form.

8 HOME MONITOR PROCEDURES

Procedures for at monitors are described in the following sections. All participant materials will be translated to Spanish and Chinese and posted on the MESA Exam 7 website.

8.1 ActiGraph Hip Activity Monitor

8.1.1 Overview of the MESA 24H-ACT Study

The MESA 24H-ACT Study, officially titled *Leveraging the 24-hour movement paradigm to preserve cognitive function and prevent Alzheimer's disease: The Multi-Ethnic Study of Atherosclerosis (MESA) 24H-ACT Study* is a four-year ancillary study funded by the National Institute on Aging (NIA; R01 AG071032). Study participants are recruited from the MESA Exam 7 cohort. This collaborative study includes Columbia University Irving Medical Center, University of Alabama at Birmingham, Johns Hopkins University, Northwestern University, University of California- Los Angeles, University of Minnesota, Wake Forest University, and additional consultants.

This Manual of Operations outlines the activity monitor (ActiGraph wGT3x-BT) protocol. **The 24-hour activity cycle components** will be assessed using “gold-standard” research-grade devices capable of quantifying these behaviors in a naturalistic setting for eight consecutive days. The ActiGraph wGT3X-BT will be used to detect waking behaviors and the GENEActiv will be used to determine sleep duration and quality (*see section 8.2 for details on the GENEActiv monitor protocol*). Participant recruitment, screening for eligibility, and instruction and distribution of the wearable devices, will occur during MESA Exam 7.

Participants will receive verbal or written instructions and a package that includes the initialized ActiGraph and an elastic belt or belt clip, detailed written wear instructions, a set of Frequently Asked Questions with responses, return checklist, magnet, Participant Diary, and contact information for study staff. Each day, in the daily **Participant Diary**, participants will indicate whether they wore their red activity monitor for the entire day today, and if not, why. Participants will also indicate 1) clock times corresponding to when they got into and out of bed and 2) whether they took a nap. If the participant took a nap, they should also indicate the clock times corresponding to when they initiated and ended a nap. See additional details in section 8.7. Two to three days after receiving the device, study staff will call to confirm device wear, address any questions, and trouble-shoot problems. Participants will return the devices and related materials to study staff using a pre-paid, self-addressed envelope (or small box, as needed).

Prior to the study visit, the ActiGraph device will be initialized by study staff using ActiLife6 software at the MESA Field Center. After the eight-day data collection period, the participant will mail the device and other materials back to the MESA Field Center using a pre-paid and addressed padded envelope. Study staff will download the raw data file from each device, using the ActiLife6 software. The GT3X file will be used to create a second reintegrated file (.agd) that will be used to derive summary estimates. Depending on the data processing method, an additional file may also be created (e.g., R ‘accelerometry’ program requires reintegrated files in CSV format). All data files will be archived via secure server maintained at the University of Washington with de-identified files sent to Columbia University for further processing.

It will take approximately 15-20 minutes (time spread over several days) to complete the activity monitor protocol (**Figure 1**), including:

1. Initialization of the activity monitor and preparation of supplemental materials that will be included in the data collection package. **Note.** The data collection package may also include sleep devices, heart monitor patches, and other relevant materials from the MESA mobile monitoring studies.
2. All participants will be called 2-3 days after the participant begins to wear the activity monitor to confirm wear, troubleshoot any issues, and remind participants to return the data collection package after 8 days of wear.
3. Receipt of returned data collection package, including downloading data file from activity monitor and transfer of activity monitor datafiles to the MESA Coordinating Center.

- The recovery protocol, consisting of reminder letter and telephone calls, is implemented when the data collection package and/or activity monitor is not returned within 2 days of the expected receipt date.






 <i>Initialize</i>									 	 <i>Download</i>
Prepare Package	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Recovery <i>as needed</i>	Receipt
24-Hour Activity Cycle Protocol										

Figure 3. Overview of the 24H-ACT Protocol.

8.1.2 Study Leadership Contact Information

PRINCIPAL INVESTIGATOR(S)

[Priya Palta, PhD, MHS](#)
[Columbia University](#)
[Email: pp2464@cumc.columbia.edu](mailto:pp2464@cumc.columbia.edu)

[Keith Diaz, PhD](#)
[Columbia University](#)
[Email: kd2442@cumc.columbia.edu](mailto:kd2442@cumc.columbia.edu)

Kelley Pettee Gabriel, PhD, MS
 The University of Alabama at Birmingham
 Email: gabrielk@uab.edu

PROJECT COORDINATOR

Margaret Murdock, MS; Columbia University
 Email: mem2356@cumc.columbia.edu

OTHER RESEARCH PERSONNEL

Erin Dooley, PhD
 Researcher V; The University of Alabama at Birmingham
 Email: edooley@uab.edu

Pablo Martinez-Amezcuca, PhD
 Postdoctoral Research Scientist; Columbia University
 Email: pm3151@cumc.columbia.edu

INVESTIGATORS

[Columbia University](#)
 Steve Shea, MD [Field Center PI]
 Jose A. Luchsinger, MD
 Joseph Schwartz, PhD, MA

[Northwestern University](#)
 Norrina Allen, PhD [Field Center PI]

University of Minnesota

James Pankow, PhD [Field Center PI]

UCLA

Karol Watson, MD [Field Center PI]

Johns Hopkins University

Seth Martin, MD [Field Center PI]

Wendy Post, MD

Wake Forest University

Alain Bertoni, MD [Field Center PI]

Timothy Hughes, PhD

Kathleen Hayden, PhD

Samuel Lockhart, PhD

University of Washington

Robin McClelland, PhD [Data Coordinating Center PI]

Consultants

Susan Redline, MD, MPH

Harvard Medical School; Brigham and Women's Hospital

8.1.3 Summary of MESA 24H-ACT Study

Alzheimer's Disease and Related Dementias (ADRD) is an emerging epidemic in the United States; Black adults are particularly vulnerable. Without effective prevention strategies to target and optimize resilience to ADRD, 14 million U.S. adults will be living with ADRD by 2060, with an associated financial burden of \$511 billion by 2040. While physical activity has been consistently identified as a modifiable, protective factor to prevent cognitive decline and delay age of dementia onset, the majority of this evidence is based on reported estimates of leisure-time moderate to vigorous intensity physical activity (MVPA), which provides an incomplete characterization of this complex behavioral phenotype. Adults spend approximately 95% of waking hours sedentary or in light intensity physical activity; however, there is limited research exploring the interrelations of these different intensity categories. Further, less than 10% of adults accumulate sufficient MVPA to meet recommendations, and this prevalence estimate is even lower in Black adults. Studies have also demonstrated that sleep disturbances, including short sleep duration, circadian rhythm disturbances, and sleep-disordered breathing may increase risk of cognitive impairment. However, this evidence is still emerging. Further, Black adults have a higher prevalence of disordered sleep compared to Whites. Despite the potential importance of both waking and sleep behaviors to optimize cognitive resilience, their impacts are often studied in isolation. To address these critical research gaps, we propose the MESA 24-Hour Activity Cycle Study (MESA 24H-ACT Study), a four-year ancillary study to the funded MESA Exam 7. The overall goal of the MESA 24H-ACT Study is to quantify 24-hour activity cycle behaviors and estimate the independent and joint roles of waking (sedentary to vigorous intensity physical activity) and sleep (duration and quality characteristics) behaviors to optimize cognitive resilience. All participants attending MESA Exam 7 and who are willing to concurrently wear an accelerometer and sleep actigraphy watch for eight consecutive days will be invited to participate. Exclusion criteria include: unable to ambulate or physician instruction not to be physically active. The MESA 24H-ACT study measures include: (1) accelerometry and (2) sleep actigraphy, which complement extant MESA data, and data that will be collected as part of Exam 7. To accomplish these goals, we propose to examine the independent and joint associations of 24-hour activity cycle behaviors with: (**Aim 1**) cognitive functioning; (**Aim 2**) subclinical markers of cerebrovascular disease (e.g., white matter hyperintensity volumes), white matter microstructural integrity, and neurodegeneration (e.g., hippocampal and total brain volumes) quantified from brain magnetic resonance imaging (MRI); and (**Aim 3**) the prevalence of mild cognitive impairment (MCI) and

dementia. Potential moderation by sex, age epoch (<65 versus ≥65 years), education/literacy, and APOE ε4 genotype will also be evaluated. The MESA 24H-ACT Study will provide novel information on the role of 24-hour activity cycles in promoting cognitive resilience in Black adults.

Specific Aims and Hypotheses:

Specific Aim 1. Using MESA 24H-ACT device-based measures of physical activity/sleep and a state-of-the-art compositional data analysis approach, we will examine the associations of the 24-hour movement cycle with (a) cognitive performance; (b) cerebrovascular disease, neurodegeneration; (c) Aβ burden; (d) plasma biomarkers of amyloid, tau, and NFL; and (e) prevalence of MCI and dementia.

Specific Aim 2. We will use self-reported physical activity and sleep measures collected in Exam 5 (2010-2013), calibrated to device-based measures to correct for measurement error, to quantify the 24-hour movement cycle and determine its associations with (a) 12-year change in global cognition and (b) 2-year change in cerebrovascular disease and neurodegeneration via compositional data analysis.

Aims 1 and 2 Hypotheses: We hypothesize that there will be cross-sectional and longitudinal associations between the 24-hour activity cycle composition and cognitive outcomes, and these relations will be stronger for the 24-hour composition than for any of the four 24-hour behaviors considered in isolation. The 24-hour movement paradigm will partially mediate the associations between race/ethnicity and cognitive outcomes.

Specific Aim 3. The association between the 24-hour movement cycle and cognitive function is likely bidirectional wherein poor physical activity and sleep could be a consequence of or a precursor to impaired cognitive function. To elucidate their interrelationship, we will examine the bidirectional relationship between cognitive function and 24-hour activity cycles over 12 years. Hypothesis: In comparing the relative strengths of the cross-lagged effects, we hypothesize the existence of associations in both directions.

8.1.4 Wearable Devices

ActiGraph wGT3X-BT (ActiGraph Corp; Pensacola, FL) is a small (4.6 cm x 3.3 cm x 1.5 cm; 19 grams), tri-axial piezoelectric accelerometer worn on an elastic belt around the waist or with a belt clip. The ActiGraph accelerometer has been extensively validated in laboratory and free-living conditions.

Raw tri-axial data will be sampled at 40 Hz. After eight days of wear, data will be downloaded and re-integrated to 15 second epochs using ActiLife software and analyzed using established algorithms, including the Troiano wear time algorithm¹ and Freedson², Matthews³ and NHANES¹ count cut-point thresholds. Primary summary estimates include: total and average accelerometer counts, time (min·d⁻¹) spent sedentary and in light-, moderate-, and vigorous-intensity physical activity. Secondary estimates, include (and are not limited to): steps (count·d⁻¹), inactive to active transitions (count·d⁻¹) and sedentary and MVPA in bouts (bouts·d⁻¹ and min·d⁻¹).



Figure 4. ActiGraph wGT3X-BT

Equipment and Supplies

The MESA 24H-ACT Study will provide the following to each MESA Field Center:

ActiGraph wGT3X-BT

- ✓ 30 wGT3X-BT accelerometers (i.e., activity monitors)
- ✓ 360 black adjustable elastic belts with plastic closures or belt clips
- ✓ 1, 7-port USB charging hubs
- ✓ 7 USB cables
- ✓ ActiGraph software license

The MESA Field Center will need to purchase the following:

- ✓ Paper supplies to print data collection package materials, written instructions with contact information, set of frequently asked questions with responses, participant diary, and a checklist to assist with returning the wearable devices and other materials
- ✓ Padded envelope or small box for return of wearable devices and other materials after the 8-day data collection period
- ✓ Mailing labels
- ✓ Postage
- ✓ Alcohol wipe for cleaning the wearable devices after each use

The Coordinating Center has the product key code to download and install the Full license, and each Field Center has a product key to download the Lite license of ActiLife6 software from the ActiGraph website: (<https://www.theactigraph.com/support/downloads/>). The Full license allows for initialization, download, data reduction and processing; the Lite license allows for initialization and download, only. Both the Coordinating Center and Field Centers should also download copies of the ActiLife 6 and wGT3X-BT manuals from the ActiGraph website: (<https://www.theactigraph.com/support/downloads/>).

8.1.5 Quick Links

Below are links to the ActiGraph Corp website, including direct links to respective device and software user guides. A paper copy of the user guides should also be kept at the MESA Field Center.

ActiGraph	https://actigraphcorp.com/
ActiGraph wGT3X-BT User Guide	https://s3.amazonaws.com/actigraphcorp.com/wp-content/uploads/2020/03/05155605/ActiGraph_wGT3X-BT_UserGuide_E.200.6003_Revision5_FINAL.pdf
ActiGraph Support	Online: https://actigraphcorp.force.com/support/s/contactsupport Telephone: (877) 497-6996

8.1.6 Labeling and Charging Activity Monitors for Field Data Collection

Research staff will prepare and regularly update an excel spreadsheet that links the ActiGraph issued serial number with a 3-digit study-issued unique monitor identification number. This 3-digit study-issued monitor ID is used to track the activity monitors in the field. This spreadsheet should be regularly updated to indicate activity monitors that were never returned after field data collection. The ActiGraph (red monitor) will be labeled as **Y-XXX** where **Y** is the Field Center Indicator (W=Wake Forest; U=UCLA; C=Columbia; N=Northwestern, J=Johns Hopkins; M=Minnesota). This spreadsheet should be regularly updated to indicate devices that were never returned after field data collection.

Contact Name	555-555-5555
Device	###

Figure 3. Device Label.

The MESA 24H-Act study team will inventory and label each of the ActiGraph devices. The labels will be attached to the backside of the activity monitor and includes: 1) name and 2) phone number of the primary study staff contact for this ancillary study (**Figure 3**). The label will also include the study-issue monitor ID number (see above). Once the label is affixed, scotch tape or a clear material will be placed over the label for protection. The devices should be inventoried and checked against the excel spreadsheet when received by the MESA Field Center.

Software Installation

Install the ActiLife6 Data Analysis Software (Figure 4).

With product keys corresponding to the **Full Activation**, study staff are able to initialize devices, download data, view/open data files, and analyze data.

With product keys corresponding to the **Lite Activation**, study staff are able to initialize devices and download data, only.



Figure 4. ActiLife 6 Software.

Charging Device Batteries

To charge the activity monitors, connect the device to the USB hub using cables and connect the hub to a powered-on computer or electrical outlet. charge all activity monitors ($\geq 98\%$) prior to distribution for field data (Figure 5). Charging a monitor takes roughly 3-4 hours.



the USB Fully collection

Figure 5. Charging ActiGraph device.

8.1.7 Recruitment and Eligibility Criteria for the Activity Monitor Component

MESA participants attending MESA Exam 7 will be recruited to participate in the MESA 24H-ACT Study. All participants will receive the information sheet (see **APPENDIX A**). If interested, eligibility criteria will be assessed, which include:

Inclusion Criteria

1. Participants attending MESA Exam 7.
2. Willing to complete the proposed ancillary study measures, including willing to wear the ActiGraph accelerometer for determination of physical activity for eight consecutive days.

Exclusion Criteria

1. Unable to ambulate (i.e., wheelchair user); and
2. Physician instruction not to be physically active.

8.1.8 ActiGraph wGT3X-BT Initialization Process

The initialization process prepares the ActiGraph for field data collection. The ActiGraph should be initialized, using the steps outlined below, prior to distributing to study participants.

1. Open the ActiLife 6 software
2. Connect the ActiGraph to the computer using a USB cable. The ActiGraph issued serial number will appear under the **DEVICES** tab (Figure 6).

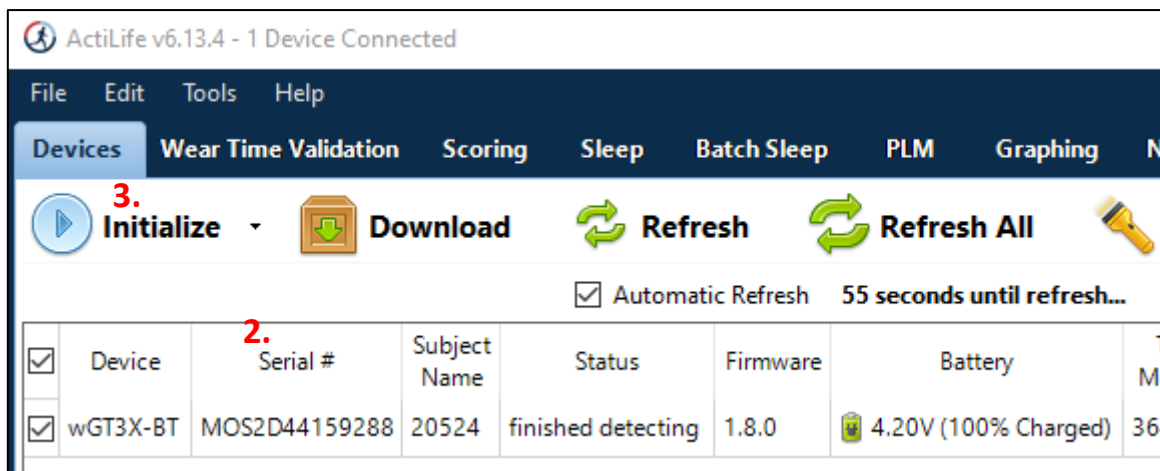


Figure 6: DEVICES tab with activity monitor connected to ActiLife Software.

3. Select **INITIALIZE** drop-down menu (Figure 6) and select **REGULAR INITIALIZATION**.
4. A dialog box (new window) will open to display the **INITIALIZATION PARAMETERS**, including 1) start and stop times, 2) device time, 3) sample rate, 4) LED Options, 5) wireless options, and 6) recording options (Figure 7).

INITIALIZATION PARAMETER #1: Start and Stop Times

5. **START DATE:** Enter the date corresponding to when the participant receives the device and take-home package (i.e., during clinic or home exam). If a mailed distribution protocol is implemented, the expected delivery date is 2-3 days after the package leaves the Field Center.
6. **START TIME:** Enter 12:00 am
7. Uncheck the **USE STOP TIME** box. No information should be included in the **STOP DATE** or **STOP TIME** fields.

INITIALIZATION PARAMETER #2: Device Time

8. Select **ATOMIC TIME**.

INITIALIZATION PARAMETER #3: Sample Rate

9. Select **40 Hertz**.

INITIALIZATION PARAMETER #4: LED Options

10. Uncheck 1) **DELAY MODE LED** and 2) **DATA COLLECTION LED**. The default is for the **WIRELESS LED** box to be unchecked.

INITIALIZATION PARAMETER #5: Wireless Options

11. Uncheck **ENABLE WIRELESS** box. The default is for the **HEART RATE** box to be unchecked.

INITIALIZATION PARAMETER #6: Recording Options

12. Select **ENABLED** for **IDLE SLEEP MODE**, which is the default option
13. Complete the initialization parameters form and select **ENTER SUBJECT INFO**.

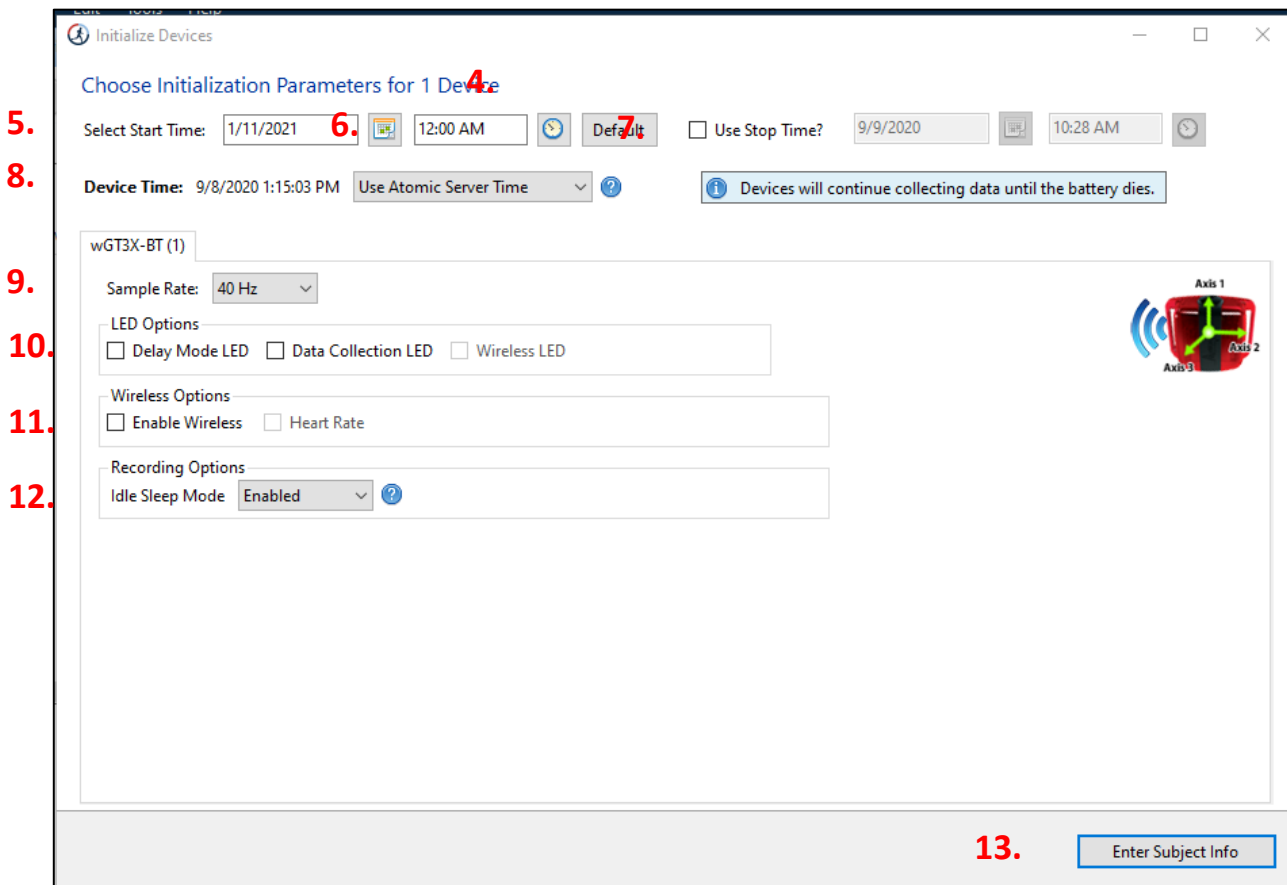


Figure 7: Initialization parameters for the MESA 24H-ACT Study.

14. The ActiGraph issued serial number for the device will appear in Column 1. In Column 2 (**SUBJECT NAME**) enter the participant’s MESA Study ID; **do not enter the participant’s name**.
Do not enter information in any other columns, including **GENDER, HEIGHT, WEIGHT, DOB, RACE, LIMB, SIDE, or DOMINANCE (Figure 8)**.
15. Click the **INITIALIZE 1 DEVICE** button. A progress bar will indicate when the initialization process is completed (**Figure 8**).

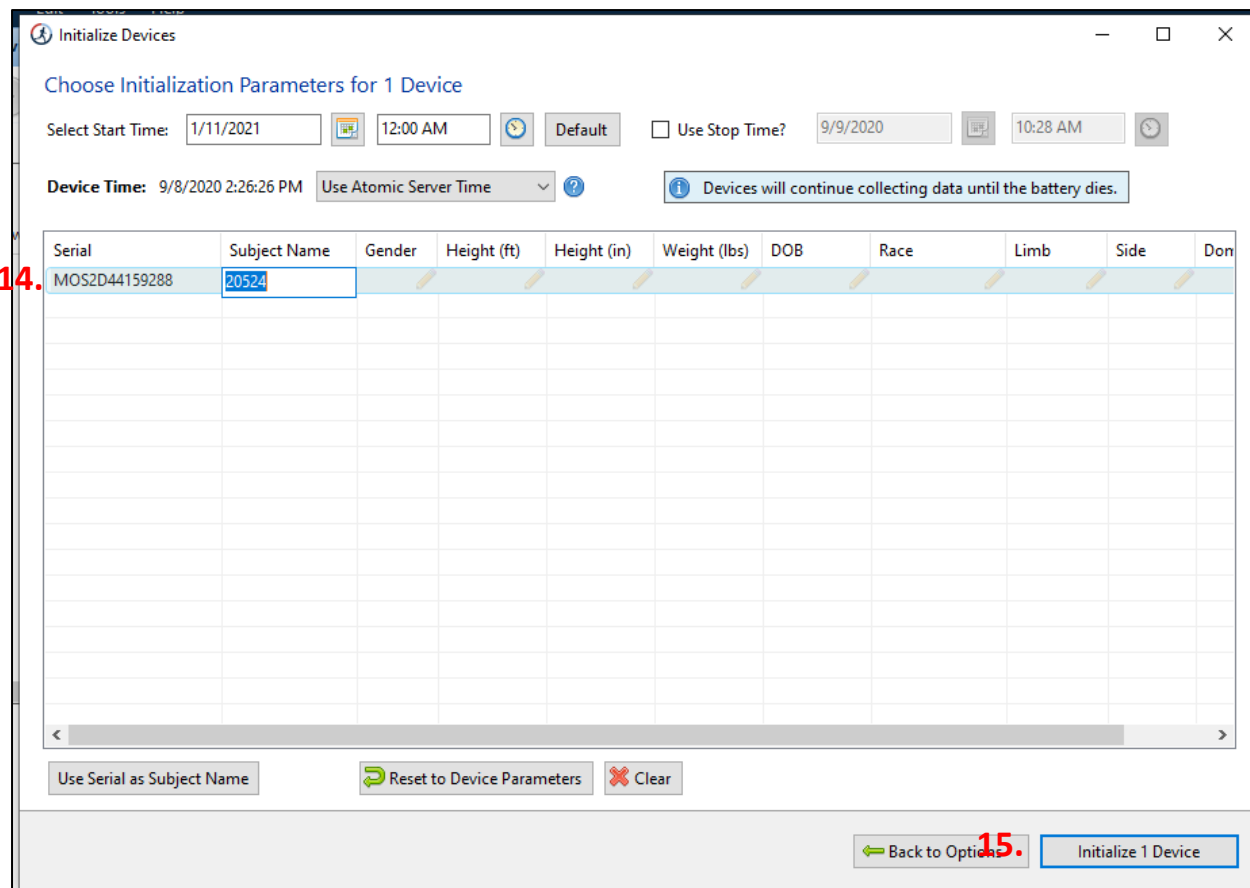


Figure 8: Initializing the device; entering the MESA Study Participant ID.

- Before removing the ActiGraph from the USB cable, connected to the computer, confirm that the **PARTICIPANT ID** (see **SUBJECT NAME**) and Initialization parameters #1-6 are correct. Finally, confirm that battery life is $\geq 98\%$ (Figure 9).

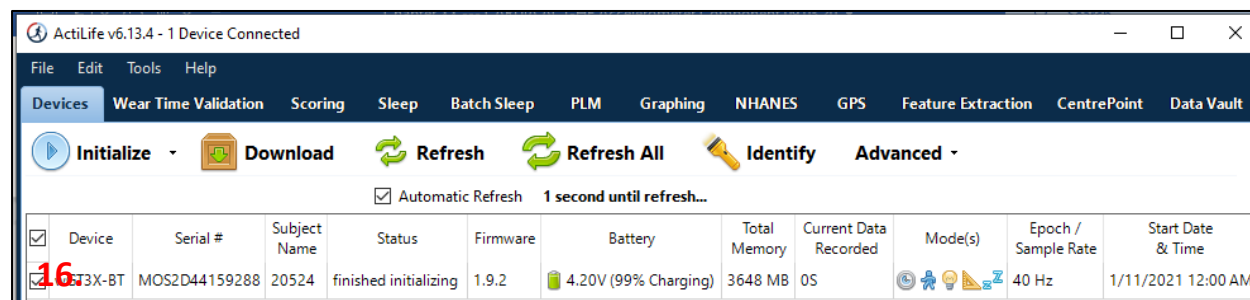


Figure 9: Initializing the device and confirmation of parameters.

- Remove the ActiGraph from the USB Cable. Using the red plastic triangle (or a dime), close the USB cover on the monitor and attach it to the elastic belt or belt clip.
- The ActiGraph will begin collecting data when the selected start day and time elapses. The device will continue to collect data until the device is downloaded and reinitialized, or the battery is depleted.

8.1.9 ActiGraph wGT3X-BT Download Process

The download process extracts data from the activity monitor to an individual-level data file for batch processing. Data is downloaded at the Field Center and the downloaded (.gt3x) file is sent to the Coordinating Center for batch transfer to Dr. Keith Diaz at Columbia University Irving Medical Center.

- Open the ActiLife software.
- Connect the activity monitor to the computer using a USB cable. The ActiGraph issued serial number will appear under the **DEVICES** tab (Figure 10).

- Verify the box in front of the device is checked and select **DOWNLOAD** from the taskbar menu (Figure 10).

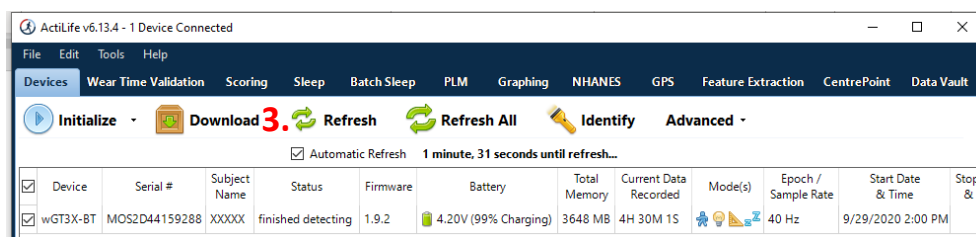


Figure 10. ActiGraph download.

- A dialog box (new window) will open to display the download options, including: 1) file download location, 2) download naming convention, 3) download options [create clinical report, create AGD file (epoch, # of axis, steps, lux, inclinometer, low frequency extension), and 4) biometric and user information (Figure 11).

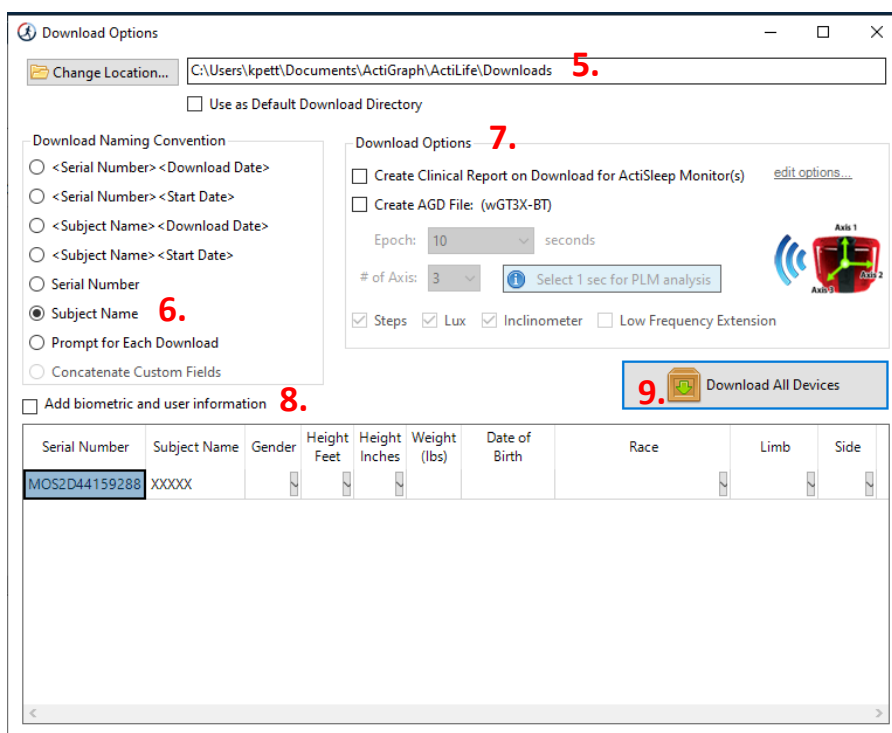


Figure 11. Downloading options.

- For **DOWNLOAD NAMING CONVENTION**, select **SUBJECT NAME**, which will correspond to the Participant ID.
- For **DOWNLOAD OPTIONS**, uncheck the box **CREATE CLINICAL REPORT ON DOWNLOAD FOR ACTISLEEP MONITORS**. Uncheck the box **CREATE AGD FILE**, and there is no need to change **EPOCH**, **# OF AXIS**, or **STEPS**. Uncheck the **LUX** and **INCLINOMETER** boxes. Uncheck the **LOW FREQUENCY EXTENSION** box.
- Uncheck the **ADD BIOMETRIC AND USER INFORMATION** box.
- Click the **DOWNLOAD ALL DEVICES** button. The dialog box will close, and a progress bar will appear under the **STATUS** column in the grid.
- When the download is complete, a **FINISHED DOWNLOADING** link will appear (Figure 12).

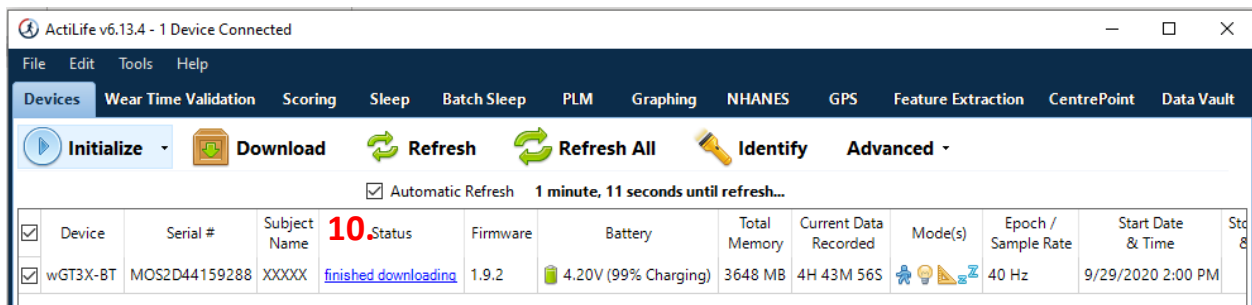


Figure 12. Downloading status.

- Go to the computer directory where the downloaded raw (.gt3x) files are saved and confirm the downloaded file is included.

8.1.10 Preparing the Data Collection Package

The **DATA COLLECTION PACKAGE**, including the initialized ActiGraph, is prepared by study staff prior to distribution. Study staff also complete Question 1 on the **Hip Activity Monitor Completion Form (APPENDIX C)**. The written materials that are included in the **DATA COLLECTION PACKAGE** are included in **APPENDIX B**.

Data Collection Package Materials and Supplies

- Fully charged and initialized ActiGraph monitor on an elastic belt or belt clip
- Written materials (see **APPENDIX B**)
 - ✓ Participant Instructions
 - ✓ Frequently Asked Questions
 - ✓ Return Checklist
 - ✓ Magnet
 - ✓ Participant Diary
- Pre-paid and addressed shipping envelope
 - ✓ Small shipping box or 8.5” x 11” padded envelope
 - ✓ Adhesive mailing labels

8.1.11 Activity Monitor Overview

Participants that meet the MESA 24H-ACT Study eligibility criteria (see **Section 8.1.7**) will be recruited for this ancillary study during the in-person component of MESA Exam 7.

The following **SCRIPT** is used by the ancillary study staff to provide MESA Exam 7 participants with an overview of the MESA 24H-ACT Study.

SCRIPT. One of the new procedures that we are offering for Exam 7 is a small monitor that you wear on your hip at home for 8 days. The purpose of this study is to help us understand how physical activity, sedentary behavior, and sleep affect brain health.

Would you like to hear more about the hip monitor?

If no, <<No problem! Thank you for your time>>.

If yes, <<Great, let me share some additional information with you. Please feel free to stop me at any time if you have questions>>.

If you decide to participate, you will be asked to wear a small device; a red activity monitor that measures physical activity and sedentary behavior (during waking hours, only) <<show participant the ActiGraph Device>> for eight straight days. It's very small device that you will wear on your hip; attached to an elastic belt or belt clip. It's very similar to a pedometer, that you might have worn or seen at the store. This monitor is what is used in research studies to collect information on how a person spends their day being active and sitting still.

During these eight days, you will also be asked to check off that you wore your red activity monitor for the entire day, each day <<show participant the MESA Participant Diary>>. You will also indicate the clock times corresponding to when you got into and out of bed. If you took any naps that day, you will fill in the times when you started and ended the nap. You will wear the red activity monitor on your hip just above your right hip bone, during the entire time that you are awake. It is very important that you wear the red activity monitor throughout the entire day. The red activity monitor cannot get wet for long periods of time, so we will ask you to take it off during showers, baths, or during other water-based activities, like swimming.

After you've been wearing the device for 2-3 days, our study staff will call you to ask if you are wearing the device and answer any questions that you may have about the device, or the study. After the 8 days are over, you will send us back the device in an envelope that already includes postage and our study address. We are not asking you to change your normal physical activity while you are wearing the device.

Do you have any questions? <<respond to all participant questions>>.

Is this something that you think you might want to participate in?

If no, <<No problem! Thank you for your time>>.

If yes, <<Great, our next step is to get you scheduled for a return visit.>>

8.1.12 Activity Monitor Overview and Participant Instruction

The following **SCRIPT** is used to provide participants with an overview of the ActiGraph device and data collection protocol, including instructions for wear and return of study materials.

SCRIPT: Hello, my name is <<insert your name, here>> and I am with the **MESA Study**.

Thank you for agreeing to be a part of our study. I'd like to take a few minutes of your time to tell you more about the device that you will wear today and for the next eight days.

This is the ActiGraph or the red activity monitor <<show participant the ActiGraph Device>>. It's a very small instrument that you will wear on your hip; attached to an elastic belt or belt clip. It's very similar to a pedometer, that you might have worn as part of MESA or have seen at the store. This monitor is what is used in research studies to collect information on how one spends their day being active and sitting still.

For this study, we are not asking you to change your normal physical activity; rather we'd like for you to go about your normal daily routine while you are wearing this device.

It is very important that you wear the red activity monitor during the entire time when you are awake. We will ask you to check off that you wore your red activity monitor for the entire day, each day, including if you nap. <<show participant the MESA Participant Diary>>. You will also indicate the clock times corresponding to when you got into and out of bed. If you took any naps that day, you will fill in the times when you started and ended the nap. You will wear the red activity monitor on your hip, during the entire time that you are awake. It is very important that you wear the red activity monitor throughout the entire day. The red activity monitor cannot get wet for long periods of time, so we will ask you to take it off during showers, baths, or during other water-based activities, like swimming.

Now, I will show you how to wear the device properly. Let's start with the red activity monitor <<show participant the ActiGraph Device>>. Please note that there is a little screw top or knob on one side of the red activity monitor <<show participant the knob on ActiGraph device >>, this knob should be facing up (towards

the sky) while you are wearing the red activity monitor <<show participant the ActiGraph device with the knob facing up>>.

If you are wearing pants with belt loops, feel free to use the elastic belt as your belt. Or you can place the elastic belt with the red activity monitor so that it fits comfortably on your waist just above the right hip bone. <<Let the participant know that they can either place the elastic belt on their waist either on top of- or underneath- a dress or skirt>>. The elastic belt is adjustable <<show participant how to adjust the elastic belt>> and you can tuck in the straps if there is excess material <<show participant how to tuck in straps >>. We ask that you please not cut the elastic belt straps. For the belt clip, clip to the waistband just above the right hip bone.

You do not need to turn the red activity monitor on, it is on now and ready to collect information. Also, you may notice a green blinking light, please disregard it. Please wear the red activity monitor during all times that you are awake; from the time you get up until the time you go to sleep. Please wear it if you nap during the day.

Do you have any questions about the red activity monitor <<answer any questions>>?

Now, I'm going to ask you to put on the device <<watch the participant put on the device and troubleshoot placement, as necessary>>. We'd like for you to start wearing the device today and continue to wear it for the next eight days. As a reminder, you will wear this red activity monitor the entire time that you are awake. The device can not tell us where you are in the community.

In 2-3 days, we will telephone you to check if you have any questions for us. In this package, we are also providing an instruction sheet <<show participant instructions >> and a sheet that goes over common questions and answers <<show frequently asked questions >> to review when you get home. Otherwise, feel free to call us << show participant the contact information included on the participant instructions >>.

After you've worn the device for eight days, you will complete the **Return Checklist** <<show participant the return checklist >>. It will remind you what needs to be returned to us. Please use this envelope to return the device and other materials to us <<show participant the return envelope >>. This envelope has our address on it, and the postage is already paid for. All you need to do is drop it in the mail, or your local U.S. Post Office. You will return the device, the elastic belt or belt clip and the Return Checklist. That's it! You can either keep or throw away the other materials we gave you.

Do you have any questions? <<answer any questions>>.

8.1.13 2-3 Day Check-in Telephone Call

The following **SCRIPT** is used to confirm wear, answer questions, and troubleshoot issues during data collection in the field. This call should be completed 2-3 days after distribution of the device and take-home package. If the participant is also wearing the wrist actigraphy monitor or Stress heart monitor patch, inquire about all monitors during this call (see section 8.2.5.7 for wrist actigraphy and 8.4.13 for heart monitor patch reminder call details).

Script. Hello, my name is <<insert your name, here>> and I am with the **MESA Study**. Thank you for participating in this study. I'm calling today to check how you are doing with wearing the device(s).

1. Have you been wearing the red activity monitor?

<< if yes >> Great! <<move to next question>>

<< if no >> Do you think you can start wearing the red activity monitor today, and continue wearing it for the next eight days?

<< if yes>> Great, we really appreciate your willingness to do so. <<move to next question>>

<< if no>> That's OK. Please send us the red activity monitor, as soon as possible, using the envelope we provided at your visit. Do you still have the return envelope we gave you?

<< if yes>> Great, please send us the red activity monitor using that envelope, as soon as possible. We would like to use the red activity monitor again for another participant. Thank you for your time <<end call>>.

<< if no>> That's OK, we will send you another envelope. Please use that envelope to send us the red activity monitor, as soon as possible. We would like to use the red activity monitor again for another participant. Thank you for your time <<end call>>.

2. Do you have any questions about the red activity monitor?

<< if no>> Great, after you've finished wearing the red activity monitor for eight full days, please remember to return it with the **Return Checklist** using the envelope we provided at your visit. Thank you for your time <<end call>>.

<< if yes, answer any questions and troubleshoot any issues>> After you've finished wearing the red activity monitor for eight full days, please remember to return it with the **Return Checklist** using the envelope we provided at your visit. Thank you for your time <<end call>>.

8.1.14 Completing the Hip and Wrist Activity Monitor Completion Form

Purpose. The **Hip and Wrist Activity Monitor Completion Form** is completed for every MESA participant who consents to the procedures. The information recorded allows for the tracking of the device in the field and returned to the Exam Center after the data collection period. It also collects reasons for monitors that are not deployed.

Record the participant ID, visit date, and initials of staff/staff ID of person completing this form.

Hip Activity Monitor Section

Q1. Indicate if the study participant received the red activity monitor by checking the yes or no box.

If **NO**:

Q1a. Indicate the reason why a participant did not receive a device. Response options include: participant refusal, unable to ambulate, physician instruction not to be physically active, red activity monitor not available, or other. If other, specify the reason.

If **YES**:

Q1b. Record the date the red activity monitor was distributed. In most cases this will be the exam date.

Q1c. Record the MESA 24H-ACT Study ActiGraph number for the device that was distributed to the participant.

Q1d. Indicate if the red activity monitor that was distributed was fully charged (or $\geq 98\%$) by checking the yes or no box. **Note:** Per protocol, all distributed devices should be fully charged prior to field data collection.

Q1e. Record the date that the red activity monitor was initialized to start data collection. **Note:** Per protocol, all red activity monitors should be initialized to start data collection on the day of the exam at 12am. This means that the initialization process must be completed before this day and time.

Q1f. Indicate if the red activity monitor was initialized to start at 12am on the day of the in-person exam by checking the yes or no box. **Note:** Per protocol, all red activity monitors should be initialized to start data collection on the day of the exam at 12am. This means that the initialization process must be completed before this day and time.

Q1g. Record the anticipated date of the 2-3 day check-in call. **Note:** This should be 2 to 3 days following the exam date.

Q1h. Record the anticipated end date of the 8-day data collection period. **Note:** This should be 7 to 8 days following the exam date.

Q1i. Record the anticipated red activity monitor receipt date following the data collection period. **Note:** This should be 2 to 3 days following the anticipated end date (see **Q1h**).

Q2. Indicate if the participant returned the red activity monitor after the data collection period by checking the no or yes box.

If **NO**:

Q2a. Indicate the reason why the red activity monitor was not returned. Response options include: lost by participant, lost by postal service, or other. If other, specify the reason.

If **YES**:

Q2b. Record the date that the red activity monitor was received by the Exam Center.

Q2c. Indicate if the data were downloaded by checking yes or no. **Note:** Per protocol, data should be downloaded as soon as the red activity monitor is received by the Exam Center. Data will stay on the device until it is reinitialized.

If **NO**: Indicate the reason why data were not downloaded. Response options include: download error, monitor damaged, staff error, or other. If other, specify the reason.

Q2d. Record the date that the red activity monitor data were downloaded.

The **Wrist Actigraph Device** section of the completion form is described in section 8.2.14

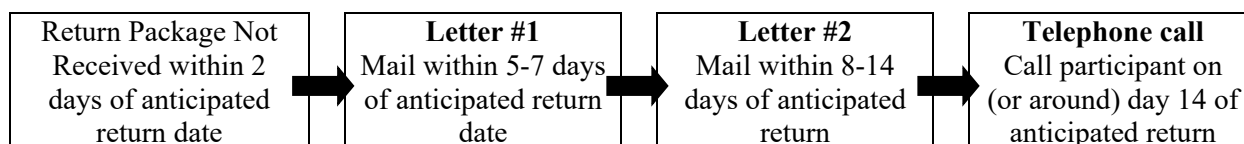
8.1.15 Recovery Protocol

Purpose. After the 8-day data collection period, participants will return the:

- ActiGraph (red activity monitor)*
- Black elastic belt or belt clip*
- Return Checklist

*Key data collection elements

The expected receipt of the return packages is 2 to 3 days following the expected data collection end date. Upon receipt, the remaining items from the **Hip and Wrist Activity Monitor Completion Form** should be completed. If the return package is not received when expected, the red activity monitor recovery protocol should be implemented.



Reminder Letter #1

Dear Participant,

Thank you for taking part in the **MESA Exam 7**. At your visit, you were asked to wear a red activity monitor on your waist for eight days. If you are not already wearing the red activity monitor, please begin wearing it as soon as possible. The monitor can only record activity for 2 weeks. After you have worn the red activity monitor for 8 days in a row, please use the padded and addressed envelope we gave you at your visit to mail the red activity monitor with black elastic belt or belt clip and the return checklist to us. If you have any questions about the red activity monitor or the study, please call **[name] at [phone number]**.

Thank you again for your time and efforts. Do not hesitate to call us if you have any questions or would like more information.

Sincerely,

[name]

Reminder Letter #2

Dear Participant,

Thank you for taking part in **MESA Exam 7**. At your visit, you were asked to wear a red activity monitor on your waist for eight days. After you have worn the red activity monitor for 8 days in a row, was asked you to return the monitor and the return checklist to us using the padded and addressed envelope we gave you at your visit.

We have not yet received this package. Because this red activity monitor is time sensitive, we ask that you return your monitor as soon as possible using the envelope you were given at your visit. If you have misplaced the return envelope, please contact **[name] at [phone number]** for a new one. It is ok if you were unable to wear the red activity monitor during the time you had it. Please return it for someone else to use.

Thank you again for your time and efforts. Do not hesitate to call us if you have any questions or would like more information.

Sincerely,
[name]

Reminder Telephone Call

When conducting this call, complete Question 2 on the **Hip and Wrist Activity Monitor Completion Form**.

Script. Hello, my name is <<insert your name, here>> and I am with the **MESA Study**.

Thank you for agreeing to be a part of this study. At your visit, we asked that you wear a red activity monitor for eight days and return it back to us after the eight days are over.

Do you still have the red activity monitor?

<< if yes >> Do you still have the return envelope we gave you?

<< if yes >> Great, please send us the red activity monitor using that envelope, as soon as possible. We would like to use the red activity monitor again for another participant. Thank you for your time <<end call>>.

<< if no >> That's OK, we will send you another envelope. Once received, please use that envelope to send us the red activity monitor back, as soon as possible. We would like to use the red activity monitor again for another participant. Thank you for your time <<end call>>.

<< if no >> OK, let me get some more information. << Complete Question 2 on the **Hip and Wrist Activity Monitor Completion Form**>> Thank you for your time <<end call>>.

8.1.16 Appendix A: Recruitment Materials

What is the MESA 24-hour Activity Cycle (MESA 24H-ACT) Study?

The MESA 24H-ACT Study is an ancillary study of the Multi-Ethnic Study of Atherosclerosis. This research study wants to learn about how movement during the day and sleep at night affects brain health. The MESA 24H-ACT Study is funded by the National Institute on Aging.

What do I have to do?

If you participate, you will wear a small red activity monitor on your waist for 8 straight days.

- ✓ The **red activity monitor** gathers information about when you are active or still. You will wear this on your waist just above your right hip bone during the entire time that you are awake. It cannot tell us where you are in the community.



Return the red activity monitor to us in the pre-paid and addressed envelope that is provided to you at your visit.

We are not asking you to change what you normally do.

What will I get out of participating in the MESA 24H-ACT Study?

You will be given \$50.00 if you wear the red activity monitor for 8 straight days. You will receive this compensation after the red activity monitor is returned to us. We will also send you a brief report about how much you move.

Why am I being asked to participate?

We are inviting all MESA participants who attend Exam 7, who are able to walk, and who have not been told by their doctors that they cannot exercise.

8.1.17 Appendix B: Take-Home Package Materials

Red Activity Monitor Instructions

We are asking you to wear a small device (red activity monitor) on your waist just above your right hip bone for eight straight days.

The red activity monitor is used in research studies to understand how a person spends their day being active or sitting still. It is very similar to a pedometer, or step counter that you might have worn or seen in the store.



How Do I Wear the Red Activity Monitor?

Each Day:

- ✓ Wear the red activity monitor snugly on your waist, using the black elastic belt or belt clip.
- ✓ Wear the red activity monitor just above your right hip bone.
- ✓ Keep the red activity monitor on the *entire time that you are awake*.



Other Wear Tips

- ✓ Try to wear the red activity monitor in the same place, every day.
- ✓ Please do not cut or permanently change the black elastic belt.
- ✓ Remove the red activity monitor any time you shower/bathe or participate in water activities, like swimming. If it gets wet in the rain, that's OK.
- ✓ If you miss a day, as soon as you remember, put the red activity monitor on and finish up the eight days. It's OK if you need to wear the red activity monitor for an extra day or two.
- ✓ The monitor is expensive, and care should be taken not to misplace or damage it. If something happens to the device, please call [MESA Study Staff Name] at [Telephone Number], immediately.

REMEMBER: For this study, we are not asking you to change your normal physical activity; rather we'd like for you to go about your normal daily routine as usual while you are wearing the device.

Returning the Red Activity Monitor

Please use the **Return Checklist** to remind you what to send back to us. Using the pre-paid and addressed return envelope that we gave you during your visit, please return the red activity monitor, participant diary, and the black elastic belt or belt clip with the Return Checklist. That's it!

Questions?

If you have any questions after you have returned home, please call [MESA Study Staff Name] at [Telephone Number], immediately.

Frequently Asked Questions

1. Question: Do I need to turn the red activity monitor on or off?

Answer: No, the red activity monitor is turned on and will stay on for the entire time you have it.

2. Question: My red activity monitor used to blink a little green light, but now it doesn't. Is it broken?

Answer: No, the blinking is only a technical feature of the monitor. The device is monitoring your activity even if it is not blinking.

3. Question: Is the red activity monitor waterproof?

Answer: No, the red activity monitor should not be worn while bathing, showering, or doing any water-based activities, like swimming. If you forget to take the red activity monitor off, it will be ok as long as it wasn't in more than 3 feet of water for longer than 30 minutes (or 1/2 hour).

4. Question: Can I wear the red activity monitor in the rain?

Answer: If outer clothing protects the red activity monitor, you can wear it when it is raining. We ask that you do not wear the red activity monitor in the shower, bath, or pool.

5. Question: I took the red activity monitor off during the day but forgot to put it back on. What should I do?

Answer: We would like for you to wear the red activity monitor for 8 straight days but realize that sometimes people might forget to put it on. Please put the red activity monitor on as soon as possible. If you had the red activity monitor off for longer than two hours, please wear the red activity monitor for an additional day.

6. Question: I forgot to wear the red activity monitor yesterday. Should I start wearing it again today?

Answer: Yes. We ask that you wear the red activity monitor for 8 straight days. If you forget a day, start wearing the monitor the next day. If you accidentally skip a day, make it up by wearing the monitor for an additional day for 8 full days.

7. Question: Does it matter if I wear the red activity monitor in the same place each day?

Answer: It is ideal that you wear the red activity monitor in the same place. Please remember to wear the red activity monitor on your waist over your right hip.

8. Question: The belt for my red activity monitor is too short (or too long) to go around my waist. How do I lengthen (or shorten) it?

Answer: Pull the belt through the black plastic tabs to shorten or lengthen the belt. Please do not make any other alterations to the belt.

9. Question: My belt has an unpleasant smell. Can I wash it?

Answer: No, please do not remove the activity monitor from the belt for any reason. If you would like a replacement, please contact study staff and we will provide further assistance.

10. Question: Should I clean the red activity monitor? If so, how do I clean it?

Answer: No, there is no need to clean the red activity monitor while you have it. We will clean it before we give it to the next study participant. If you need to clean it, just wipe it down with a damp cloth.

11. Question: I've accidentally dropped the red activity monitor. Is it okay?

Answer: *The red activity monitor is a delicate piece of equipment and should be handled with care. However, minor accidents should not impair their functioning. Please contact study staff if you are concerned.*

12. Question: My red activity monitor is hard to keep in place when I wear skirts and dresses. Do you have any suggestions to make this easier?

Answer: *Most people find that wearing the red activity monitor with pants is the most comfortable. If the pants have belt loops, you can string the red activity monitor and belt through the loops as if it were a normal belt. You can also wear the red activity monitor under a dress or skirt, if necessary.*

13. Question: Does the red activity monitor tell you where I am in the community?

Answer: *No, the red activity monitor collects information on how much time you spend active or still during the time you are awake. The monitor cannot tell us where you are in the community.*

14. Question: Do I need to do anything with the red activity monitor or shut it off before I return it?

Answer: *No, you do not need to do anything or shut it off before returning it to us.*

15. Question: I misplaced the pre-paid and addressed return envelope. What do I do?

Answer: *No problem. Please contact study staff and we will provide further assistance.*

Participant Diary

See section 8.7 for Participant Diary instructions.

Exam 7
Participant Diary

Participant ID #:

Acrostic:

Please complete this form daily for every day that you wear a home monitor. The questions on the first page should be answered in the morning. The second page should be completed at night. Be sure to put your hip monitor on when you wake up.

Date: / /

Month Day Year

What time did you get into bed yesterday?

: AM
 PM

How long did it take you to fall asleep?

hours minutes

How many times did you wake up (not counting your final awakening)?

times

What time was your final awakening? Record the last time you woke up in the morning.

: AM
 PM

What time did you get out of bed for the day?

: AM
 PM

Last night your sleep was:

Very poor
 Poor
 Fair
 Good
 Very good

Do you remember dreaming last night?

Yes No

Please continue with questions on page 2

MESA Exam 7 | Participant Diary | Self-Administered | v1
1/31/2022
Page 1 of 2

Exam 7
Participant Diary

Participant ID #:

Acrostic:

Complete these questions at night before you go to bed:

Did you wear your red hip monitor for the entire day today? Yes No

If no, why?

Did you take a nap today?

Yes No

Nap 1:

Start time : AM PM

End time : AM PM

Nap 2:

Start time : AM PM

End time : AM PM

Nap 3:

Start time : AM PM

End time : AM PM

What time did you eat today?

Breakfast: : AM PM

Lunch: : AM PM

Dinner: : AM PM

Snack 1: : AM PM

Snack 2: : AM PM

Snack 3: : AM PM

Snack 4: : AM PM

Please continue with questions on page 2

MESA Exam 7 | Participant Diary | Self-Administered | v1
1/31/2022
Page 2 of 2

Return Checklist

Please carefully complete this checklist before returning or mailing back the red activity monitor and this sheet to us in the pre-paid and addressed padded envelope that we gave you at your exam visit. These items should be returned to us immediately after you have worn the red activity monitor for 8 straight days.

During the 8 days, please:

- Wear the red activity monitor on your waist over your right hip for **the entire time you are awake for 8 straight days.**
- Each day, in your **Participant Diary**:
 - ✓ Check off that you wore your red activity monitor for the entire day, each day.
 - ✓ If the red activity monitor was not worn for the entire day, please indicate why.
 - ✓ Record the clock times corresponding to when you got into and out of bed.
 - ✓ If you took a nap, record the date and time the nap started and ended.


After you have worn the red activity monitor for 8 days, please return the following items in the pre-paid, pre-addressed envelope:

- Participant Diary
- Return Checklist (i.e., this form)
- Red activity monitor and black elastic belt or belt clip →



Thank you for participating in the MESA Exam 7!

8.1.18 Appendix C: Tracking Activity Monitors in the Field



Exam 7
Hip and Wrist Activity Monitors Completion Form

Participant ID #:

Acrostic:

Technician ID:

Date: / /

Month Day Year

Hip Activity Monitor

Did the participant receive a hip activity monitor?

No →

Yes

Reason:

Participant refusal

Unable to ambulate

Physician instruction not to be physically active

Monitor not available

Other: _____

Skip to page 3

Date distributed: / /

Month Day Year

ActiGraph Monitor ID: _____

Fully charged battery?

No

Yes

Start date: / /

Month Day Year

Initialized to start at 12AM?

No

Yes

Check-in call*: / / *Estimated as 2-3 days (or first business day) after start date

Month Day Year

End date*: / / *Estimated as 9 days (or first business day) after start date

Month Day Year


Receipt date*: / / *Estimated as 9 days (or first business day) after start date

Month Day Year

MESA Exam 7 | Hip and Wrist Activity Monitor Completion Form | Interviewer-Administered | v1

12/28/2021

Page 1 of 4



Exam 7
Hip and Wrist Activity Monitors Completion Form

Participant ID #:

Acrostic:

Technician ID:

Date: / /

Month Day Year

Did the participant return the hip activity monitor?

No →

Yes

Reason:

Lost by participant

Lost by postal service

Other: _____

Date received: / /

Month Day Year

Data downloaded?

No →

Yes

Reason:

Download error

Monitor damaged

Staff error

Other: _____

Date data downloaded: / /

Month Day Year

MESA Exam 7 | Hip and Wrist Activity Monitor Completion Form | Interviewer-Administered | v1

12/28/2021

Page 2 of 4

8.1.19 Appendix D: Research Staff Certification Checklist

MESA 24H-ACT Study– Certification Check Sheet

Field Center	Date
Study Staff	Observer

Prepare Data Collection Package		Yes	No
1.	Data collection package includes: Participant Instructions, Frequently Asked Questions, Return Checklist, pre-paid and addressed return envelope/package	<input type="checkbox"/>	<input type="checkbox"/>
2.	Completed Question 1 on Hip Activity Monitor Completion Form	<input type="checkbox"/>	<input type="checkbox"/>
3.	ActiGraph battery fully charged ($\geq 98\%$)	<input type="checkbox"/>	<input type="checkbox"/>
ActiGraph Initialization		Yes	No
4.	Start date is the expected day of in-person, ancillary study exam	<input type="checkbox"/>	<input type="checkbox"/>
5.	Start time is 12:00am	<input type="checkbox"/>	<input type="checkbox"/>
6.	Use stop time? box is unchecked.	<input type="checkbox"/>	<input type="checkbox"/>
7.	Atomic server time is selected	<input type="checkbox"/>	<input type="checkbox"/>
8.	Sampling rate is 40 hertz	<input type="checkbox"/>	<input type="checkbox"/>
9.	LED and Wireless options are unchecked	<input type="checkbox"/>	<input type="checkbox"/>
10.	Idle Sleep Mode Enabled	<input type="checkbox"/>	<input type="checkbox"/>
11.	MESA ID entered as Subject Name	<input type="checkbox"/>	<input type="checkbox"/>
Participant Instruction		Yes	No
12.	Followed Script	<input type="checkbox"/>	<input type="checkbox"/>
13.	At the end, asked participant if they had any questions	<input type="checkbox"/>	<input type="checkbox"/>
2-3 Day Check-in		Yes	No
14.	Followed Script	<input type="checkbox"/>	<input type="checkbox"/>
15.	At the end, asked the participant if they had any questions	<input type="checkbox"/>	<input type="checkbox"/>
ActiGraph Data Download		Yes	No
16.	Subject Name (i.e., MESA ID) was used as the file naming convention	<input type="checkbox"/>	<input type="checkbox"/>
17.	Data file was downloaded to the specified computer directory	<input type="checkbox"/>	<input type="checkbox"/>

8.1.20 References Cited

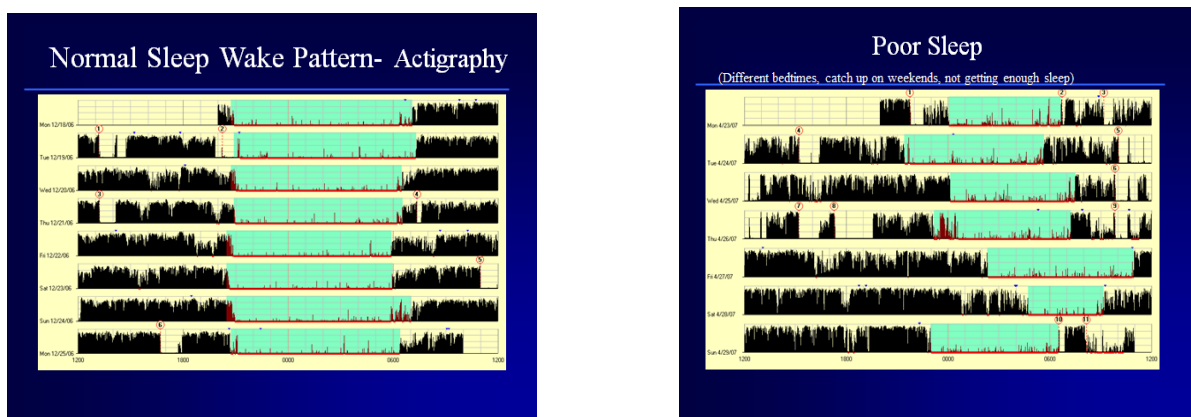
1. Troiano RP, Berrigan D, Dodd KW, Masse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc.* 2008;40(1):181-188.
2. Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc.* 1998;30(5):777-781.
3. Matthews CE, Hagstromer M, Pober DM, Bowles HR. Best practices for using physical activity monitors in population-based research. *Med Sci Sports Exerc.* 2012;44(1 Suppl 1):S68-76.
4. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc.* 2011;43(2):357-364.
5. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. *Med Sci Sports Exerc.* 2012;44(10):2009-2016.

6. Evenson KR, Wen F, Herring AH, et al. Calibrating physical activity intensity for hip-worn accelerometry in women age 60 to 91 years: The Women's Health Initiative OPACH Calibration Study. *Preventive medicine reports*. 2015;2:750-756.

8.2 GENEActiv Wrist Actigraphy Sleep Monitor

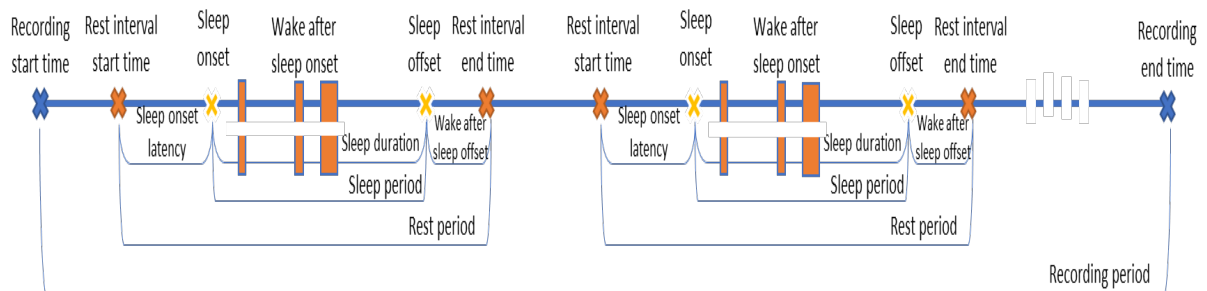
8.2.1 Purpose

Actigraphy is a method for collecting objective information related to movement. The data output shows activity and inactivity levels- when worn on the wrist, the information provides reliable wake/sleep estimates. (In contrast, waist-worn devices are better at estimating physical activity). The use of actigraphy in epidemiological studies has accelerated in the last decade as research has shown the importance of sleep patterns and circadian rhythms as key drivers of health and functioning. Typical parameters calculated from actigraphy are: sleep duration, sleep efficiency (percentage of the sleep period spent sleeping), WASO (wake time after sleep onset), and sleep latency (the amount of time it takes to fall asleep: lights off-sleep onset). The following depict 7 days (one day per row) of information from a wrist actigraph. The black marks indicate movement- inferred to be wake while periods with lack of movement (green) are sleep periods. Note how sleep can vary from night to night in someone with poor sleep.



Research shows that actigraphy is a cost-effective method for evaluating specific sleep disorders, including insomnia, circadian rhythm disorders, or excessive sleepiness. Unlike polysomnography, a wrist actigraphy device can be worn for 24-hours over extended periods, thus providing more representative data for some measures (sleep duration) than single night tests. Additionally, data from actigraphy can reduce reporting and recall issues common with questionnaire data. When combining actigraphy data with a sleep diary (log), there may be even further improvement in the accuracy of the data.

Actigraphy data can be summarized per day or averaged over the recording period (multiple days). Other metrics that can be derived include daytime naps, average sleep timing (bedtime, wake time, mid sleep), sleep fragmentation (frequency of brief movements during sleep), variability on sleep timing and duration across the recording period, and circadian rhythm estimates. The following schema describes some of the key measurements made over the sleep period.



We are particularly interested in using wrist actigraphy in MESA due to MESA’s goals of understanding cardiovascular disease and cognitive decline risk factors. Actigraphy data will be combined with data from polysomnography and questionnaires to provide a comprehensive understanding of the multi-faceted aspects of sleep that influence health. Many participants in MESA Exam 5 also underwent actigraphy. Collecting actigraphy in Exam 7 will provide an opportunity to

understand how sleep patterns change over 10 years in aging adults, and how those changes associate with health outcomes.

8.2.2 Equipment and Supplies

The equipment used for this study, the GENEActiv® Original actigraph (watch) device (from Activinsights Corporation), is a wrist-worn device designed for multiple 24-hour wear measuring activity, light, and temperature. The GENEActiv actigraph contains a tri-axis solid-state accelerometer, a silicon photodiode light sensor (with a wavelength range of 400-1100nm), a capacitive wear time sensor, a rechargeable lithium-polymer battery with battery life for up to 30 days, 0.5Gb of raw data memory, and associated circuitry. The device has an “event marker” that participants can use to indicate changes in behavior (e.g., in bed times). The efficacy and sensitivity of the accelerometer are optimized for highly effective sleep-wake inference from wrist activity, which has been previously validated in small-scale studies and large international cohorts. The device is designed to be compact, lightweight, fully waterproof, and to detect movement, environmental light, and temperature, give information on daily behaviors, and to classify sedentary behaviors.

Supplies:

- GENEActiv instrument
- GENEActiv PC software
- Wrist strap
- USB cable
- Charge cradle

8.2.3 Staff Training and Certification

Site staff will be trained on the use of the wrist actigraphy devices by qualified Brigham Sleep Reading Center (SRC) staff or by site staff who underwent central training. Training will include all steps necessary to obtain high-quality study data, including device initialization, study participant instruction on device use, device distribution and retrieval, downloading of data from study devices, data transmission to the SRC, and proper cleaning, disinfection, and maintenance of equipment. All staff will be required to obtain certification from the SRC before performing study procedures and administering devices to study participants.

Each site staff member is required to obtain protocol certification before performing data collection from MESA participants. Each site staff member involved with actigraphy data collection using the GENEActiv device is required to successfully complete:

- Training under the direction of a member of the SRC or by a centrally trained site staff member.
- Submission of one (1) successful certification study demonstrating:
 - Successful GENEActiv device initialization using the GENEActiv PC software.
 - Collection of at least 24 hours of data recorded on a non-participant volunteer.
 - Download of data from the GENEActiv device.
 - Successful transmission of study data to the CC.

Each new actigraph device should also be tested for one night before use in research participants. For device testing, volunteers should wear two devices on each wrist concurrently (can wear a total of 4 devices by using both wrists) for 24 hours. Data will be transmitted to the CC to ensure comparable data collection (sleep duration and recording times within 2% of one another.)

8.2.4 Actigraphy Data Acquisition

8.2.4.1 Setting Up the GENEActiv Software and Device

GENEActiv PC Software is a Windows-compatible program used to initialize the GENEActiv Original actigraphs and download data from the devices. The SRC will also use this software to score the actigraphy data and generate reports. To install the software:

1. Download the GENEActiv software from the following website. The SRC will confirm the appropriate software version that should be installed:
<https://www.activinsights.com/expertise/geneactiv/downloads-software/>
2. Install the software following the instructions in the wizard. Click “Allow” if any security prompts appear.
3. When the GENEActiv installer completes, download the GENEActiv drivers from the following link:
<https://www.activinsights.com/wp-content/uploads/2017/07/GENEActivDrivers-1.0-W10.zip>
4. Extract the files from the .zip file to a folder on your computer. Run the install file and follow the prompts to complete installation of the drivers.
5. Once the software and drivers are downloaded, open the GENEActiv software. For the first use, load one single GENEActiv device into the charging cradle. Connect the charging cradle to the computer using the USB cable.

Make sure that the device ‘clicks’ into place (if it has a strap fitted, the strap may need to go behind the mounting clip to ensure a good connection)

6. Allow GENEActiv devices to charge for 3 hours before using the software. A red light will flash to show that it is charging. When fully charged, a green light will flash, and the device can be removed.

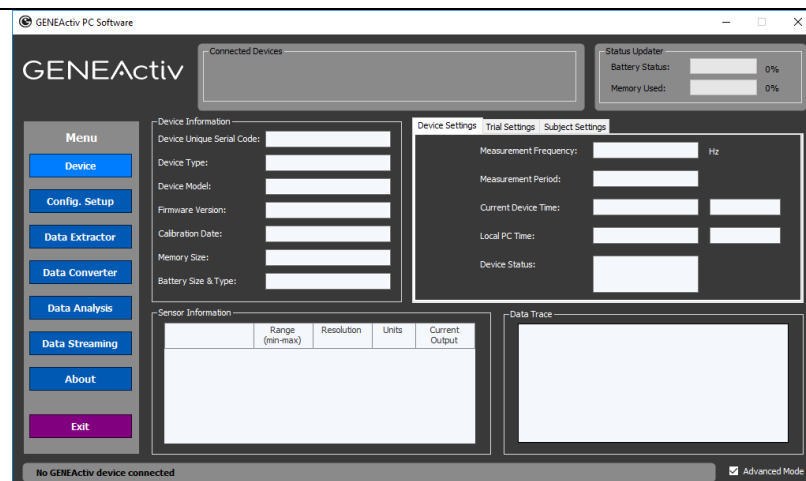


Figure 5: GENEActiv software

8.2.4.2 Preparing the GENEActiv Device for recording

7. Launch the GENEActiv software.
8. Select “Advanced Mode” in the bottom right corner.
9. Connect the charging cradle to your computer using the USB cable.
10. Place a GENEActiv device into the charging cradle. Allow the GENEActiv device(s) to charge for at least 3 hours before configuring the software. The light on the device will flash red while it is charging and green once it is charged. To ensure the device is fully charged, it must be left in the charging cradle until the green light is flashing.
11. When connected, the software will show information about the device and any data previously stored on it.
12. Click ‘Config. Setup’ from the left-hand menu.

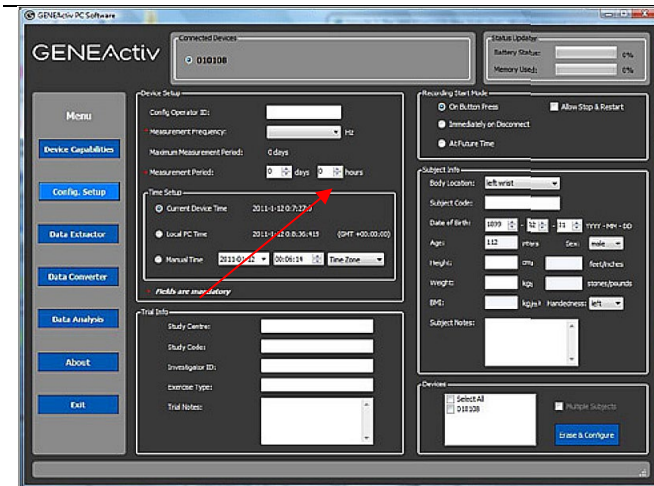


Figure 2: GENEActiv Device Connected

13. Set the Measurement Frequency to 60 Hz. Note that 12 days will automatically appear in the “Measurement Period” field. Do not change this number. Participant data collection will occur for 8-9 consecutive days, including the initial PSG night and the night when 24 ABPM is used.
14. Select “Local PC Time” in the Time Setup field.

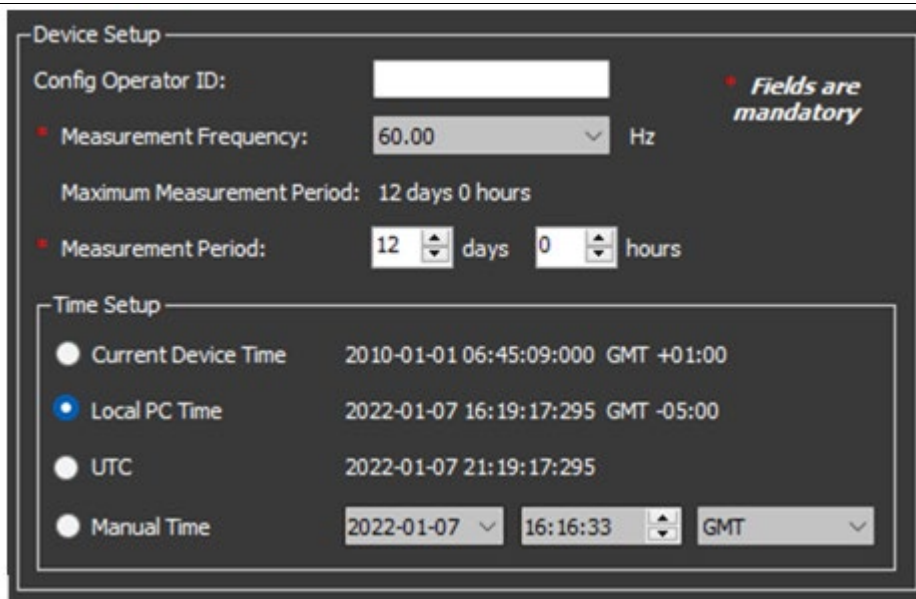


Figure 3: GENEActive Device Setup

15. In the Recording Start Mode field select “At Future Time”. The date and time of the study visit should be used for the start date and start time.
16. Enter the participant identification number for the study participant in the “Subject Code” field. No other subject information or PHI should be entered.

Note: The subject identification number convention is the Participant ID and date of visit as follows:

Participant ID-YYYYMMDD

YYYY=Year, MM= Month, DD= Day

17. In the Devices field select the desired GENEActiv device. The Devices field will show the device serial number. The serial number is displayed on the front of the GENEActiv device.

The screenshot shows the GENEActiv Configuration Settings interface. It is divided into several sections:

- Status Updater:** Shows Battery Status at 100% and Memory Used at 80%.
- Recording Start Mode:** Includes radio buttons for 'On Button Press', 'Immediately on Disconnect', and 'At Future Time' (which is selected). Below are date and time pickers set to 2022-01-11 and 12:00:00.
- Subject Info:** Contains fields for Subject Code (ParticipantID-YYYYM), Subject Notes (text area), Body Location (dropdown), Date of Birth (1900-01-01), Age (years), Sex (dropdown), Height (cm and feet/inches), Weight (kg and stones/pounds), BMI (kg/m²), and Handedness (dropdown).
- Devices:** A list of devices with '046430 (GENEActiv)' selected. There are checkboxes for 'Select All' and 'Multiple Subjects', and a blue 'Erase & Configure' button.
- Advanced Mode:** A checkbox at the bottom right that is checked.

Figure 4: GENEActiv Configuration Settings

18. Click the button “Erase and Configure.” A pop-up window will appear informing of any issues with the selected device – such as mandatory information missing or low battery charge – and warn that configuring will erase any existing data. The configuration will take about 10 seconds, and a pop-up will confirm that it has been completed successfully.
 - Note: Please ensure that the data on the device has been downloaded and saved to the appropriate folder prior to configuring the GENEActiv device for the next participant’s use.
19. Data will start recording at the selected date and time of the study visit.
20. Double-check the battery is fully charged and the Start Date & Time are correct.

21. Remove the device from the charging cradle and deliver it to the participant.
22. After the data collection period has ended, the participant will return the device to the study site, following instructions provided by the study staff. The recording will cease when the GENEActiv device is plugged into the USB charging cradle once again.



Figure 4: GENEActiv fully charged in USB charging cradle

8.2.5 Participant Instructions

The participant will be provided a GENEActiv device, a Participant Diary, and written instructions on how to use the actigraphy device. All procedures for wearing the actigraph and completing the Sleep Diary should be explained to the participant before beginning sleep data acquisition. Sufficient time should be allowed for questions and demonstrations.

8.2.5.1 5.1 Wearing the GENEActiv Actigraph

The actigraph should be worn on the **non-dominant wrist** and should be securely fastened. It should be worn just as a wristwatch would be worn. The participant should be fitted with a wristband so that the device fits snugly on the wrist and there is no loose movement. However, the watch should not be too tight. A small finger should be able to be fit under the watch band. The device should not dangle from the wrist or slide around. If possible, measure the wrist and select the appropriate wrist strap size (see participant instructions).

The device should be worn against the skin and not over or under clothing, to ensure an accurate wear time sensor and light meter readings. While not always be possible (e.g. outdoors in the cold), participants should be encouraged to roll up long sleeves so the actigraph is exposed to light.

The device should be worn from the time the participant is given the watch until the day it is returned to the clinic staff (an approximate 8-day period, including the night of 24 ABPM, and if possible, the PSG). The watch should only be removed when engaged in contact sports (e.g., football). It can be used when bathing, swimming, etc. The participant should remove the device briefly after the activity, drying the skin and band with a towel, and then replacing the device. This minimizes skin irritation related to wearing a wet band. Participants should also be told when it is okay to stop wearing the device, which is the morning of the day the actigraph is to be returned.

The actigraph has an “event marker” located on the top of the device under the serial number. Participants should be asked to firmly press the hidden event marker button under the six-digit number each day, when trying to fall asleep (e.g., in bed. Lights out) and at final awakening.



Figure 5: Pressing the GENEActive event marker

When instructing participants, please refer to the participant instruction sheets.

Sample participant instructions:

This wrist watch-like device is used to estimate your sleep and wake-estimating your sleep duration and how many awakenings per night you have. MESA is collecting this information because the quantity and quality of sleep are important for daily functioning and heart and brain health. Because the device is small and can be worn over several days, it provides information on day to day patterns of sleep and waking that complement information obtained with the one night sleep study (which measures level of oxygen, breathing/air flow, and brain activity during sleep). The device used in this exam is similar to the one you may have worn in MESA Exam 5- but somewhat lighter. We ask you to wear the watch on your wrist (the one you don't use for writing) for about 8 to 9 days and nights—including the night of the sleep study (if you agree to do this) and ending on the day of ABPM monitoring (if you agree to do this). If you do not do ABPM monitoring, you will wear the device for 8 days from the time the device is attached. We will arrange for the device to be returned using a mailer (or note other means). After the information is processed, you will receive a letter with the results of key measurements from the actigraph.

The device is completely water-proof- so you don't need to remove it when bathing or swimming. However, if it gets wet, please remove it and blot dry the watch and skin and then replace it. If you do contact sports (football) please remove the device during that activity.

There is a small button on the device (point to it) that we ask you to press when going to bed and waking up in the morning. Don't worry, though, if you forget to press the button.

We have gone over a lot of information. I want to be sure I explained everything clearly. Can you explain it back to me so I can be sure I did?.

If the participant is not able to teach back correctly, explain the directions again and re-check.

8.2.5.2 Completing the Participant Diary

Staff will explain how to complete a daily sleep diary (log) while using the actigraph. In this Diary, the participant will record bed and wake-up times, quality of sleep, naps, and dreams. Clinic staff will fill out Day 1 of the Diary with the participant. The Diary will be completed for 8-9 days and nights, coinciding with GENEActiv data collection and including ABPM. If the participant is reluctant to complete the Diary, they should still be given a device to wear and should be encouraged to fill in as much data as possible. This Diary will be integrated into the logs used by other ancillary studies with wearables.

Sample script:

While wearing the watch, we ask you to complete a Participant Diary, indicating the times you went to bed, woke up, sleep quality, and whether you had dreams. (Refer to the diary and demonstrate how to complete).

8.2.5.3 Removing the GENEActiv actigraph

The actigraph is waterproof but participants should be instructed to remove the device and wipe the underlying skin dry if the device or band gets wet to avoid possible irritation. Once the skin and band are dry, the watch can be replaced and worn as described earlier. The device should be removed during contact sports. Please refer to the Participant Instruction Sheet.

8.2.5.4 *Reminder Phone Calls*

Clinic staff will call participants 2-3 business days after the day on which devices (wrist and waist actigraphs) are first administered. At the time of the call, clinic staff will answer any questions, trouble-shoot potential problems and reinforce use of the devices and diary, remind the participant of the day when devices can be removed and will be returned, following a script provided and integrated for the Sleep and 24 ACT studies. Prior to calling participants, staff should check whether participants agreed to use both the wrist and waist/hip devices or only one, and choose the appropriate script.

8.2.5.5 *Returning the GENEActiv device to the Site*

Sites should explain to participants that the actigraph must be returned as soon as possible after the period of data collection. Clinic staff should clarify the stop date of wearing the wrist actigraphy and provide details on how the device will be returned (e.g., by a pre-paid mailer). As possible, return of devices should be coordinated across home-based ancillary studies.

8.2.6 Downloading Data from the GENEActiv Software

8.2.6.1 *Data extraction from the GENEActiv device*

Data from the actigraph will be downloaded and stored in a folder on the same computer used to initialize the device. If more than one site staff member will initialize watches and download data, make sure the Actigraphy Data folder is created in a folder that all research staff can access.

23. Create a folder on the computer desktop to house the GENEActiv actigraphy data.
24. Create a folder inside the Actigraphy Data folder for each participant before downloading data from the actigraphy watch.
25. Name the new folder using the participant identification number and the visit date. This folder will contain the actigraphy data for the participant and a copy of the participant's Sleep Diary data.
 - a. Sample folder name: Participant ID-20210428
26. Open the GENEActiv software.
27. Connect the GENEActiv device to the computer using the charging cradle connected via USB cable.
28. Open the GENEActiv software and click the "Data Extractor" button.

The Data Converter and Data Analysis tabs (selected from the left-hand menu) can convert .bin files to .csv files or compressed .csv files that can be handled more efficiently. This feature means that .bin files can be saved and then converted to another format at a later date if required. Click the 'extract' button. The data can take up to 20 minutes to download and a pop-up will confirm completion.

29. Complete the following on the Data Extractor screen (Figure 5):
 30. Choose the participant folder as the file location and create a .bin format file. The default data format is a compressed .bin that can be interpreted, with a suitable script, by most mathematical analysis software packages, but not Excel.
 31. Note - The Data Converter and Data Analysis tabs can convert the default .bin files to .csv files or compressed .csv files that can be handled more efficiently. This means that .bin files can be saved and then converted to another format later if required.
 32. Click the 'extract' button. The data can take up to 20 minutes to download and a pop-up will confirm completion. Multiple units can be downloaded simultaneously.

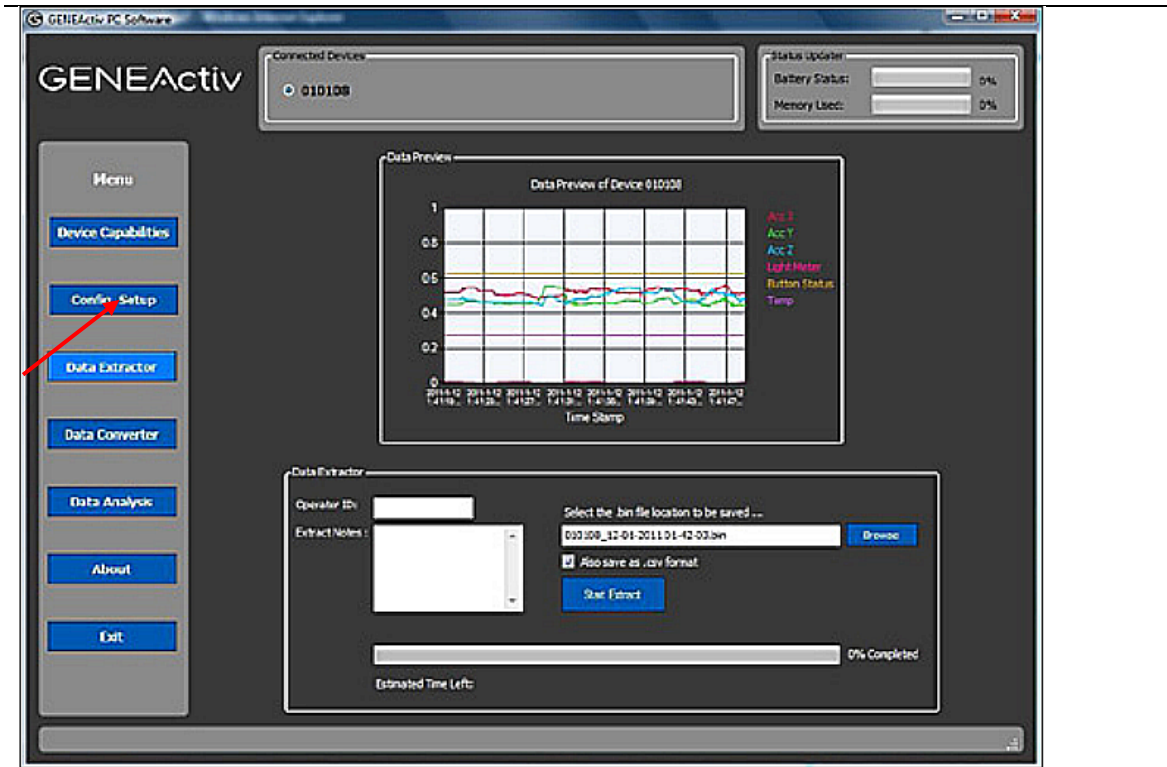
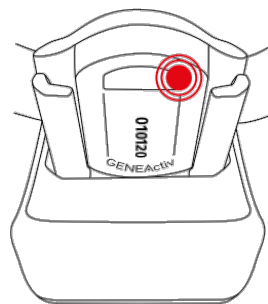


Figure 6: GENEActiv Data Extractor

33. Recharge device and disconnect from computer. Inspect the device for any signs of damage, specifically cracks in the plastic. The device will display a repeating flashing red light when connected to the charging cradle and charging. When the light becomes steady and green, the device is fully charged.
34. **Set device aside until the Sleep Reading Center confirms data has been received.** Once the data has been reviewed, the device can be reinitialized for a new subject or put in a low power mode for storage.



Constant = communicating

Flashing = charging

Figure 7: GENEActiv device charging in USB charging cradle

8.2.6.2 Participant Diary Management

The Participant Diary will be collected using REDCap and should be reviewed upon receipt for completeness/consistency. If obvious errors of missingness are identified, the clinical staff can attempt to call the participant to clarify ambiguous entries. The actigraphy study data and the Participant Diary will be transmitted to the CC (see instructions provided by the CC) where the Sleep Reading Center (SRC) will access these for actigraphy scoring.

8.2.7 Equipment Maintenance, Cleaning and Disinfection

8.2.7.1 Battery Management

The GENEActiv device has a Lithium Ion Polymer battery. The battery can be charged by connecting the device to a computer by placing it in the charging cradle and connecting via the USB cable. When connected, the battery status is displayed on the *Status Updater* field in the “Configuration Setup” page, and a red LED indicator light will flash while the device is charging. A steady green light indicates the battery is fully charged. **Each device should be charged for three hours, or until fully charged, within 24 hours of administering to a participant.** After charging is complete, devices should not remain connected to the computer via the USB cable for extended periods or during storage.

8.2.7.2 Cleaning and Disinfection

The GENEActiv device should be cleaned and disinfected between each use- ideally when it first arrives back in the clinic and before downloading. Using a CaviWipe or similar disinfecting wipe should be used to thoroughly wipe the device, including the band, allowing it to dry.

8.2.7.3 Device Logs

A log should be maintained for tracking purposes, so the location of all devices is known at all times. The serial number for each device can be found on the GENEActiv device face. An id will be

8.2.7.4 Device Quality Control

At approximately 6 month intervals, site clinic staff should check each GENEActiv device to verify that any given device had not “drifted” over time. A staff member should wear two devices on the same wrist for 24 hours. A quality control log should be kept tracking all device pairs and test dates. The SRC will review the study pairs and compare the data collected by each device. The SRC will work to resolve quality control issues through further testing.

8.2.8 Data Transmission to the CC

REDCap Diaries and the GENEActiv data exports will be transmitted to the CC where the SRC will access them, identify whether sufficient data were collected, and edit and annotated the record, generating full reports and analytical files. Please see instructions provided by the CC for data transmission.

8.2.9 Repeat Studies

A minimum of 5 days of data, including 6 hours during the sleep period is considered adequate for analysis. If studies are shorter, the site will be alerted that the study does not meet quality criteria. The SRC and field center staff should consult to determine likely source of poor data: device failure (including batteries), participant usage, or other. The study staff should ask participants to repeat the study and inform the SRC if the study will be repeated, taking care to identify participant-related barriers to collecting sufficient data.

8.2.10 Sleep Reading Center Contacts

Please contact the SRC with any concerns about wrist actigraphs or the monitoring procedure: mesasupport@bwh.harvard.edu

8.2.11 Appendix A: Participant Diary

Exam 7
Participant Diary

Participant ID #:

Acrostic:

Please complete this form daily for every day that you wear a home monitor. The questions on the first page should be answered in the morning. The second page should be completed at night. Be sure to put your hip monitor on when you wake up.

Date: / /

Month Day Year

What time did you get into bed yesterday?

: AM
 PM

How long did it take you to fall asleep?

hours minutes

How many times did you wake up (not counting your final awakening)?

times

What time was your final awakening? Record the last time you woke up in the morning.

: AM
 PM

What time did you get out of bed for the day?

: AM
 PM

Last night your sleep was:

Very poor

Poor

Fair

Good

Very good

Do you remember dreaming last night?

Yes No

Please continue with questions on page 2

MESA Exam 7 | Participant Diary | Self-Administered | v3
6/23/2022
Page 1 of 2

Exam 7
Participant Diary

Participant ID #:

Acrostic:

Complete these questions at night before you go to bed:

Did you wear your red hip monitor for the entire day today? Yes No

If no, why?

Did you take a nap today?

Yes No

Nap 1:

Start time : AM PM

End time : AM PM

Nap 2:

Start time : AM PM

End time : AM PM

Nap 3:

Start time : AM PM

End time : AM PM

What time did you eat today?

Breakfast: : AM PM

Lunch: : AM PM

Dinner: : AM PM

Snack 1: : AM PM

Snack 2: : AM PM

Snack 3: : AM PM

Snack 4: : AM PM

Answer this question if you wore the blood pressure monitor in the past day or night:

If you take blood pressure medication, at what time(s) did you take it today?

Time 1: : AM PM

Time 2: : AM PM

Time 3: : AM PM

MESA Exam 7 | Participant Diary | Self-Administered | v3
6/23/2022
Page 2 of 2

8.2.12 Appendix B: Participant Instructions

Wrist Actigraph Information & Instructions

➤ What is an actigraph?

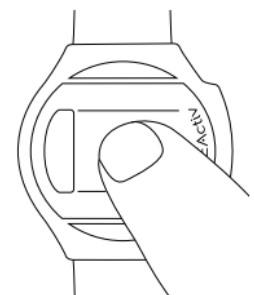
This small device records information about body movement during everyday activities such as walking and sleeping. The actigraph is safe and uses a battery similar to a watch battery for power. It is **not** a GPS tracking device, nor does it record heart rate.



➤ What am I supposed to do with the actigraph?

The actigraph will start recording data today and will continue to record 24 hours a day for 8 to 9 days.

1. We ask that you wear the monitor for the full 8 days, all day and night. It is worn on the **non-dominant wrist** like a watch and should fit snugly around your wrist.
2. The monitor is water-resistant so it can be worn when taking a bath, shower, or swimming. If the monitor and wrist strap get wet, you may blot them dry with a towel and dry the skin under the monitor.
3. If you must take the actigraph off for any reason, remember to put it back on the same wrist as soon as possible.
4. If the actigraph is removed, please keep it away from small children and pets to avoid accidents.
5. Please firmly press the hidden event marker button under the six-digit number when you are trying to fall asleep and at your final awakening.




➤ Who do I contact if I have questions?

If you have any questions about the monitor, please call the sleep study project coordinator.

8.2.13 Appendix D: Actigraph Device Completion Form

Participant ID	GENEActiv Serial Number	Date Device Given to Participant (MM/DD/YYYY)	Staff ID (provided device)	Date Device Returned (MM/DD/YYYY)	Staff ID (received device)	Comments
		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	
-----		___ / ___ / ____	-	___ / ___ / ____	-	



Exam 7
Hip and Wrist Activity
Monitors Completion
Form

Participant ID #:
Acroscopic:
Technician ID:
Date: / /
Month Day Year

Wrist Actigraph Device

Did the participant receive a wrist actigraph device?

No Yes

Reason:

Participant refusal

Unable to ambulate

Physician instruction not to be physically active

Device not available

Other: _____

End of form

GENEActiv serial #: _____

Programmed recording start:

/ / : AM PM

Month Day Year

Device on wrist start:

Mo Tu W Th F Sa Sun

/ / : AM PM

Month Day Year

Device on wrist stop:

Mo Tu W Th F Sa Sun

/ / : AM PM

Month Day Year


Comments (any difficulties with application, uploading, participant wear):

PRINT FORMS FROM MESA WEBSITE

MESA Exam 7 | Hip and Wrist Activity Monitor Completion Form | Interviewer-Administered | v1

12/28/2021

Page 3 of 4



Exam 7
Hip and Wrist Activity
Monitors Completion
Form

Participant ID #:
Acroscopic:
Technician ID:
Date: / /
Month Day Year

Did the participant return the wrist actigraph device?

No Yes

Reason:

Lost by participant

Lost by postal service

Other: _____

Date received:

Mo Tu W Th F Sa Sun

/ / : AM PM

Month Day Year

Data downloaded?

No Yes

Reason:

Download error

Monitor damaged

Staff error

Other: _____

Date data downloaded:

Mo Tu W Th F Sa Sun

/ / : AM PM

Month Day Year

Comments (any difficulties with application, uploading, participant wear):

PRINT FORMS FROM MESA WEBSITE

MESA Exam 7 | Hip and Wrist Activity Monitor Completion Form | Interviewer-Administered | v1

12/28/2021

Page 4 of 4

8.3 Continuous Glucose Monitor

8.3.1 Background, Rationale and Context

Type 2 diabetes (T2D) accelerates cognitive decline, and increases risks for Alzheimer's disease and Alzheimer's disease related dementias (ADRD) by 50% or more. Prediabetes also increases the risk of cognitive decline, so risk associated with dysglycemia likely occurs along a continuum. The rapidly increasing prevalence of dysglycemia (currently 25% with T2D and 48% with prediabetes) in adults aged >65 suggests that a better understanding of the relationship between glucose homeostasis and Alzheimer's and ADRD could have a major public health impact on our aging population. How dysglycemia (high, low, or unstable blood sugar) affects these risks is less clear. 1) Evidence that differences in fasting glucose levels across the normoglycemic and pre-diabetic ranges are associated with cognitive decline and Alzheimer's and ADRD is less consistent. 2) Intensive glycemic control in T2D has not been shown to prevent cognitive decline in trials, highlighting the challenges for prevention in this area. 3) There are similar gaps in the literature about the role of hypoglycemia, not measurable by HbA1c, in the development of dementia. Taken together, the literature points to early and consistent control of circulating glucose within the 'normal range' as a potential prevention strategy for metabolic contributions to Alzheimer's and ADRD. More detailed data are critically needed to comprehensively assess dysglycemia and investigate the effects of glucose homeostasis, including diurnal variation such as postprandial spikes and nocturnal dipping, on cognitive trajectories and Alzheimer's and ADRD risk.

8.3.2 Objectives

The purpose of this proposal is to address critical knowledge gaps in our understanding of which aspects of dysglycemia increase risks of cognitive decline and Alzheimer's and ADRD by adding continuous glucose measurements to MESA Visit 7 that can be paired with longitudinal characterization of cognition, incident mild cognitive impairment (MCI), and Alzheimer's and ADRD biomarkers. The first objective is to collect CGM data on MESA Visit 7 participants, and investigate the determinants of glucose homeostasis (CGM glucose variability and time in range) (n=2000) and change over 2 years (n=1000-2000). The second objective is to determine whether CGM markers of dysglycemia are associated with cognitive decline, incident cognitive impairment (including MCI and Alzheimer's), and Alzheimer's and ADRD biomarkers. (n=2000). The third objective is to understand the contributions of dysglycemia to Alzheimer's and ADRD pathology by sex and race/ethnicity. (n=2000).

8.3.3 Methods and Measures

A. Design

This is an ancillary study to MESA Visit 7.

B. Setting

MESA Glucose will include all six MESA field centers.

C. Subjects selection criteria

MESA participants that agree to participate in MESA Visit 7 either in person, through a home visit, or by virtual visit.

Exclusion Criteria

- Type 1 diabetes
- Unwilling to wear a continuous glucose monitor

D. Sample Size

We anticipate approximately 2000 participants.

E. Measures

The primary measure for this study is the continuous glucose monitor (CGM). A supplementary daily diary is paired with the CGM to calculate additional secondary data elements. The only other measure for this study is the assay of fasting insulin that can be paired with the assay for fasting glucose and can be accomplished without any additional blood collection.

Continuous Glucose Monitoring: Participants will wear a blinded FreeStyle Libre Pro CGM starting at Visit 7. CGM devices will be placed by participants with the assistance of MESA staff either in person or by video call. When a virtual visit is requested CGM sensors and readers will be mailed to participants and a member of the study team will video call participants to provide instructions and real time guidance on attachment and activation of the CGM. A handout for participants and scripts for walking participants through CGM placement and removal are found in Appendix A-D. In addition, a video will be provided to participants before their virtual visit to help them visualize the CGM placement procedure.

The participants will wear the CGM for 14 days. Study staff will call participants on day 14 to remind them to remove the sensor and provide instructions and guidance if needed for removal. Participants will return the continuous glucose monitors, readers, and daily diaries to the study coordinator by mail using prepaid mailers.

Daily Diary: During CGM wear time, participants will complete daily diaries documenting the timing of sleeping, waking, eating, and exercise (Appendix E). Only the time of the activity start will be recorded with no additional details. Start time of the CGM device will be recorded for the purpose of combining these data sources.

8.3.4 Reports for Participants

A 1-page report with a summary of the 14-day glucose data will be provided back to participants together with a cover letter for them to share with their health care provider if they choose. If the CGM registers values $<50\text{mg/dL}$ or $\geq 400\text{mg/dL}$, the letter will include a note that the participant should consider discussing the results with their primary care doctor or endocrinologist at their next visit.

8.3.5 Training and Certification Procedures

A. Initial Training and Certification

Training and certification of MESA staff responsible for placing CGM devices can be completed at Central Training or at individual field centers. The same training is required for staff who will place devices in person as well as staff who will support participants in placing the devices themselves during remote virtual visits. Training for CGM placement requires the following steps:

1. Read and understand the CGM protocol in the MOP.
2. Observe the CGM placement process in the training videos, and handouts, and read the FAQ document.
3. Practice applying up to 3 CGM sensors as needed on volunteers and activating the device following the protocol. Practice using the reader to download the data (both PDF reports and raw data files). Complete the check list for device placement, activation, removal, data download, and data saving, CGM applicator disposal, and CGM sensor storage.
4. Certification is based on review of a video recording of successfully applying **ONE** CGM device with appropriate placement on **ONE** volunteer and activating the device as described in the protocol.

If training is not done at central training, then the practice applications must be videotaped and the video should be transmitted to Lenore Crago at the Wake Forest Field Center for certification.

B. Maintaining Certification

Maintaining certification is based on continued CGM device placement at an acceptable level. This requires the following:

1. Successfully perform the following CGM device application and activation procedures as well as data download, storage, and CGM reader cleaning as described in the protocol and in accordance with certification checklist under supervision of the lead person in the clinic.
2. Place and activate CGM devices and/or direct participants in self placement and activation of devices on least 6 MESA participants every 2 months.

8.3.6 Procedures for Placing and Removing CGM Sensors

FIELD CENTER SET UP

1. Download CGM software onto all computers that will be used to download CGM data (NOTE: You will need Admin rights on the computers)
2. Prepare folders on secure servers for data storage
3. Ensure staff have a flat and stable place to prepare CGM devices

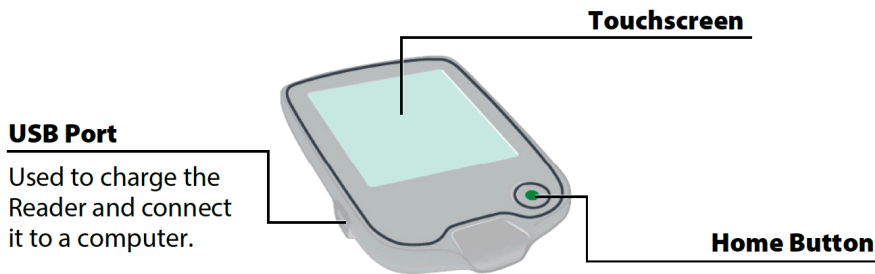
HOW TO DOWNLOAD CGM SOFTWARE

1. Go to the MESA website
2. On the Left side on the purple task bar click on: *Exam 7*
3. Click *Links*
4. Click on *Continuous Glucose Monitoring software download on NextCloud*
5. Download the software “*FreeStyle Libre Pro Installer exe*”
 - a. Note you will need administration rights on your computer to run/install the exe file.
6. Follow the directions to download the software.
 - a. Note there is not a license fee for the software.

**DO NOT USE THE FREESTYLE LIBRE WEBSITE FOR DATA DOWNLOADS.
THE WEBSITE IS NOT NEEDED FOR ANY MESA GLUCOSE ACTIVITIES.**

NEW READER SET UP

1. Turn on (**Green** Home Button)
2. Set data and time correctly
3. Set target glucose range as: **80 – 120**
4. Check that reader is charged



PREPARATION FOR CGM PLACEMENT

1. Check required items: Alcohol wipe, sensor pack, applicator, adhesive patch, reader



Sensor Pack

Used with the Sensor Applicator to prepare the Sensor for use.



Sensor Applicator

Applies the Sensor to the patient's body.

2. Check that reader is charged and has the correct date, time, and glucose range (80-120)
3. Check sensor pack's expiration date

CAUTION: Do NOT use if the Sensor Pack or the Sensor Applicator seem to be damaged or already opened. Do NOT use if past expiration date.

4. Use the barcode reader to put sensor kit serial number in **tracking form** with participant ID
 - a. The serial number is encoded in the 2D QR code NOT in the regular barcode
5. Record the date that the CGM is being placed in the **tracking form**
6. Have a solid surface available to prepare the applicator
7. Wash hands or use hand sanitizer

CHOOSING A SITE FOR THE CGM-Things to consider

Did you consider which arm is their non-dominant arm?

CGM placement is generally preferred on the non-dominant arm.

Did you ask whether they side sleep on one arm in particular?

Exclusively sleeping on the side with the CGM can lead to compression of blood flow around the device and can lead to artificially low readings.

Will they be wearing an ambulatory blood pressure monitor at any point while also wearing the CGM?

If yes, then make sure the CGM sensor goes on the arm that WILL NOT have the ABPM.

Do they already use a CGM device worn on the arm for management of glucose?

If they already have a CGM, they should wear the study CGM sensor also. The study CGM sensor can be placed on the same arm as their other sensor, but ensure that there is plenty of space around each of the sensors and that they are not too close together. There should be enough room to place the adhesive patch over the study sensor without it touching the other CGM device.

Other placement considerations

Avoid areas with scars, moles, stretch marks or lumps. Select an area of skin that generally stays flat during normal daily activities (no bending or folding). If relevant, choose a site that is at least 1 inch (2.5 cm) away from any insulin injection site.

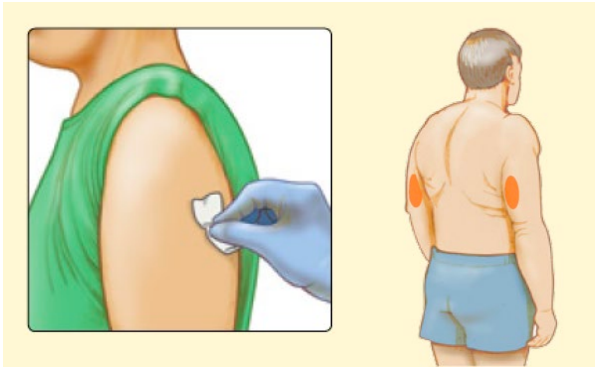
Did you make sure that the chosen site is reachable by the participant if they will be removing the device themselves?

PLACING THE FREESTYLE LIBRE PRO CGM SENSOR (A VISUAL GUIDE)

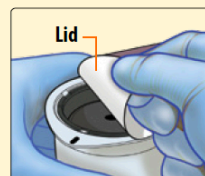
The estimated time for placing the CGM sensor is 5 to 15 minutes.

PLEASE TRY TO WALK PARTICIPANTS THROUGH WHAT YOU ARE DOING. MANY OF THEM WILL BE ASKED TO DO THIS AGAIN BY THEMSELVES AT HOME.

1. Clean hands prior to sensor handling/insertion to help prevent infection.
2. Use alcohol wipe to clean the chosen site for device placement.

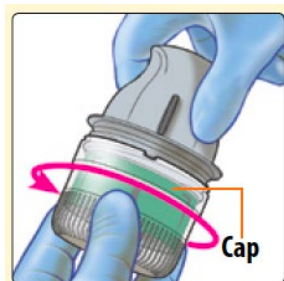


3. Wait until area is dry.
Note: The area MUST be clean and dry, or the sensor may not stick to the site.
4. Open the sensor pack by peeling off the lid.



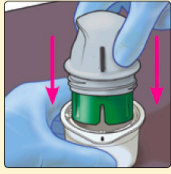
Open the Sensor Pack by peeling the lid off completely. Unscrew cap from the Sensor Applicator and set the cap aside.

5. Remove the applicator cap by twisting it off.



6. Line up the dark line on the applicator with the sensor pack.

7. On a solid surface, press firmly and **straight down** until the applicator stops.



Line up the dark mark on the Sensor Applicator with the dark mark on the Sensor Pack. Press firmly down on the Sensor Applicator until it comes to a stop.

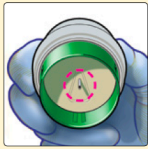
**WAIT! ARE YOU READY TO PLACE THE SENSOR?
AFTER YOU LIFT IT OUT OF THE PACK YOU **MUST** PLACE IT IMMEDIATELY!**

8. Lift the applicator out of the sensor pack



Lift the Sensor Applicator out of the Sensor Pack.

9. **AT THIS POINT THE SENSOR MUST BE PLACED! DO NOT TOUCH THE INSIDE OF THE APPLICATOR OR PUT IT BACK IN THE SENSOR PACK. DO NOT SET THE APPLICATOR DOWN.**



The Sensor Applicator is prepared and ready to apply the Sensor.

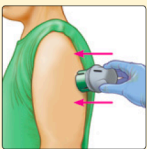
CAUTION: The Sensor Applicator now contains a needle. Do NOT touch inside the Sensor Applicator or put it back into the Sensor Pack.

10. Place sensor applicator over prepared site and push down firmly until there is a loud click.



The Sensor Applicator is prepared and ready to apply the Sensor.

CAUTION: The Sensor Applicator now contains a needle. Do NOT touch inside the Sensor Applicator or put it back into the Sensor Pack.

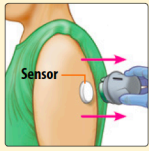


Place the Sensor Applicator over the prepared site and push down firmly to apply the Sensor to the body.

CAUTION: Do NOT push down on the Sensor Applicator until placed over prepared site to prevent unintended results or injury.

11. Wait 5 seconds

12. Slowly pull the applicator away from the body



Gently pull the Sensor Applicator away from the body. The Sensor should now be attached to the skin.

Note: Applying the Sensor may cause bruising or bleeding. If there is bleeding that does not stop, remove the Sensor, and apply a new one at a different site.

13. Put the cap back on the applicator by twisting it back on.

14. Dispose of the applicator in the sharps container.

**MAKE SURE YOU ARE ONLY DISPOSING OF THE APPLICATOR!
IT LOOKS LIKE THIS AND GOES IN THE SHAPRS CONTAINER.**



15. Gently check that the sensor is secure



16. **Gently press on the sensor and adhesive** from the center out to ensure that the adhesive is well attached.

17. Place the adhesive patch over the sensor with the hole centered over the CGM sensor.



**DID YOU REMEMBER TO PLACE THE ADHESIVE PATCH OVER THE CGM SENSOR?
THIS PATCH WILL HELP PREVENT EARLY LOSS OF THE SENSORS.**

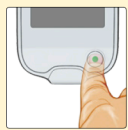
18. Gently press on the patch from the center out to ensure that the adhesive patch is well attached.

WHAT IF THE SENSOR DOES NOT START?

- Try again using the TOP of the reader (the home button is on the bottom).
- Wait 7 minutes and then try to start the sensor again with the reader.
- If it still doesn't start, then remove the first sensor and replace with a new sensor.
- You can place the new sensor in the same place on the same arm, but it might be sore and participant may want to switch arms.

STARTING THE SENSOR WITH THE READER

1. Turn on the reader(**green** Home Button)



Press the Home Button to turn on the Reader.

2. Press the “Start the new sensor” icon

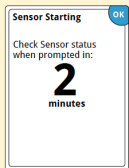


Touch **Start New Sensor**.

3. Hold the reader up to the sensor. It need to be close and it works best if the top of the reader is closest to the sensor. The reader should beep immediately.



Hold the Reader within 1.5 inches (4 cm) of the Sensor to start it. If sounds are turned on, the Reader beeps when the Sensor has been started. You can check the Sensor has successfully started in 2 minutes.



Note: If communication is not established within 15 seconds, the Reader displays a prompt to try again. Touch **OK** to return to the Home Screen and touch **Start New Sensor** to start the Sensor.

4. Wait 2 minutes or until the reader prompts
5. Touch “yes” when prompted
6. Verify the sensor is working
7. Touch “OK”
8. If the reader does not establish communication with the sensor, you can go back to “start the new sensor” and try again.
9. Remind the participant that they will receive a phone call to walk them through removing the sensor at the scheduled date and time.
10. **Write down the date and time that the participant is scheduled to receive a call to remove the CGM sensor on the participant letter.**
11. **Make sure the participant has their letter and the padded return mailer for the CGM with the biohazard bag.**

DOES THE PARTICIPANT HAVE THEIR RETURN MAILER AND LETTER WITH THE DATE AND TIME OF THEIR CGM REMOVAL?

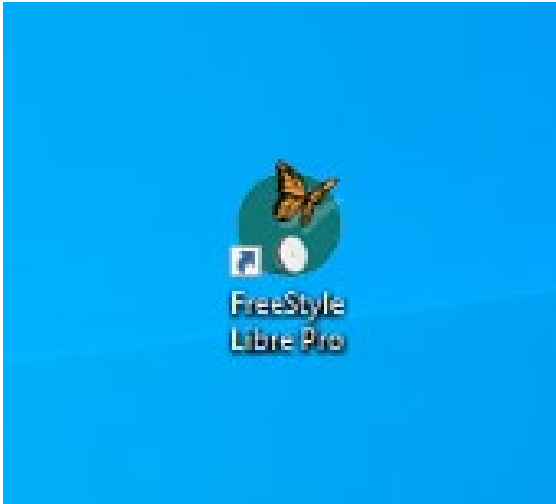
12. Turn off reader (**green** button)
13. Clean reader
14. Check reader charge level and place on charge if needed
15. Record the time that the CGM was placed in the **tracking form**
16. Record the tracking information for the return shipping in the **tracking form**

PLEASE ENSURE THAT THE TRACKING FORM IS COMPLETE

RECEIVING A COMPLETED SENSOR AND DOWNLOADING RAW DATA AND REPORTS

1. Use the barcode reader to check that you have the correct participant ID and that the serial number on the sensor matches the one recorded.
2. **You do NOT need to remove the sensor from the biohazard bag**
3. Record in the tracking form the date that the sensor and/or diary were returned from that participant
4. Open CGM software

8.3.7 Glucose Software: FreeStyle Libre Pro



**ALL CGM DATA DOWNLOADS REQUIRE THIS LOCAL SOFTWARE.
THERE IS NO REASON TO USE THE FREESYTYLE WEBSITE FOR THIS STUDY.**

5. Turn the Reader on with the **GREEN** Home Button
6. Click ***Get Sensor Data***
7. Scan the sensor with the reader
 - a. Be sure to scan from the **TOP** of the reader or an error will occur
 - b. Will take a couple of seconds for the reader to read data from sensor
8. Connect the Reader to the computer with the **YELLOW USB** cord.
 - a. Follow the directions on the reader to connect to the computer.
9. The reader asks for a “name” for downloading the data.
 - a. Put your field center as the “First name”
 - b. Put Mesa Participant ID as the “Patient ID”
10. Click **Create Reports**
11. Double check that the participant ID and serial number match those on file in the **tracking form**.
12. Check that the Date matches the period that the participant wore the sensor.
13. Make sure all 3 reports are selected on the left (Daily Patterns, Daily Glucose Summary, and Glucose Pattern Insights)

Home Double check the serial number FreeStyle Libre Pro

Create Reports

Select Reports

- Daily Patterns
- Glucose Pattern Insights
- Daily Glucose Summary

Sensor Profile

WAKE

PATENT ID#: test SERIAL #: 1MH009W3F3W SENSOR DATA AVAILABLE: 2022/03/08 - 2022/03/22

Set Report Parameters

Timeframe

FROM 2022/03/08 TO 2022/03/22

Target Glucose Range

80 - 120 mg/dL

Changes will not be saved to the Reader.

For Glucose Pattern Insights Only: Edit

DAILY EVENTS:

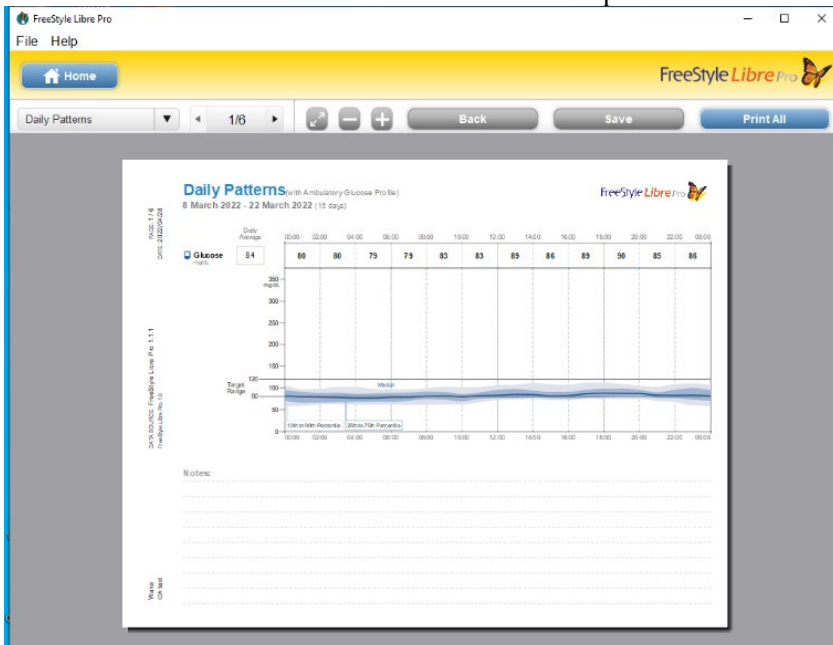
- BREAKFAST 08:00
- LUNCH 12:00
- DINNER 18:00
- BEDTIME 22:00

MEDIAN GOAL: 154 mg/dL

LOW GLUCOSE ALLOWANCE: Medium

Total Pages: 6 Print Reports View Reports

14. Click **View Reports** in the software to view the data downloaded from the sensor.
15. Then click **Save** (name Field Center- PPT#) using (COLU, JOHNS, MINN, NWTN, UCLA, WAKE)
 - a. Save in the folder created for CGM Reports as a CSV file.

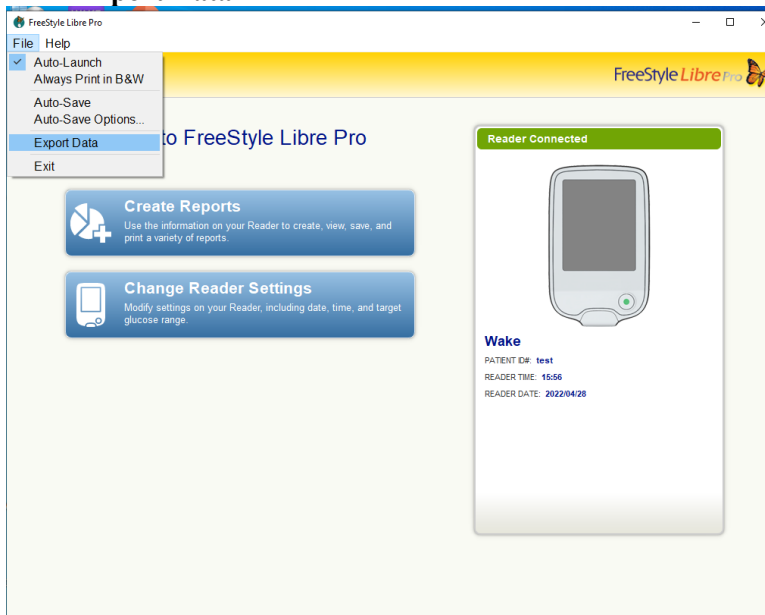


****Please note that this report will save in a PDF format, the raw data report will save as a CSV file. You can name them exactly the same because the file formats are different**

16. Click **Home**

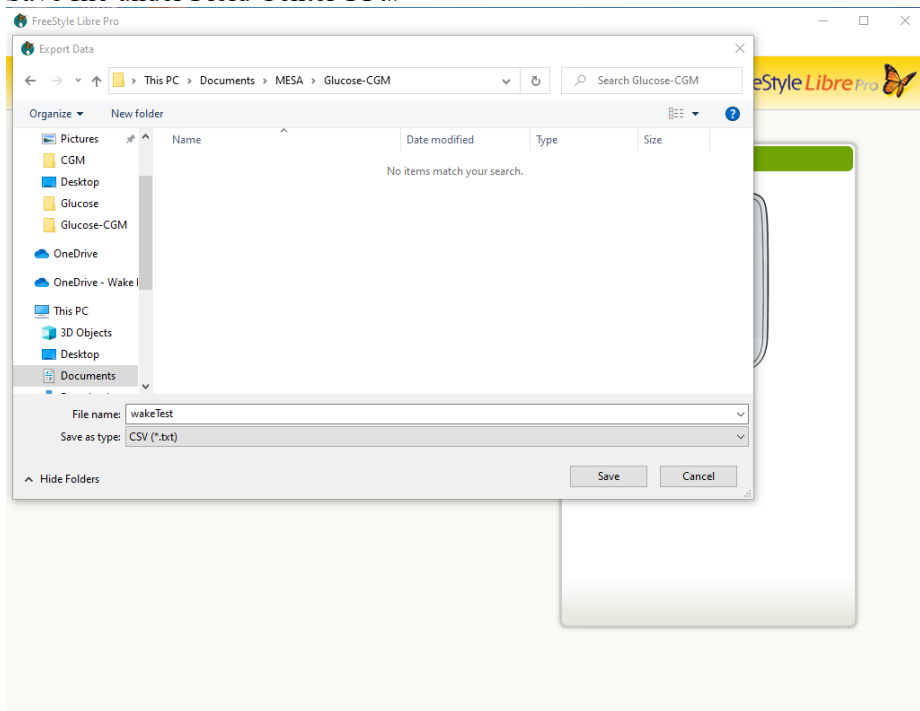
17. Click **File** (top left corner)

18. Click **Export Data**

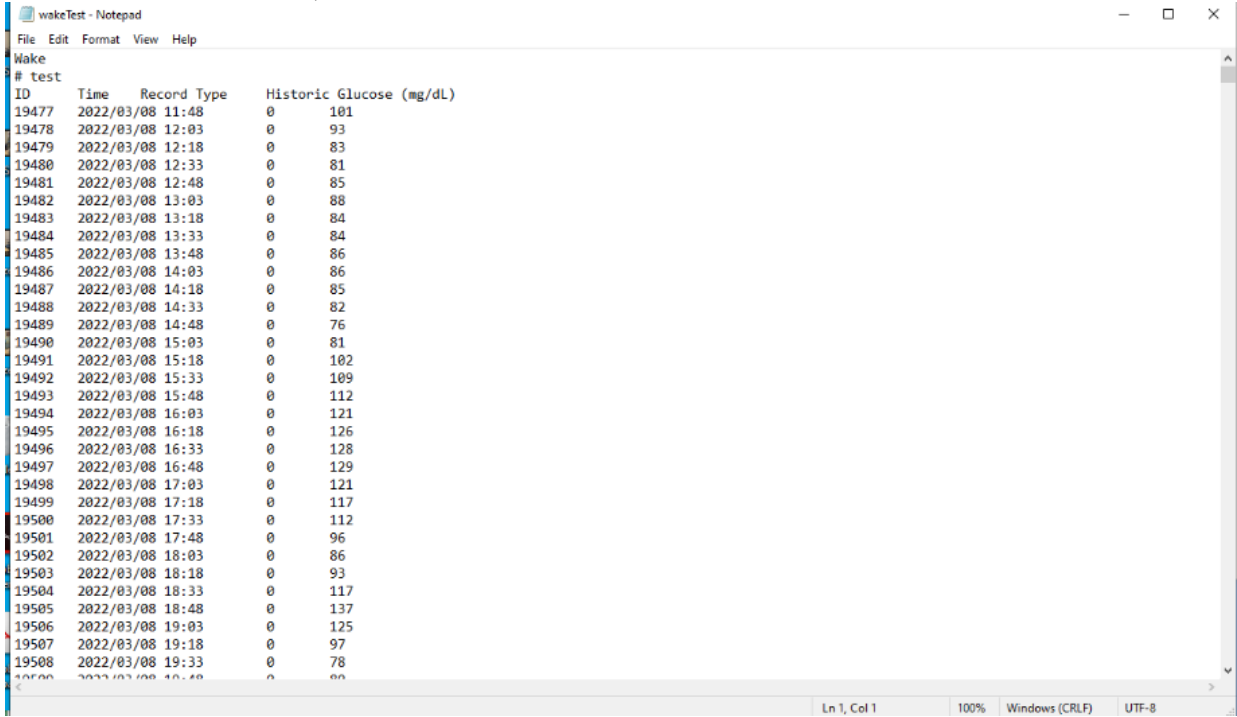


19. Window to Save file will pop up

20. Save file under Field Center-PPt#



21. File will save to the folder, double check that it was saved. File should look like this:



- 22. Place MESA ID label on biohazard bag
- 23. Double check that all data including raw data are stored with correct MESA participant ID
- 24. Make sure that all fields for this device have been filled in the **tracking form**.
- 25. Label the bag that the sensor is in with the participant ID barcode label.
- 26. Place sensor in its bag in storage box.

STORE ALL CGM SENSORS FOR NOW.



8.3.8 Appendix C.1. Script for CGM Removal Call

MESA Glucose Script CGM Removal

(Basic introduction greeting)

Hello, I'm _____ (research team member) with the MESA. Is now a good time to go over the removal of your CGM sensor?

As we discussed when we saw you, your 14-day window for wearing the sensor is over today. Now I'm going to assist you with the removal of your glucose monitor and return instructions. This won't take more than 5 min.

- First, if you are wearing an adhesive patch over the sensor, remove the adhesive patch.
- Now remove sensor from your body by peeling it slowly off from the edge in one smooth motion (as if you were taking off a regular bandage)
- Place the sensor in the biohazard bag
- And place the sensor in its prepaid mailer, along with your diary if you haven't already sent it back.

Now you can seal the return mailer and put it in the mail to us. The postage is pre-paid, so you don't need to have it stamped or anything.

Thank you for participating in the MESA Glucose Ancillary Study!

8.4 Heart Monitor Patch Monitor and Daily Stress Questionnaire

8.4.1 Introduction and Background

Racial and ethnic minority adults are at higher risk for Alzheimer’s disease and related dementias (ADRD). Minority adults are not only exposed to more intense and frequent stressful situations in their daily lives, but they also have fewer resources to manage these situations in healthy ways. Limited resources among these adults may lead to impaired physiologic stress responses (i.e., stress reactivity), specifically dysregulation of the sympathetic nervous system and the hypothalamic-pituitary-adrenocortical (HPA) axis. Our understanding of the impact of stress reactivity on ADRD risk comes from animal studies and experiments in humans using controlled, laboratory stressors. This is a major limitation because laboratory stressors cannot capture the variety, severity, or duration of stressors that individuals face in their daily lives. Thus, there remains a need to more rigorously evaluate relationships of stress reactivity with ADRD risk in natural settings.

We propose to fill this critical gap in the literature by adding more personalized and objective indicators of stress and stress reactivity to a longstanding community-based cohort, the Multi-Ethnic Study of Atherosclerosis (MESA). We will collect repeated measurements of stressful experiences, negative affect (emotions), and heart rate to develop participant-specific markers of affective and autonomic stress reactivity, respectively. Our overall goal is to use these measures to examine associations of the body’s response to stressful experiences with risk of ADRD in a natural setting. We will leverage existing and ongoing repeated assessments of cognitive function as well as ongoing assessments of neuroimaging biomarkers of both vascular and AD pathology including cerebral blood flow (CBF), white matter hyperintensities, A β deposition, and gray matter volume loss. Our proposed study will allow us to begin to disentangle the pathways through which stress exposure and stress reactivity impact vascular dementia pathology and/or AD positivity. Findings will inform stress management interventions and precision medicine initiatives designed to prevent ADRD and/or slow its progression.

8.4.2 Eligibility and Exclusion Criteria for the MESA Stress Reactivity Study

MESA participants will be recruited for the MESA Stress Reactivity Study during Exam 7. Individuals of all ages, race/ethnicity groups and both sexes will be invited to participate, including Spanish and Chinese language speakers. To be included in the MESA Stress Reactivity Study, participants must be willing to wear the Cardea SOLO sensor and answer daily phone surveys for a 7-day period.

Exclusions relevant to the MESA Stress Reactivity study are:

- a. A history of allergy to skin adhesives is an exclusion.
- b. Unwillingness to shave upper left chest (in participants with hair on their chest) is an exclusion.
- c. Implanted electronic devices including pacemaker, nerve stimulator, cochlear implant, or infusion pump are NOT OK and are exclusions.

If the participant has an upcoming MRI, CT scan, or mammogram for their own health care, the heart rhythm monitor should be rescheduled for after those tests have been completed.

8.4.3 Supplies:

Cardea SOLO Sensor Pouch (place sticker on outside of pouch to record MESA ID and application date/time)

- Cardea SOLO ECG Sensor
- Application template
- Skin prep materials: alcohol pad, abrasive sponge, abrasive paper, and gauze pad.
- Paper participant diary: only give participant adhesive remover to take home, rip off and throw out paper participant diary that is included in the pouch.

Participant take-home materials

- USPS Pre-paid bubble mailing envelope

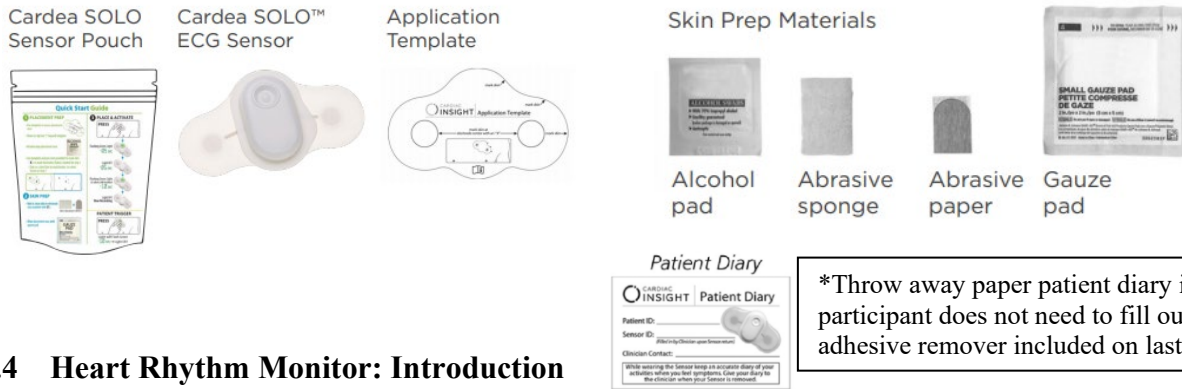
- All About Cardea SOLO Participant Brochure (includes removal and return instructions)
- Daily phone survey reminder postcard

Marker or ballpoint pen

Gloves

Gown (if participant is not wearing loose fitting top)

Razor (if needed for chest hair removal)



8.4.4 Heart Rhythm Monitor: Introduction

The Cardea SOLO sensor is a single-use continuous recording ECG monitor that is much easier for the participant than a Holter monitor. It is worn for up to 8 days at a time, through normal daily routines such as light exercise, showering and sleeping. Each device is brand new for every participant. Participants will have the Cardea SOLO sensor applied by clinic personnel at the end of the Exam 7 day, or as determined by individual Field Center schedules. Participants will answer a daily survey for 7 consecutive days. At the end of the 7-day study period, the participant will return the Cardea SOLO sensor in a prepaid mailing envelope. Neither clinic staff nor participants should throw away any Cardea SOLO sensor; they must all be returned.

8.4.5 Prepare Materials

Sensors come in 5-pack boxes, and the expiration date is marked on the outside of the box. As you prepare sensors for participants, make sure to use the sensor with the soonest expiration date to ensure using sensors before they expire. Do not open the pouch until the participant arrives and you are ready to apply sensor. This will keep the adhesive tacky.

8.4.6 How to Prepare the Skin and Apply the Cardea SOLO Patch

Refer to [Cardea SOLO Application guide and training video](#) for more information.

Skin Preparation

Proper skin preparation is crucial for accurate heart rate recording of the Cardea SOLO sensor. The preparation process has several steps which must be followed to ensure good signal recording and quality. The participant must be standing or sitting upright, with their arms at their sides. The participant should be wearing a loose-fitting top, so that you have good access to the area of skin that needs to be prepared. If the participant is not wearing a loose-fitting top and you do not have access to the upper left chest area, have the participant change into a gown.

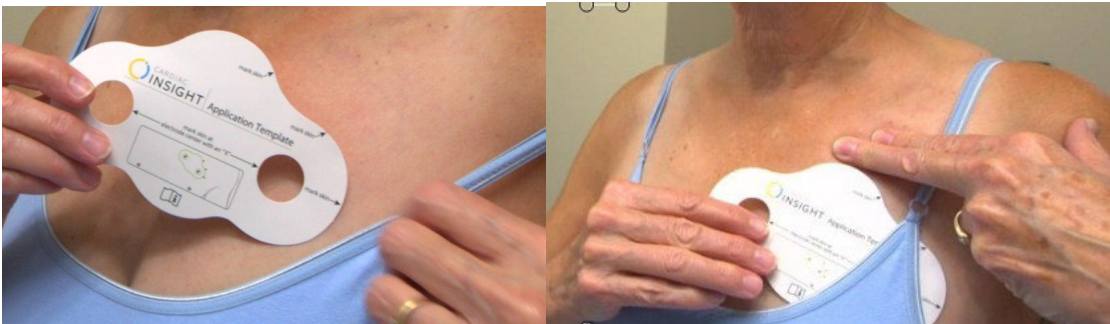
Make sure that the skin in the upper left chest is clean, dry, and free of oils, lotions, powders, and hair. Do not place the sensor over an open wound. Wet shave all chest hair on the participant's upper left chest (from the sternum to the armpit and from the collarbone to just above the nipple line) using the provided disposable razor. See image below for the area that needs to be shaved.



Sensor Placement

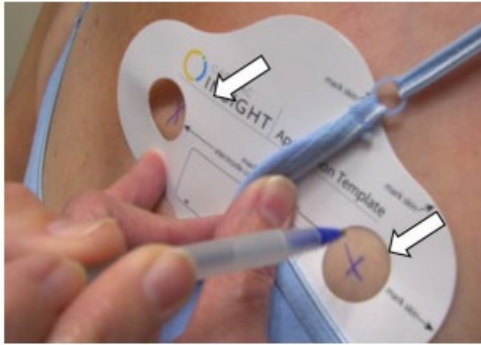
Next, determine placement of the Cardea SOLO sensor on participant's **UPPER LEFT CHEST** using the application template. Placement of the device is the same for both male and female participants. Template should be placed two fingers below the clavicle bone, and above the LEFT breast. The template can be placed on a slight diagonal, angled down toward the armpit, or straight across.

Note: avoid placing the sensor too low and/or over breast tissue or within the armpit area. Also for a participant with a smaller chest area, placing the sensor more horizontal might be more comfortable for the participant.



Next, use the alcohol pad to wipe clean an area slightly larger than the Cardea SOLO placement area. Let the skin dry for 30 seconds.

Place the application template two fingers below the LEFT clavicle. Use a pen or marker to mark these areas on the skin:



A. With the Application Template in place, draw an **X** in each of the two holes.



B. Mark **dots or short lines** along the outside border of the template. These dots will guide your Sensor application. You may also trace around the entire Application Template.

Cleaning and Prepping Skin

Choose one of the two included skin abrasion pads and over each of the two X's, rub skin gently in a circular motion.

- Note: Use only the Sponge, more gauze-like abrasion pad if participant is taking a blood thinner or if they have sensitive skin.



Next, briskly wipe the Cardea SOLO placement area three times with the dry, sterile gauze sponge to remove dead skin cells and debris. Failure to follow these skip preparation steps may cause skin irritation, decrease signal quality, or decrease device wear time.



Skin-Tac

Only use if you know the participant is an endurance athlete or participates regularly in activities that would cause excessive sweating. Wipe Skin-Tac on the placement area after skin prep steps and before placing the sensor. Skin-Tac enhances the adhesive in the sensor to ensure that the sensor stays in place if the participants sweats.



Applying the Cardea SOLO Sensor

Remove the clear plastic liner from the LEFT side of the sensor. Take care not to wrinkle or fold the outer adhesive border when removing the liner. Align the left sticky side onto the left chest—make sure that the grey circular electrode aligns over the X on the lower left of the chest.



Remove the right plastic liner, then place grey electrode over the right X and stick the Cardea SOLO sensor on completely.



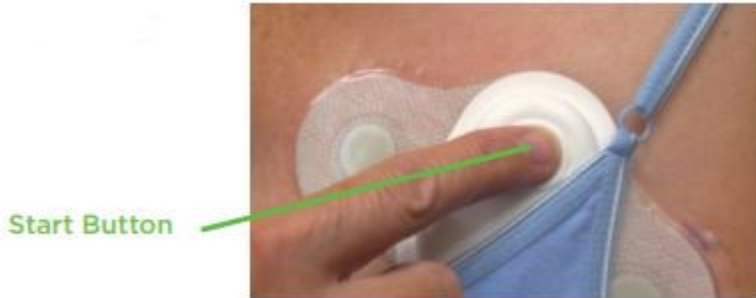
Make sure the Cardea SOLO sensor is firmly attached, lying smooth and flat across the chest. **Firmly press down and smooth out the SOLO Sensor against skin again, including top, bottom, middle and all around the sides.**



Starting the Cardea SOLO Sensor

Make sure participant remains still during the following steps.

Press the Cardea SOLO's round start button once to turn on sensor.



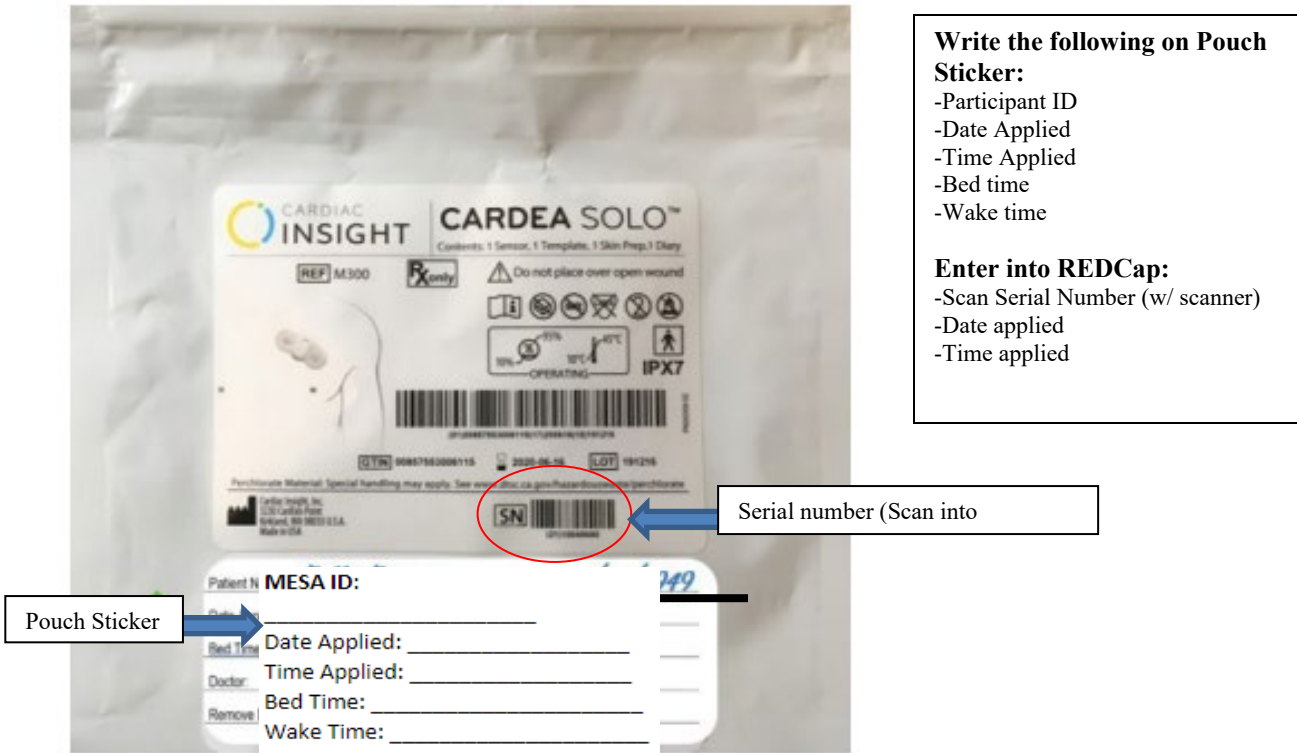
Watch and verify that you see the start-up light sequence below:

- First, a **green** light will flash for about 5 seconds.
- Second, the **green** light will turn off for another 5 seconds.
- Third, the **green** light starts flashing again in the same rhythm of the participant's heartbeat for about 10 seconds.
- Fourth, the **green** light will then turn off completely, indicating that it has started correctly.



Record Start Date and Time

When the green light turns completely OFF, write the Start date and time on the Cardea SOLO Pouch label. Include the participant's usual Bedtime and Wake time, date of birth and participant ID number (in patient name field). No need to fill in Doctor field on outside of pouch. Also record date and time the monitor was activated and serial number of the sensor in the **REDCap Stress Reactivity Completion Form**.



8.4.7 Step-by-step instructions for applying the sensor and what to tell the participant

The participant should be wearing a loose-fitting top with easy access to the **upper left chest**. If the participant is not wearing a loose-fitting top, have the participant change into a gown.

Wash hands and put on gloves.

“I am going to apply your heart rhythm monitor in the clinic today. The battery in the sensor allows it to record your heartbeat for 7 days. The heartbeat information is stored on the sensor, so it’s very important for you to return the sensor at the end of the monitoring period so we can get the heartbeat information.”

First, I am going to prepare your skin.

(If participant has hair on their upper, left chest) I’m going to shave your upper left chest. This ensures that the sensor will remain in place and that the reading of your heartbeat will be accurate. Wet shave all chest hair on the participant’s upper left chest (from the sternum to the armpit and from the collarbone to just above the nipple line) using the provided disposable razor and soap.

Next, I am going to decide where to place the sensor on your chest. I’m going to use this template to find the best place to put the sensor. Find the placement using the application template, two fingers below the clavicle and slightly angled down towards the armpit. Avoid placing sensor in armpit, on sternum, or on breast tissue.

I’m going to use an alcohol wipe to clean your skin. Wipe an area slightly larger than placement area with alcohol wipe and let dry for 30 seconds.

Now I'm going to use this pen to mark the area on your skin where I'm going to place the sensor. Use pen/marker to mark placement on skin using application template.

*Next, I am going to clean your skin really well so that the sensor will really stick to the skin.
Use abrasion pad to rub over each of the two Xs in a circular motion.
Wipe placement area three times with gauze sponge.*

*Now I'm going to remove the backing and apply the sensor. Remove clear plastic one side at a time. First remove clear plastic from the LEFT, and place on participant's left side. Remove clear plastic from RIGHT side next, and place on participant's right side. Firmly press and smooth out sensor against skin
Make sure to press down the outer border of the sensor all the way around.*

Finally, I'm going to activate (turn on) the sensor. Press the monitor's start button. The indicator will blink green, pause, and then flash green in cadence with the heartbeat for 10 sec. Once the light turns off, the monitor will start recording.

**If the light flashes red and green, the sensor did not activate...see troubleshooting section below and try to activate again.*

The sensor is activated and is currently recording your heart rhythm!

Record Start Time

When the green light turns completely OFF, immediately write the activation date and time on the Cardea SOLO Pouch label and in REDCap. Include participant's usual Bedtime and Wake time and participant ID number (in patient name field) on outside of pouch. Use the barcode scanner to scan the sensor serial number into REDCap. The serial number is the smaller, bottom barcode. Click on the serial number field in REDCap and then scan the SN barcode and the serial number should populate in REDCap. The participant will take the Cardea SOLO pouch home with them so please place the pouch inside the USPS take home envelope.

8.4.8 Explain how to care for the Sensor (show inside-left of brochure)

"We would like you to wear the sensor for a full 7 days if possible. The Cardea SOLO Sensor should be worn during all normal daily activities, including showering, and sleeping. However, it should not be submerged under water, so you should not go in a swimming pool, hot tub, or bath during the duration of the study. Keep your showers brief, with your back to the flowing water if possible. Hold the sensor down with your hand when you dry yourself after a shower and just pat it dry. It would be best if you don't take a shower today but wait until tomorrow to give the sensor a chance to really stick to the skin. Soaps and cleansers are ok to use but avoid applying lotion in the placement area.

Heavy sweating may cause the sensor to come loose or fall off, so please try to avoid activity that causes heavy sweating. It is natural over time for the edges to lift slightly or loosen. If they do, push the edges back down. Call us if the sensor falls off or if you have itching that is severe. A little itching is OK. If the sensor does come off before the end of the seven days, make a note of exactly when the sensor came off. Even if the sensor comes off early, we'd still like you to return the sensor in the pre-paid envelope."

8.4.9 Show Participant Instructions

All About Cardea SOLO Guide Brochure

"The sheet has additional information about your sensor."

Show participant FAQs on All About Cardea SOLO Guide Brochure.

"If you have any questions about the heart monitor, please call us at the number shown here."

Show participant contact info on back of brochure.

Button Press—Stressful situations

“If anything happens to you that most people would consider stressful, like an argument, a situation at work or an instance of discrimination, while you are wearing the sensor, push the button on the front. Remain still for about a minute after pressing the button. In addition to pressing the button, when you experience a stressful situation, you will also answer questions about these situations in your daily phone call.”

Take the participant’s finger and show them how to press the button when they experience a stressful situation. They will feel a “click.”

8.4.10 Daily Phone Surveys

“Starting tomorrow, you will be completing a daily phone survey that will ask you some questions about various stressful and supportive experiences you may have encountered throughout your day. We will schedule this automated phone call to call you at the same time each day during the 7-day study. Just to confirm is (participant phone number in REDCap) the best phone number to reach you at?”

Record participant’s preferred phone number into the Stress Reactivity Study Completion form in REDCap.

“Great! And what is the best time for us to schedule your automated daily phone calls? You can choose any time after 4pm. Please choose a time on the hour or half hour (ex: 4pm, 4:30pm, 5pm, 5:30pm, etc)”

Record the date and time of the first phone call in REDCap. Please fill in language and time zone variables too. The date of the first phone call is the day after sensor placement. The time is the participant’s preferred time to be contacted for the daily surveys (make sure it is 4pm or later and enter in 24-hour time). Also, record date/time of first phone call on the Daily Survey Reminder postcard to be sent home with the participant.

“Great! You will receive an automated phone survey at (time participant chose) for seven evenings in a row starting tomorrow. The call will come from 206-775-7589. If you happen to miss a call at the scheduled time, you will receive a call back 15 minutes later. Do you have any questions?” (Show participant reminder postcard.)

If participant is worried about remembering which phone number the survey is coming from, or if they screen their calls, you can let the participant know that the number should show up as “MESA Study” on caller ID on a landline. If the participant is using a cell phone, ask if they would like help programming the phone number 206-775-7589 into their contacts as MESA Study.

Demo Phone Survey

“To make sure you are familiar with how the phone surveys work, we are going to have you complete a quick practice survey today. In just a minute, you are going to call **206-593-2595**, and the survey will ask a few questions that are similar to the one’s you will be answering during the study. You will use the numbers on your phone to answer each question. If you need a question repeated at any time just press 9. Please let me know if you have any questions during the practice phone survey!”

*If the participant has a cell phone, have the participant call 206-593-2595 using their personal phone. If they do not have a cell phone, have the participant call the practice number **206-593-2595** using the clinic phone. Once the participant calls the number, the practice survey will start. Please answer any participant questions that come up. After about 5 minutes of practice questions and if the participant seems to have an understanding of how to answer the survey questions, feel free to end the practice survey by hanging up.*

8.4.11 Removal and Return of the Sensor

“After your 7th and final phone survey on (date--7 days after visit) at (time of phone call), you can refer to this Removal and Return Guide to help you remove the sensor.”

Show participant Removal and Return Guide in brochure while explaining sensor removal. Make sure to fill in removal/return date in the brochure.

“Use the adhesive remover to wipe around the edges of the sensor. Gently lift and slowly peel the sensor from your skin. Hold your skin down with your opposite hand.”



“Cleanse the skin with mild soap and water after removal of the sensor.”

“Then fold the two wings together under the middle and insert your folded sensor back in its original pouch. Put the pouch into the pre-paid US Postal Service bubble mailer and seal. Put the envelope in any US Postal Service blue mailbox or give it to your postman. The postage is already pre-paid.”

Record tracking number of USPS return envelope in REDCap.

Make sure participant has all take home materials:

- 1. USPS Pre-paid envelope with Cardea SOLO pouch inside.*
- 2. Adhesive remover (rip off from paper patient diary and throw paper away. Only give participant adhesive remover.)*
- 3. Cardea SOLO brochure with removal date written inside.*
- 4. Phone survey reminder card with date/time of first phone survey written on the front.*




ersion 12



8.4.12 Fill out the Stress Reactivity Study Completion Form

On the tablet, please complete the Stress Reactivity Study Completion Form:



Exam 7

Stress Reactivity Study Completion Form

Participant ID #:

Acrostic:

Technician ID:

Date: / /
Month Day Year

1. Was the Cardea SOLO sensor applied?

Yes →

No (go to Q2)

Application:

Self-applied

Replacement Sensor (self-applied)

Applied by FC staff

↳ Technician ID: _____

Date applied: / /
Month Day Year

Time applied: : *Use military time*
4:00pm = 16:00.

Serial number: _____

Date for first call:
Day after sensor is placed

/ /
Mon

Preferred language:

English Spanish Mandarin Cantonese

Participant preferred contact time for daily phone surveys (after 4pm): :
Use military time
4:00pm = 16:00.

Time Zone:

Eastern Central Mountain Pacific
 Arizona East Indiana Indiana-Starke Michigan

Participant phone number for telephone surveys:

() -

Tracking number for return envelope:

Enter date and exact time sensor was applied

Use barcode scanner to scan bottom barcode on Cardea SOLO pouch (labeled SN)

Go to Question 3

8/8/2023

Version 12

252



Exam 7

Stress Reactivity Study

Completion Form

2. If no, why sensor was not applied?

- Participant refused
- Unknown
- Other: _____

3. Check-in call at day 1-2 after sensor placed?

- Yes →
 - No
- Date: / /

Month Day Year

4. Reminder phone call to return sensor (8 days after sensor placement)?

- Yes →
 - No
- Date: / /

Month Day Year

5. Was replacement sensor needed due to wear time less than 48 hours?

- Yes →
 - No
- Date replacement sensor mailed to participant:

/ /

Month Day Year

Start a new completion form if a replacement sensor is shipped.

6. Should all future phone calls be cancelled? *Mark yes if a new sensor is sent.*

- Yes
- No

Comments: _____

PRINT FORMS FROM MESA WEBSITE

8.4.13 Clinic Staff Reminder Calls

- 1) Contact participant **2 days after sensor placement**, which should be after they have completed their first phone survey. Record date of this call on the Stress Reactivity Study Completion Form.

“Hello! This is (your name) calling from the MESA study, how are you? I’m calling to check in on how your heart monitor is doing, have you had any issues?”

If the sensor fell off, try to get an estimate of the date and time that the sensor fell off. Record this in the comments section in REDCap. Follow the troubleshooting protocol below and ask the participant if they would be willing to be mailed a new sensor.

If no issues...

“Great! Were you able to complete your first phone survey last night?”

Have you had any issues with the phone survey?”

If no issues...

Great! Do you have any additional questions? Thank you again for being an important part of the MESA study and have a great day!”

- 2) Contact participant **8 days after sensor placement** to remind them of sensor removal and confirm that they are mailing the sensor in the pre-paid mailer—record date of this call on the Stress Reactivity Study Completion Form in REDCap.

“Hello! This is (your name) calling from the MESA study, how are you? I’m calling with a friendly reminder to please remove your heart rate monitor and return in the pre-paid USPS envelope if you have not done so already. Have you been able to remove and return the heart monitor in the mail yet?”

If yes...Great, thank you so much! Do you have any additional questions?”

Thank you again for being an important part of the MESA study and have a great day!

If no... No problem at all! As a reminder you can use the adhesive remover to wipe around the edges of the sensor. Gently lift and slowly peel the sensor from your skin. Then fold the two wings together under the middle and insert your folded sensor back in its original pouch. Put the pouch into the pre-paid US Postal Service bubble mailer and seal. Put the envelope in any US Postal Service blue mailbox or give it to your postman. The postage is already pre-paid. Do you have any additional questions?”

Thank you again for being an important part of the MESA study and have a great day!”

8.4.14 Spanish or Chinese language materials

The Coordinating Center has prepared Spanish and Chinese language versions of all printed materials needed for the heart rhythm monitoring and will mail them to the appropriate Field Centers.

8.4.15 Troubleshooting

Green light sequence does not occur at the start of monitoring.

First, try to press the sensor's button again. It is possible that recording did start, but that the confirmatory flashing green light was not observed. If recording is in progress, the light will flash green in cadence with the heartbeat.

There must be no red light displayed at any time. If you see a red and green light flashing, the device is not making good contact with the skin. Make sure the Cardea SOLO is lying flat on the participant's chest without wrinkles or folds. Smooth all parts of the sensor against the skin. Press the start button again to see if the correct green light sequence occurs.

If the sensor does not activate after smoothing out and ensuring the adhesive is attached firmly, wait 5-10 minutes and try again to activate the sensor. Sometimes the sensor needs to warm up to body temperature if it is too cold.

If the sensor does not activate after a third attempt, remove, and return this sensor to its pouch and apply a new one. Try relocating sensor higher and more midline. Press the start button again to see if the correct green light sequence occurs.

The Sensor comes off after less than 48 hours

If the participant calls to tell you (or you learn) that a Sensor has come off less than 48 hours after activation, and if the participant is willing to try again, ask them to mail the sensor that has come off back to Northwestern using the pre-paid USPS bubble mailer they received. Prepare a new sensor for mailing and send them the replacement sensor in the mail using a USPS pre-paid bubble mailer. Please also include another brochure, reminder card, **an instruction packet for applying the sensor** and another USPS mailer for the participant to mail the sensor back in after they wear it. Record that you have sent a replacement sensor on the Stress Reactivity Study Completion Form. Please notify Lauren Hoffer (lauren.hoffer@northwestern.edu) of the patient ID and the serial # of the sensor that came off whenever you send a replacement sensor.

Also, please answer "Yes" to question 6 (Should all future phone calls be canceled?) on the Stress Reactivity Study Completion Form in REDCap. Then, please fill out a new Stress Reactivity Study Completion Form for the replacement sensor.

Track the USPS mailer that you sent to the participant. It should arrive to their home in ~2 days. Once the package has arrived at the participant's home, please call them to confirm that the participant applied the sensor and inform them that the phone surveys will start again the next day.

"Hello! This is (your name) calling from the MESA study, how are you? I'm calling to see if you've received the new heart rate monitor in the mail yet?"

If yes...Great! Were you able to apply it and write the date and time on the outside of the sensor pouch?

If yes...Great! We are going to start your phone surveys again. Is (participant phone number) still the best number to reach you at? And what is the best time for us to schedule your automated daily phone calls? You can choose any time after 4pm. Please choose a time on the hour or half hour (ex: 4pm, 4:30pm, 5pm, 5:30pm, etc)

You will receive your first phone survey at (time participant chose) tomorrow. You will then receive a call with your phone survey at the same time each evening for 7 days in a row. After completing all 7 phone surveys, you can remove the sensor following the directions in the study brochure and mail it back in the pre-paid mailer. Do you have any questions?

Thank you again for being an important part of the MESA study and have a great day!”

After confirming that the participant has applied the sensor and they have chosen a time for the phone surveys, please fill out the rest of the Stress Reactivity Study Completion Form in REDCap.

*Please email Lauren Hoffer with any questions about replacement sensors lauren.hoffer@northwestern.edu.

Participant loses the USPS Pre-paid mailer

If the participant loses the pre-paid mailer, direct participant to mail sensor to the following address:

Lauren Hoffer
Northwestern University
680 N Lake Shore, Suite 1400
Chicago, IL 60611

If the participant is unable to mail the sensor on their own, please send the participant another pre-paid USPS bubble mailer and direct them to mail the sensor back in that envelope.

Participant loses the adhesive removal packet

If the participant loses the adhesive removal packet used to help remove the sensor at the end of the monitoring period, they can use a little baby oil or Dawn dishwashing liquid on a piece of paper towel to help remove it.

Documenting participant reported concerns

Please note any problems or concerns reported by the participant (such as adhesive/skin reaction, sensor falling off, etc.) on the “Notes” section of the Stress Reactivity Study Completion form.

8.4.16 Technician Certification

Field Center technicians will complete the following to become certified in applying the Cardea SOLO sensor:

- Attend MESA Central Training in January 2022 and Dr. Kiarri Kershaw's presentation on the MESA Stress Reactivity Study. Apply a demo Cardea SOLO sensor on a volunteer and provide all the participant information as directed in the MOP. For those who miss the Central Training session, complete the application of a demo Cardea SOLO sensor on a volunteer, providing all the information as directed in the MOP, with the lead technician at their site. A completed certification checklist for every tech should be sent to the CC for each technician who will be applying the heart monitor. This must be overseen/administered by the lead technician at each site.
- Complete and pass the Cardea SOLO University Skin Prep 101 Knowledge Test

8.4.17 Contact information

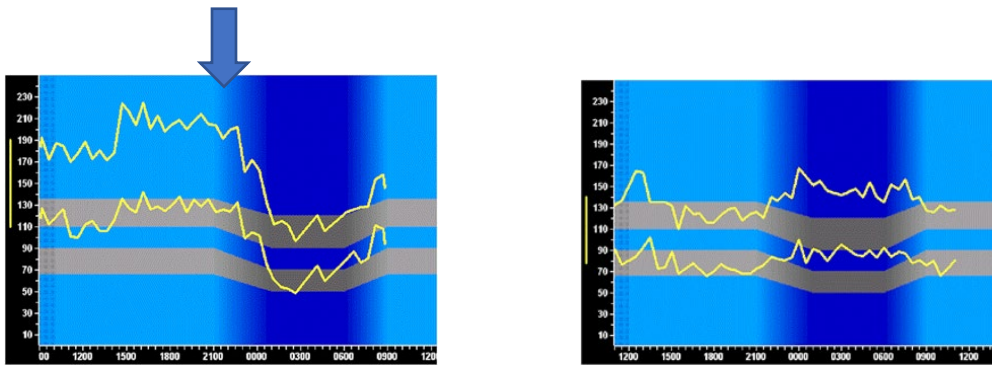
Lauren Hoffer (MESA Stress Reactivity Project Manager)
Northwestern University
680 N Lake Shore, Suite 1400
Chicago, IL 60611
Phone: 312-503-3182
Email: lauren.hoffer@northwestern.edu

Kiarri N. Kershaw, PhD (MESA Stress Reactivity PI)
Northwestern University
680 N Lake Shore, Suite 1400
Chicago, IL 60611
Phone: 312-503-4014
Email: k-kershaw@northwestern.edu

8.5 24-Hour Blood Pressure Monitor

8.5.1 Purpose

24-hour Ambulatory Blood Pressure Monitoring (ABPM) is used to measure blood pressure (BP) at regular intervals over the day and night over a 24-hour period. Multiple measurements yield estimates of average BP that are more reliable and representative than measures made at a single point in time. In research studies, ABPM may better predict outcomes such as stroke and mortality compared to clinic blood pressure. ABPM also provides temporal information about how BP varies with circadian rhythms and behavioral factors that change over the day (eating, exercise, sleep). Normally, BP falls by about 10% or by 10 mmHg during the night compared to the day. For example, the right-hand figure below shows the normal expected drop in BP during the night (starting around 12 AM), while the left shows no drop in BP and even a small rise in the night hours. This pattern would not be apparent with clinic BP.



By comparing the average of measurements made during the day (or during wakefulness) to the night (sleep), it is possible to identify the following abnormal patterns:

- Non-dipping BP: a less than 10% fall in BP during the night compared to the day.
- Reverse-dipping: a paradoxical rise in BP during the night compared to the day.
- Nocturnal hypertension: elevation in average nocturnal systolic (>130) or diastolic (>90) blood pressure.

In MESA, the purpose of conducting 24-hour ABPM is to investigate the role that changes in blood pressure plays in sleep patterns and to assess the role of nocturnal hypertension as a mediating pathway linking sleep disturbance with vascular disease and cognition/Alzheimer Disease susceptibility.

8.5.2 Introduction to the Ambulatory BP Monitoring

The ABPM (OnTrak; Spacelabs) is a lightweight, and portable device validated to measure ambulatory blood pressure. Participants will wear a blood pressure cuff on the non-dominant arm for approximately 24 hours- from the time when it is placed and starts recording until one day later. The cuff will be programmed to inflate every 30 minutes. The monitor must be worn for 24 hours because it is important to collect awake and asleep blood pressures and a minimal number of valid measures for each time period is needed for valid assessment. Note that the device should not be worn in the bath or shower. Participants will be instructed how to suspend readings and put the monitor back on after the participant's bath or shower. ABPM will overlap with the one night of wrist sleep monitoring but not with the polysomnography. The combination of actigraphy data with ABPM data will allow changes in blood pressure to be evaluated during epochs identified as sleep or wake by the actigraph.

8.5.3 Recruitment and Eligibility

The Sleep Ancillary Study will take place at the six MESA sites: New York, NY; Los Angeles, CA; Baltimore, MD; Chicago, IL; St. Paul, MN; and Winston Salem, NC. All participants previously enrolled in MESA Exam 7 will be invited to participate.

Whenever possible, participants will be invited to participate when they attend Exam 7. In some cases, the RA may need to recruit participants over the phone or further consent the participant at the home exam.

Approximately 300 participants will be recruited at each site during MESA Exam 7, aiming to recruit 1800 of the 2000 participants targeted for the MESA Sleep Study. Participants who agree to participate will sign the appropriate consent form during Exam 7.

Inclusion Criteria

- MESA participants attending Exam 7
- Willing to complete the 24-hour ABPM and provide informed consent

Exclusion Criteria

There are no exclusion criteria other than inability to understand the procedure and consent, and inability to attach the cuff to an arm.

Participant Reimbursement

Participants will be reimbursed a total of \$50 for their participation after they complete ABPM (i.e., return device).

Sleep Reading Center Contact Information

Any questions or problems with the protocol can be addressed to:

Our MESA Sleep support email: bwhmesasupport@bwh.harvard.edu

8.5.4 Training and Certification

Initial training will be conducted by video conference call after clinic staff read the ABPM MOP and watch a related video before attending the training. The presentation will include information related to the objectives of the study, the use of the ABPM device, data collection and transmission procedures, and providing follow-up to participants. Centrally trained/certified staff may train other local staff.

The steps for certification of the Research Assistants (RAs) applying ABPM are:

1. Read the ABPM MOP and review the training video
2. A practical exam, demonstrating ability to explain the procedure to participants, proper measurement of the arm and selection of cuff size, proper application of the device, checking comparability with a manual BP read, and completion of forms. A checklist will be used by the trainer to verify that all procedures are performed correctly by the RA
3. Complete and pass a written exam
4. Submit one acceptable practice study that records data over 24 hours on a volunteer- showing a minimal of 20 day and 7-night valid readings.

The certified RA may certify other technicians on-site by observing the procedures and sending one completed checklist, one completed study, and the exam to the SRC.

Maintenance of certification requires completing the procedure with at least one participant every 4 weeks.

The Certified RA will observe another certified technician once every two months for the purpose of monitoring. A checklist will be completed at each supervision and sent to the SRC.

8.5.5 Equipment and Supplies

Each site will receive 4 ABPM devices with associated supplies and cuff covers (devices may be reallocated if needed should recruitment differ from expectation). Before using a device on a MESA participant, each device should be used on

one staff volunteer to ensure it is appropriately recording. In addition, all staff distributing ABPMs are encouraged to wear the device for 24 hours to enhance understanding of the experience of wearing the device.

Equipment:

- The ABPM (OnTrak; Spacelabs), which includes the monitor, 2 belts, and a carrying case.
- Cuffs: 4 sizes, with tubing attached to each cuff
- Disposable cuff covers: 2 sizes
- Tubing support clip
- USB cable for connecting the OnTrak to the computer
- Sentinel 11.5 software with ABPM software module kit containing 3 USB drives

Supplies:

- Disinfectant wipe for cleaning the device and cuffs after each use
- Mailing labels
- AA alkaline batteries
- Mailers to use to return the device (per site specific approaches)
- Measuring tape to measure arm and determine cuff size
- China marking pencil for marking arm for cuff placement

Forms:

- [Participant Instruction](#)
- [24h ABPM Home Tracking and Alert Form](#)
- [24h ABPM Accountability Log](#)
- [Participant Diary](#) (given at the time of the actigraphy)

8.5.6 Method

8.5.6.1 Setting up the ABPM Device in the Clinic

In the clinic, prior to making the home visit, it is important to initialize the device and bring two fresh AA alkaline batteries. Detailed instructions for device initialization can be found in an Appendix to this manual. When initializing the device, you will enter the following information in the Sentinel software “Add Patient” screen:

- Participant ID—do not enter any identifying information (PHI). Please only enter the MESA participant ID number. The participant’s study ID number will be entered into the “Patient ID” field. This is a required field.
- ABPM unit ID will be entered into the “Second ID” field. The SRC will work with each site to assign unit ID that will be associated with the serial number of each OnTrak device.
- Staff member ID for the staff member initializing the device will be entered into the “Third ID” field.

After participant information has been entered, you will initialize the recorder using the MESA Sleep Protocol on the “Configure ABP recorder” screen. The MESA Sleep data collection protocol will be preconfigured and selectable from a dropdown menu within the Sentinel software and will be used to initialize all devices for the MESA study. The protocol will initialize the device with the following collection parameters:

- The frequency of recording: every 30 minutes
- The time for day readings: 0800 with Tone set to audible to alert when a reading will start
- The time for night readings: 2200 with Tone set to silent

Review the forms needed for the visit. If the arm had been measured for a clinic BP, record that circumference in the Blood Pressure Home Tracking form (Field 3).

8.5.6.2 Home Visit Procedures

As part of the actigraph data collection, the RA will call the participant two or three days after the initial home visit (when actigraphy recording began) to reinforce instructions on using devices and completing questionnaires/diaries. An additional call may be required to remind the participant of the ABPM home visit date and time, or to confirm whether the device was mailed.

Explaining the procedure

Consent participants to the procedure if needed.

General guidelines for working in the home setting:

- Call the participant prior to the visit to confirm the visit and let them know to expect you (your team) and check on any specifics in accessing the participant's home. Remind the participant to wear loose fitting clothing with short sleeves if possible- bedclothes with short sleeves are ok if the visit is in the early evening. Ask the participant to avoid exercising heavily or going swimming the day of monitoring.
- Dress professionally but not conspicuously; wear your professional ID badges
- Introduce yourself and ask to find an area where the set up can take place—i.e., an area with a table or surface to place the equipment and a chair for the participant to sit comfortably and without distractions
- Review the procedures with the participant, getting consent if not already obtained
- Bring a chuck, towel, or other material to place on the surface you will use to set out equipment- this shows respect for the participant's furniture and provides a clean surface to work from.

Explanation of procedures/consent: The RA will reinforce what had already been explained during recruitment and highlight what to expect for this visit. The RA could use this script or a similar one when initiating the home visit:

This visit will take between 30 and 45 minutes. We will first review the use of an ambulatory blood pressure monitor and how information collected from it is used. We may recheck your arm size to select the blood pressure cuff that fits you best. We then will fit the ABPM cuff on your arm and check manually two blood pressure readings- to make sure the device is working correctly. If needed, we will adjust the cuff and repeat the blood pressure check. We will show you how to remove the cuff and device and stop recording if needed. We will show you how to carry it and sleep comfortably with it. We will talk about how to return it.

Review of the ABPM with the participant

Review why we collect ABPM:

- Three measures in clinic are not enough to show how BP changes over the course of the day and night.
- Multiple measurements improve the “representativeness” of the information and can show whether there are large blood pressure swings as we do our daily activities.
- Measuring blood pressure at night allows us to know if there is a normal reduction in blood pressure at night, or abnormal increases related to sleep problems or other factors.

Record initial information

First, confirm whether the ID and acrostic displayed on the [24h ABPM Home Tracking and Alert form](#) belong to the participant. Then, record ABPM monitor number and date of the visit. Record time of attachment later when ABPM is attached.

Ascertaining which arm to use for ABPM

Measure the arm circumference if this had not been previously measured during the clinic exam within 3 months of the ABPM exam. Otherwise, use the recorded arm circumference from the clinic exam.

ABPM cuff will be placed on the non-dominant arm. Ask participant: Which hand do you use most for writing and prefer? Choose the other arm, which will be the non-dominant arm.

Ascertain whether there are any contraindications to using that arm for ABPM (prior surgery with lymphedema, surgical shunt), etc. If contraindications, use the other arm.

Record on the [24h ABPM Home Tracking and Alert Form](#) (field 5), what arm you are using for the blood pressure readings.

Cuff size selection

Measuring arm circumference:

This procedure should be performed if the arm circumference had not been measured at the clinic exam within 3 months of the ABPM exam. The measurement of arm circumference during the ABPM study should be like the measurement of arm circumference made during the [seated BP of the Core MESA Exam](#). Ask the participant to sit or stand holding their forearm horizontal, i.e., parallel to the floor. Using a non-distensible metric tape, measure the arm length of the non-dominant arm from the top outer edge of the bony protuberance of the shoulder to the bony prominence of the elbow. Mark the midpoint on the back surface of the arm using a black or blue China Marker (making a small dot). Ask the participant to relax the arm alongside the body and then draw the measuring tape around the arm at the midpoint, keeping the tape horizontal and perpendicular to the long axis of the arm. Record the arm circumference in cm on the [24h ABPM Home Tracking and Alert Form](#) (field 3).

Select the cuff size for the ABPM using the table below:

Arm Circumference	Cuff size
17-26 cm	Small adult
24-32 cm	Adult
32-42 cm	Large adult
38 – 50 cm	Extra large

If the arm circumference measure overlaps the two cuff sizes, choose the larger cuff, i.e., if the arm circumference you obtained is 32 cm, use the large adult cuff.

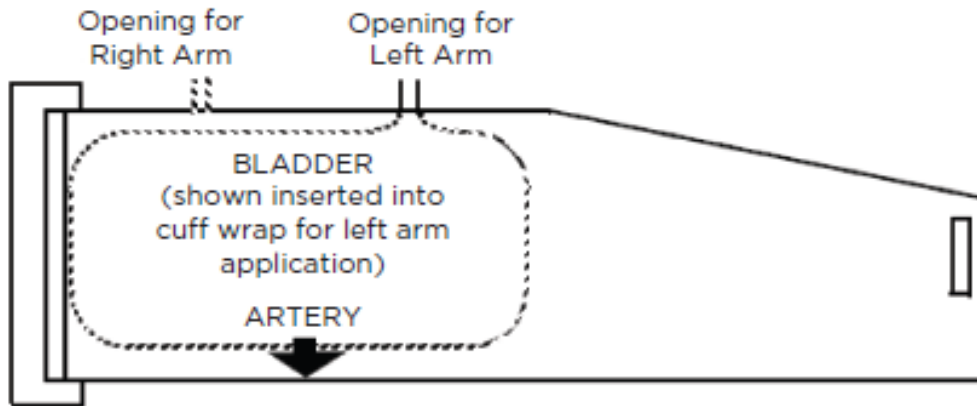
Select the disposable cover for the ABPM cuff:

We will use a disposable cover for the cuff that is placed over the arm, that the ABPM sits on. The cover is disposable and makes wearing the ABPM cuff more comfortable and keeps the ABPM cuff clean.

- Large cover for the Extra large and Large Adult
- Small cover for Small Adult and Adult

Cuff placing for the ABPM

The cuff will be applied on a non-dominant arm with the palm facing up. If the non-dominant arm cannot be used, use the other arm. Once you have determined which arm will be used, check that the bladder is inserted correctly into the cuff wrap. If the right arm is used, the bladder is inserted so that the tubing extends from the right side of the cuff wrap when the cuff is placed on the arm. For left arm use, the bladder is reversed and the tubing comes out of the left side of the cuff wrap when the cuff is placed on the arm. Please refer to the image below for proper bladder configuration.



Place the non-dominant upper arm through the cuff cover so it covers most of the upper arm and extends below the elbow.

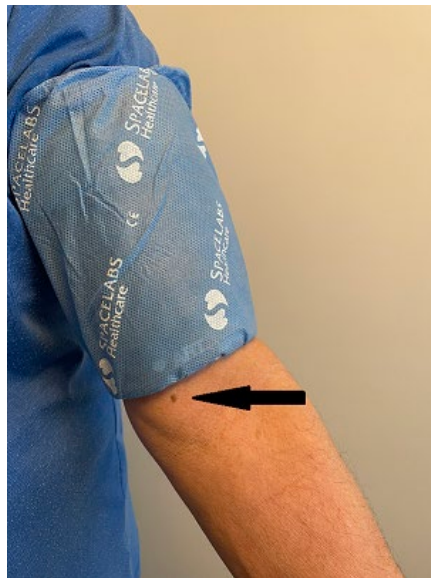


The ABPM will measure blood pressure by sensing the pulsation of blood through the brachial artery. Find the brachial artery by gently but firmly placing two fingers below the creases in the elbow- with the arm extended- finding the pulse maxima in this spot. Put a dot over the spot- show this spot to the participant and emphasize that this is the landmark to be used when replacing the cuff (the white arrow on the cuff should be above this dot).

The cuff selected to be appropriately sized should be wrapped over the cover, placed about 2 cm above the crease in the elbow, with tubing going up toward the shoulder. The arrow printed on the cuff must point at the dot placed approximately in center of the participant's arm at the bend over the brachial artery. In the image below, a black dot has been drawn on the cuff cover for illustrative purposes to indicate the placement of the black dot on the arm beneath the cuff cover. Wrap the cuff firmly but not uncomfortably tight, so two fingers can be inserted below the cuff.



Bring the tubing behind participant's neck and down the other side of the front of participant's body toward the waist. Fold the lower half of the cuff cover up and over the cuff. The blood pressure cuff will now be fully wrapped inside the cuff cover as show in the below image. Note that the black arrow indicates the location of the small black dot that was placed on the participant's arm.



Next show the participant how the cuff connects to the recording device.

Click the tubing into the OnTrak monitor so you hear a click and insert two AA alkaline batteries. You may now manually check blood pressure values to make sure the device is working correctly (see "Initiating the ABPM recording"). Record first and second manual blood pressure reading from the OnTrack on the [ABPM Home Tracking and Alert Form](#) (field 5) and use the second reading to determine alert (field 6.1). Proceed to place the OnTrack monitor into the case, and then on either the provided belt or shoulder strap

To place the device on the grey belt for the participant to wear around the waist, simply feed the grey belt through the loop on the back of the black OnTrack monitor case. Secure the belt around the participant's waist as shown in the image

so that it fits securely but is not uncomfortably tight. The belt is secured using the two black D-rings attached to the end of the belt.



The participant can also wear the device over the shoulder using the black shoulder strap. Attach the Velcro at each end of the shoulder strap to the Velcro inside each side of the ABPM case. Adjust the strap so the device is at a comfortable level near the participant's waist and place the shoulder strap around the neck so that the device is worn on the opposite side of the blood pressure cuff.



Wearing the ABPM during sleep:

To minimize sleep disruption from noise that occurs during the inflation of the cuff, ask the participant to remove the device from the pouch, place on a folded towel on the mattress and then cover with a pillow (or towel) to muffle the noise. If needed, the device can be also placed on a side table or nightstand close to the bed (using a towel and pillow).

Initiating the ABPM recording

Insert two AA alkaline batteries. To power on the monitor, hold down the round Action button located on the right side bottom front of the monitor for 3 seconds until a beep is heard. The monitor will switch on within 7 seconds. Make sure the “Start New Test” option is highlighted on the device screen. When the device is powered on, it is in “Office Check” mode. This allows the operator to obtain up to 5 manual blood pressure readings before the 24-hour data collection begins. Push the round Action button to inflate the cuff and start readings. When the Action button is pressed, the monitor will beep and count down before inflating the cuff and taking a reading. Take two readings, 60 seconds apart. Note that the monitor will enforce a 30 second pause between readings. Between readings, raise the participant’s arm for 15 seconds.



When ready to take the second reading, press the Action button. Record the first and second readings on the [24h ABPM Home Tracking and Alert Form](#) (Field 5). Note that you can only attempt 5 readings with the ABPM monitor before the 24-hour readings start.

After the second successful reading is obtained, the device must be taken out of “Office Check” mode for the 24-hour recording to begin. To exit Office Check mode, press the Action button to start a reading. When the cuff begins to inflate, press the Action button to interrupt the reading. An error message reading “EC03” will display on the screen to indicate that the reading was cancelled. No action is needed after this message is displayed. Place the monitor inside the pouch, and the OnTrak will begin recording blood pressure measurements at the next scheduled reading time.

Suspending Readings

If at any time the cuff does not deflate or becomes uncomfortable, press the Action button on the monitor to stop the blood pressure reading. The cuff should deflate until the next scheduled reading time. If the cuff does not deflate, remove the cuff, and follow the instructions to power off the monitor. These steps should also be used if participants need to temporarily suspend blood pressure readings for the purposes of taking a bath or shower. (also see Participant Instructions).

To Power Off:

Press and hold the Action button for 3 seconds.

A message will appear on the monitor display asking you to confirm a decision to power the unit off.



Press the Down arrow button once to highlight the “Yes” option.

Press the Action button once to confirm the selection, and the unit will shut down. Wait for the cuff to deflate.

Participant Diary

Participants will be asked to use the wrist actigraph and complete a [Participant Diary](#) (log) that includes the night of ABPM monitoring. If the participant is unwilling or unable to use the actigraph the night of ABPM, then they should be asked to complete the Diary alone for the day of ABPM recording to provide information on reported sleep and wake times.

Participant Instructions

Recruiting participants to the study

Sample text that the RA can use when recruiting the participant to the ABPM study:

We invite you to participate in a sub study called the MESA Sleep Study. [If appropriate: As you may recall, you participated in the MESA Sleep study a few years ago]. This part of the MESA Sleep study investigates the effects of blood pressure patterns on heart disease and brain health. Blood pressure may vary a lot of the day and night—therefore a single blood pressure measurement in clinic alone may not tell us all we need to know about the level of blood pressure over the day and night. Measuring blood pressure multiple times during the day and night may help us understand which people are at most risk for problems related to high blood pressure, such as stroke. Identifying differences between night and day blood pressure also may help us understand how sleep problems influence blood pressure. If you agree to participate, we will schedule a home visit that will take about 30 minutes to attach the blood pressure device. This blood pressure monitor measures your blood pressure every 30 minutes. You also will be asked to use the wrist actigraph and complete a Diary. You will wear a light blood pressure cuff and carry a small box on your waist for 24 hours, including sleep. You will take it off to bathe or shower. The blood pressure monitor could be uncomfortable, and the blood pressure cuff will cause pressure when it inflates on your arm like what you feel when your blood pressure is checked in clinic. Very rarely, the blood pressure cuff can cause bruising in the arm. You will fill out a form to record your sleep times. After you return the blood pressure monitor, we will reimburse you \$50 for this part of the study. We ask that you don't exercise heavily or go swimming the day of monitoring. After the blood pressure information is analyzed, we will provide you a report that you -and if you wish- your doctor can use to understand your day and night blood pressure.

Participant Instructions for Using the ABPM

Before ending the visit, the RA should review all aspects of the monitoring—reminding the participant how to place the device, the duration of recording, how to walk/sleep with the device, how to remove it for bathing, etc., and how to return the device and who to call with questions or concerns. Use the Participant Instruction sheet as a reference. After reviewing with the participant, ask the participant to describe what they understand- as a check of how well YOU explained things. Make sure they understand how to replace the monitor.

The participant also should be reminded to continue completing the Participant Diary and using the wrist actigraph until after the ABPM recording is completed. Use this visit to also reinforce the use of the Participant Diary. Ask the participant to show you what has been filled out so far and reinforce correct completion of the diary.

Below is a script that RA can use to explain the data collection procedures to the participant during the home visit.

The ABPM will begin measuring blood pressure after the blood pressure cuff is placed and the unit is powered on and will continue recording for the next 24 hours. You should carry the ABPM with you all day and night for this time period.

Before the machine starts to inflate for daytime readings, there will be a beep. Please sit down if possible and don't cross your legs, place your arm at the level of your chest, and rest (if you can't sit, please stay still standing). Please do not talk, eat, or drink while the cuff is inflating and try to stay still for the few minutes that it takes for the machine to take your BP. When the cuff gets tight and/or the tone sounds, STAY STILL and KEEP YOUR ARM STILL until the cuff is loose again. For nighttime readings, the monitor will not beep before the cuff inflates to measure blood pressure.

When you go to bed, please remove the monitor from its pouch and place on a folded towel on your mattress. Then put a small pillow (or another towel) over the monitor to muffle the sound. When you wake up, please put the monitor back in its pouch and attach the pouch to the belt or strap. Continue wearing the monitor until XXX. You can then take it off and place it in the box to pick up or mail back. Please put all supplies- belt, strap, monitor- in the box.

If the cuff does not deflate, remove the cuff, turn off the device, let the cuff deflate, reattach the cuff, and turn the device back on by pressing the Action button for 3 seconds. If at any time the cuff becomes uncomfortable while it is inflating, press the Action button to stop the blood pressure reading. The cuff should deflate until the next scheduled reading time. Follow the instructions for powering off the device if you need to temporarily suspend blood pressure readings to take a bath or shower. After your bath or shower, replace the cuff and then press the Action button for 3 seconds to turn the monitor back on and resume readings. If you have problems replacing the cuff or it does not seem to be working, please call your clinic staff number.

While wearing the monitor, check that the tubing from the cuff is not twisted or bent.

Please, treat the equipment gently. Please, no hard knocks, bumps, or drops. And please do not bathe or shower with the device attached to you.

Common questions and answers:

Do I need to do anything different because I'm being tested? No. Because the test is being carried out to find out what your normal daily blood pressure is, please continue your normal routines. However, you should avoid heavy exercise such as going to the gym or running.

What clothes should I wear for the appointment? You should wear loose clothing, preferably a short-sleeved top. The monitor will be fitted underneath your top. You may wear loose bed clothes with short sleeves if you don't plan to go out after the visit.

Do I have to sleep with the monitor on? Yes, this will help us understand what your blood pressure is doing while you are sleeping. However, the recorder can be placed next to you on the mattress or a bedside table while you are sleeping.

May I take a bath/shower whilst undergoing monitoring? It is best not to shower or bathe during the day that the blood pressure monitor is used. If you take a bath or a shower you will need to take off the monitor and cuff as these are not waterproof and you must not get them wet.

May I exercise with the monitor on? Please try not go to the gym or exercise heavily while the monitor is attached. A gentle or brisk walk is fine.

Sites may add additional information. Participants who agree to participate will sign in the appropriate place in the consent form.

Participants should be provided the instruction brochure before leaving the visit.

Let them know they will get a feedback letter with results of the monitor.

8.5.6.3 Removal and return of ABPM

Participants should be provided instructions on when and how to return equipment, identifying the time when the ABPM can be removed and the dates that it should be mailed or otherwise returned. If the ABPM device was placed to overlap the last day of actigraphy, the participant could mail both the ABPM device and the actigraph along with the [Participant Diary](#) in one mailing.

- There is flexibility for when and how the ABPM device and accessories should be returned after the 24h wear period, and sites can plan for return based on what day the monitoring will finish. For participants who wear the monitor early in the visit, sites might want to have the device returned right away so they can download data and prepare the ABPM for another participant visit. If the ABPM device is worn late in the visit, it can be returned along with the actigraphy device.
- If the ABPM device is shipped, it should be shipped in a rigid shipping box and not in an envelope (even if padded). FedEx Small Box (dimensions: 10 7/8” x 1 1/2” x 12 3/8”) and UPS Express Small boxes are examples of appropriately sized boxes. These supplies are usually provided at no charge to customers with shipping accounts, and we have successfully shipped many monitors in this size box.
- Ensure the ABPM unit is powered off before placing the unit inside the shipping box.
- The ABPM unit should be placed inside the black carrying pouch before placing in the shipping box to help protect it during shipping.
- Remember to include in the shipping box the cuff with tubing, carrying strap/support belt that attaches to the carrying pouch, and tubing support clip (if used).
- Insure the box for \$2400.

Tracking participant data and equipment

Clinic staff will keep a log of the participants who have received a device and the dates on which collection will occur using the [ABPM Accountability Log](#). Please enter the device ID for each ABPM OnTrak device as it is distributed, recording return dates, any problems, or service required.

Receiving ABPM monitor and transferring data

When the participant returns the device, clinic staff will review all the participant's material and transfer data as detailed in section 8.5.10.

8.5.7 Alerts and Referrals

As in the MESA Exam 7, we will use the 2004 Report of the Joint National Committee on detection, evaluation, and Treatment of High Blood Pressure (JNC 7) to define categories of blood pressure criteria for alerts and referrals.

8.5.7.1 Alerts and Referrals for the Manual Reading

At attachment of the ABPM monitor, the cuff will inflate twice. Record the first and second BP readings. Use the 2nd reading to determine an alert. Participant should be seated for these manual readings.

BP values	Alert Level	Action
1. Systolic blood pressure > 210 mmHg OR Diastolic blood pressure > 120 mmHg	Immediate referral	<i>Notify immediately</i> to the PI or health care provider.
2. Systolic blood pressure 180 - 210 mmHg OR Diastolic blood pressure 110 - 120 mmHg	Urgent referral	Inform the participant to contact their health care provider within one week

Record the action taken in field 6.a on the [24h ABPM Home Tracking and Alert form](#) and write down any comment of action taken including names of professionals approach (PI/health care provider) for the immediate alert, and date the participant was notified for an urgent alert.

8.5.7.2 Alerts and Referrals for the 24h ABPM

This measure is from using the ABPM device after completion of the study and site has transmitted the data to the CC. After the Sleep Reading Center reviews this data, it will report the average BP of the 24h ABPM.

BP values	Alert level	Action
1. 24 hr Average Systolic blood pressure \geq 180 OR Diastolic blood pressure \geq 110 mmHg	Urgent referral	Inform the participant to contact their health care provider as soon as possible to discuss follow-up

Record when alert was received and when participant has been notified in field 6.b on the [24h ABPM Home Tracking and Alert Form](#) and write down any comment of action taken.

8.5.8 Calibration of ABPM Monitors

Calibration checks should be performed at least once a year.

Complete the MESA ABPM Calibration Log form for all your ABPM devices at your site and send the document via email to the SRC to Emily Kaplan (ekaplan1@bwh.harvard.edu), and cc Dan Mobley (dmobley@bwh.harvard.edu), and Cecilia Castro-Diehl (ocastro-diehl@bwh.harvard.edu).

Procedure:

- Take two automatic readings on the OnTrak per the ABPM MOP. Record the first and second readings on the MESA ABPM Calibration Log.
- Take one reading on the calibrated Onron or Dinamap machine used for MESA Exam 7 and record the reading on the MESA ABPM Calibration Log
- Write any comment on the Log

8.5.9 Form Completion

Following forms should be completed following the guidance provided by the CC

1. [24h ABPM Home Tracking and Alert Form](#)
2. [Participant Diary](#)
3. MESA ABPM Calibration Log

8.5.10 Appendix A: Participant Instructions

8.5.10.1 24-hour Blood Pressure Home Monitoring Instructions

To understand your day and night blood pressure patterns, we ask that you wear a blood pressure cuff for approximately 24 hours- from the time it is placed until one day later. Please don't remove the cuff until _____. The cuff will inflate about every 30 minutes.

Some tips while wearing the monitor:

1. During the day, before the monitor starts to inflate, there will be a beep. Please sit down and don't cross your legs (if standing), place your arm at the level of your chest, and rest (don't talk during cuff inflation). At night, there will not be a beep before the monitor start to inflate.
2. When the cuff gets tight and/or the tone sounds, STAY STILL and KEEP YOUR ARM STILL until the cuff is loose again.
3. While wearing the monitor, check that the tubing from the cuff is not twisted or bent.
4. Treat the equipment gently. Please, no hard knocks, bumps, or drops.
5. Keep the equipment dry. Remove the cuff when showering or bathing.
6. Try not do to do heavy physical activity during the day you wear the monitor.
7. During sleep, take the monitor out of its pouch, place on a folded towel, and cover the monitor with a pillow or towel (to muffle the sound). You may place the monitor under a pillow or at the side of the bed.

Stopping a Reading or Pausing Readings:

If at any time the cuff does not deflate or becomes uncomfortable, press the Action button to stop the blood pressure reading. The cuff should deflate until the next scheduled reading time. If the cuff does not deflate, remove the cuff, and follow the instructions below to power off the monitor. The following steps should also be used if you need to temporarily suspend blood pressure readings for the purposes of taking a bath or shower.

To Power Off:

1. Press and hold the Action button for 3 seconds.
2. A message will appear on the monitor display asking you to confirm your decision to power the unit off.
3. Press the Down arrow button once to highlight the "Yes" option.
4. Press the Action button once to confirm the selection, and the unit will shut down. Wait for the cuff to deflate.

To Power On and Resume Readings:

1. Put the cuff back on your arm as described below in "Replacing the Blood Pressure Cuff."
2. Press and hold the action button for 3 seconds to turn the unit back on. An audible beep will confirm the unit has powered on.



3. Wait approximately 10 seconds and then press the action button. The cuff will inflate, and the monitor will take a blood pressure reading.
4. The unit will automatically resume readings.
5. If the unit did not power on or would not take a blood pressure reading, please contact a study staff member for instructions.

Replacing the Blood Pressure Cuff after removing it:


1. Hold your arm out with your palm facing up.
2. The cuff will be inside a soft cover and should not be removed from the cover. Wrap the cuff around your arm with tubing pointing up towards the shoulder.
3. Point the arrow on the cuff toward the center of your arm near the bend inside of your elbow as shown in the image (and over the spot that the MESA research assistant showed you). Tighten the cuff so that it is snug and stays in place but is not uncomfortably tight.
4. Bring the tubing behind your neck and down the other side of the front of your body toward the waist.
5. Hold down the round Action button located on the front of the monitor for 3 seconds until a beep is heard. The monitor will switch on within 7 seconds.
6. Push the round Action button to inflate the cuff and start readings



Remember: We want **awake and asleep** blood pressures, so it is important to wear the monitor for **24 hours**. **HOWEVER, do not wear the unit into the bath or shower. Follow the instructions for suspending readings, and please remember to put the monitor back on after your bath or shower.**

When you are finished wearing the monitor, take the monitor off and follow the instructions to power off the monitor. Follow the instructions provided by the study staff to return the monitor.

8.5.10.2 24h ABPM Home Tracking and Alert Form



Exam 7
24h ABPM Home
Tracking and Alert
Form

Participant ID #:

Acrostic:

Technician ID:

Date: / /

Month Day Year

Monitor number:

1. Record date and time at Attachment

Date: / /

Month Day Year

Time: : AM PM

2. Record date and time at Removal

Date: / /

Month Day Year

Time: : AM PM

3. Arm circumference: . cm

4. Cuff size:

Small adult (17 - 26 cm)

Adult (24 - 32 cm)

Large adult (32 - 42 cm)

Extra large (38 - 50 cm)

5. ABPM reading at attachment (check the arm used for final attachment):

Select one: Right arm Left arm

1st reading

SBP DBP Pulse

2nd reading

SBP DBP Pulse

Note: The ABPM monitor will inflate the cuff twice at attachment. Record first and second reading. Use the 2nd reading to determine alert in next section.


6. Alerts and Referrals

6.1. Manual Blood Pressure using ABPM device (awake, seated, 2nd reading)

Blood Pressure Values	Action
1. Systolic blood pressure > 210 mmHg -OR- Diastolic blood pressure > 120 mmHg	Immediate referral to the PI or a health care provider? <input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> N/A Date: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
2. Systolic blood pressure 180-210 mmHg -OR- Diastolic blood pressure of 110-120 mmHg	Was the participant notified? <input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> N/A Date: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

Comment of action taken: _____

PRINT FORMS FROM MESA WEBSITE



Exam 7
24h ABPM Home
Tracking and Alert
Form

6.2. Blood Pressure using ABPM device (average 24h BP)

Alerts Reporting:

Date study report received from the SRC: / /

Month Day Year

Was the alert reported to the Participant?

Yes No

Date: / /

Month Day Year

Comment: _____

MESA Exam 7 | 24h ABPM Home Tracking and Alert Form | Interviewer-Administered | v1

3/21/2022

Page 2 of 2

8.5.10.3 24h ABPM Accountability Log

24H ABPM Accountability Log

Clinic Site #	
Page #	

MESA Subject ID	ABPM Serial Number	Date Device Given to Participant	Staff ID (provided device)	Date Device Returned	Staff ID (received device)	Comments																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												
		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		<table border="1"> <tr> <td></td><td></td><td>/</td><td></td><td>/</td><td></td><td></td> </tr> <tr> <td>M</td><td>M</td><td></td><td>D</td><td>D</td><td>Y</td><td>Y</td> </tr> </table>			/		/			M	M		D	D	Y	Y		
		/		/																														
M	M		D	D	Y	Y																												
		/		/																														
M	M		D	D	Y	Y																												

Calibration Form

Field Center:

Device #	Date of the calibration	Measures from the OnTrak		Measure from the Omron (O) or Dinamap (D) (one reading)	O / D Used	Comments
		First Reading	Second Reading			

8.5.11 Appendix B: Instructions for OnTrak ABPM Monitor

Instructions for OnTrak ABPM Monitor Initialization, Data Download, and Study Export

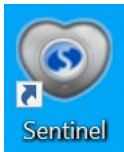
Sentinel software (Spacelabs Healthcare) is used to initialize the OnTrak ABPM monitor and to download data from the monitor after data collection is complete. Sentinel is also used to export participant studies for transmission to the SRC for review and analysis. The software and a license is provided by the SRC, and the SRC will work with each site to install the software. The SRC will also provide ongoing support for the ABPM monitor and Sentinel software and will be your site’s primary point of contact for questions and troubleshooting. The SRC can be reached at bwhmesasupport@bwh.harvard.edu.

OnTrak Device Initialization

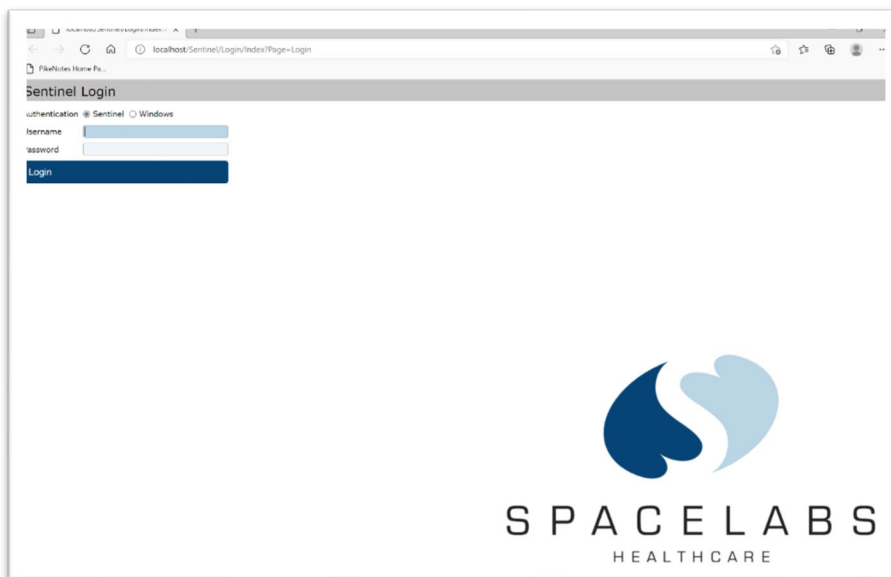
There are two primary tasks which must be completed within Sentinel software to initialize the OnTrak monitor and collect 24-hour ABPM data—adding the patient (study participant) record to the Sentinel database and configuring the ABP recorder.

Log into Sentinel software

1. Locate the Sentinel icon on the computer desktop and open Sentinel.



2. The Sentinel Login screen will display. Enter the Username and Password provided to your site by the SRC and click “Login”.

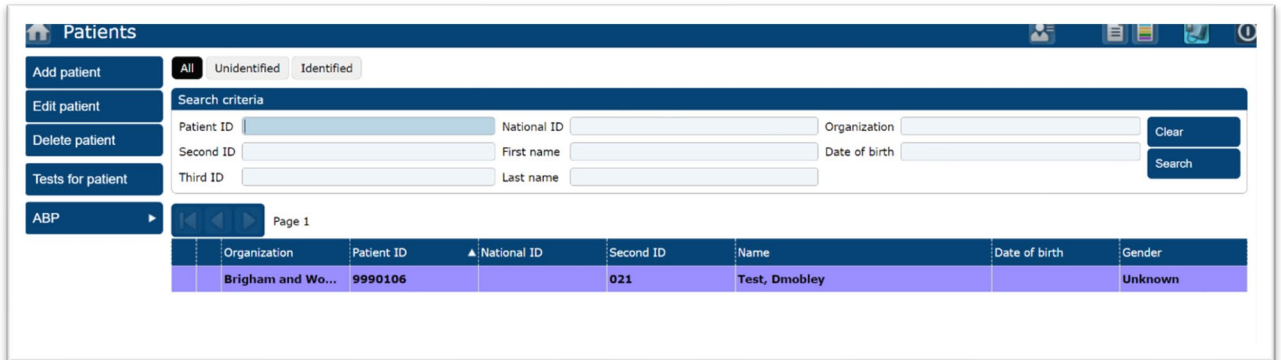


3. The Sentinel Home screen will display.

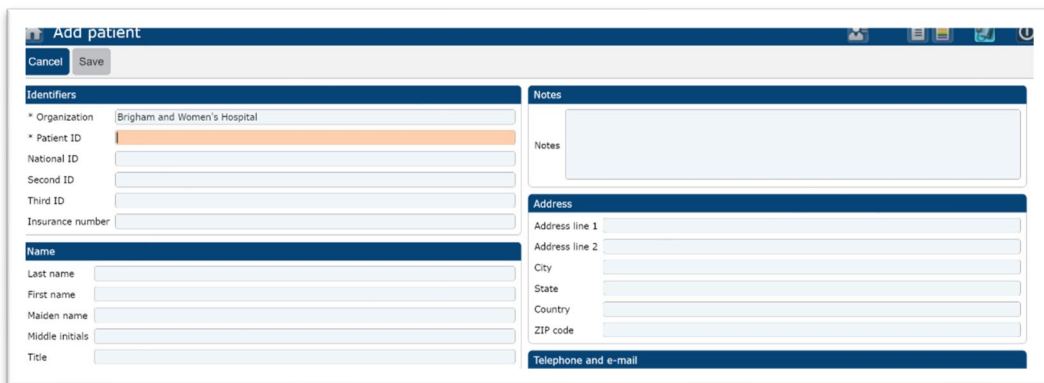


Create the Patient Record

4. Click the “Patients” menu item on the left side of the screen to display the “Patients” screen (note your screen might look different before your first study participant is added).



5. Click the “Add patient” menu item on the left side of the screen to display the “Add patient” screen. The image below only shows part of the screen. We will only use the “Identifiers” section on this screen.



6. As a reminder, no patient information (PHI) should be entered on the “Add patient” screen. Enter the following information only into the three fields listed:
 - a. Patient ID—Enter the participant’s MESA study ID
 - b. Second ID—ABPM unit ID
 - c. Third ID—Study site staff member idea

Note: The screenshot below contains sample information as an example of data entered into the Identifiers section of the screen. You will replace the information in the three fields with the information appropriate for your participant and study site.

The screenshot shows the 'Add patient' form with the following data entered in the 'Identifiers' section:

- Organization: Brigham and Women's Hospital
- Patient ID: 9012345
- National ID: (empty)
- Second ID: 34
- Third ID: 988
- Insurance number: (empty)

7. Click “Save” to save the participant record in Sentinel. The “Add patient” window will close, and the “Patients” screen will display. You should see the newly added patient record in the patient list.

The screenshot shows the 'Patients' screen with a table of patient records. A red arrow points to the first row of the table, which is highlighted in blue. The table has the following columns and data:

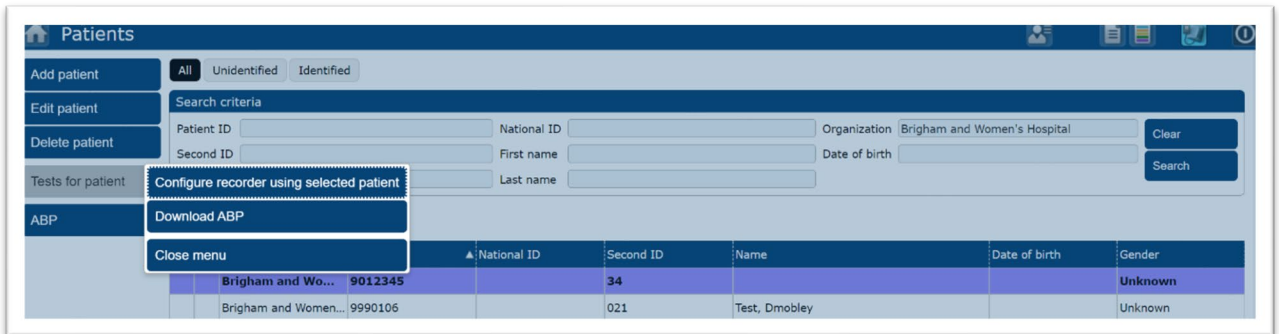
Organization	Patient ID	National ID	Second ID	Name	Date of birth	Gender
Brigham and Wo...	9012345		34	Test, Dmoble		Unknown
Brigham and Women...	9990106		021			Unknown

Configure the OnTrak ABP Monitor

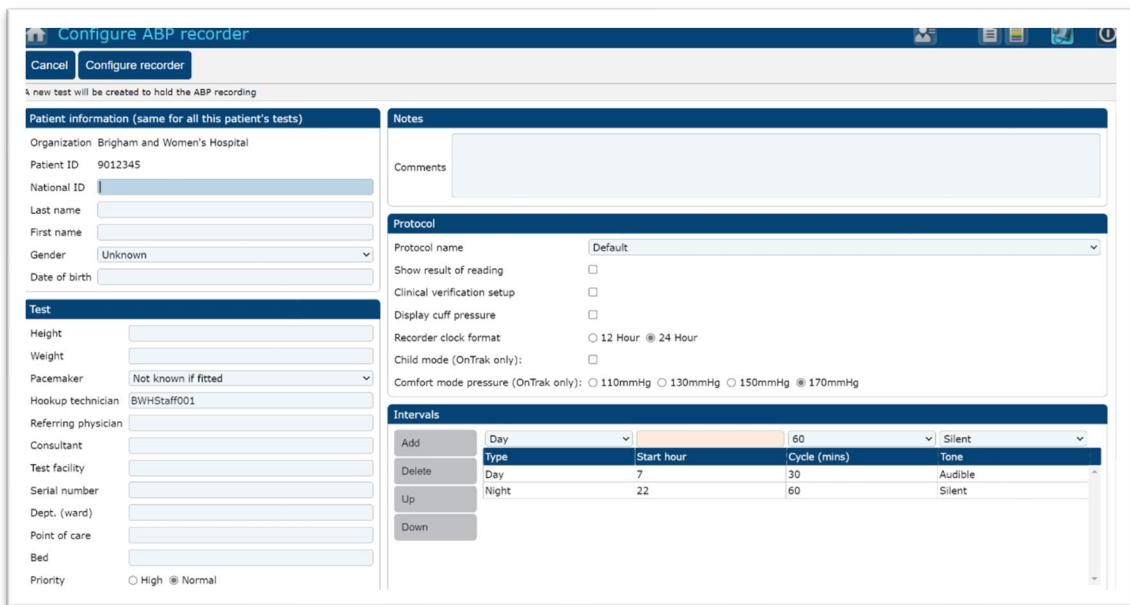
8. Connect the OnTrak ABP monitor to the computer using the USB cable supplied with the device. The port on ABP monitor is located on the bottom of the device beneath a small protective cover. Be careful not to pull the protective cover out of the device when opening the cover to expose the port.



9. Press and hold the Action button for 3 seconds to power on the monitor. The monitor will power on and display the “Connected to PC” message on the display.
10. Select the participant record the ABP monitor is being prepared for in the patient list by clicking once on the patient’s record. The participant’s record will be highlighted (refer to image in step 7).
11. Click the “ABP” menu item on the left side of the screen to display the ABP submenu.



12. Click the “Configure recorder using selected patient” menu item on the ABP submenu, and the “Configure ABP recorder” screen will display. Verify the Patient ID displayed is the correct study participant ID.



- In the Protocol box on the right side of the screen, select the “MESA Sleep” protocol from the “Protocol name” dropdown menu. Note that the information in the intervals box will display day and night start hours and frequency of readings as described in the Manual of Procedures. The device will be programmed to record every 30 minutes. *(Note the following screen will read start hour for day at 8).*

Protocol

Protocol name: MESA Sleep

Show result of reading:

Clinical verification setup:

Display cuff pressure:

Recorder clock format: 12 Hour 24 Hour

Child mode (OnTrak only):

Comfort mode pressure (OnTrak only): 110mmHg 130mmHg 150mmHg 170mmHg

Intervals

Type	Start hour	Cycle (mins)	Tone
Day	8	20	Audible
Night	22	30	Silent

- Click the “Configure recorder” button at the top of the “Configure ABP recorder” screen to initialize the OnTrak monitor. A dialogue box will display as follows:

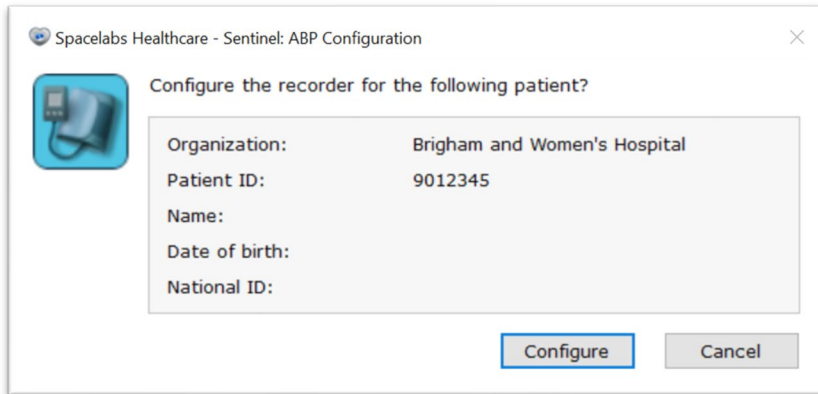
Open this file?

Do you want to open Spacelabs.Abplinitialise.application from localhost?

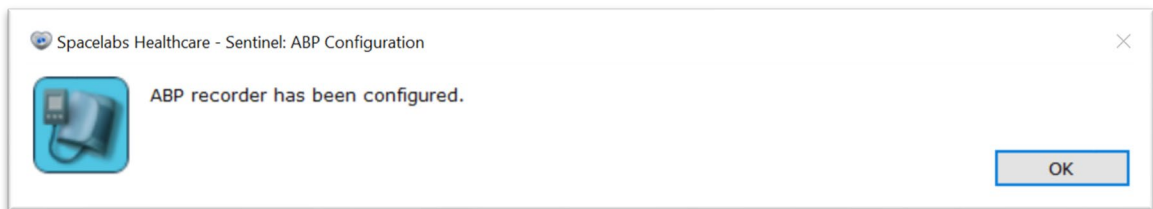
[Report file as unsafe](#)

Open Cancel

- Click “Open” in the dialogue box. A new dialogue box will display asking if you want to configure the recorder. Once again, verify the correct participant ID is displayed in the Patient ID field. Click “Configure”



16. A progress bar will briefly display followed by a dialogue box confirming the ABP monitor has been configured. Click “OK”.



Remove batteries from ABPM monitor. Disconnect the USB cable from the port on the ABP monitor.

17. Click the Home (house) icon at the top of the Sentinel screen and click “Log out” on the menu to log out of Sentinel software. The web browser window can now be closed.
18. Insert batteries immediately before powering on the ABPM monitor to take manual readings.

OnTrak Device Cleaning and Data Download

When the OnTrak ABPM device is received at the study site from the participant, the device must be properly cleaned and disinfected, and the participant’s 24-hour test data must be downloaded into Sentinel software.

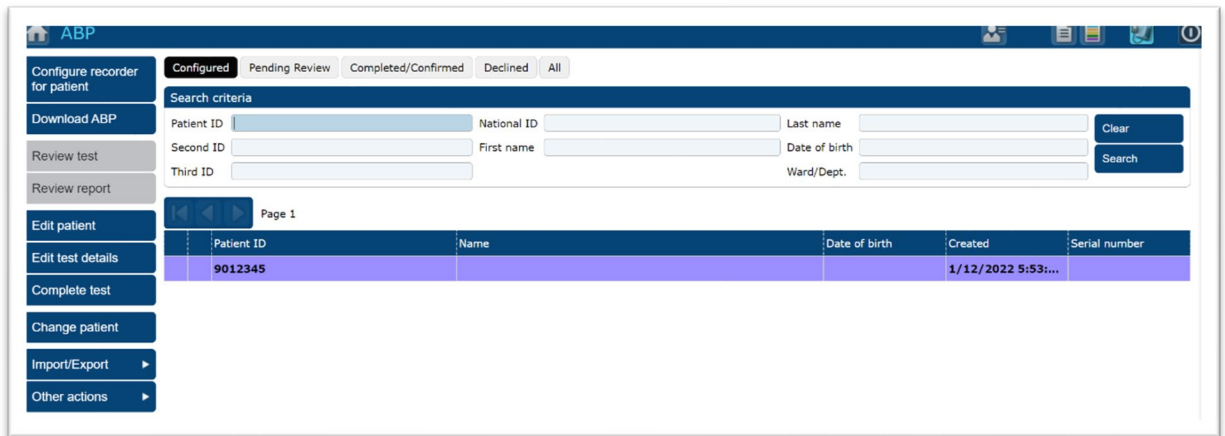
Cleaning and Disinfecting the OnTrak ABP Monitor and Equipment

1. **Gloves and appropriate eye protection should be worn when cleaning and disinfecting the ABPM equipment.**
2. **Inspect the ABPM monitor, tubing, bladder, bladder cover (cloth cuff cover with Velcro), protective case, and waist belt/shoulder strap for signs of damage. If any damage is noted, contact the SRC at bwhmesasupport@bwh.harvard.edu.**
3. **If the participant returned the disposable cuff cover, dispose of it in the trash.**
4. **Warm water and a mild soap or detergent solution on a soft cloth can be used to wipe away any visible dirt or debris from all equipment. Wring the cloth out thoroughly before wiping the device to prevent water from entering the device.**
 - a. **If visibly soiled or dirty, the waist belt, shoulder strap, and the cloth bladder cover can be washed in warm water and soap/detergent solution and laid on a flat surface on a clean towel (or draped over a hanger) to dry.**
5. **Wipe the ABPM device, tubing, bladder, bladder cover, and protective case with a disinfecting wipe such as a PDI Sani-Cloth wipe.**

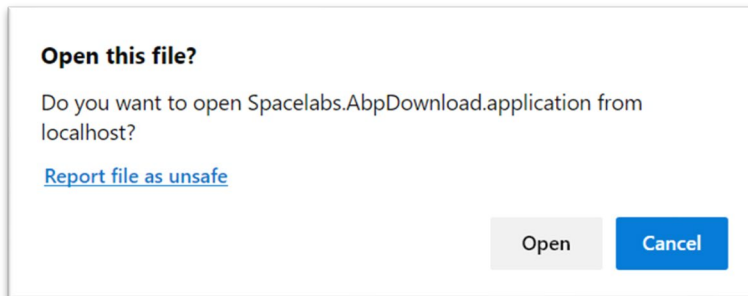
6. Allow the device and all parts to dry completely before handling.

Downloading Data into Sentinel Software from the ABPM

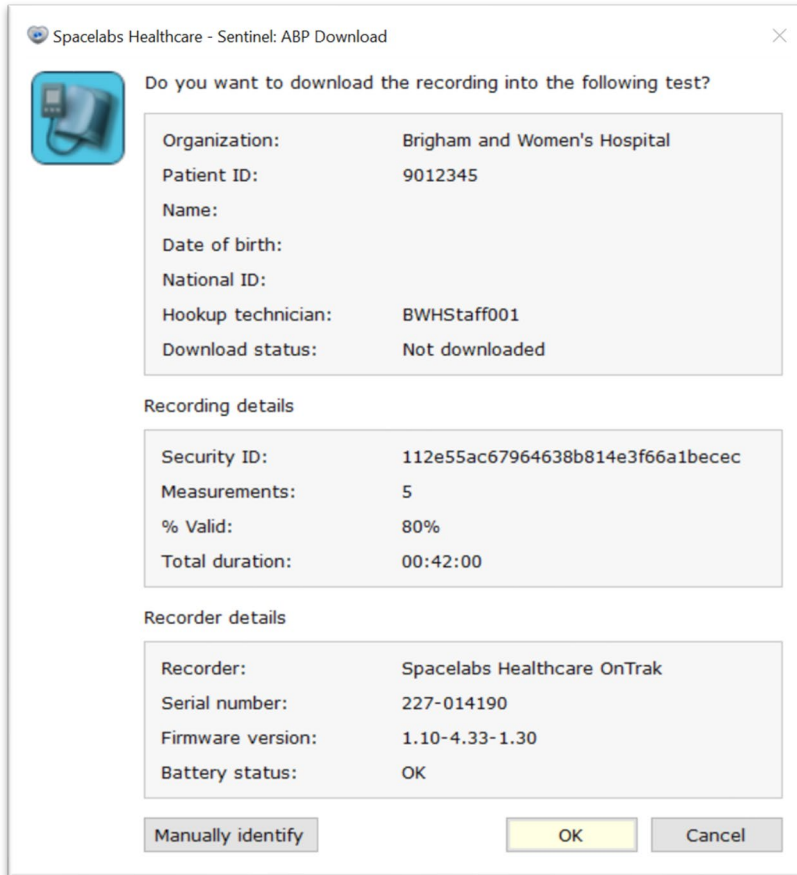
1. Log into Sentinel software as described earlier in these instructions.
2. Press and hold the Action button for 3 seconds to power on the monitor.
3. The “End Test” screen displays when the device powers on. Use the down arrow button to highlight “Yes” and press the Action button to end the test.
 - a. If the “End Test” screen does not display, simultaneously press and hold the up and down buttons on the front of the ABPM device.
 - b. The “Edit Test” screen will display. Use the down arrow button to highlight “End Test” and press the Action button.
 - c. When asked to confirm you want to end the current test, use the down arrow button to highlight “Yes” and press the Action button.
4. Connect the OnTrak ABP monitor to the computer using the USB cable supplied with the device as described earlier in these instructions. The “Connected to PC” message will appear on the device display.
5. Click the “ABP” menu item on the left side of the Sentinel Home screen to display the ABP screen.



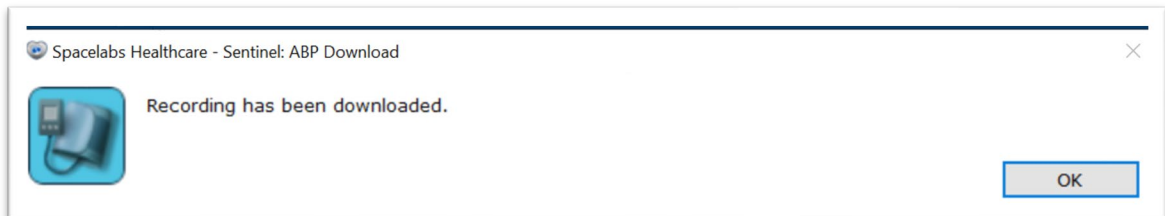
6. The patient list, by default, opens to display study participants with a monitor that has been configured for data collection.
7. From the ABP screen, click the “Download ABP” menu item on the left side of the screen. Note that you do not need to select a study participant’s record. The patient ID will be read from the recorder and the data downloaded to the appropriate record. The software will disregard any patient record selected on the screen. A dialogue box will display as follows:



- Click “Open” in the dialogue box. A new dialogue box will display asking if you want to download the recording. The participant ID will display in the Patient ID field in the dialogue box.



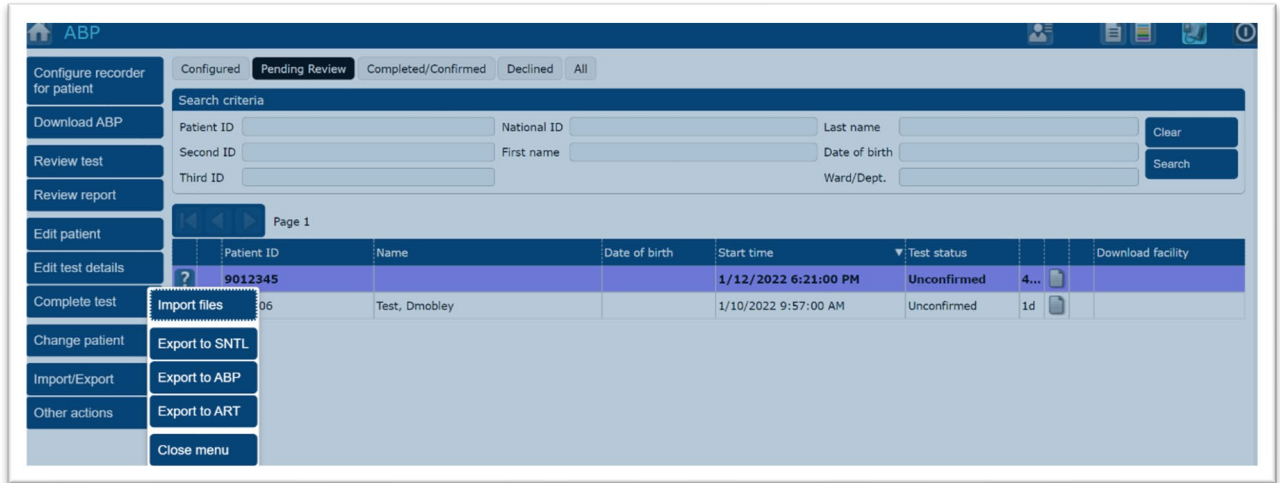
- Click “OK” to download the recording. When download is complete, the following dialogue will display:



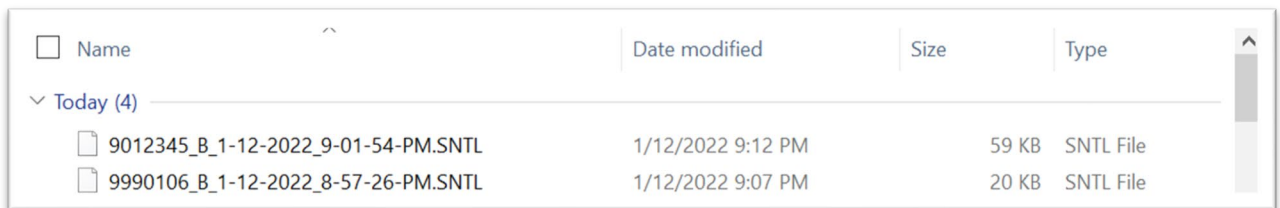
- Click “OK” to close the dialogue box and return to the Sentinel “ABP” screen and proceed to the next section to export the recording.

Exporting the Recording for Transmission to the CC

1. Select the participant’s test to be exported by clicking once on the participant ID number in the Patient ID list. The participant’s record will be highlighted.
2. From the “ABP” menu, click the “Import/Export” menu item to display the Import/Export submenu.



3. Click the “Export to SNTL” submenu option. A dialogue box stating “Exporting tests...” will briefly appear, and the test will be exported to the Downloads folder on your computer. When the dialogue box closes, export is complete.
4. If you are finished exporting tests for transmission to the CC, click the Home (house) icon at the top of the screen to return to the Sentinel Home screen, and click the “Log out” menu item to log out of the software. The web browser can now be closed.
5. To locate the exported recordings on your computer, open File Explorer and navigate to your Downloads folder. The file name of the recordings will start with the participant ID number and in with SNTL. This example shows two exported recordings (for participants 9012345 and 9990106).



Data Transmission to the CC

Sentinel 24-hour ABPM recordings will be transmitted to the CC. When the SRC receives the data from the CC, the data will be reviewed to identify whether sufficient data were collected and will review the data for urgent alerts. Please see instructions provided for data transmission to the CC in section 13.6.

8.6 Home Sleep Study

8.6.1 Brigham Sleep Reading Center Introduction

The MESA Sleep Exam will be overseen by the Brigham Sleep Reading Center (SRC). This Center is embedded in the Brigham and Women's Hospital and will benefit from the extensive sleep research expertise related to sleep data collection and analysis. Data analyses are performed by trained personnel who undergo frequent testing to ensure high levels of reliability. Scorers within the Center participate in regular quality control activities, including assessment of inter- and intra-scorer reliability. Advanced sleep study processing and data exploration tools have been developed and a well annotated archive of sleep studies and data dictionaries has been created to further support the scientific goals of the study.

The Sleep Reading Center (SRC) will:

- Provide centralized training for aspects of MESA related to the performance of the sleep-related procedures.
- Provide ongoing technical support for the performance of sleep studies, providing advice regarding troubleshooting of problem studies and acting as a liaison with the equipment supplier to identify equipment problems and solutions.
- Provide timely review (for quality and medical alerts) and scoring of all records, generating reports needed for participant feedback and data files for central (Coordinating Center - CC) processing.
- Provide complete scoring of all sleep studies, with generation of reports that summarize key sleep and respiratory data.
- Participate in on-going quality assurance efforts to maintain high levels of scoring accuracy and technical performance of tests at the field sites. These include assistance in trouble-shooting site-specific and study-wide problems, perform site visits, report generation, and lead regular conference calls with technicians and co-investigators.
- Produce and archive a clean, edited data set of raw and scored polysomnograms.
- Maintain a data dictionary relevant to polysomnogram variables.

8.6.2 Staff training and certification

Project staff will be trained on use of the Nox A1s device by qualified SRC staff. Training will include all steps necessary to obtain high quality study data including device initialization, instruction on device use, device distribution and retrieval, download of data from study devices, transmission of data to the Coordinating Center (CC) for retrieval by the SRC, and proper cleaning, disinfection, and maintenance of equipment. All staff will be required to obtain certification from the SRC prior to performing study procedures and administering devices to study participants. Certification for the Nox A1s device procedure is described later in this manual.

The SRC has implemented a rigorous quality control program to ensure all scoring staff are appropriately trained to score overnight sleep study data. All scoring staff team members undergo routine training and participate in reliability scoring exercises to assess both inter- and intra-scorer reliability. Studies are selected by the Chief Polysomnologist, and scorers are blinded to the original study information. When

scoring is complete, the SRC Data Manager generates summary statistics for each scored study for review by the study team. If significant differences are detected, studies are individually reviewed with the scoring team and differences discussed. If necessary, staff are retrained, and further exercises performed to reevaluate scoring quality.

8.6.3 Overview of the Multi-Ethnic Study of Atherosclerosis (MESA) Sleep study

Background: MESA is a longitudinal study that has followed a community-based cohort since 2000 for risk factors for cardiovascular disease and cardiovascular outcomes, and more recently for cognitive impairment, as well as multiple other health parameters. Between 2013-2016, the first MESA Sleep exam occurred, when up to 2026 MESA Exam 5 participants were studied with in-home polysomnography (PSG), 7-day actigraphy, and sleep questionnaires. That study led to the publication of over 50 papers that characterized the prevalence of sleep disorders in MESA and reported how multiple aspects of sleep (apnea, duration, quality, etc.) varied with a wide variety of risk factors and health outcomes. Notably, over 60% of MESA participants were shown to have mild or more severe sleep apnea, and sleep apnea was shown to be a risk factor for hypertension, coronary artery calcium, atrial fibrillation, and other cardiovascular outcomes. Marked variations in sleep duration, sleep patterns, and sleepiness by gender and race/ethnicity also were observed, and these sleep traits also were shown to predict health outcomes. With the aging of the cohort and expected increase in cognitive impairment, there is now an opportunity to further understand how sleep influences cognitive aging.

Objectives: MESA Sleep Exam 7: The MESA Sleep exam now will add comprehensive sleep and overnight (24 hour) blood pressure assessments to the MESA Exam 7 and MESA MIND studies, leveraging the rich data on vascular and cognitive outcomes these core studies are collecting, which include detailed cognitive tests, advanced brain imaging, and comprehensive Alzheimer's Disease (AD)/AD-related disease risk factors. We will utilize these varied data to understand *age-related changes in sleep physiology and circadian rhythms relevant to AD/ADRD*. The Sleep protocol adds the following to MESA Exam 7, aiming to recruit approximately 1800 MESA participants to undergo:

- State-of-the-art in-home polysomnography (PSG)
- 7-10 day wrist actigraphy
- 24-h ambulatory blood pressure monitoring (ABPM)

These measurements will provide advanced quantitative metrics of sleep and circadian rhythm to characterize the evolution of sleep disturbances over critical aging periods. The addition of 24-hour ABPM uniquely will provide information on how variation in blood pressure over the day- and particularly during sleep- are linked to cardiovascular and cerebrovascular disease. Together with data from MESA Sleep Exam 5, these data will allow the following novel study questions to be answered:

1. Over 10+ years, how does sleep change, and how do those changes predict changes in cognition, including neurodegeneration and AD/ADRD biomarkers (from brain imaging)?
2. Which sleep metrics—sleep apnea, sleep duration, sleep depth, sleep variability, etc- most strongly predict cognitive decline and markers of AD/ADRD?
3. What are the links between sleep, vascular disease risk factors and cognitive function? For example, does poor sleep increase risk vascular disease, and in turn, does sleep-related vascular changes increase risk for cognitive decline? Are sleep-related increases in blood pressure risk factors for cognitive impairment?

MESA sample eligible for the Sleep Exam: All MESA Exam 7 participants will be invited to participate. Participants who use a CPAP machine or oxygen ($\approx 2\text{-}5\%$ of participants) or who use nightly hypnotics will not be excluded but will be asked to use these therapies as they would typically do, thus providing

representative sleep data. Our objectives are for each FC to enroll 300 participants at a rate of 3 to 4 participants per week (total n=1800). We will monitor enrollment, and if we exceed these goals, we will prioritize enrollment of participants who are also in the MESA MIND Exam.

General PSG Procedures: Due to the pandemic and the multiple ancillary studies, there will be flexibility in the protocol. The wrist actigraph and 24 ABPM can be fit in the clinic or at the in-home visit. The standard PSG requires an in-home visit to attach the head (EEG) leads. If those visits prove difficult, an alternative method that involves participants using self-applied EEG leads will be considered. ABPM monitoring should NOT occur on the same night as the PSG. Actigraphy should be used on ABPM monitoring days, and if possible, also during the PSG.

For the in-home visits, staff safety and participant comfort are addressed *by* use of a 2-member research team who will directly secure sensors, minimizing participant burden. Each visit (for PSG placement) is projected to take 60-90 mins. Research assistants, certified for this procedure, will review with the participant the purpose of the test, instructions on wearing study equipment, and then apply sensors. After the sleep study, the PSG unit will be retrieved by study personnel or courier. PSG study data will be electronically transmitted to the University of Washington Coordinating Center and then accessed by the Sleep Reading Center (SRC) personnel for quality control analysis, standardized scoring, and off-line processing for quantitative phenotypes. Ideally the PSG should capture the participant's entire sleep period (6 to 8 hours). Studies with less than 2 hours of artifact free data on key channels will be repeated, if possible.

8.6.4 Sleep Study Data Collection Overview

Polysomnography (PSG) is the gold standard for objectively measuring sleep neurophysiology, sleep-related breathing abnormalities and sleep-related movements, providing information not available from actigraphy. A single night PSG using the Nox A1s device will provide quantitative assessments of levels of overnight hypoxemia, apneas and hypopneas, leg movements, ECG parameters, and sleep stage distributions. The recording montage will include electroencephalograms (EEG), electrooculograms (EOG), electrocardiography (ECG), leg and chin EMG, thoracic and abdominal respiratory inductance plethysmography, airflow (nasal pressure), and finger pulse oximetry. Methods will be similar to those used in the initial MESA Sleep exam. Specifically, during the home visit, trained staff members will perform the setup of the device and connection of the electrodes and sensors. Instructions will be given on how to move about with the recording device, and the participant will be provided instruction on removal of all equipment the morning after the sleep study. The Nox A1s equipment will be retrieved by study personnel or returned to the site using instructions provided by study personnel. PSG studies will be downloaded from collection equipment by study site staff and securely transmitted to the Coordinating Center (CC), and the SRC will retrieve the data from the CC for scoring, reporting, and quality control review. The PSG data will be reviewed at the SRC, and an assessment will be made about whether each study meets minimum quality criteria as well as thresholds for Urgent Medical Referral. Appropriate study personnel will be notified of any failed study or of other technical problems. Studies that meet criteria for potential Urgent Referrals will be triaged for priority scoring; the rest will be scored as they are received and within 5 business days. Studies will be attempted to be repeated if there are less than 2 hours of predominantly artifact-free tracing on key channels.

1.1.1.1 Polysomnography Sensors and Measurement Tools

The following describes the key sensors that will be used to measure breathing abnormalities, sleep stages, leg movements, and ECG.

EEG, EOG, chin EMG. Provide the information about sleep quality and quantity (enabling sleep staging)

Nasal Cannula Flow. Produces a signal from pressure changes to a nasal cannula during inspiration (pressure drop) and expiration (pressure increase). Allows changes in breathing amplitude to be measured.

Respiratory Effort (Inductance plethysmography). Qualitative assessment of effort associated with breathing (allows distinction of central from obstructive events). Recorded with bands around the thorax and abdomen that measure changes in distention/movement with breathing (inductance).

Finger Pulse Oximetry. Measures oxygen saturation levels in the blood by passing light through the finger and measuring absorption patterns (made by the oxygen carrying pigment-hemoglobin in the blood). Also measures pulse.

Leg Movement Sensors. Provide additional information for identifying the source of arousals during sleep (Periodic Limb Movements of Sleep) as well as disorders which may cause sleep disruption (Restless Leg Syndrome).

Body Position. To distinguish supine (on back), prone (on front), and side positions. This permits identification of the extent to which any sleep-related breathing problems are positional. This sensor is internal to the Nox A1s device.

ECG. Allows assessment of heart rate responses to breathing-related stresses, and arrhythmia detection.

Respiratory Events

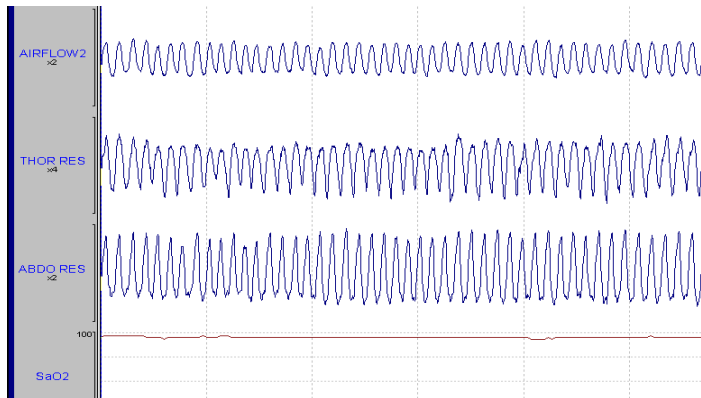
The respiratory irregularities which are one focus of the sleep study are classified as apneas and hypopneas.

An **apnea** is a complete or almost complete cessation of airflow, lasting ≥ 10 seconds, and usually associated with desaturation or an arousal.

A **hypopnea** is a reduction in airflow ($< 50\%$ of a "baseline" level), associated with desaturation or arousal.

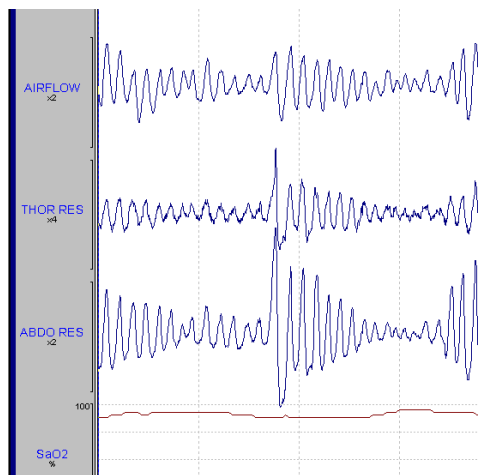
Events (apneas or hypopneas) are also classified on the basis of the extent of the associated respiratory effort. **“Obstructive”** events (the most common form in sleep apnea) are associated with chest and/or abdominal respiratory effort (occurring in face of an obstructed throat [upper airway]). **“Central”** events are associated with insufficient or highly irregular breathing efforts; and may or may not include an obstructed upper airway. This pattern may be seen in heart failure or after strokes. Thus, accurate recording of these events requires measurement of airflow, oxygen saturation, respiratory effort, and EEG, EOG, and EMG. On the following page are examples of breathing as measured by polysomnography.

NORMAL BREATHING

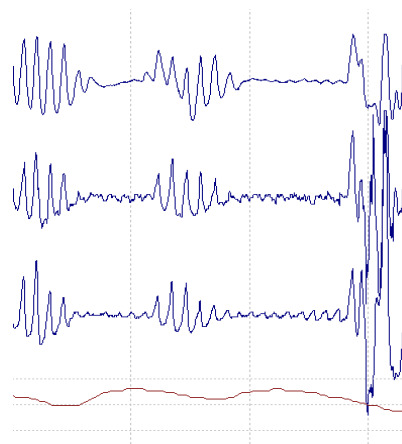


OBSTRUCTED BREATHING. Note changes in oxygen saturation corresponding to changes in respiration.

Hypopnea



Apnea



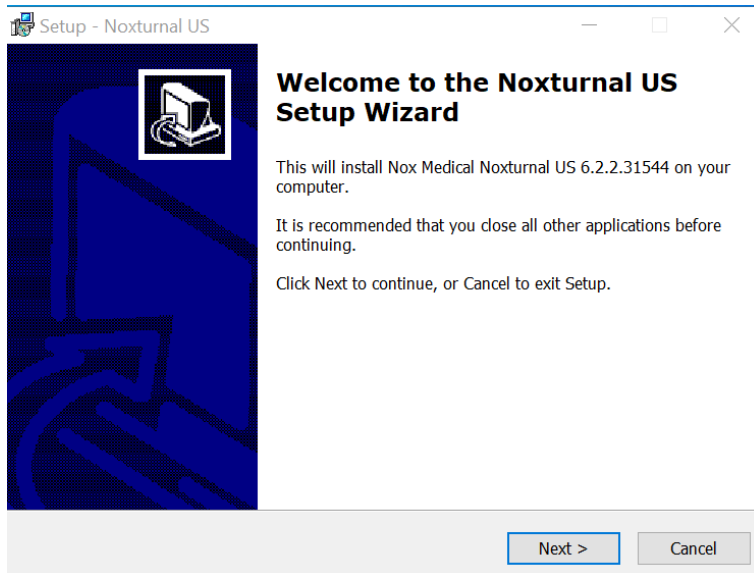
1.1.1.2 Software Requirements and Installation

Noxturnal software will be installed on each Field Center computer. A software download link will be provided by the SRC. Noxturnal software is required to configure the Nox A1s device and its corresponding Nonin WristOx device for overnight sleep study data collection and to download the overnight sleep study data after a recording is completed. Minimum system requirements for installation are:

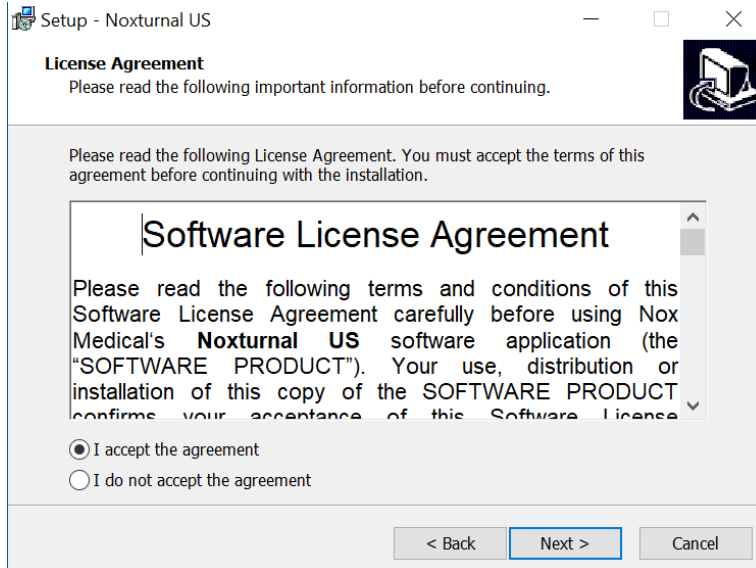
Hardware Type	Minimum Requirement
Operating System	Windows 8.1
Processor	x64 based Intel or AMD
Processor Clock Speed	1.7 GHz or faster
Memory	2 GB or more
Free Hard Drive Space	4 GB or more
Graphics Resolution	1024x768 or higher

To install Noxturnal software, the user performing the install must be logged into the computer with administrator privileges. Please consult with your local IT department if their assistance is required for software installation.

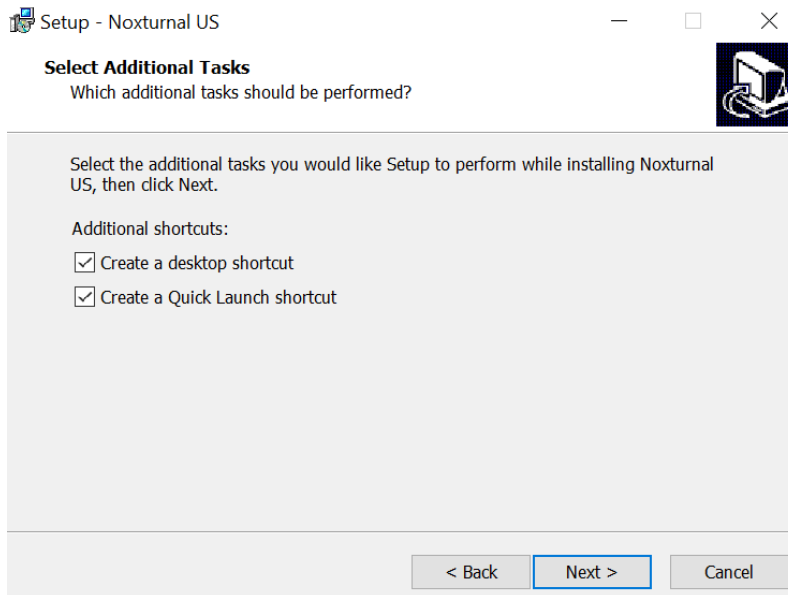
1. Run the Noxturnal installation file to start the software installation, and follow the instructions provided by the Noxturnal Setup Wizard.



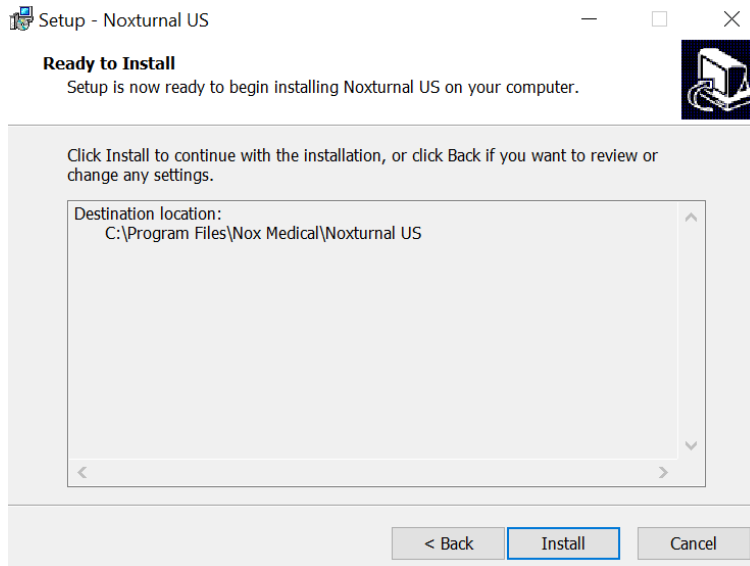
2. Click next to advance to the License Agreement screen. You must accept the license agreement before clicking Next to continue.



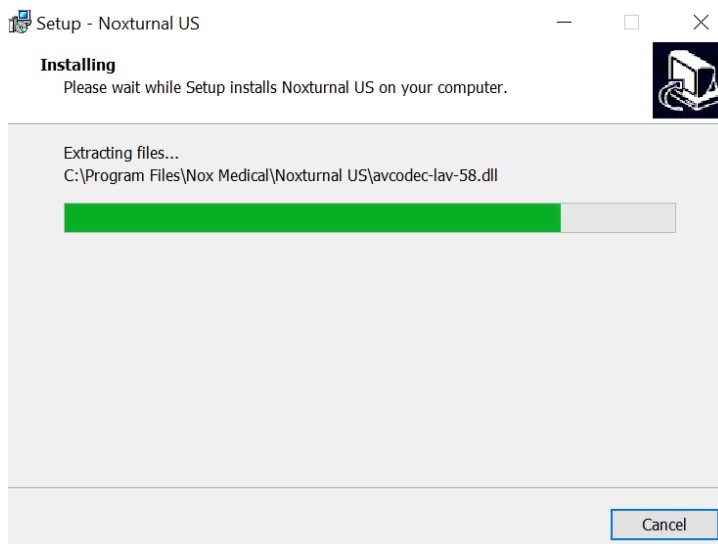
3. If you would like to create a desktop and/or Quick Launch shortcut, select the checkboxes on the "Select Additional Tasks" screen and click Next.



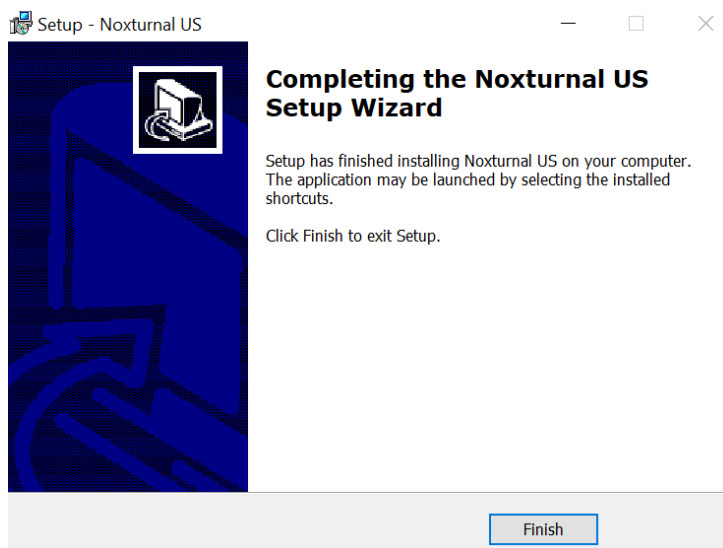
4. When ready to install, click the Install button on the "Ready to Install" screen.



5. The install process will begin, and a progress bar will display.



6. When software installation is finished, click Finish to close the wizard and complete the installation process.



1.1.1.3 Equipment Description

The Nox A1s device (Figure 1) is lightweight (~4 ounces with battery installed) and can record a minimum of 10 hours of data. The monitoring device was chosen because it can acquire high quality signals with sampling rates ranging from 200 Hz (flow/pressure signals) to 512 kHz (unipolar and bipolar channels) with advanced noise reduction and anti-aliasing. The system uses 13 unipolar channels to record EEG, EOG, and chin EMG data, and 4 bipolar channels for recording ECG and limb movement data. Respiratory data for identifying apneas and hypopneas consistent with American Academy of Sleep Medicine recommendations will be collected via a nasal pressure cannula and respiratory effort bands (high resolution thoracic and abdominal inductance plethysmography). Pulse oximetry will be collected via a wrist-worn Bluetooth-enabled finger pulse oximeter (Nonin WristOx2 model 3150, Figure 2) paired to the Nox A1s device. The Nox A1s device and the Nonin WristOx are battery powered, and details about battery use are provided below.

Please note that each Nox A1s device is paired to a corresponding Nonin WristOx device, and these devices must remain together in the kits. The Nox A1s device will only work with its paired Nonin WristOx device, and the devices should remain paired in their kits as distributed by the SRC unless the SRC provides guidance to change device pairings.

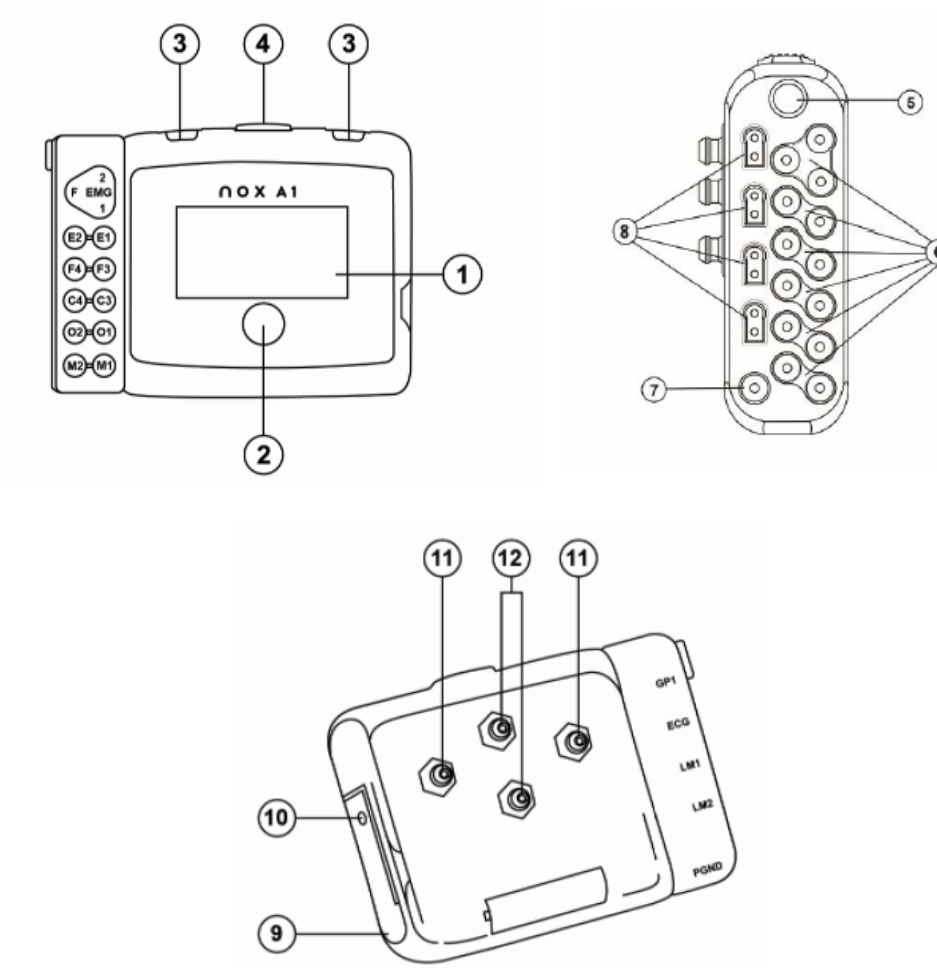


Figure 6: Nox A1s Device

Source: Nox Medical.

Refer to the list below to identify parts of the Nox A1s.

1. Device display
2. Push button (light sensor and indicator light located under button)
3. 2 clip strap loops
4. Microphone for recording respiratory sounds/snoring
5. Pressure lock for connecting nasal cannula
6. 13 Unipolar touch proof inputs (10 EEG/EOG, 3 chin EMG)
7. Reference ground input
8. 4 Bipolar touch proof inputs (ECG, leg movement cables)
9. Battery lid (covers the battery and the USB connector)
10. Battery lid pin (used with Nox battery lid key to open lid)
11. Metal snaps (2 to connect thorax RIP belt)
12. Metal snaps (2 to connect abdomen cable)



Figure 7: Nonin WristOx 3150 with finger pulse oximeter

Source: Nonin Medical.

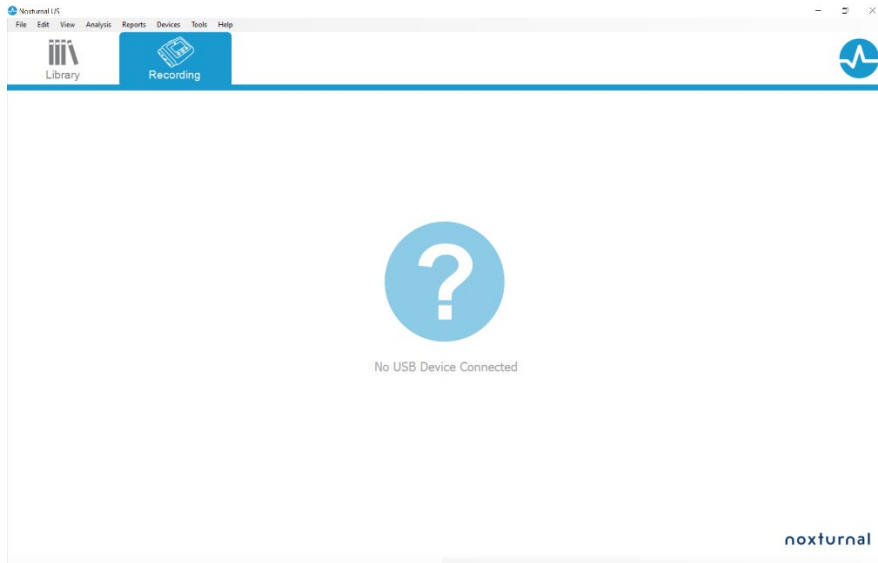
1.1.1.4 Battery Information

Nox A1s: A single size AA lithium battery will be used to power the Nox A1s device. A new AA battery should be used for each recording. The battery will be inserted into the device after device configuration is complete and prior to providing the device to a participant. The used battery will be removed from the Nox A1s device after the device is returned to the center when the battery lid is opened to access the USB connector for data download. Please follow site specific guidance for disposal or recycling of AA lithium batteries.

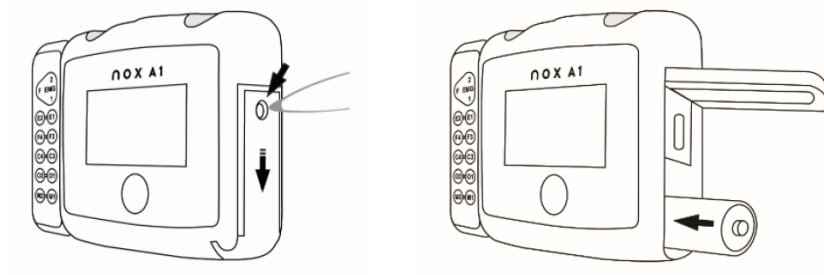
Nonin WristOx: Two alkaline AAA batteries will be used to power the Nonin WristOx. New batteries should be inserted into the WristOx at the time of Nox A1s device configuration. Batteries are required to power the device during the initialization and pairing process. The used batteries will be removed from the Nox A1s device after the device is returned to the center. Please follow site specific guidance for disposal of AAA alkaline batteries.

8.6.5 Preparing the Nox A1s for Data Collection

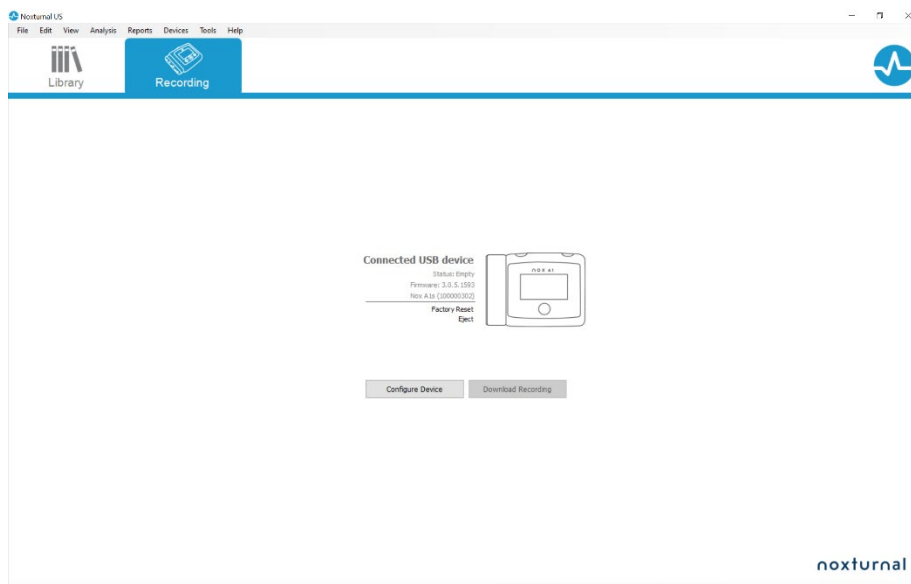
1. Start the Noxturnal application and select the “Recording” tab at top of the screen.



2. Connect the Nox A1s device to the computer with the supplied USB-C cable. To access the USB port on the Nox A1s device, use the Nox battery lid key to press the battery lid pin and gently slide the battery lid down, towards the bottom of the device. The battery lid door will open. A battery does not need to be inserted while the device is connected to the computer.



3. When the Nox A1s recorder is connected to the computer, the device display lights up and displays “Connected” at the bottom of the display. The Noxturnal software Recording tab will change to display the “Connected USB device” message and will show details about the connected Nox A1s device. Note: It can take several seconds for the software to recognize the device. If the software does not recognize the device after approximately 10 seconds, move the mouse pointer to the question mark on the “Recording” screen and click to scan for the Nox A1s device.



4. Prepare the Nonin WristOx device, as it will be paired with the Nox A1s device in the following steps.
 - a. Insert 2 AAA batteries into the WristOx by sliding open the battery cover on the back of the device. There are printed battery guides inside the device to show the direction of insertion for each battery. Replace the battery cover.
 - b. Plug the finger pulse oximeter cable into the top of the Nonin WristOx device.

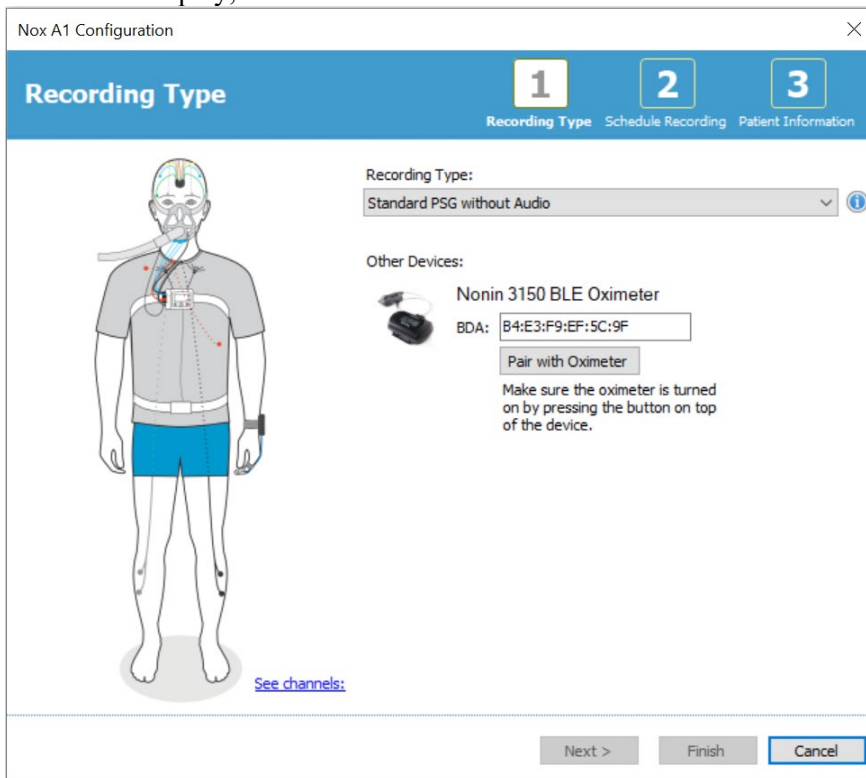


- c. Insert the shorter tab of the Velcro strap through the strap holders across the back of the WristOx as shown in the image below. Fold the longer part of the strap over the back of the device and secure the Velcro.

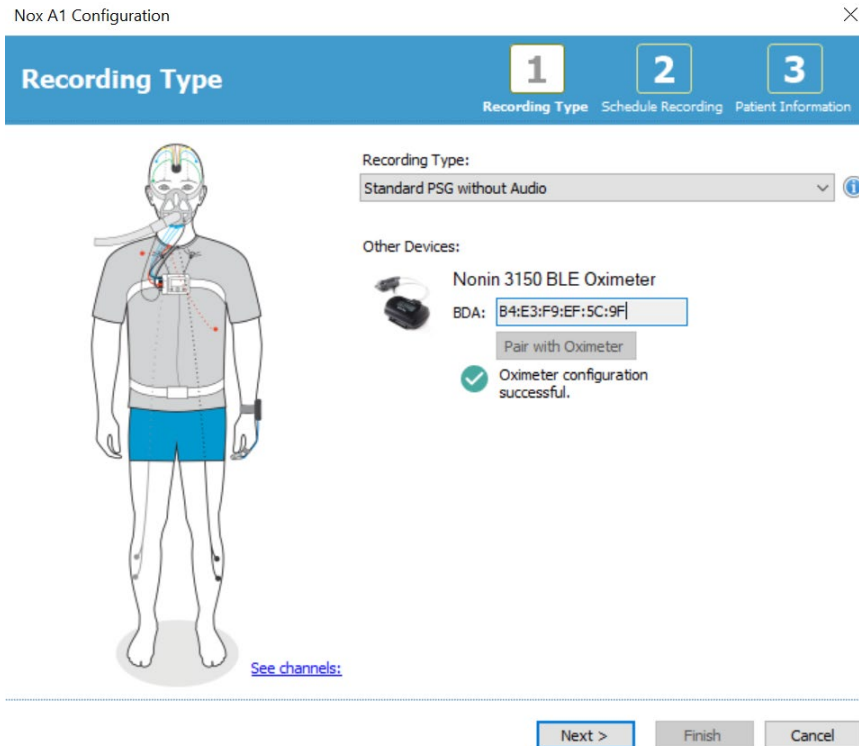


d.

5. Click Configure Device. The Nox A1 Configuration “Recording Type” screen will display.
 - a. In the Recording Type field, select “Standard PSG without Audio”
 - b. In the BDA field, enter the BDA address found on the back of the Nonin WristOx.
 - c. Press the small button on top of the WristOx near the cable connector to turn the WristOx on.
 - d. After the WristOx powers on and the small Bluetooth icon appears on the right side of the display, click the Pair with Oximeter button



6. After successful pairing of the Nox A1s device with the WristOx, a message saying “Oximeter configuration successful” will display, and the Next button will be available. Click Next. (Note: If pairing is not successful, ensure the BDA number was entered correctly and the Nonin display is powered on. If not, refer to step 5c.)



The WristOx device will automatically turn off a few minutes after device pairing and configuration is complete. A small Bluetooth symbol will periodically blink on the WristOx screen indicating the WristOx is in Bluetooth Wake up mode, and the WristOx will turn on when the Nox A1s begins recording the sleep study.



7. The “Schedule the recording time” screen will display with the Manually Start Recording option selected. We will not ask participants to manually start recordings but will schedule the Nox A1s device to begin recording at a predetermined time. This will help eliminate potential errors with participants not turning on the device or not starting the recording correctly. The duration of all recordings will be 12 hours. Click the Start Recording At radio button to display the scheduling options. Set the options as follows:
 - a. Number of Nights: 1
 - b. Start Time: One hour prior to study participant’s reported bedtime.
 - c. Date: Choose the date on the calendar for the date the sleep study will occur.
 - d. Duration: Click the radio button next to the Hours box and enter 12.

e. Click Next

Nox A1 Configuration ×

1 2 3
Recording Type Schedule Recording Patient Information

Manually Start Recording

Start Recording At:

Number of Nights:

Start Time:

Date:

February 2022
Sun Mon Tue Wed Thu Fri Sat
27 28 1 2 3 4 5
6 7 8 9 10 11 12
Today: 2/25/2022

Duration:

7 Hours, 8 Hours, 10 Hours, Hours, Unspecified

8. The “Patient Information” screen will display. It is very important that no PHI is entered on this screen. Please enter only the following information in each field:
 - a. First: MESA technician ID number
 - b. Last: MESA participant ID
 - c. ID: MESA participant ID (enter a second time, do not copy and paste)
 - d. Leave all other fields as displayed and click Finish

Nox A1 Configuration ×

Patient Information

1
2
3

Recording Type
Schedule Recording
Patient Information

Name

First: 999	Last: 9912345	ID: 9912345
---------------	------------------	----------------

Gender

Male
 Female

Date of Birth

1/ 1/1960
 N/A

Body Metrics

Height: cm
 Weight: kg
 BMI:

Tags

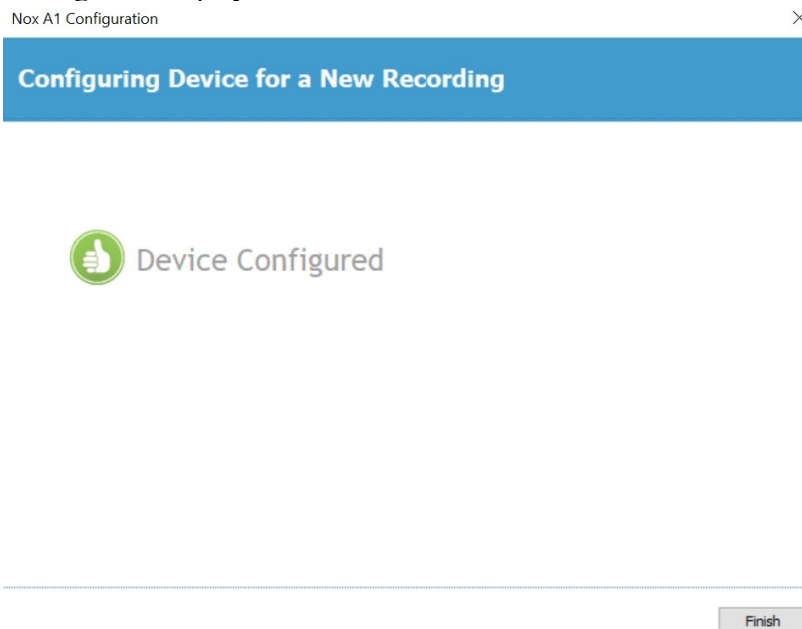
[Click to edit tags...](#)

Notes

Edit... change device pin...

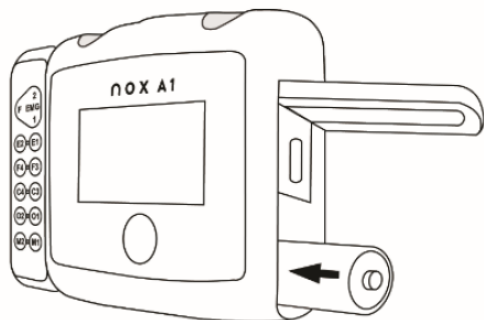
< Previous
Finish
Cancel

9. The “Configuring Device for a New Recording” screen will display a progress bar during device configuration. When configuration of the Nox A1s is complete, the Device Configured message will display.



10. The display on the Nox A1s device will turn off. Disconnect the device from the USB cable.
11. If you are completing the sleep study visit within 24 hours of device configuration, proceed with inserting the battery into the Nox A1s device. If the visit will occur more than 24 hours from device configuration, insert the battery into the device prior to the study visit. To insert the AA lithium battery into the Nox A1s device, insert the negative (flat end) of the battery into the battery slot first as shown in the image below. Gently close the battery compartment by

pressing the lid back towards the device, then slide the battery lid back into position towards the top of the device.



12. The Nox A1s device configuration is now complete and ready for data collection.

8.6.6 Supplies and Equipment Required for the Study Visit

Site staff should create a sleep study supply kit that contains the following items. This kit should be transported to the home on the evening of the sleep study visit and should leave the home with study staff at the end of the visit. The supply kit should not be left with the study participant. For items where quantities are provided in the table, the quantity represents the number of each item required for a single study. Many supply items (e.g., NuPrep tube, Ten20 paste jar, rolls of gauze/tape) will be used for multiple study visits, and product use may vary per participant. These items are marked with an asterisk, and ample supply should be available during each study visit.

Item	Quantity	Description/purpose
Nox A1s kit containing Nox A1s device, Nonin WristOx with soft tip sensor, and cables (Grey and black leg cables, orange ECG cable, Nox head cable with EEG 5 lead gold cup electrode cables (2) attached, abdominal belt cable)	1	Overnight sleep study recording device. Items listed are standard items provided inside each Nox A1s kit.
Size AA Lithium battery	1	Powers Nox A1s device
Size AAA alkaline battery	2	Powers Nonin WristOx
Nox RIP belt set (2 effort belts per set)	1	Measure breathing effort
Nox nasal cannula with filter	1	Measure airflow at the nose
Ambu BlueSensor N electrode	5	Measure leg movement (4), Nox forehead cable attachment (1)
Ambu BlueSensor M electrode	2	Measure ECG/heart rate (2)
Ambu Neuroline 715 electrode	3	Measure chin muscle tone
Medicine cups	1 to 2	Holding NuPrep, conductive paste/gel
Tongue depressors	1	Removing Ten20 paste from container
Cotton-tipped applicators, 6"	2 to 4	Application of NuPrep to skin
Ziploc bag	1	Participant use when removing equipment after sleep study
Blue under pad (Chux pad)	1	Protection of participant's furniture
NuPrep skin prep gel tube	*	Preparing skin for electrode application
Tensive conductive adhesive gel tube	*	Gold cup electrode application
Ten20 conductive paste jar	*	Gold cup electrode application

Prep-n-Stay bottle	*	Skin prep for diaphoretic patients, helps secure electrodes
Tape measure, 60” long	*	Measuring head for proper electrode placement
Blue peel-off China marker	*	Marking measured electrode sites
Nylon hair comb	*	Parting hair during electrode measurement/application
Hair clips	*	Securing longer hair during electrode application
Bandage scissors	*	Cutting gauze strips and tape
Gauze rolls	*	Cut to 1 to 1.5” strips to cover electrodes
4” x 4” gauze squares	*	Can be cut to cover electrodes and used for cleanup
Cover-Roll Stretch Tape	*	Cut to 1” strips to secure electrodes
Paper surgical tape, 1”	*	Secure electrodes, good for sensitive skin
Gloves	*	Protective supplies

8.6.7 Preparation for the Study Visit, Arrival in the Home, and after Visit Overview

For in-home application of PSG, two staff members will attend study visits. This formula helps ensure staff safety and reduces the time required to complete the visit, as both staff members can assist in visit activities. (Note, to meet participant needs, an alternative approach for dispensing equipment from clinic using self-applied electrodes may future be a study option). The following shows an example of steps to consider in preparing, conducting, and follow-up PSG data collection, noting that these steps may vary by center and participant.

Pre-visit

Recruitment and Scheduling

Approximately 1-2 weeks before the home visit or at the Exam 7 clinic visit

- Study staff will perform phone calls to participants and determine eligibility and interest in participating; Obtain informed consent at clinic if able.

Within two days of the home visit

- Staff will confirm the appointment and give participants instruction to be prepared for the visit of the study staff.
- Prepare a study folder per participant, including the consent form (if not already obtained), completion forms, Participant Diary form, and Sleep Questionnaire. Confirm ID and Acrostic in each form correspond to the scheduled participant.

- Set up equipment and supplies for the in-home visit
 - NOX A1 PSG
 - (Actigraph if applicable)
 - Enter device information in the PSG Accountability Log

Instructions to participants:

- The participant should be instructed to shower and dress in comfortable clothing for sleeping prior to the study team's arrival. Comfortable clothing is needed because the Nox A1s device and respiratory effort sensors should not be placed directly on the skin.
- Have participants have a separate shirt and pajama bottoms (if possible) to facilitate placement of ECG sensors on the torso and cover and protect leg EMG sensors during sleep.
- The participant should be instructed to apply no hair products (e.g., hairspray, gels, mousse, and/or oils), lotions, moisturizers, or other types of creams before the study, as these items prevent the electrodes and sensors from adequately adhering to the skin and cause interference with data collection.
- The participant should remove artificial nails and have nails free of products or polish prior to the arrival of the study staff, as nail polish can interfere with the pulse oximeter, causing readings to be absent or inaccurate, leading to an invalid study. Preferably, have the middle (ring) finger of the non-dominant hand free of artificial nails or polish.

In-home sleep visit

Upon arrival to the participant's home, obtain informed consent (if not already obtained). Review the overall procedure, explaining:

PSG will provide information on the quality and characteristics of:

- **Sleep** measured by sensors placed on the scalp to record brain wave activity. To distinguish dream (rapid eye movement) sleep from non-dream sleep also requires sensors measuring eye movements and sensors measuring muscle tone near the chin.
- **Breathing and levels of** oxygen in the body will be measured using a nasal cannula to measure airflow at the nose, effort bands placed around the torso, and a sensor placed on the fingertip to measure blood oxygen levels.
- **Leg movements** by sensors placed on each leg.
- **Heart rate** by an ECG measured overnight using sensors on the torso.

Emphasize that the participant should try to sleep as they would normally do. Once the sensors are attached, they should not worry about them. The device is portable, so they are free to move about and use the restroom.

Study participants who wear oral appliances/devices, an oxygen cannula at night, or who use a PAP device should be studied while using their usual treatment. If an oxygen cannula or a PAP mask is worn, note that the participant will not wear the Nox A1s nasal pressure cannula.

Ask the participant where they would prefer to apply the sleep study device to occur.

- Staff will request that the participant use a table, such as a kitchen table, so the study staff has adequate space to prepare for device application. Ideally, the light should be good, and there should be sufficient room for two staff members to work.
- Protect the cleanliness of eating surfaces with a barrier. Chux/under pads are recommended, but a paper or other type of covering will suffice. Be sensitive that your equipment, carry case, and instruments are less sanitary than the participant's environment.
- Staff will clear a flat surface area to set up supplies. Set all materials on the protective barrier and position items for easy access.
- The participant should sit close to the supply tray during the application of the Nox A1s device.
- Study staff will make sure they have easy access to the participant's head, torso, and legs, as electrodes and sensors will be placed in these areas.

Before leaving the home:

- Study staff will record whether any sleep apnea treatment was used during the study on the PSG Tracking Form.
- Demonstrate to the participant how to fill out the Sleep Questionnaire
- Review Participant Dairy with the participant and complete Day 1 with the participant
- If actigraphy is applied the same day, Study staff will demonstrate how to wear the actigraph (refer to Actigraphy MOP)
- Staff will hook up participant to the PSG
- Complete PSG Tracking Form
- Study staff will provide instructions for equipment use and return of equipment. Review the Participant Instructions form with the participant and give a copy to the participant.

Receiving NOX A1 device (the day after hooking up)

- Participants will mail the Nox A1s equipment and electrodes and sensors, or study staff will retrieve PSG equipment and Sleep Questionnaire if applicable.
- Staff will clean and disinfect electrodes and sensors.
- Staff will download data from the study and save it on the computer.
- Complete PSG Tracking Form
- Upload data file to the NextCloud.
- Verify Sleep Questionnaire for completeness and accuracy.
- Complete Accountability Log.

8.6.8 Suggested Order of Nox A1s Sensor Application

The following order of placement is recommended based on the design of the Nox A1s device and sensors. Placing equipment and sensors in the order described should help minimize the time required to prepare the participant for the study, thus reducing burden. This order also helps ensure easy access to electrode placement sites on the body before other equipment is placed that might impede access to electrode sites and cables. Step-by-step detailed instructions that follow this order are included later in this manual.

Nox A1s Recorder	Secure to clothing with clips near the neckline of sleepwear.
ECG (1 cable, 2 snap electrodes)	Orange cable, short end with adhesive snap electrode placed below right clavicle, long end with adhesive snap electrode at base of lower rib on left side.
Leg EMG sensors (2 cables, 4 snap electrodes)	Below knee on outside of the upper shin on belly of tibialis anterior muscle. Black cable for left leg, grey cable for right leg, 2 snap electrodes per cable. Have participant place cables inside clothing as described, attach electrodes to cable, and place electrodes on leg.
Respiratory belts (2)	Thoracic belt below armpits, abdominal belt around abdomen just below umbilicus and attached to Nox Abdomen Cable. Adjust belts as described so they are snug but not uncomfortable.
Nox Head Cable	Attach Ambu BlueSensor N snap electrode to Nox Head Cable and place at Fpz location on forehead.
EEG electrodes (10)	Attach Head Cable to Nox A1s device and EEG Electrode Cables to Head cable. There are 10 electrodes (5 each per head cable) that we be attached at the following sites: F ₃ , F ₄ , C ₃ , C ₄ , O ₁ , O ₂ , E ₁ , E ₂ , M ₁ , M ₂ .
Chin EMG electrodes (3)	Ambu Neuroline 715 self-adhesive with wires already attached are used. Plug into Nox A1s at inputs labeled EMG 1, 2, and F and affix to chin as described.
Nasal cannula	Apply between nose and upper lip and secure with tape to maintain placement. Connect cannula to PRES port on Nox A1s.
Wrist Oximeter	Apply the Nonin Wrist Oximeter to the participant's non-dominant wrist using Velcro strap. Place soft tip sensor on finger and secure cable with tape to maintain placement.

1.1.1.5 Electrode Placement Measurement

Proper sensor placement is very important for effectively recording sleep patterns and for consistency of data between sites. The technician may prefer to measure and mark the head before beginning to apply the body sensors and electrodes other than scalp electrodes or might prefer to measure and mark the head after applying leg sensors and other sensors applied to the body. Either method is acceptable, but head measurement is required. Estimated placement of scalp electrodes is not acceptable.

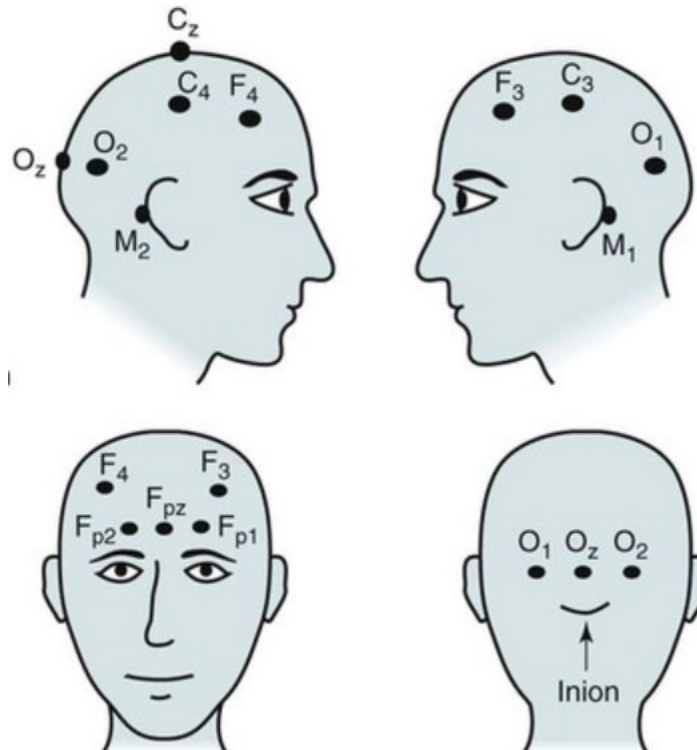
The process for placing EEG sensors on the participant will follow the 10-20 system for electrode placement. This standard was developed to provide consistent application of EEG electrodes for the collection of brain wave recordings. This system is based on measurements from 4 standard points (landmarks): the nasion, inion, and left and right pre-auricular points.

Before beginning head measurement (and subsequent placement of the device on the participant), it is important to explain each step of the process and give the participant ample opportunity to ask questions.

You will be identifying the following key areas for sensor attachment. Sites associated with odd numbers (1, 3) are located on the left side of the head, and sites associated with even numbers (2, 4) are located on the right side of the head. Sites with the letter “z” are sites along the midline of the head. Sites that begin with “Fp” are along the frontal plane (forehead). Note that some sites you locate will not have sensors attached (e.g., Fp₁, Fp₂, Cz). Those sites must be located because they are required to find other sites. The letter preceding the number describes the region where the electrode will be placed:

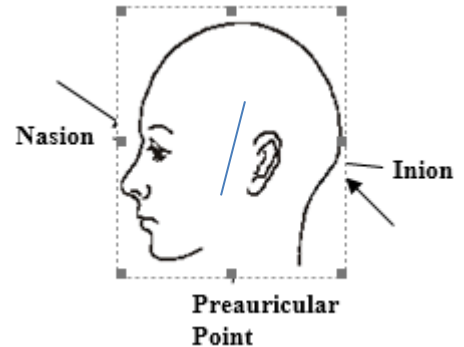
- C: Central electrode (near middle of head)
- F: Frontal electrode (front area of the head)
- M: Mastoid electrode (behind ear)
- O: Occipital electrodes (back of the head)
- Fp: Frontal plane (forehead area)
- E: Eye electrodes (next to each eye)

This image illustrates approximate locations of these sites, which will be located on each participant by taking measurements of the head as described in the steps below. Images showing placement of eye sensors are provided later in the manual.



Identify your landmarks:

1. **Pre-auricular points:** Standing at the side of the participant, look at the ear. In front of the ear canal is a small flap of cartilage called the tragus. Just above the tragus is the point at which the top of ear lobe begins to form. The small dimple-like indentation between the tragus and the formation of the top of the ear lobe is the pre-auricular point. If in doubt, ask the participant to open and close his jaw. Look and feel for movement at the indentation above the tragus. Using blue china marker, lightly mark these landmarks on both the right and left sides of the participant.



2. **Nasion:** Facing the participant, look into his/her eyes. Find the small dip at the bridge of the nose between the eyes. This point at which the forehead meets the nose is the nasion. Lightly mark the nasion.
3. **Inion:** Using a comb, unpadded cotton swab end or hair clip, part the participant's hair down the center, in the back of the head. Starting at the nape of the neck, run a finger up the back of the participant's head until a bony ridge, or bump, can be felt. Having the participant move his/her head up and down may help you to identify this bony ridge. The slight hollow just beneath this bony ridge is the inion. Lightly mark the inion. This landmark may be difficult to feel on some individuals. When the inion cannot be easily determined use the following method:
 - *Re-identify the nasion, which has been lightly marked.*
 - *Re-identify both pre-auricular landmarks, which have been lightly marked.*
 - Standing on the side of the participant, visualize an imaginary line forming a band around the head using the nasion and pre-auricular sites that have been marked. The back of this imaginary band should identify the inion. Mark the inion lightly.

1.1.1.6 Measure for electrode sites:

- Distance measurements are done with a **metric** tape measure and taken in centimeters (cm). When computing percentages to find the electrode site, a quick measurement guide is provided below to assist with providing the percentage values for measurements. The guide can be photocopied and kept with your prep materials for handy reference.
- All marks on skin must be done with a non-toxic, non-permanent implement, such as a wax-based china marker. Bright blue is most easily seen against dark hair. Red markers can be misidentified as blood by the participant or family members and is discouraged.
- When working with participants having long or thick hair, create a part in the hair by means of a comb or the unpadded end of a cotton-tipped swab; then hold the hair in place with hair clips while you work. The skin must be visible at the electrode sites because the **electrode must rest on the skin, not on hair.**

1.1.1.7 Quick Reference: Measurement Chart

Total Measurement Value (cm.)	50% Value (cm.)	20% Value (cm.)	10% Value (cm.)	5% Value (cm.)
25	12.5	5.0	2.5	1.25
26	13.0	5.2	2.6	1.3
27	13.5	5.4	2.7	1.35
28	14.0	5.6	2.8	1.4
29	14.5	5.8	2.9	1.45
30	15.0	6.0	3.3	1.5
31	15.5	6.2	3.1	1.55
32	16.0	6.4	3.2	1.6
33	16.5	6.6	3.3	1.65
34	17.0	6.8	3.4	1.7
35	17.5	7.0	3.5	1.75
36	18.0	7.2	3.6	1.8
37	18.5	7.4	3.7	1.85
38	19.0	7.6	3.8	1.9
39	19.5	7.8	3.9	1.95
40	20.0	8.0	4.0	2.0

Note: If the *total* value measurement contains a fraction, continue to use the percentage values as the whole number.

Example: Total measurement = 35.2, 35.5, 35.7 continue to use the percentage values for 35.

Remember: The 50% values are used to determine Cz.
The 20% values are used to determine C₃ and C₄.

Measure from Nasion to Inion and mark preliminary sites along center line of the scalp:

1. Have the participant sit in a chair. Standing at the side of the participant, place the zero line (0) of the tape measure on the marked nasion. Holding the tape measure in place with your non-dominant hand, stretch the tape measure over the crown of the head until it reaches the marked inion. Determine the total distance between the nasion to inion, in centimeters. Remember this number (it may help to write it down). Compute 50% of this total measurement (or use your measurement guide).
2. Mark the value for 50% of the nasion to inion total (near top of head). When marking these sites, make a large enough line so it can be easily found. This is your preliminary Cz mark.
3. With the tape measure still in place at the marked nasion, compute 10% of the nasion to inion total. Mark the 10% value as a straight horizontal line across the participant's forehead above the marked nasion. Extend this line to just above each eyebrow. This is your preliminary Fpz mark.

4. Use the same 10% value computed in step 3 and mark 10% up from the marked inion. Draw a horizontal line across the back of the head at this mark. This is your preliminary Oz mark.

To determine Cz:

5. Remove the tape measure and stand behind the participant. Place the zero line of the tape measure on the left pre-auricular mark. Stretch the tape measure over the top of the head, and along the mark made in step 2 until it reaches the right pre-auricular mark. Determine the total distance from pre-auricular to pre-auricular in centimeters. Remember this number (it may help to write it down). Compute 50% of this total measurement (or use your measurement guide).
6. While firmly holding the tape measure at the left preauricular mark, allow the tape measure to drape over the crown of the head while marking the value for 50% of the total measurement. This mark should intersect the mark made in step 2. The point at which the lines intersect is the Cz site.
7. With the zero line of the tape measure still at the left preauricular mark, compute 10% of the total distance between the pre-auricular marks. Mark a horizontal line across the side of the participants head at the 10% value above the left ear. Repeat this step on the right side of the head and mark a horizontal line at the 10% value above the right ear. These marks above each ear will be used to assist with measurements in the following steps.

To determine Fpz (for placement of snap electrode attached to Nox Head Cable):

8. Looking straight at the participant's face make a dot in the middle of the eyebrows then extend this dot into a vertical line that intersects the previously marked horizontal line from step 3. The point at which the lines intersect should be the middle of the forehead. **This location is known as Fpz.** This location should be in line with Cz. A snap electrode will be placed at this site in a later step.

To determine Fp₁ and Fp₂:

9. Measure the circumference of the participant's head by placing the zero line of the tape measure at the Fpz mark. Using the lines marked at 10% above each ear and the mark you made at 10% above the inion at the back of the head as a guide, encircle the head with the tape measure. Remember this number (it may help to write it down). Compute 5% of this total measurement. Place the zero line of the tape measure on the mark for Fpz and mark a vertical line at the 5% measurements to the left (Fp₁) and right (Fp₂) of Fpz. Double check your marks by measuring the distance between Fp₁ and Fp₂. The distance between these 2 locations should equal 10% of the total circumference measurement.

To determine O₁ and O₂:

10. Place the zero line of the tape measure on Fpz, wrap the tape measure around the side of the head using the mark made at 10% above the ear as a guide, and measure 50% of the total circumference (from step 9). Mark a vertical line at the 50% location at the back of the head. This

line should intersect the horizontal line you made at 10% above theinion (step 4). The point at which the lines intersect is the Oz site.

11. Compute 5% of the circumference total. Place the zero line of the tape measure on the mark for Oz and mark a vertical line at the 5% measurements to the left (O_1) and right (O_2). **These are the O_1 and O_2 electrode site locations.** Double check your marks by measuring the distance between O_1 and O_2 . The distance between these 2 locations should equal 10% of the total circumference measurement.

To determine C_3 and C_4 :

12. Place the zero line of the tape measure on Cz and allow the tape to stretch downwards toward the left ear. Remembering the total distance from pre-auricular to pre-auricular, compute 20% of the total measurement. While holding the tape in place between Cz and the left ear, make a horizontal line across the side of the participants head at the 20% value. This is your preliminary C_3 mark.
13. Place the zero line of the tape measure on the O_1 mark. Stretch the tape forward to the mark for Fp_1 , making sure the edge of the tape runs along the horizontal line you just made in the prior step. Compute 50% of the total distance between O_1 and Fp_1 and make a vertical line to intersect with the horizontal line marked in the prior step. **This intersection on the left side of the head is the site for the C_3 electrode placement.**
14. Repeat steps 11 and 12 on the opposite side of the head to determine C_4 , marking the 20% horizontal line between Cz and the right ear, and using the distance between O_2 and Fp_2 to compute the 50% vertical line. **The intersection on the right side of the head is the site for the C_4 electrode placement.**

To determine F_3 and F_4 :

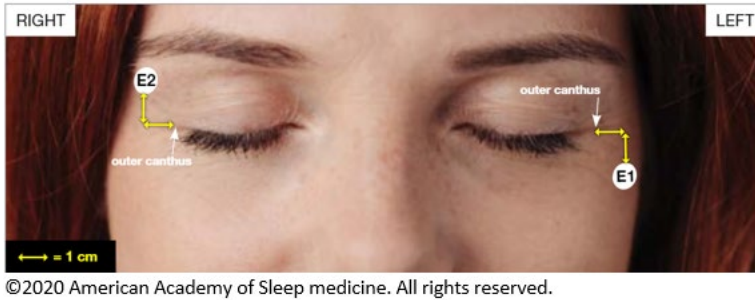
15. Lay the tape measure between the mark for Fp_1 (above the left eyebrow) and C_3 . Measure the distance between these locations and make a horizontal mark at 50% of the total distance. This mark should be in line with Fp_1 and C_3 . **This is the site for the F_3 electrode placement.**
16. Lay the tape between the mark for Fp_2 (above the right eyebrow) and C_4 . Measure the distance between these locations and make a horizontal mark at 50% of the total distance. This mark should be in line with Fp_2 and C_4 . **This is the site for the F_4 electrode placement.**

To determine M_1 and M_2 :

17. These placement sites are on the mastoid process (bone behind the earlobe). The electrode should be placed on the skin between the crease of the earlobe and where the hairline begins. Lightly mark these sites. **M_1 is placed on the left mastoid, M_2 on the right.**

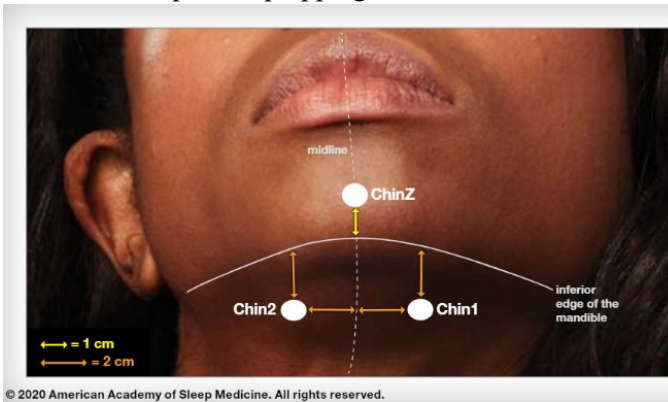
To determine EOG E_1 and E_2 placements:

18. The EOG recording electrodes are placed about **1 cm (one finger breadth) lateral to and 1 cm below the outer canthus of the left eye (E_1), and 1 cm above for the right eye (E_2).** Lightly mark these sites, and then stand in front of the participant to make certain that they are correct.



To determine chin EMG placement:

19. The EEG waveforms in REM sleep resemble the waveforms of wakefulness. The facial muscles, however, relax in REM sleep; therefore, these EMG electrodes are crucial in correctly identifying REM sleep. These electrodes must be attached firmly to prevent displacement and to yield quality data through the recording period. Attachment of these electrodes is described later in the manual. Two chin EMG electrodes are placed on each side of the geniohyoid muscle, which is a large muscle located underneath the chin. Having the participant activate this muscle may be helpful for determining the placement of the EMG electrodes. To activate the muscle, place your hand under the participant's chin, between the tip of the chin and the neck. Ask the participant to swallow. You will feel the geniohyoid muscle move. The electrodes are placed on each side of this muscle 2 cm below the inferior edge of the mandible and 2 cm to the right and left of the midline. A center electrode is placed on the ledge of the chin in the midline 1 cm above the inferior edge of the mandible (below the lower lip) as shown in the figure below. It can be helpful to lightly mark these electrode sites prior to prepping the skin.



- a. For participants with facial hair that prevents placement of electrodes in the locations described above, the two lower electrodes can be moved further back along the geniohyoid muscle. The midline electrode can be moved to an area along the jawline near the cheek on either side of the face.

1.1.1.8 Electrode Site Preparation Guidelines

- Electrodes must be placed in the correct locations to yield valid data.
- Electrode sites must be properly prepared prior to electrode placement to insure tight bonding and proper recording of the electrical signals (low impedance values).

- *Secure attachment of gold disk electrodes is crucial to successful recording of data. Before the attachment of gold disk electrodes, the skin at the marked sites must be properly cleansed and lightly abraded. Excessive impedance defeats the passage of signals into the electrode and, in turn, to the recorder. Successful skin preparation prior to electrode placement helps to reduce the level of impedance thereby improving the quality of signal.*
- Skin preparation requires abrasion to the top layer of the participant's skin at the electrode site. Although blood is not evident, the technician must understand that these areas are now non-intact skin and pose a risk for blood borne pathogens. Personal protective equipment (PPE) must always be worn when working with non-intact skin and equipment which has been in direct contact with non-intact skin (i.e.: used electrodes).
- Use an abrasive preparation. NuPrep has been provided for this purpose and contains a mild abrasive that is gentle and safe for sensitive skin.
- Abrade only the area at the marked site. Gold disk electrodes have a diameter of 1 centimeter; therefore, the abrasion should be limited to an area the size of or just slightly larger than the electrode. On marked sites, remember that the electrode should be placed where the 2 lines intersect.
- The participant should know what to expect! Please communicate. You may choose to use the following script: "Before I attach the electrodes, I have to get your skin ready. I will be using a special cleaner that sets the skin up for a good contact. You may feel a little bit of scratching on your skin, but it should not hurt, and it will not harm your skin."

1.1.1.9 Application of Skin Preparation Product

- 1. You will prep 20 sites on the participant's skin:*
 - a. Fpz at the forehead, and F₃, F₄, C₃, C₄, O₁, O₂ on the scalp*
 - b. M₁ and M₂ behind each ear*
 - c. E₁ below the left eye and E₂ above the right eye*
 - d. The left, right, and center chin electrode sites*
 - e. The left and right ECG electrode sites*
 - f. Two sites on each leg for leg electrodes*
- 2. Place a small amount of NuPrep skin prep abrasive onto a clean disposable surface (i.e.: 4x4 gauze square or small plastic med. cup). The product can also be placed on the glove near the thumb for easy access during skin preparation.*
- 3. If working in a hairy area, separate the hair to see the skin. You may find a comb or hairclips useful to create a part and hold the hair back.*
- 4. Use a cotton-tipped applicator to transfer a small amount of skin prep directly onto the electrode site. Before lifting the applicator, apply a moderate pressure and make small circular motions repeatedly on the skin. Take care that you include the center of the site, not just make circles around it leaving the center un-prepped. You may prefer to use a combination of back-and-forth strokes along with some circular motions.*
- 5. Continuing with moderate pressure, slowly count to 5 while you scrub the site (1 one-thousand, 2 one-thousand, 3 one-thousand, 4 one-thousand, 5 one-thousand). You are done when the skin "pinks up". Expect some participants to have more fragile skin than*

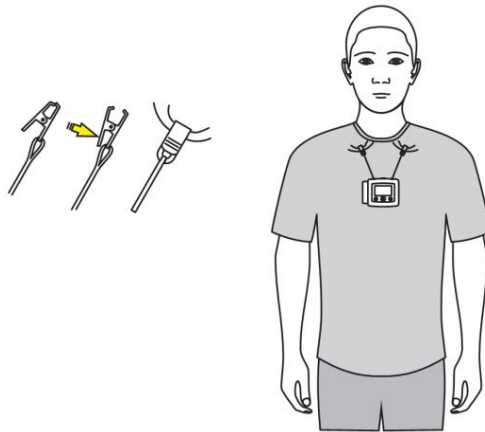
others; keep an eye on what you do. You may have to adjust the pressure or the count time.

6. *Prep abrasives are not designed as conductors; remove any excessive prep abrasive from the skin using a gauze pad prior to electrode placement.*
7. *Repeat the above steps for each electrode site. You might find it easier to prep 2 or 3 sites, and then to apply those electrodes, provided you do not lose your prepped sites. Use a clean applicator for applying prep to electrode sites on the face.*
8. *Discard the applicator and prep abrasive when finished. Never contaminate your original tube or bottle.*

8.6.9 Applying the Nox A1 Equipment to the Study Participant

Apply the Nox A1 Recorder

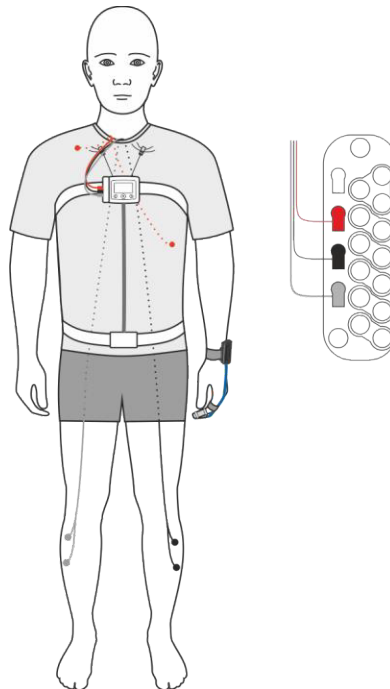
- Snap the clips that are attached to the Nox A1 recorder to the participant's shirt near the neckline as in the image below. This will help hold the Nox A1 device in place.



1.1.1.10 Apply the ECG and Leg EMG Electrodes (See following picture)

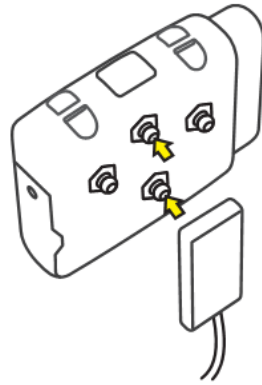
- Connect the orange ECG cable to the ECG keyhole connector on the Nox A1 recorder.
 - a. Ask the participant to place the ECG cable inside the neck opening of their sleepwear, and gently pull the longer side of the cable down the left side near the bottom of the ribcage.
 - b. Using a small amount of NuPrep, clean the skin just beneath the right clavicle.
 - c. Snap a self-adhesive electrode to the cable and apply the electrode to the cleaned area.
 - d. Ask the participant to lift their shirt just to the bottom of the rib cage on the left side.
 - e. Using a small amount of NuPrep, clean the skin just beneath the last rib on the left side of the rib cage.
 - f. Snap a self-adhesive electrode to the cable and apply the electrode to the cleaned area.
- Connect the black leg EMG cable to the LM1 keyhole connector on the Nox A1 recorder and connect the grey leg EMG cable to the LM2 keyhole connector on the Nox A1 recorder.

- a. Ask the participant to pass the black leg EMG cable through the neck opening of their sleepwear and through the waist of the sleepwear (if not wearing a nightgown or nightshirt) and down the left leg. Do the same with grey leg EMG cable and place it down the right leg. Placing the cable through the neck and inside the shirt helps protect the cables during sleep. However, if a participant is very tall, the leg cables can be connected to the device and passed through the waistband only.
- b. If the participant is wearing pajama bottoms, ask them to raise the pant legs to just below the knee and gently use your fingers to locate the tibialis anterior muscle in each leg. This muscle is situated on the lateral side of the tibia. To help locate the muscle, you can ask the participant to tap the foot up and down.
- c. Using a small amount of NuPrep, clean the skin on each leg over the area of the muscle where greatest movement occurs (usually ~2" to 4" below the bottom of the knee).
- d. Snap 2 self-adhesive electrodes to each cable and apply the electrodes to the cleaned area on each leg. The electrodes should be placed 2-3 cm apart.

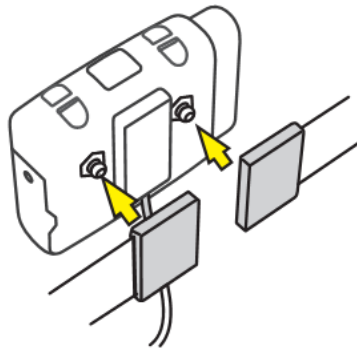


1.1.1.11 *Attach Abdomen Cable and Respiratory Belts*

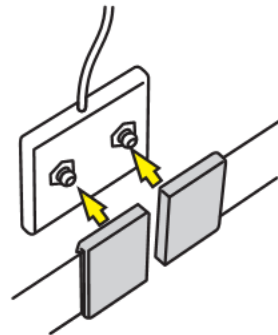
- Snap the Nox abdomen cable to the back of the device. The abdomen cable length can be adjusted by wrapping the cable around the connection unit to shorten the cable. The snap connector should be adjusted to hang just beneath the umbilicus.



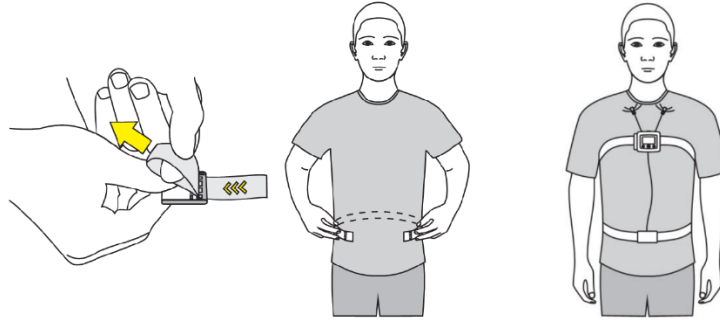
- Wrap a Nox disposable RIP belt around the participant’s thorax, passing it under the arms just beneath the armpits, and snap the effort belt to the snap connectors on the back of the right and left sides of the Nox A1 device. The belt should rest above the breasts and across the top of the thorax.



- Wrap a Nox disposable RIP belt around the participant’s abdomen, positioning the abdomen connector and belt just beneath the umbilicus, and snap the effort belt to the snaps on the back of the abdomen cable.

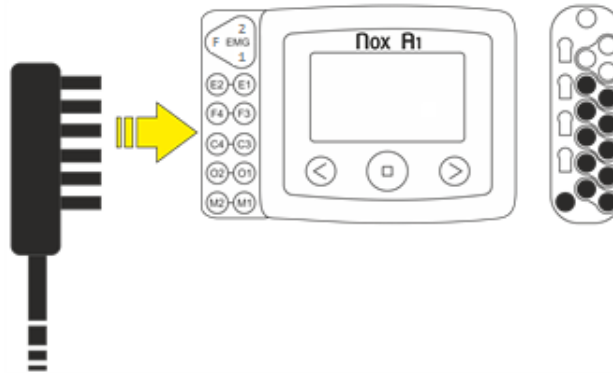


- Adjust the RIP belts around the participant’s thorax and abdomen so that they are snug but not so tight that they are uncomfortable. Adjustments can be made by pulling the elastic belt material through the plastic loops next to any of the 4 snap connectors. The plastic “teeth” visible in each loop will prevent the belt from loosening.

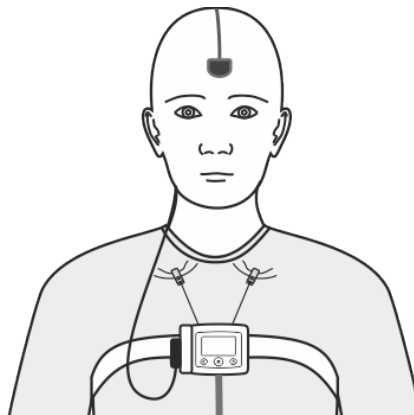


1.1.1.12 *Connect the EEG Head Cable and EEG Electrode Cables*

- Connect the Nox EEG Head Cable to the inputs on the side of the Nox A1 recorder. The Head Cable will connect to the E₂-E₁, F₄-F₃, C₄-C₃, O₂-O₁, M₂-M₁, and PGND inputs on the Nox A1 recorder.



- Snap a self-adhesive electrode to the Nox EEG Head Cable. Route the Nox EEG Head Cable behind the participant's head and adhere the electrode you prepped near the middle of the participant's forehead at the Fpz location.



- Connect two Nox 5 lead EEG electrode cables to the head cable placed at the Fpz location, one on each side of the head cable connector.



1.1.1.13 Attach Gold Disk Electrodes

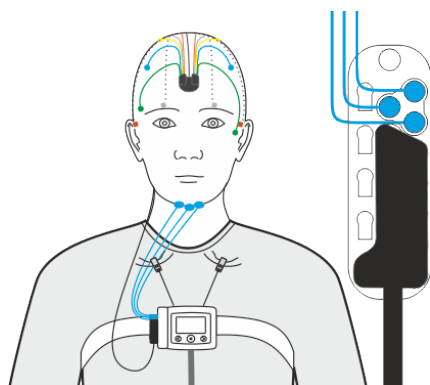
- The gold disk electrodes are applied to the prepared sites with an electrolyte paste. Ten20 Conductive Paste is preferred for most applications. Tensive Gel is also provided and might be preferred for participants with thin or no hair. Note that Tensive gel dries and creates a strong bond. Electrodes placed with Tensive Gel can be removed by holding a warm washcloth over the electrode site to loosen the gel. These products serve a dual purpose: providing both a conductive pathway for the signal to enter the electrode cup, as well as holding the electrode in place on the skin.
- Assemble your supplies in advance. Have several pieces of cut gauze or pieces of tape ready to place on top of the electrode once it is placed on the skin. For participants with hair on the scalp, gauze strips cut to 1 to 2" lengths are preferred. Tape can be used for participants with no hair. Cover-Roll Stretch tape cut to 1" strips or paper tape can be used behind the ears, for the eye electrodes, and to help secure chin electrodes. Gravity can move the electrode from its proper site if not supported, so it is important to ensure the electrode remains in the proper location during application.
- Place a small amount of electrolyte paste onto a clean disposable surface (i.e.: 4 x 4 gauze square, small plastic med. cup or the back of your gloved non-dominant hand).
- If working in a hairy area, separate the hair to see the skin. The electrode site should still be visible from the prep phase.
- If the participant is expected to sweat, there are additional skin preparations that reduce the moisture of the skin (such as Prep-N-Stay) and help improve the electrode contact with the skin. Generally, these liquids are applied very sparingly to prepped skin using a small piece of gauze and allowed to dry before continuing with electrode application.
- Before using tape, ask the participant about sensitivity to tape, latex or adhesives. All adhesives provided by the SRC are latex-free. Paper tape can be used on sensitive skin.
- Discard the unused electrolyte paste when finished. Never contaminate your original tube or bottle.
- Attach the gold cup electrodes for the EOG and EEG electrodes per the table below, ensuring the correct wire color is used for each electrode site. Use all wires connected to the left EEG

electrode cable for the odd numbered electrode sites on the left side of the face and head, and use wires connected to the right EEG electrode cable for the even numbered electrode sites on the right side of the face and head.

Wire color	Electrode site
Green	E ₁ and E ₂
Blue	F ₃ and F ₄
Yellow	C ₃ and C ₄
Grey	O ₁ and O ₂
Red	M ₁ and M ₂

- a. For the E₁, E₂, M₁ and M₂ electrodes:
 - i. Using the gold cup of the electrode as a scoop, fill the electrode cup with electrolyte paste so it is slightly rounded above the gold cup (there must be no “air pockets” inside the gold cup, as this can cause a poor signal).
 - ii. For the M₁ and M₂ electrodes, place the electrode onto the prepped site paste side down with the tail of the electrode (end where wire attaches to gold cup) pointing down toward the shoulder, and cover with a piece of non-latex skin tape. Cover-Roll Stretch tape is excellent for attaching these electrodes. Paper tape can be used on participants with sensitive skin. Cover the black tail of the electrode where the wire attaches to help ensure the electrode stays firmly in place.
 - iii. Press lightly on the top of the electrode as well as firmly around the rim of the cup to insure a good seal. Hold in place until electrolyte begins to set and the electrode feels secure.
 - iv. For the E₁ and E₂ electrodes, place the electrode onto the prepped site paste side down with the tail of each electrode pointing away from the participant’s eye and towards the hairline. Cover with a piece of tape as you did for the electrodes behind each ear ensuring the tail of the electrode is covered.
 - b. For the F₃, F₄, C₃, C₄, O₁, O₂ scalp electrodes:
 - i. Separate hair to make sure skin is visible at the prepped electrode sites.
 - ii. Using the above technique, fill the electrode cup with electrolyte paste so that the paste is lightly slight rounded above the gold cup and attach to prepped site on the scalp by pressing the electrode firmly to the scalp.
 - iii. Cover the electrode with cut gauze pressing firmly on electrode and hold in place until electrode paste begins to set and feels secure. A second piece of gauze can be used with a small amount of paste on the gauze to help stabilize the electrode. The participant’s hair can also be used to gently cover the gauze to help further protect the electrode. Note that for participants without hair, tape can be used instead of gauze to secure electrodes.
- Attach the chin EMG electrodes. Ambu Neuroline 715 electrodes will be used. Insert the chin electrode leads into the EMG channels of the Nox A1 recorder.
 - a. The left chin electrode (black wire) plugs into the **1** input on the Nox A1 device.
 - b. The right chin (red wire) electrode plugs into the **2** input on the Nox A1 device.

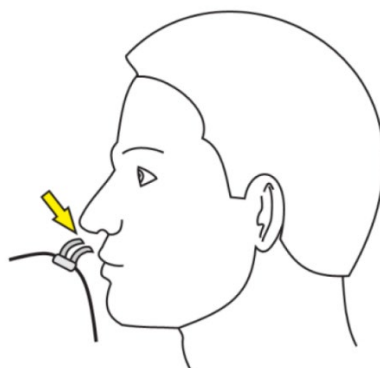
- c. The center chin (green wire) electrode plugs into the **F** input on the Nox A1 device.



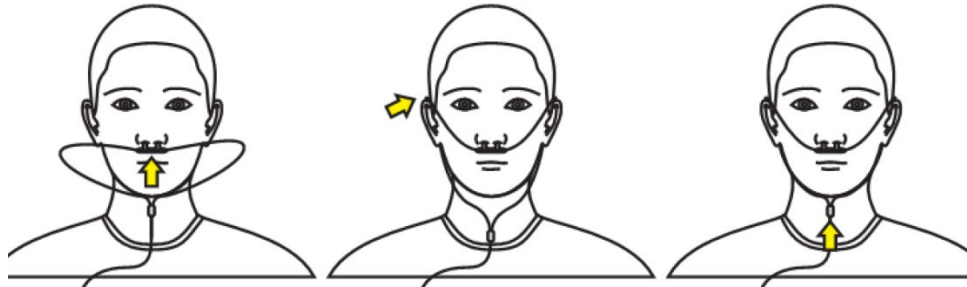
- d. The chin EMG electrodes are self-adhering and contain a silver/silver chloride sensor. No electrolyte paste is used. Gently peel each electrode from the backing and apply each sensor to the locations you identified and prepped earlier on each side of the geniohyoid muscle and midline 1 cm above the edge of the mandible (below the lower lip).
- i. Special note for participants with facial hair: Placement of electrodes may need to be modified. Electrodes should be placed along the geniohyoid muscle behind the hairline of the beard. The center electrode may be placed along the jawline near the cheek if a beard is present.

Apply the Nasal Cannula: Skip this step and go to “Apply the Wrist Oximeter” if the participant wears an oxygen cannula or a PAP mask during sleep.

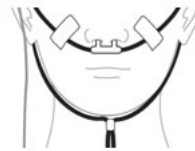
- Plug the nasal cannula firmly into the PRES port on the side of the Nox A1 recorder.
- Place the nasal prongs gently in the participant’s nostrils. The prongs should point downwards inside the nostrils as in the image.



- Pull the cannula tubing over the ears and then position it under the chin and slide the fastener snugly under the chin to hold the cannula tubing securely in place. The fastener should be snug but not tight or uncomfortable.



- Use a small piece of tape on both sides of the nose to secure the cannula.

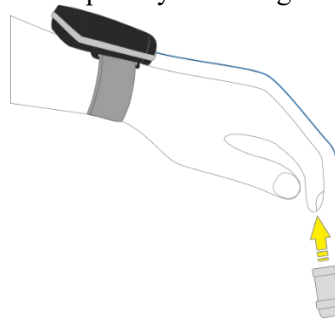


1.1.1.14 Apply the Wrist Oximeter

- Place the Nonin WristOx device on the non-dominant wrist. The device should fit like a wristwatch and is secured with the Velcro strap attached to the device. The strap should be adjusted so that the device is secure against the wrist but not uncomfortable or tight.



- Place the finger probe on the finger that fits best into the soft tip sensor. The middle finger or ring finger is recommended. The fingertip should be near the end of the probe but should not extend through the opening at the end of the probe. Note that the oximeter will power on when the finger is inserted and might turn off again. This is normal, and the oximeter will power on and begin collecting data when the sleep study recording is started.



- The largest part of the soft tip sensor, the raised square, should be positioned over the bed of the fingernail. Improper placement will result in an invalid recording, so proper placement is important.
- Use a small piece of tape to secure the cord of the finger probe cable by wrapping the tap around the finger just behind the soft tip sensor. A small piece of tape should also be used to secure the wire on the back of the hand.
- The participant should be instructed not to get the oximeter finger probe wet. If necessary, the finger probe can be removed to use the restroom and wash hands and then replaced.

8.6.10 Starting the Nox A1 Sleep Study Recording

- The recording will start automatically at the time provided during device initialization. This time should correspond to one hour prior to the participant's reported bedtime. No action is required by the participant to start the recording.
- When the device turns on and begins recording, a small indicator light beneath the button on the front of the Nox A1s device will blink green while the recording is in progress. Participants should be instructed not to press any buttons on the device.
 - Pressing the button before the recording has started will turn on the display, and a countdown to the specified start time of the recording will display. See left image below.
 - Pressing the button after the recording has started will turn on the display, and the current duration of the recording will display. See right image below.



- When the participant wakes up and is ready to get out of bed for the day, they should follow the participant instruction sheet for removing all sensors and equipment, placing all items into the Nox Medical carrying case, and returning the equipment to the study site. The device will turn off automatically after 10 hours of recording time.

8.6.11 Receiving and Cleaning/Disinfecting the Nox A1 kit

- After the Nox A1 kit is returned to the study staff, the following steps should be performed to properly clean and disinfect the equipment. The device should be cleaned immediately upon receipt.

1.1.1.15 General Guidelines:

1. Appropriate PPE should be worn when performing device cleaning and disinfection. At a minimum, gloves should always be worn.
2. Designate a specific area in your workspace for equipment that has been returned from a participant but has not yet been cleaned and disinfected. Equipment that has not been cleaned and disinfected should always be kept separate from clean equipment. Consider a plastic container or tub that can be easily cleaned with a disinfectant wipe for this purpose.
3. After receiving a Nox A1 kit back from a participant, place the entire kit in the area or container you have designated for soiled equipment.
4. Designate a clean area in your workspace for storing equipment that has been cleaned, disinfected, and is ready for participant use.

1.1.1.16 Cleaning Instructions for the Nox A1 Device, Cables, Carrying Case

Materials/equipment:

1. Mild detergent (soap) and water solution. Endozime® AW Plus cleaner can be used if your hospital prefers an enzymatic detergent.
2. Lint-free cloths
3. Gloves (and other PPE as required by your institution)
4. PDI Sani-Cloth Plus Germicidal Disposable Cloth or equivalent validated disinfectant wipe. If your institution has a preferred product, please make sure it is safe to use on metals and plastics.

Cleaning/Disinfecting the Nox A1 Device and Cables:

1. Put on gloves before beginning the cleaning/disinfecting process.
2. Prepare a solution of mild detergent and water or prepare Endozime® AW Plus cleaner per manufacturer's directions for use.
3. Open the carrying case and dispose of following items in the trash:
 - a. Nasal cannula
 - b. Thoracic and Abdominal RIP belts
 - c. Single-use, self-adhesive, snap electrodes, chin electrodes
4. Carefully disconnect the ECG, LM1, and LM2 cables from the Nox A1 recorder. Also disconnect the EEG electrode cables from the EEG head cable. You do not need to disconnect the head cable from the Nox A1 device. **Do not discard these items.** All cables provided by Nox Medical for the Nox A1s device are reusable.
5. The gold cup electrodes at the end of the EEG electrode cables can be briefly soaked in a cup containing hot water and mild soap to dissolve electrode paste. A nylon brush (e.g., a toothbrush) can be used to gently scrub paste out of the gold cups. Once clean, allow the gold cup electrodes to dry before disinfecting.
6. Dampen a lint-free cloth with the detergent and water solution (or the Endozime solution).
 - a. Do not pour or spray any liquids on the Nox Recorder
 - b. Do not allow any liquids to enter any openings on the Nox Recorder
 - c. Do not fully immerse the cables in liquid
 - d. Avoid contact of the cleaning solution to cable/electrode connectors
7. Wipe all surface areas of the Nox A1s device and all cables and connectors thoroughly to remove all visible soil and contaminants. Wipe each component for at least 2 minutes.
8. Visually inspect the cleaned components to ensure no soil remains. Be sure to check gold cup electrodes carefully.

9. Allow the device and all cables to air dry completely before disinfection and for a minimum of 3 minutes.
10. For disinfection, remove a PDI Sani-Cloth Plus Germicidal Disposable Cloth or your institution's equivalent disinfectant wipe from the container.
11. Wipe all surface areas of the Nox A1s device and all cables with the disinfectant wipe for at least 3 minutes if using the PDI Sani-Cloth wipe. If your institution recommends a different wipe, please follow instructions for the appropriate contact time. Pay special attention to the gold cup electrodes and ensure all surfaces are carefully cleaned with the disinfectant wipe.
12. Allow the device and components to air dry completely before next use.
13. Visible soil can be removed from the Nox A1s carrying case with the mild detergent solution. When completely dry, thoroughly wipe down the Nox A1 carrying case with a disinfectant wipe and allow the case to air dry.

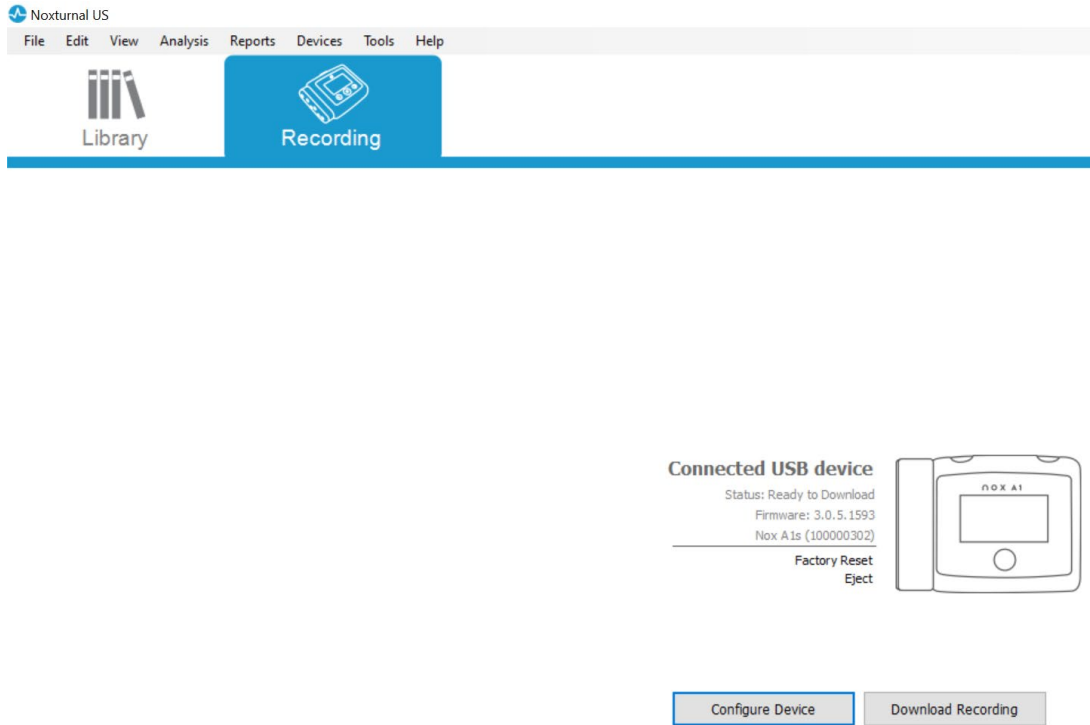
Cleaning the Nonin WristOx

1. Wash the Velcro wristband in a mild detergent with warm water and allow to air dry.
2. Open the battery cover and remove the batteries from the device.
3. Replace the battery cover.
4. Unplug the sensor cable from the side of the WristOx device.
5. Clean the sensor by wiping all surfaces of the cable and fingertip sensor for 3 minutes with a PDI Sani-Cloth wipe or use your institution's equivalent disinfectant wipe for the appropriate contact time. Remember to clean the inside of the fingertip sensor.
6. Allow the fingertip sensor and the Nonin WristOx device to dry thoroughly before next use.

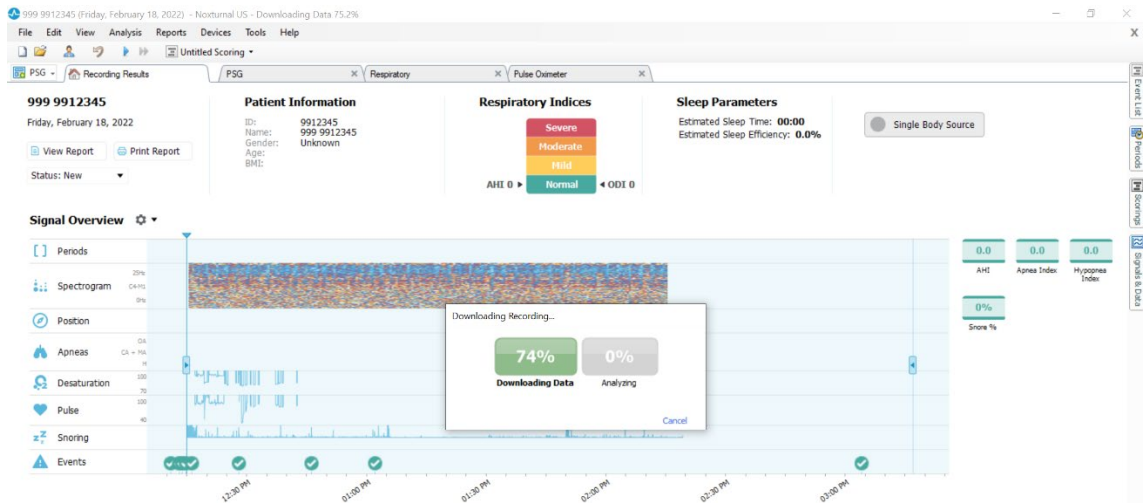
Remember to wash hands thoroughly after handling soiled equipment. Always wash hands thoroughly before handling equipment that is clean and ready to be packed into the kit for participant use.

8.6.12 Downloading Sleep Study Data and Sending the Study to the Coordinating Center

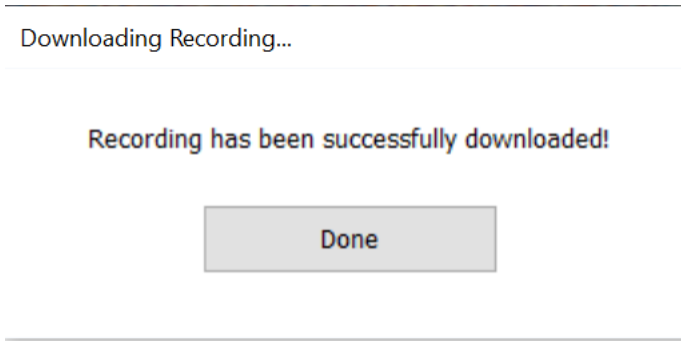
1. Start Noxturnal software and select the "Recording" tab at the top of the screen.
2. Open the battery lid on the Nox A1s device with the key pen provided, remove the AA lithium battery and discard per your facility's instructions.
3. Connect the Nox A1s device to the computer with the USB-C cable.
4. When the Nox A1s recorder is connected to the computer, the device display lights up and displays "Connected" at the bottom of the display. The Noxturnal software Recording tab will change to display the "Connected USB device" message and will show details about the connected Nox A1s device. Note: It can take several seconds for the software to recognize the device. If the software does not recognize the device after approximately 10 seconds, move the mouse pointer to the question mark on the "Recording" screen and click to scan for the Nox A1s device.
5. The status message on the screen should say "Ready to Download." Click the Download Recording button.



- The study will begin downloading, and a status message will display the progress of the download.



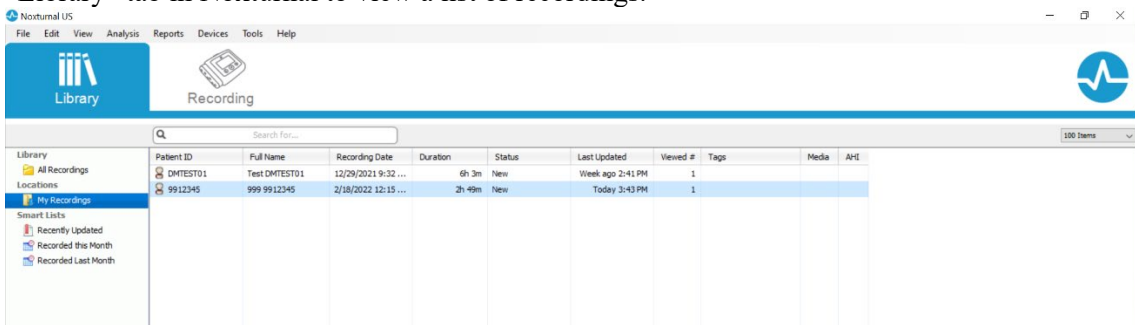
- When downloading is complete, a notification will appear stating the download was successful. Click Done.



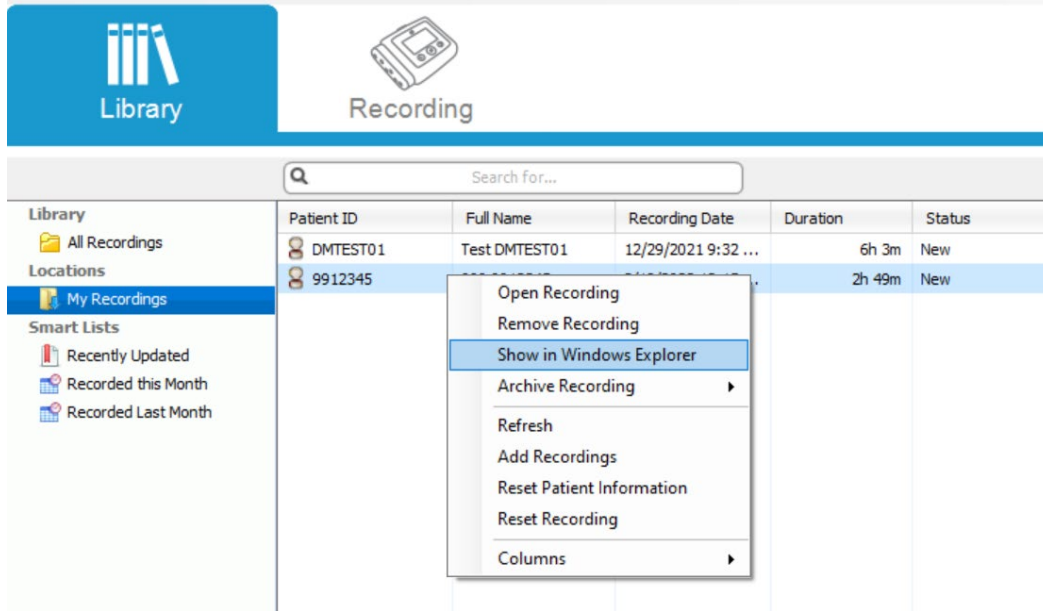
- On the Noxturnal File menu, choose the “Close & Save Workspace” menu item. The Noxturnal “Recording” tab will display, and the “Download Complete” status message will display.



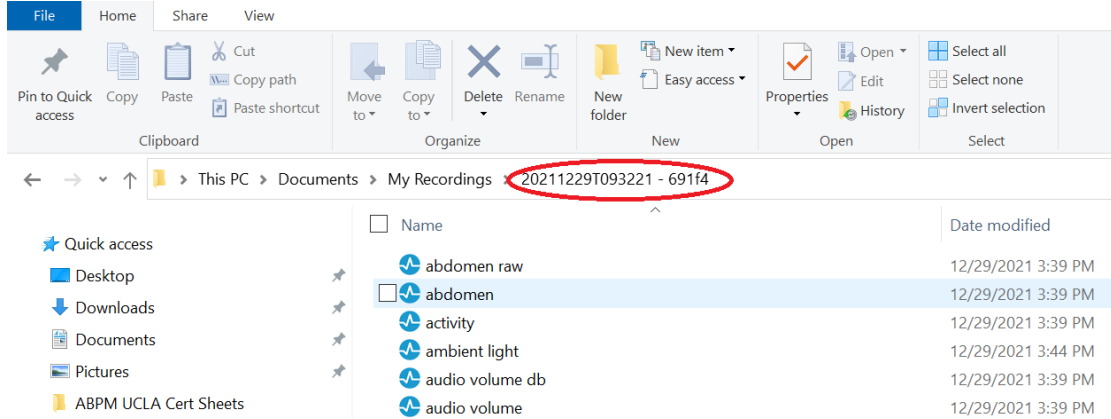
- To locate the study and prepare it for transmission to the Coordinating Center, click the “Library” tab in Noxturnal to view a list of recordings.



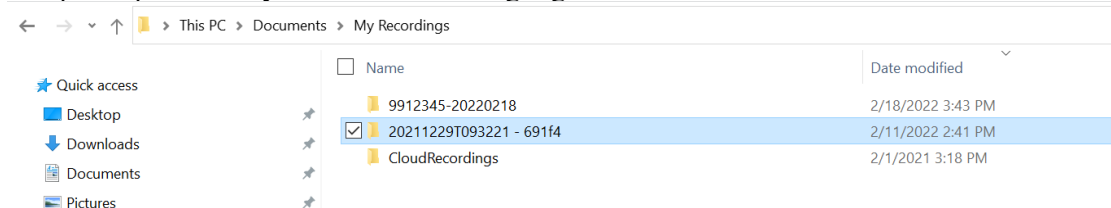
- Locate the participant’s study ID in the Patient ID field. You can use the search box above the list to enter the participant ID.
- Right-click on the participant’s record in the list and select the “Show in Windows Explorer” menu option.



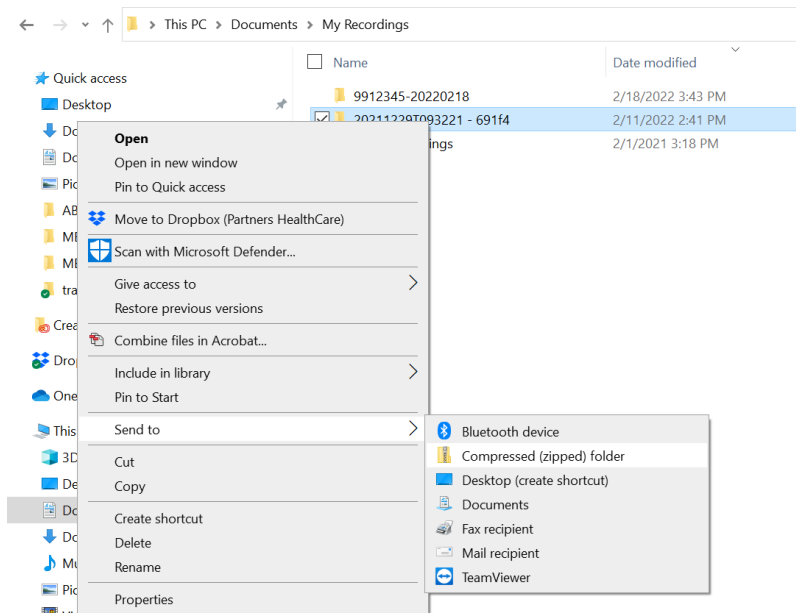
- Nocturnal sleep studies are saved in the Documents folder on your computer in a folder named My Recordings. The folder containing the participant’s study will open. Make a note of the folder name that is displayed in Windows Explorer. In this example, the folder name is circled in red.



- Navigate up one folder level by clicking on “My Recordings” to the left of the folder name. The participant’s study folder should be highlighted.



- Rename the folder using the following format: Participant ID-YYYYMMDD.
- Right-click the newly renamed folder, choose the “Send to” menu option, and then the “Compressed (zipped) folder” menu option to create a compressed copy of the participant’s sleep study.



16. Transmit the compressed sleep study to the Coordinating Center. The SRC will access sleep studies from the CC and will review studies to ensure sufficient data was collected, score the studies, generate reports, and monitor studies for sufficient signal quality. Please see instructions from the CC for data transmission procedures.

8.6.13 Scored Reports, Study Acceptability and Urgent Alerts

The SRC will provide consistent and accurate scoring of all data, blinded to participant information, identifying any studies that require repeating due to insufficient data, studies with severe physiological abnormalities requiring timely notification (urgent alerts), and for quantifying quantitative metrics for use for predictive modelling. Sites will receive urgent referral notifications within two business days of receipt of the study by the SRC.

Failed Studies: Studies that do not meet minimal criteria for acceptability (> 2 hours of artifact free data during the sleep period on respiratory bands, airflow and oximetry) will be attempted to be repeated.

Repeat Studies: If a participant is willing to repeat a failed study, follow the same device configuration steps to create the new participant. The same Participant ID should be used. When the sleep study is downloaded, a new recording will display in the Noxturnal Library with the new recording date.

Urgent Alerts: Alerts will be reported using the CC REDCap system if any of the following are identified during scoring of the sleep study:

- PSG: O₂sat <85% for >= 10% Total sleep time
- PSG: Baseline (wake) O₂ saturation <88% for >= 1 minute
- AHI > 50 and no history of diagnosed OSA
- A-fib/flutter not previously diagnosed
- A-fib/flutter previously diagnosed but HR >120 bpm or <50 bpm for 2 min
- HR >=150 bpm or <=30 bpm for >= 2 consecutive mins (no A-fib/flutter)
- PSG: Acute ST segment (suggests ischemia)
- Heart Block Complete AV block, 2nd degree AV Block, Mobitz 2; pause > 6 secs
- Non-sustained wide complex tachyarrhythmia (3 beat run at rate >120)

The staff member receiving the urgent alert email from the SRC should “reply all” and acknowledge receipt of the email. Within 48 hours of being notified of an urgent alert, the study coordinator will notify their site PI for follow-up. The study PI will review this information and determine appropriate follow-up, which may include review of medical records for evidence of a prior condition or referring the patient for further follow-up.

8.6.14 No Show or Blank Studies

If the Nox A1 is prepared for a participant and the participant is unable to complete the study at the programmed time, the device can simply be configured for a new recording for a later date. If the Nox A1 records a study but is not worn, there is no need to download the study data. The data can be erased during configuration for a new study.

8.6.15 Device Accountability Logs

Maintenance and repair log shall be kept for each instrument including date and description of any software installation or upgrades. Sites will be provided with device logs that should be used to track PSG equipment. The log will contain the device serial number, participant ID number, date sent home with the participant, and the date the device was returned to the clinic. In the event a device needs to be sent to Nox Medical for repair, an entry should be made in the log with “Nox Repair” noted in the participant ID field, and the date the device was sent for repair and received back at the site will be recorded.

All leads and peripherals used should be labeled and kept with the same unit to enable accurate troubleshooting methods. Date of replacement should also be recorded in the maintenance and repair log.

8.6.16 Training and Certification

All site staff must be certified by the SRC to perform the PSG procedure using the Nox A1s device. Certification requires completion of the PSG Written and Practical Exams. Each staff member who will be responsible for configuring the Nox A1s device, applying the device to a study participant, and downloading data must complete a certification recording that will be reviewed by the SRC. The certification recording process should follow all procedures outlined in this manual and should be conducted on a non-participant volunteer or study staff member. Each staff member certifying must successfully configure the Nox A1 recorder, apply the device per the instructions in this manual to the volunteer, receive and clean/disinfect the device, and successfully download the overnight sleep study and transmit the data to the CC for review by the SRC.

In addition to certification recordings for each staff member, all Nox A1s devices at each site should be tested before they are first used to collect sleep study data on a consented participant to ensure the device functions properly. The test recording can be performed simultaneously with the overnight certification recording. For any Nox A1s device not used for staff certification, a brief recording (1 to 2 hours) while the device is worn during the day can be submitted. The SRC will provide feedback on study quality and any problems observed during study review. Certification and device testing studies will not be fully scored.

When configuring the Nox A1s device for a certification study, the “Last” name field and “Identification” field on the Patient Information screen in Noxturnal should contain the staff ID number preceded by the

letters “CR” (e.g., CR9001) so the SRC can easily identify the certification studies and staff member associated with the study. For equipment test studies only, precede the staff ID number with the letters “EQ” in the “Last” name field and “Identification” field (e.g., EQ9001) to indicate an equipment test study. Note that the 1-to-2-hour equipment test studies cannot be used for staff certification.

1.1.1.17 Recommended Staff Responsibilities

It is recommended one PSG Technician/Research Assistant at each site be identified as the Lead Technician responsible for maintaining equipment records and tracking any problems identified, including any resulting in returns of the unit to the Manufacturer. Because proper maintenance is a key aspect for the quality of the PSGs, the lead technician will be responsible to ensure that all equipment is checked at the time it is returned to the site and before it is scheduled for use on a home visit. PSG technicians are responsible for maintaining the unit in good working order and identifying and replacing any electrodes or other peripherals that were damaged in the home or are no longer functioning properly.

8.6.17 Ongoing Quality Control

Following initial certification PSG technicians will be evaluated continuously to monitor and assure quality control.

The quality of each signal and overall study quality will be assessed at the time of scoring of the record. The Scorer will code each channel according to the duration of i) scorable signals; ii) duration of artifact free signals during sleep, and iii) an overall QA grade to each study. The total duration of the study (from Time to Bed to the lights on) and the total duration of sleep will also be indicated. Scoring notes regarding staging, event identification, outliers, and specific physiological signal issues are also recorded on the QS form. All data contained in the QS form (quality grades and scoring notes) will be entered into a REDCap database. This QS data is reported to the site for individual reports and used to generate Quality summary reports. (Sample QS Form is included in the Appendix)

The SRC will generate periodic summaries on overall quality of the PSG sleep studies by site, by technician, and by unit using the QS form data. Sites and Technicians are expected to maintain quality of 85% of studies in the Very Good, Excellent, and Outstanding range. If a Technician is noted to fall below the 85% performance level (and it is not due to faulty equipment or identified participant issues in the home), the site will be notified so that the technician can be observed by another on site tech to improve performance and be retrained as needed.

1.1.1.18 Participant Confidentiality and Field Site Data Management

Procedures to assure confidentiality will be strictly observed. All certification and research data transmitted to the SRC will have identification numbers and no personal identifiers (other than study dates). All documents and the sleep files should be checked to ensure no personal or identifying information is contained in these files before transmitting the files the SRC.

Each field site will use designated computers that comply with their institution’s security regulations. A copy of the PSG should be retained at the site until final reports are received from the Sleep Reading Center indicating the SRC has a final archived copy. Periodically the sites will want to check the available storage on the computers where studies are downloaded and delete copies of older PSGs that have been finalized with reports from SRC if needed.

1.1.1.19 Data Security and Archival at the SRC

All systems are secured behind the MGB firewall and follow MGB Information Security policies for authenticated, minimum access. All systems are patched, monitored and scanned routinely for vulnerabilities and intrusions by the systems administrator and MGB Information Security. Data is encrypted, where applicable, in compliance with state and federal government standards, regulations, and in accordance with Partners Security and Privacy policies. All configuration changes that could affect accessibility or security are approved by management.

The virtual services and databases are backed up nightly via the enterprise backup system, IBM Tivoli Storage Management, and maintained on encrypted storage tapes for tapes that are stored off site. All systems administrative personnel and support staff have completed the NIH training program in Computer Security and have additionally completed their certification in The Collaborative IRB Training Initiative (CITI) program. CITI was developed by experts at PHS, MGH, and BWH and with outside institutions in the "IRB community" and consists of courses in the Protection of Human Research Subjects for Biomedical research.

8.6.18 Appendix A. Definitions and Descriptions of Common Sleep Terms

Sleep Apnea

Sleep Apnea (also referred to as obstructive sleep apnea syndrome (OSA), sleep apnea-hypopnea (SAHS), and sleep disordered breathing (SDB)) is a condition characterized by loud disruptive snoring, snorting/gasping (during sleep), and daytime sleepiness. These symptoms result from abnormal breathing during sleep occurring as a result of brief, repetitive episode when there is collapse or partial collapse of the throat (upper airway tissues). When the throat totally collapses (obstructs), breathing completely stops (momentarily), and an apnea occurs. When the throat partially collapses, a hypopnea (or partial obstruction) occurs (breathing continues but is diminished). In order to resume breathing after a complete or partial throat obstruction, the body sends signals to the lungs and chest to breathe harder. Eventually (usually only seconds), enough force is developed to open the throat muscles, allowing normal breathing to resume. As the throat tissues are pulled open, a loud snort or gasp may result. Snoring may be heard as the throat tissues vibrate during breathing through a partially blocked throat.

Why does this occur? Normal breathing depends on many factors, including airway (bronchial) size and function, lung tissue factors, the lung's blood supply, and breathing muscles (chest, diaphragm, and throat). The brain controls many of the lung's activities. While we are awake, the brain usually sends the appropriate signals to the muscles of the chest and the throat, maintaining normal breathing. However, during sleep, many of the throat muscles relax too much. When this happens, especially in people with a small throat opening (from big tonsils, a big tongue, fat, or a small jaw), a partial or complete throat collapse (hypopnea or apnea) may occur.

In whom does this occur? Not too long ago, sleep apnea was thought to be a rare condition. Now that doctors know more about it and have access to sleep laboratories (where sophisticated monitoring equipment aids in making this diagnosis), many people are being diagnosed. What is more, epidemiologists (scientists who study diseases and risk factors in communities) have begun measuring sleep and breathing in large numbers of people in the community. Because of this, we now know that sleep apnea is quite common (perhaps as common as high blood pressure). It is estimated that between 6 and 20% of adults have sleep apnea, with rates as high as 60% in older adults. Although one of the biggest risk factors for sleep apnea is obesity, thin people may also have sleep apnea.

What does sleep apnea do to a person? Most of the consequences of sleep apnea are due to three phenomena: snoring, sleep disruption, and irregular breathing. One of the most troubling consequences of sleep apnea is the snoring and loud breathing noises that can disturb the sleep of the affected person as well as his/her bed-partner. This may cause embarrassment and marital discord. The intermittent disruptions to sleep also interfere with the brain's normal sleep pattern- causing "arousals," and reducing the amount of sleep time spent in deep sleep and REM (Rapid Eye Movement, or "dream") sleep. This may prevent "restorative" sleep, causing the person to feel sleepy and irritable during the day, and, possibly, "slowing" the person (physically and mentally). The breathing irregularities often cause the body's oxygen levels to drop. The drops in oxygen levels are thought to cause stress on the heart, contribute to high blood pressure, to other heart ailments (heart attacks, angina, irregular heart rhythms) or stroke. A major purpose of the MESA Sleep Study is to now better understand how sleep apnea affects blood pressure over the day and influence risk for cognitive impairment.

How is sleep apnea diagnosed? Sleep apnea is diagnosed in people who have symptoms of snoring, snorting, and sleepiness, and by an overnight sleep that shows repetitive periods of obstructed breathing. During sleep, every apnea and hypopnea that lasts at least 10 seconds (and usually also is associated with some drop in oxygen or change in brain waves [arousals]) is counted. If the total number of apneas and hypopneas per hour of sleep is greater than a given threshold (5 to 20, according to local physician practices), a diagnosis of sleep apnea is made.

How is sleep apnea treated? Several fairly simple things are usually recommended to improve breathing during sleep: weight loss (if overweight), sleep posture (side rather than back), nasal decongestants,

avoidance of alcohol, and good sleep habits (regular bed/awake times, sufficient sleep time, etc). People who are symptomatic often are prescribed a breathing aid, nasal CPAP (continuous positive airway pressure), a bedside device that blows air, under pressure, through the nose into the mouth, acting as a pneumatic stent, keeping the throat open. People who are prescribed this wear a small plastic mask over their nose (to permit the passage of this air). It is recommended that this machine be used nightly. Other therapies include surgery (removing tissue in the throat), neurostimulation of the tongue, and dental devices that bring the jaw forward. New medications are under development for sleep apnea. There is a great deal of controversy, however, concerning the role of specific treatments in people who do not complain of excessive daytime sleepiness. The information proposed for collection in the MESA Sleep Study, will better define the role of sleep apnea in heart and brain disease, and, thus, provide data useful for deciding which patients should be treated for sleep apnea.

Insomnia and Sleep Duration Variation

Insomnia refers to problems initiating (getting to) or maintaining sleep, including early morning awakenings. Chronic insomnia (lasting > one month) affects about 10% of people; however, 30 to 50% of people have suffered from insomnia from time to time. Insomnia may be found in 40% of elderly (>65% years). Insomnia is commonly associated with underlying medical (e.g., arthritis, chronic lung problems, renal failure, etc.) or psychologic conditions, including anxiety, depression, and responses to life stress. In the elderly, pain from physical problems is a common cause of insomnia. Those with insomnia often complain of daytime sleepiness and poor waking function. Diagnosis of insomnia usually requires a careful medical history. Sometimes a 7-day sleep diary along with actigraphy (to measure movement and estimate sleep-wake time) is useful. Sometimes an overnight sleep study is needed to rule out other conditions that may disrupt sleep, including sleep apnea and periodic limb movement disorder (PLMD). If an overnight sleep study (PSG) is done, some typical findings in patients with insomnia are a long sleep latency (long period of awake before sleep onset; e.g., > 30 minutes) and low sleep efficiency (low percentage of time asleep compared to time in bed; e.g., < 65%). Treatments for insomnia vary according to its cause, including treatment of any underlying medical and psychological conditions. Behavioral treatments (e.g cognitive behavioral therapy for insomnia) are considered first line treatments, although medications can be used judiciously in specific settings.

Periodic Leg Movements Disorder (PLMD)

PLMD is a disorder characterized by repetitive stereotypical movements, usually of the legs, but sometimes of the arms, that occur during sleep. Most of the movements individually last 0.5 to 5 seconds and recur every 20 to 40 seconds in clusters that can last minutes or hours. Often the big toe extends and ankle dorsi-flexes (points upwards). With movements, there are often “arousals” –or lightening of sleep or even awakening. PLMD occurs in > 40% of the elderly. Many people with PLMD also have restless leg syndrome (RLS) –a syndrome where the subject reports feeling “creeping or crawling” sensations in the legs-especially while resting. PLMD may be a cause of insomnia and/or daytime sleepiness. Much, however, is not known about PLMD. One goal of MESA is to better identify what the health impact of PLMD is. Identification of PLMD will be accomplished by measuring leg movements during sleep.

Sleep Stages

Although we all know the value of a good night's sleep, most people do not realize that sleep is a complex process. At the onset of sleep, the brain's electrical impulses slow down. As sleep progresses, the brain's electrical activity fluctuates in certain very specific patterns and locations. These patterns define specific sleep stages. Based on the patterns of the electrical activity of the brain, sleep is characterized as:

Stage 1 (N1): Light sleep, occurring in transitions from wake to sleep. Typically, <5% of sleep time. Higher amounts usually indicate poor sleep.

Stage 2 (N2): Light sleep with specific electrical characteristics (spindles, K complexes). Typically, the most common sleep stage (>50% of sleep time)

Stage 3 (N3, also known as “slow wave sleep”): Deep sleep, characterized by large, slow brain waves. Considered to be “restorative” and important for memory. Typically, 20-25% of sleep time, but lower in men and in older adults.

Stage REM (NR, Rapid Eye Movement Sleep): Also known as “dream sleep”. This stage of sleep is more common in later parts of the sleep period, often associated with dreaming. REM sleep appears important for learning and memory and can be reduced with sleep apnea and other sleep disturbances.

During a normal sleep period, there is a regular progression of sleep stages. A sleep cycle is a period of non-REM sleep followed by a period of REM sleep. Generally, there are 4-6 sleep cycles per sleep period.

With disorders such as insomnia, sleep apnea, or periodic limb movements, sleep architecture (the progression and distribution of sleep stages) may be disrupted. These disorders can be associated with abrupt changes in brain activity (arousals), sometimes waking up the person, and other times, moving him/her to a lighter sleep stage (e.g., Stage 1). Frequent arousals may be associated with shorter total sleep time and reduced slow wave, Stage 3 and REM sleep. Excessive numbers of arousals and/or movements can lead to poor quality sleep, sleep fragmentation, and sleep deprivation resulting in daytime sleepiness, mood disturbance and poor daytime functioning.

Sleep Duration and Efficiency

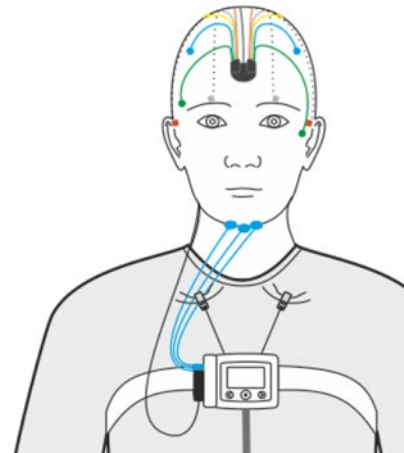
In addition to information on sleep quality (i.e., sleep stage distributions), there is also interest in sleep time. “Normal” sleep time in adults is thought to be 7 to 8 hours. People who sleep much less or much more often have poorer health and may even be at greater mortality risk. Sleep efficiency refers to the percentage of time in bed in which the subject actually sleeps. An alternative way to quantify sleep and wake periods is WASO- the absolute amount of Wake After Sleep Onset. People with a sleep efficiency of < 85% often have poorer sleep (15% of the sleep time was actually spent awake.) Similarly, WASO of > 60 minutes is considered to be an elevated amount of wake time duration sleep. Sleep patterns may be measured with PSG or with actigraphy. Both tools will be used in MESA.

8.6.19 Appendix B. Nox A1 Equipment Removal Instructions

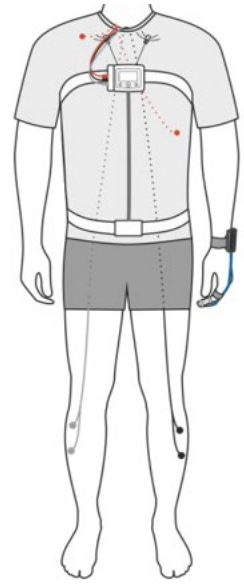
Nox A1 Equipment Removal Instructions

The morning after the sleep study, all equipment should be removed as instructed below. Please note there is no need to turn off the device, as the device will stop recording on its own.


1. Finger Pulse Oximeter:
 - a. Remove any tape from the hand and remove the oximeter finger probe from the tip of the finger.
 - b. Loosen the Velcro wrist strap and remove the Nonin unit from the wrist.
 - c. Place the pulse oximeter unit and cable into the black Nox Medical case.
2. Nasal Cannula:
 - a. Remove the nasal cannula from the nose and gently pull the cannula out of the side of the Nox A1 unit.
 - b. The cannula can be discarded into a trash bin.
3. Head and Face Sensors: There are 6 sensors on the scalp, 1 on the forehead, 1 behind each ear, 1 beside each eye, and 3 on the chin as shown in the image. These sensors will have conductive paste on them when they are removed. There is a Ziploc bag provided in the Nox bag. The ends of the sensors that contain paste can be placed into the Ziploc bag when they are removed.
 - a. Taking care not to pull on the flexible wire, begin by removing the 6 sensors on top of the head. Carefully grip each sensor and gently peel the sensor away from the scalp.
 - b. The sensors behind each ear are held in place with tape. Being careful not to pull on the sensor wire, gently peel the tape from each sensor and remove the sensor from behind each ear.
 - c. The sensors next to each eye are held in place with tape. Being careful not to pull on the sensor wire, gently peel the tape from each sensor and remove the sensor next to each eye.
 - d. Carefully unsnap the black sensor cable from the adhesive patch on the forehead. The cable and all sensors can be placed inside the plastic Ziploc bag provided by study staff. Carefully peel the adhesive patch off the forehead and discard the path.
 - e. The sensors on the chin may be held in place with tape or gauze. Being careful not to pull on the sensor wires, gently peel the tape or gauze from each sensor and remove the sensors from the chin. The ends of the sensors containing paste or gel can be placed in the Ziploc bag with the other sensors.
4. Respiratory Effort Belts: The respiratory effort belts are held in place by snaps. There are 2 snaps on the back of the Nox A1 unit that secure the white belt around the chest, and two snaps on the back of the small black abdominal cable unit that secure the white belt around the stomach.
 - a. Carefully unsnap all 4 snaps attached to the white effort belts and remove the belts.
 - b. The effort belts can be discarded into a trash bin
 - c. NOTE: Please be sure NOT to discard the small black cable the belt around the stomach is attached to.
5. Leg and Torso Sensors:



- a. There are 2 adhesive sensors on each leg as shown in the image on the right. Taking care not to pull on the flexible wire, grip each round sensor snap and carefully unsnap each of the snaps from the left and right leg sensors.
 - b. There are 2 sensors on the torso, indicated by the red dots on the image, that each have a single snap. One sensor is located just below the collarbone on the right side, and one sensor is located just below the rib cage on the left side. Unsnap each of the snaps from the sensors.
 - c. Gently pull the red wire that runs down through the shirt that was attached to sensors on the torso outside of your shirt. Gently pull the wires that run down the left and right legs outside of your clothing.
 - d. The adhesive sensors on the legs and torso can be gently removed immediately or in the shower after all equipment is removed and discarded. The red, grey, and black wires should remain connected to the Nox A1 device.
6. While holding the Nox device in one hand to prevent it from dropping, gently squeeze one of the silver clips to release the device from the neck strap.
 7. Place the Nox device and cables into the black Nox Medical case.
 8. Return the Nox A1 equipment to the study site as instructed by study staff



8.6.20 Appendix C. PSG Tracking Form



Exam 7
Polysomnography
Tracking Form

Participant ID #: Acrostic:

Technician ID: Date: / /

Month Day Year

NOX ID: _____

At the time of hook-up:

Time of arrival: : AM
 PM Time of departure: : AM
 PM

Participant's reported
planned time to bed: : AM
 PM

Is there a history of diagnosed sleep apnea?

Yes
 No
 Don't know

Is there a history of atrial fibrillation?

Yes
 No
 Don't know

Does the participant plan on using the following during the sleep (if so, do not use the nasal pressure cannula):

	Yes	No
CPAP/APAP/BIPAP	<input type="radio"/>	<input type="radio"/>
Oxygen	<input type="radio"/>	<input type="radio"/>

Were there any problems with the hook-up?

Yes →

Explain: _____

No

MESA Exam 7 | Polysomnography Tracking Form | v13/21/2022Page 1 of 2



Exam 7 Polysomnography Tracking Form

After retrieving the PSG study:

Recording Assessment:

Is the study ID on the recording correct and does it match the ID on paperwork? Yes No

└─ If no, explain below

Were any electrodes or cables visibly broken upon the Nox return and cleaning? Yes No

└─ If yes, explain below

Was the Sleep Recording Center emailed to notify them that a study was uploaded (include study ID, MR#, and date of upload)? Yes No

└─ If no, explain below

Explanation or additional specific comments/complaints from the participant that may have affected this study. Also, any comments regarding problems with the study upload (short upload time, etc.):

Alerts Reporting:

Date study report received from the SRC: / /
Month Day Year

The following **Urgent alert** was reported by the Sleep Reading Center:

Alerts will be auto-populated from the PSG Quality Summary Form

If no alerts were reported, the REDCap Form will display "None"

Was the alert reported to the Participant?

Yes → Date: / /
 No Month Day Year

Comment: _____

8.6.21 Appendix E. PSG Accountability Log



MESA MIND NOX A1 Device
Accountability Log

Site: ____
Page: ____

Subject ID	Nox A1 Serial Number	Date Device Given to Participant (MM/DD/YYYY)	Staff ID (provided device)	Date Device Returned (MM/DD/YYYY)	Staff ID (received device)	Comments
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	
_____		___/___/_____	___-___	___/___/_____	___-___	

MESA MIND Nox A1s Accountability Log [NOXLOG] – V1-7DEC2021 Please note that if sending the A1s unit in for repair, please record that as a separate entry Page 1 of 1

8.7 Participant Diary

PURPOSE

This questionnaire is designed to track the wearing of the hip actigraph monitor and collect some daily information on participants' sleeping and eating habits. The data is needed for the first 8 days for all monitoring devices, including hip activity, wrist activity, continuous glucose monitor, heart patch monitor, overnight sleep study, and 24H blood pressure monitor. If the participant continues to wear the continuous glucose monitor for more than 8 days, they only need to complete the Participant diary for the first 8 days.

The Participant Diary will be collected on paper by the participant and entered in REDCap by study staff. It should be reviewed upon receipt for completeness/consistency. If obvious errors of missingness are identified, the clinical staff can attempt to call the participant to clarify ambiguous entries.

METHODS

This is a **self-administered** questionnaire. Show the diary to the participant and ask them to complete the two-sided form every day that a monitor is worn. Go over the questionnaire with the participant in clinic and ask if they have any questions. Ask the participant to try to answer all questions, unless instructed to skip the question.

The participant should to complete the diary in two sittings; the first page is completed in the morning and the back page is completed at the end of the day.

Specific Instructions.

Review the Participant Diary at the in-clinic or home visit with the participant. The first Diary will be about the current day and the night before coming in to clinic/home visit.

Sample introductory text: *For 8 days while wearing a monitor, we ask that you complete a Participant Diary indicating the times you went to bed, woke up, sleep quality, and whether you had dreams. This form will also ask about your eating habits and naps throughout the day. If you continue to wear the glucose monitor on your arm for more than 8 days, you can stop recording the diary information after the 8th day.*

Make sure the participant knows the difference between AM and PM. Remind the participant that midnight is 12:00 AM and that noon is 12:00 PM.

What time did you get into bed yesterday? We really care about the time they got into bed in preparation for their longest sleep, not about getting into bed for a nap, or to read a book, or to watch TV. Record the time they shut the lights off with the intention to go to sleep.

How long did it take you to fall asleep? Encourage them to estimate to the best of their ability.

How many times did you wake up (not counting your final awakening)? Count the number of times between when they fell asleep, and the last time they woke up for the day. Include any time that they were aware that they were awake, regardless of whether or not they got out of bed.

What time was your final awakening? Record the last time you woke up in the morning. Many people wake up multiple times and have a hard time getting back to sleep. Record the last time they woke up before getting out of bed for the day.

What time did you get out of bed for the day? Record the time they got out of bed after their final awakening.

Last night your sleep was: Response options include:

Very poor

Poor

Fair

Good

Very Good

Participant should select the best option that describes their overall sleep last night.

Do you remember dreaming last night? We do not need to know every detail of their dreams or how many different dreams they may have had; just if they recollect dreaming at all last night. Emerging data suggests that people who do not remember their dreams may have more cognitive impairment than those who do remember their dreams. Responses are Yes or No.

The following questions should be answered at night just before going to bed.

If participant did not agree to wear the hip monitor, skip to the next question. If he/she agreed to wear the monitor, ask:

Did you wear your red hip monitor for the entire day today?

Yes

No

If no, why? Record if participant did not wear the red hip monitor at all that day or for any brief periods of time.

Did you take a nap today?

Yes

No

Include any naps that lasted 5 minutes or longer, regardless of whether the participant intended to nap or just fell asleep.

What time did you eat today? Record approximate start time for breakfast, lunch, dinner and up to 4 snacks.

This last question is only answered if the participant wore the 24H Blood Pressure monitor in the last day or night. It is also skipped if the participant does not take prescription blood pressure medication.

If you take blood pressure medication, what time did you take it today? Record up to three times in the past 24 hours.

9 ALERTS

The alerts notification process ensures that the participant and their health care provider are aware of any significant medical findings discovered during MESA procedures.

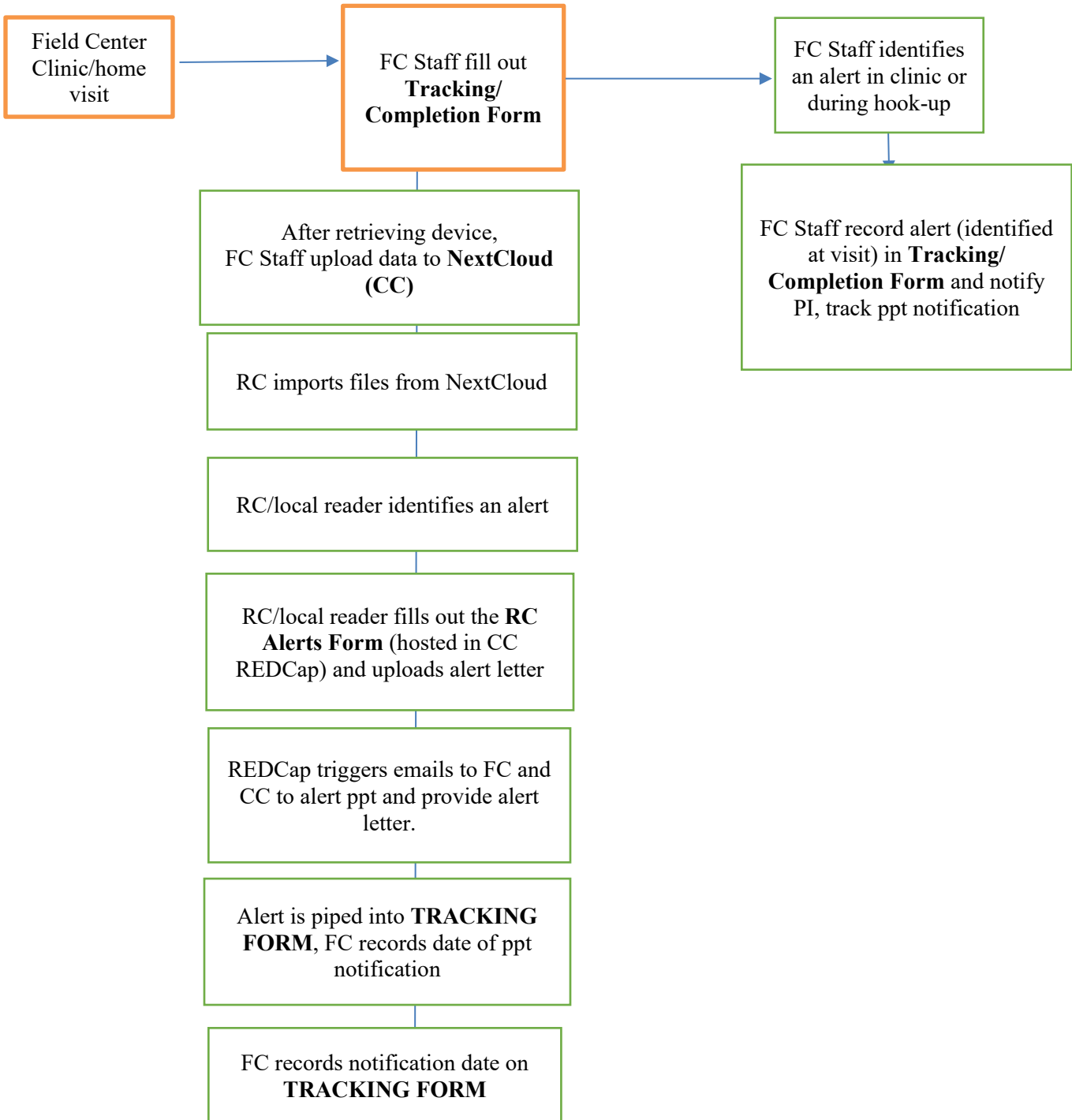
Alerts are medical findings that may have adverse health consequences to the participant if untreated. Table 1 describes the alerts identified and tracked for Exam 7. Each alert is categorized as either immediate or urgent.

Immediate Referrals are medical emergencies that require immediate notification of both the participant and their primary health care provider. Immediate referrals usually require the participant to go directly from the Field Center clinic to their health care provider or hospital. Immediate notification of the participant should occur during the clinic visit. The participant's health care provider is contacted by telephone before the participant leaves the clinic. A follow-up letter documenting the findings and phone call discussion are sent to the participant's health care provider.

Urgent Referrals include abnormalities that require non-emergency medical attention. If an urgent alert is found while the participant is in clinic, the study staff or PI will discuss the issue and provide follow-up instructions to the participant at that time. If an urgent referral is discovered after the clinic visit, the participant is contacted by phone by the MESA Field Center PI or clinic staff member. Notification of an urgent finding is shared with the participant's health care provider by mail or phone within one week of its discovery.

The actions above are documented in the Exam 7 REDCap program when an immediate or urgent alert is identified. Participants provide and update contact information during annual follow-up calls and clinic visits. Participants specify if results should be shared with each listed health care provider. All Exam 7 results that the participant chooses to receive will be shared with each health care provider who the participant approves for receiving results. Field Center PIs or physicians share immediate and urgent alerts with participants. Non-immediate and non-urgent exam results letters are prepared at the MESA Coordinating Center, sent to the Field Centers for review and mailed to the participant from the Field Center.

The figure below summarizes the process of identifying and tracking alerts and participant notifications. In general, alerts are identified either at the clinic visit or when data are reviewed at a reading center. If identified in clinic, the alert value and participant notification are recorded in the procedure completion form. For alerts identified at a reading center, reading center staff enter the alert in a reading center alert form, which triggers an email notification to the FC. After the FC notifies the participant, the date is recorded in the procedure completion form.



The following table describes where alerts are identified, in what form alert and participant notification details are recorded, and whether the reading center provides an alert report to share with the participant and their health care provider.

Procedure	Identified by:	REDCap Tracking		Is a report provided by RC?
		Form where Alert is described:	Form where Participant notification is documented:	
Blood Pressure	Clinic staff	Seated Blood Pressure	Seated Blood Pressure	No
Oxygen Saturation	Clinic staff	Seated Blood Pressure	Seated Blood Pressure	No
Pulse	Clinic staff	Seated Blood Pressure	Seated Blood Pressure	No
Brain MRI	MRI tech/MRI RC	Brain MRI Alert	Brain MRI Acquisition	Yes – attached in Brain MRI Alert Form
Heart Monitor Patch	NWU RC	Heart Monitor Alert	Stress Reactivity Completion	Yes – attached in Heart Monitor Alert Form
Lipids/Blood tests	Central Lab	n/a (reported with lab datasets)	n/a (reported with Lab Results Letter)	No
Lung CT	CT tech/CT RC	Lung CT Alert	Lung CT FORCE (4,5,8) Completion Lung CT FLASH (3,6) SOMATOM DRIVE (7) Completion	No, nothing attached to Lung Alerts Form. CC provides alert letter for central reads (Col, WFU, MINN, UCLA)
PSG	Sleep RC	PSG Quality Summary	Sleep PSG Tracking	Yes – Attached in PSG Quality Summary Form
ABPM	Sleep RC	ABPM Quality Summary	24H ABPM Tracking and Alert	No

9.2 MESA Alerts and Alert Levels

The alert values for each procedure are listed in the table below with an alert level classification of immediate or urgent.

Finding	Alert Level	Study
Systolic BP > 210 mmHg	Immediate	Core
Diastolic BP > 120 mmHg	Immediate	Core
Systolic BP 180-210 mmHg	Urgent	Core
Diastolic BP 110-120 mmHg	Urgent	Core
Oxygen Saturation (resting) <88%	Urgent	Core
Pulse >130 bpm	Urgent	Core
Brain MRI: Acute subdural or epidural hematoma	Immediate	MESA-Mind
Brain MRI: Subarachnoid hemorrhage	Immediate	MESA-Mind
Brain MRI: Acute intraparenchymal hematoma	Immediate	MESA-Mind
Brain MRI: Acute infarct	Immediate	MESA-Mind
Brain MRI: Abscess	Immediate	MESA-Mind
Brain MRI: Suspected tumor with significant mass effect	Immediate	MESA-Mind
Brain MRI: Tumor without significant mass effect	Urgent	MESA-Mind

Finding	Alert Level	Study
Brain MRI: Subacute infarct	Urgent	MESA-Mind
Brain MRI: Arteriovenous malformation	Urgent	MESA-Mind
Brain MRI: Aneurysm	Urgent	MESA-Mind
Brain MRI: Obstructive hydrocephalus	Urgent	MESA-Mind
Heart rhythm monitor: Wide QRS tachycardia >110 bpm and sustained for >30 seconds	Urgent	Stress Reactivity
Heart rhythm monitor: Complete AV block	Urgent	Stress Reactivity
Heart rhythm monitor: 2nd degree AV Block, Mobitz II	Urgent	Stress Reactivity
Heart rhythm monitor: Pause >4 seconds	Urgent	Stress Reactivity
Heart rhythm monitor: Bradycardia <40 bpm and sustained for >30 seconds during waking hours	Urgent	Stress Reactivity
Heart rhythm monitor: Atrial fibrillation/atrial flutter with average heart rate <40 bpm or >180 bpm and sustained for 60 seconds	Urgent	Stress Reactivity
Heart rhythm monitor: Atrial fibrillation that is sustained for more than 6 minutes	Urgent	Stress Reactivity
Heart rhythm monitor: Narrow QRS tachycardia >180bpm and sustained for 60 seconds	Urgent	Stress Reactivity
Heart rhythm monitor: Other abnormalities deemed important by the ECG center readers	Urgent	Stress Reactivity
Total cholesterol > 360 mg/dL	Urgent	Core
Triglyceride > 1000 mg/dL	Urgent	Core
Calculated LDL cholesterol > 260 mg/dL	Urgent	Core
Fasting glucose < 50 mg/dL or > 400 mg/dL	Urgent	Core
Creatinine > 2.0 mg/dL	Urgent	Core
Any abnormalities identified by CT tech	Urgent	Lung
CT RC Alert	Urgent	Lung
PSG: AHI > 50 and no history of diagnosed OSA	Urgent	Sleep
PSG: O2sat <85% for >= 10% Total sleep time	Urgent	Sleep
PSG: Baseline (wake) O2 saturation <88% for >= 1 minute	Urgent	Sleep
PSG: A fib/flutter or HR PSG ECG <ul style="list-style-type: none"> A-fib/flutter not previously diagnosed A-fib/flutter previously diagnosed but HR >120 bpm or <50 bpm for 2 min HR >=150 bpm or <=30 bpm for >= 2 consecutive mins (no A-fib/flutter) 	Urgent	Sleep
PSG: Acute ST segment (suggests ischemia)	Urgent	Sleep/PSG
PSG: Heart Block Complete AV block, 2 nd degree AV Block, Mobitz 2; pause > 6 secs	Urgent	Sleep/PSG
PSG: Non-sustained wide complex tachyarrhythmia (3 beat run at rate >120)	Urgent	Sleep/PSG
PSG: Other	Urgent	Sleep/PSG
ABPM: 24-hour average SBP \geq 180 mmHg and/or 24-hour average DBP \geq 110 mmHg	Urgent	Sleep/ABPM

9.3 Heart Rhythm Monitor Alerts

The ECG patch monitor will be applied at the Exam 7 clinic or home visit. After 7 days of ambulatory ECG monitoring, the participant will mail the patch to Northwestern University for analysis. The technologist at Northwestern will generate a report using the Cardea SOLO software, and if they see a concerning ECG finding, they will contact the study cardiac electrophysiologist, Dr. Rod Passman. Dr. Passman will evaluate the finding and, if he confirms the finding to be an urgent alert, he will contact the FC PI. Dr. Passman will also conduct a cardiologist over-read of the findings of each report, transmit any alert findings to the appropriate FC PI, and summarize the results that will be included in a letter for participants. The ECG monitor alerts are as shown in Table 1.

9.4 Chest CT Alerts

Significant Alerts

Alerts of potential and established significance are aortic aneurysms, dense aortic valve calcifications (aortic stenosis), lung masses (> 3 cm), pneumonia, pneumothorax and large pericardial effusions. These will be communicated to Field Center PIs, or designee, directly.

- a. Aortic diameter > 45 mm – aortic aneurysm screening is the only cardiovascular imaging modality ever shown to improve outcomes.ⁱ
- b. lung masses (>30 mm)
- c. lobar pneumonia,
- d. pneumothorax and
- e. large pericardial or pleural effusions, along with unusual findings deemed significant by the reading center.

Other Findings

Other findings of potential significance that may require follow-up include pulmonary nodules and hepatic or splenic lesions. These will be communicated to via the high-tech results letter.

- a. Nodules (non-calcified densities in the lung < 30 mm). In December 2013, the U.S. Health U.S. Preventative Services Task Force issued a Grade B recommendation for lung cancer screening **for individuals at increased risk of lung cancer** (criteria below).¹ Based on this recommendation, participants meeting these criteria (“high-risk individuals”) with lung nodules will receive an alert in accordance with the LungRADS™ assessment categories.²⁻⁴
For low-risk individuals (those not meeting the USPSTF criteria), there is no current data to suggest that intervention on small nodules provides benefit, and some data that there may be harm reporting asymptomatic nodules (cost, anxiety, follow up tests, morbidity and mortality). Consistent with prior MESA Exams, a nodule size threshold of 8 mm will be used. Scans with nodules ≥8mm in size will prompt an evaluation of older scans for comparison. Nodules will not be reported if unchanged from prior MESA scans (if available), as these are considered benign. Only solid nodules will be considered. Nodule size was collected systematically in Exam 1 and all nodules (including 1-2 mm) were reported. The prevalence of reported nodules among low-risk individuals is expected to be <10%.
- b. Dense (non-cystic) lesions in the liver and spleen will be reported. These are rare.

Radiologist Review Chest CT scans will be reviewed for pulmonary alerts and other findings that may require clinical follow-up either locally by a board-certified radiologist at the Field Center or centrally by Dr. John Austin, a board-certified thoracic radiologist and member of the Fleischner Society, who has extensive experience in lung imaging or locally. If Dr Austin is not available, another board-certified thoracic radiologist will perform the read. Central reads will occur for the University of Minnesota and UCLA. Local reads will take place at: Wake Forest University, Columbia University, Johns Hopkins University, and Northwestern University.

For local reads, the local radiologist will perform either a safety read for alerts and other findings, as defined above, or a full clinical read, according to local practice, and complete the CT Safety Reading form. If a safety read is performed, a report will be generated only in the event of an alert or other finding; if a full clinical read is performed, the result will be returned to the participant along with a cover letter explaining the significance of the report in lay language.

For central reads, Dr. Austin will perform a safety read and complete the CT Safety Reading form. For alerts and other findings, he will provide the clinic and participant with a report on letterhead documenting the potential issue in clear language with a recommended next action. In addition to the reports, the CT reading center is ready to help participants obtain copies of their images upon request if this proves difficult from the primary source, the site where the CT exam is performed.

Drs. Austin, and Barr will also consult and discuss cases with FC local radiologists, physicians and PIs as requested and have done this in the past on several occasions.

The table below describes a summary of findings and the appropriate action

Finding	Action
Alert: aortic aneurysms, dense aortic valve calcifications, lung masses (≥ 3 cm), pneumonia, large pericardial, pleural effusions or large perfusion defect	If the radiologist feels that an alert is warranted, they will write a report and this will be transmitted immediately to the field site PI, coordinator and a copy sent to the coordinating center. The participant will receive a letter that describes the finding and suggests that the participant share the letter with their physician. The PI will contact the participant directly.
Other findings: Lung nodules (<3 cm) in participants who meet US Preventative Task Force eligibility criteria for lung cancer screening CT ¹ (Adults ages 55 to 80 years who have a 30 pack-year smoking history AND who currently smoke OR have quit within the past 15 years).	The radiologist will write a report in accordance with the LungRADS™ assessment categories. ²⁻⁴ The participant will receive a letter that describes the finding and suggests that the participant share the letter with their physician. For findings requiring follow-up in 6 months or less, the PI will contact the participant directly.
Other findings: Lung nodules (<3 cm) in participants who do NOT meet US Preventative Task Force eligibility criteria for lung cancer screening CT ¹ (Participants over age 80 years OR who have a less than 30 pack-year smoking history OR who have not smoked cigarettes for more than 15 years).	The radiologist will write a report for non-calcified lung nodules ≥ 8 mm, unless they are stable and have not increased compared to a prior CT scan. The participant will receive a letter that describes the finding and suggests that the participant share the letter with their physician. For findings requiring follow-up in 6 months or less, the PI will contact the participant directly.
Other Findings: non-water density lesions of the liver or spleen, etc.	The radiologist will write a report, and this will be transmitted to the field site for inclusion in the high-tech results letter. The participant and their physician, if approved, will receive this letter that describes the finding
Routine: Emphysema Extent.	The participant will receive a letter that provides these results and suggests that the participant share the letter with their physician.

9.5 Brain MRI Alerts

For MESA Mind, safety reads will be performed locally by radiologists at each Field Center, unless a Field Center made prior arrangements with the University of Pennsylvania MRI Reading Center to perform safety reads. Any of the medical findings listed in Table 1.1 may have immediate adverse health consequences to the participant if untreated.

9.6 Geriatric Depression Scale Alerts

Appendix A of the cognitive battery manuals of procedures provides follow-up questions and procedures for use by certified interviewers when they suspect ‘significant emotional distress’ as suggested by a score on the GDS-Short Form >8 or by any of the responses during the encounter that suggest significant emotional distress such as statements regarding suicide, hopelessness or lasting depressed mood.

9.7 Continuous Glucose Monitoring Alerts

Continuous glucose monitor results from the Freestyle Libre Pro are blinded and are therefore not reviewed in real time. Acute glucose excursions in the past are not considered clinically meaningful; however, significant time spent at the extremes of the glucose range may be indicative of poor glucose control and may warrant non-urgent follow up with a physician, especially for those being treated for diabetes. If the continuous glucose monitor registers any readings <50mg/dL or any readings \geq 400mg/dL then the glucose summary letter will suggest that the participant discuss their glucose summary report with their primary care doctor or endocrinologist at their next appointment.

9.8 Ambulatory Blood Pressure Monitoring Alerts

Immediate and Urgent Blood Pressure alerts may be generated at the time of ABPM placement, which will include use of the study Omron BP device to confirm ABPM readings. Using the Omron readings, site personnel should follow the same guidelines for BP alerts as specified in the clinic exam protocol for BP alerts.

Urgent ABPM alerts will be generated after central reading at the Brigham Sleep Reading Center (SRC). PSG studies should be transmitted by the FC to the SRC as soon as possible after study completion and device retrieval. A trained research technician will review studies within two business days of receipt. If Urgent Referral Criteria are met, the study is reviewed by the SRC Director or her designee. If the Urgent Alert is confirmed, the site will be electronically notified and receive the full report within a week after final scoring is completed. This information will be emailed to the FC personnel identified to receive Urgent Referral notices. The DCC will also receive a copy of this e-mail. The site is expected to acknowledge receipt of the alert from the SRC and notify the participant (and/or family), appropriate physicians, and site personnel. The site will provide alternate staff contacts should personnel normally receiving these notices be unavailable.

All Urgent Referral Alerts will be logged by SRC personnel into a PSG Alert Log indicating the date reviewed and date the site coordinator was notified. A copy of the acknowledged receipt of the Urgent Referral by the site will be kept with the PSG Quality documents.

At the FC, FC staff are expected to keep a local log documenting receipt of each Urgent Alert, date when the participant was contacted, whether the participant’s health care provider was notified and a note of the “action plan” (e.g., referred to specialist, etc.), and other relevant comments (e.g., participant reported this is a known condition).

Urgent Alert criteria include: 24-hour average SBP \geq 180 and/or 24-hour average DBP \geq 110.

9.9 Polysomnography (PSG) Alerts

Polysomnography Alerts will be generated after central reading at the Brigham Sleep Reading Center (SRC). PSG studies should be transmitted by the FC to the SRC as soon as possible after study completion and device retrieval. A trained research polysomnologist will review studies within two business days of receipt. If Urgent Referral Criteria are met, the study is reviewed by the SRC Director or her designee. If the Urgent Alert is confirmed, the site will be electronically notified and receive the full report within a week after final scoring is completed. This information will be emailed to the FC personnel identified to receive Urgent Referral notices. The DCC will also receive a copy of this e-mail. The site is

expected to acknowledge receipt of the alert from the SRC and notify the participant (and/or family), appropriate physicians, and site personnel. The site will provide alternate staff contacts should personnel normally receiving these notices be unavailable.

All Urgent Referral Alerts will be logged by SRC personnel into a PSG Alert Log indicating the date reviewed and date the site coordinator was notified. A copy of the acknowledged receipt of the Urgent Referral by the site will be kept with the PSG Quality documents.

At the FC, FC staff are expected to keep a local log documenting receipt of each Urgent Alert, date when the participant was contacted, whether the participant's health care provider was notified and a note of the "action plan" (e.g., referred to specialist, etc.), and other relevant comments (e.g., participant reported this is a known condition).

Urgent Alert criteria include:

- Baseline oxygen saturation $<88\%$ for ≥ 1 minutes.
- AHI > 50 (with no history or prior OSA).
- O₂sat $<85\%$ for $\geq 10\%$ Total sleep time.
- Abnormal heart rate rhythm/rate: A-fib/flutter not previously diagnosed; A-fib/flutter previously diagnosed but HR >120 bpm or <50 bpm for 2 min; HR ≥ 150 bpm or ≤ 30 bpm for ≥ 2 consecutive minutes (no A-fib/flutter).
- Acute ST segment (suggesting ischemia).
- Complete AV block or 2nd AV, Mobitz 2 block; non-sustained wide complex tachycardia (3 beats duration at rate >120).

10 REPORTING PARTICIPANTS' RESULTS

MESA investigators and coordinators recognize the importance of sharing information with participants and their health care providers. Return of results with the appropriate interpretation in language the participant will comprehend is an important goal of the study and essential to build and maintain trust among participants and investigators. Return of results will first be discussed during the informed consent process, when participants will be given clear details about what results will be provided, and how and when results will be made available. Participants need to understand the utility of the results and what information the results can or cannot provide. Participant expectations for returning results should be addressed during the informed consent process to aid in their decision about whether to participate in the study each exam component. Participants should update their contact information if there are any changes on who should receive results (i.e. change of primary care provider).

I. METHODS

1. Reporting Participants' Results

Participants receive three results reports.

- The Exit Report
 - The lab results report contains the results of the blood values. This letter informs the participant if any of the results are abnormal. In addition, a letter is sent to the participant's physician, along with a page of reference ranges and the participant's lab results.
 - The "high-tech" results report contains the results of the MRI, and CT scans and informs the participant of any abnormal finding. A letter containing a more detailed report of the scan results is also sent to the physician.
- All results letters should be carefully reviewed before they are sent to participants and physicians.

10.1 MESA Core Exam

- Exit Report: BP, height, weight, BMI
- Lab Results Letter: fasting glucose, lipids, eGFR, hemoglobin

10.2 MESA Stress Reactivity

- Cardea SOLO ECG Patch Results Letter. This letter is mailed to participants after the results of their ECG patch have been read.

10.3 MESA Lung

- Spirometry FEV1, FVC, % of predicted lung function

10.4 MESA-MIND

- MRI Retention Letter: This letter is mailed to participants after they have an MRI and their scans have been processed. It does not provide any clinically meaningful results to the participant and is for retention purposes only.
- Cognitive Status Letter. This letter is mailed to participants after the results of their cognitive testing have been assessed.

10.5 MESA Continuous Glucose Monitoring

- Glucose summary letter and report with summarized metrics of glucose across the wear time and graphs.

10.6 MESA Sleep

- Polysomnography report with AHI, % in REM and deep sleep, PMLI
- Actigraphy report with hours of sleep and sleep efficiency
- ABPM report with average night, day and 24-hour SBP and DBP

10.7 MESA 24H-ACT

Participants will receive summaries of the following activity patterns from the hip activity monitor:

- Time spent sedentary, minutes per day
- Time spent in light intensity physical activity, minutes per day
- Time spent in moderate intensity physical activity, minutes per day
- Time spent in vigorous intensity physical activity, minutes per day
- Time spent in moderate and vigorous intensity physical activity, minutes per week
- Steps per day

11 DATA Management

11.1 Data Collection Tablet Best Practices

All data collection applications for Exam 7 will be web-based with password protection. Access to these applications will not be restricted to MESA-provided tablets or laptops or computers.

Instructions for MESA-provided SurfacePro tablets can be found in section 11.2. All data collection applications used by MESA Exam 7 will be web based and data entry will not be limited to SurfacePro devices. If a Field Center has or other computers/tablets they can also be used for data entry.

Security best practices for all devices used for MESA data access including tablets:

- Password protection should be enabled, and devices should be locked when not in use.
- All MESA applications and other programs containing participant information should be closed and logged out of when not in use.
- Never share personal passwords between employees.
- Ensure all computers have updated anti-virus software installed.
- Software updates to the operating system and applications should be completed promptly when available

11.2 Microsoft Surface Pro 4 Basics

Terminology

- **Touch** – A gentle press and release with your finger (corresponds to a mouse click)
- **Swipe** – Touch the screen and move finger in the indicated direction
- **Sleep mode** – Power conservation state for the Surface. Press the power button once to enter or exit sleep mode.
- **Charge** – Amount of battery power available. Make sure the tablet has sufficient charge before seeing patients
- **Kickstand** – Built-in stand for use on flat surfaces

Logging in

When you turn on the device or return from sleep mode you can log in using facial recognition by looking into the front facing camera.

Setting up Facial Recognition

These are Microsoft's instructions for setting up the facial recognition.

Step 1: Go to Start , and select **Settings > Accounts > Sign-in options**.


Step 2: Under **Windows Hello**, locate the infrared (IR) camera or fingerprint setup option.
Select **Set Up > Get Started**.

Step 3: You may be asked to set up your account with a PIN. If so, follow the on-screen instructions.

Follow the on-screen instructions to scan your face using the IR camera built into your Surface or to scan your finger using the fingerprint reader on Surface Pro 4 Type Cover with Fingerprint ID until Windows notifies you that the setup process is complete.

Step 5: Select Finish.

Connecting to Wi-Fi

Touch the [] icon in the bottom right corner of the screen. In the menu that appears, make sure airplane mode is turned off and Wi-Fi is turned on. Select your network from the list, touch Connect, and enter the network password.

You can check the 'Connect automatically' box when choosing a network if you plan to use it again.

Using this manual

Important sections of screenshots are highlighted with blue boxes.

Additional tips are listed in *italics*.

Please send any additional questions about the Microsoft Surface Pro 4 tablet or the MESA data entry program to Kayleen Williams (kmfw@uw.edu), or Jerry Watson (jerryw@uw.edu)



Power button

If the device is turned off, hold this button for 1-2 seconds to turn it on.

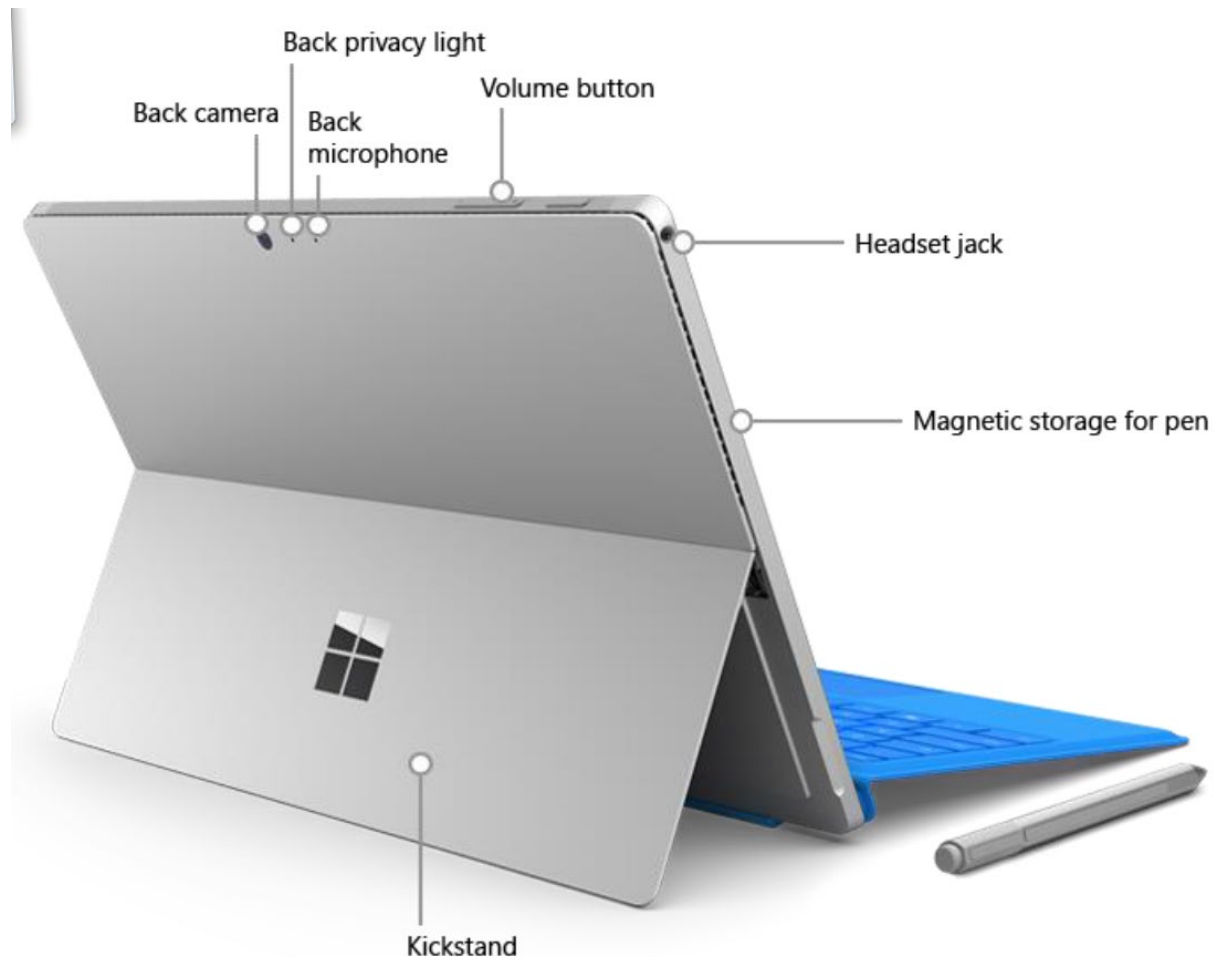
If the device is on, press the power button once or close the keyboard to enter sleep mode (conserves battery).

The device will enter sleep mode automatically after 2 minutes of inactivity to conserve power. Your data will be saved. Press the power button once to return from sleep mode and continue where you left off.

If the device is asleep, press the power button once to turn it back on. Swipe the screen upwards, then enter your username and password if prompted.

Swiping downwards instead of upwards will enter Camera Mode. Press the 'Unlock' icon in the bottom left corner to exit this mode.

To turn the device off, hold the power button until the screen changes, then release the button and follow the on-screen prompt. The device is designed to stay on, so this is usually not necessary unless it will not be used for a long period of time.



Kickstand

Pull out from the bottom edge of the device to use the Surface on a desk.

USB 3.0 port

If desired, a USB mouse can be plugged into the port. All functionality is available with touch or mouse controls.

Micro USB charging port

Plug in the charging cable here. Charging takes between 2-4 hours. **Please ensure the device is charged before a visit.** The battery meter in the right-hand corner of the screen will show you how much power is left.

Charge your Surface Pro 4

1. Connect the two parts of the power cord
2. Connect the power cord securely to the charging port.
3. Plug the power supply into an electrical outlet.

Connect the Type Cover

Snap the type cover into place and open the kickstand.





Keyboard and Touchpad

With the keyboard connected, you can enter data in form fields.


- Press Tab to move to the next field (or select the field using the touchpad)
- Press Shift+Tab to go back to the previous field

Use the touchpad to navigate the forms if you do not want to use the screen's touch feature.

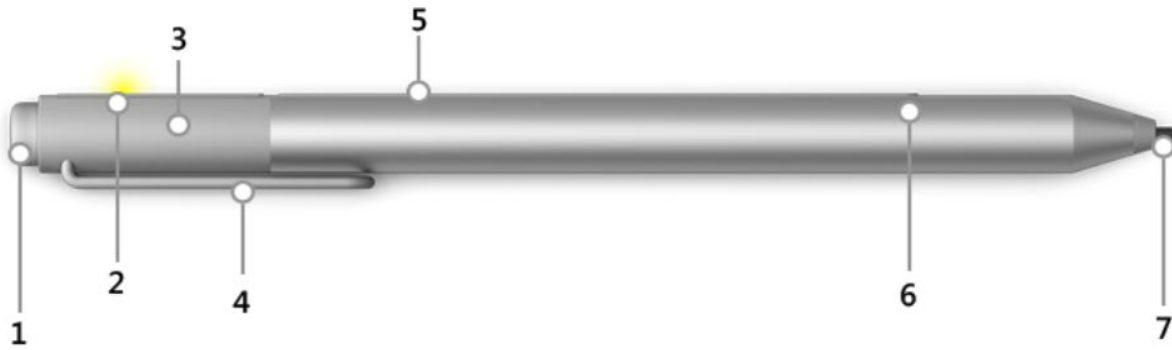
- Move your finger across the touchpad to move the on-screen mouse
- Touch the pad once to select objects, like a mouse click
- Double-touch to open apps, including the Exam 7 program
- Push on the bottom left or right of the pad to physically click like a mouse button

The keyboard can be removed by pulling it out from the bottom of the tablet. To put it back on, align the silver connector pins with the bottom of the tablet.

On-screen Keyboard

To activate the on-screen keyboard, touch the keyboard icon [] in the bottom right corner of the screen. The keyboard will block part of the screen but can be repositioned by touching and dragging the top of the keyboard. Touch the '&123' key to type numbers and symbols.

Surface Pen



- 1 – Top button: To erase, flip the pen over and use the top as an eraser
- 2 – LED: When the pen is in pairing mode, the LED glows white. When the battery is low, the LED glows red.
- 3 – Cap
- 4 – Clip
- 5 – Magnet: Use the magnet on the flat side of the cap to attach your Surface Pen to the edge of your Surface Pro 4.
- 6 – Right-click button: the tip end of the raised area on the flat side of the pen works as a right-click button.
- 7 – Tip

Battery Status

Battery status appears on the right side of the taskbar.



Other tips

To change the screen brightness, swipe from the right edge of the screen to the left, then touch Settings, then hold your finger on the Screen icon and move it up or down. Touch an area outside the Settings menu to exit.

Other settings can also be viewed by swiping to the left.

To switch between full screen and window mode, touch the bar labeled 'MESA Exam 7' at the top of the screen and drag it toward (full screen) or away from (windowed) the top.

The Exam 7 program is also accessible from the Start menu. Press the Windows button, then swipe your finger to the left until it is visible.

You can enter data using the stylus to select a response, or by writing the numbers and letters into the text box. You can also tap the box where you want to type data and use the keyboard to type your response.

Care and cleaning

To minimize wear and tear, fold the keyboard cover over the Surface screen when not in use.

To clean the screen, wipe it with a soft cloth (dampened slightly with water or eyeglass cleaner if desired). **Do not use any other cleaning products on the screen.** The keyboard can be cleaned with a cloth dampened in soapy water. Stains on the cover can be treated with small amounts of rubbing alcohol.

To sanitize the tablet, Microsoft makes the following suggestions:

"Healthcare customers can sanitize Microsoft Surface Pro 4 devices using one of our recommended solutions—PDI Sani-Cloth Plus, CaviWipes, Covidien Alcohol Prep Pads, any similar wipes with IPA (Isopropyl Alcohol) solution under 70%, Total Solutions Full Spectrum Disinfectant Wipes, or Clorox Healthcare Bleach Germicidal Wipes--without risk of damaging the device.

The alcohol-based solutions can also be used to clean the entire Surface Type Cover 3 without damage. Total Solutions Wipes may leave cotton fibers on the bottom side of the Type Cover 3, but these can be removed by hand. Clorox Healthcare Bleach Germicidal Wipes may discolor the bottom surface of the Type Cover with prolonged use, and therefore are not recommended to sanitize the Type Cover.

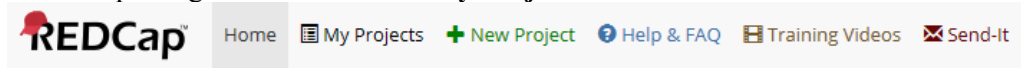
Users should not douse the items with solution, but rather use pre-moistened wipes or apply IPA to application cloth and use the cloth on the unit."

11.3 MESA Exam 7 REDCap Instructions

11.3.1 Using REDCap

Log into REDCap at the site <https://redcap.iths.org/>, entering “University of Washington” as the institution. Contact Jerry Watson (jerryw@uw.edu) for a username and password.

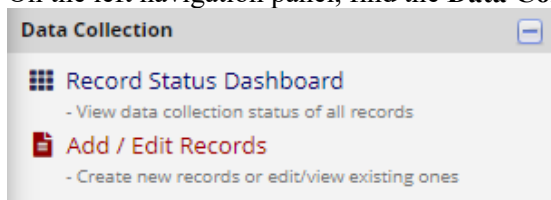
On the top navigation menu choose **My Projects**.



From the My Projects screen choose **MESA Exam 7**

There are two ways to select participants from the Project Home page.

On the left navigation panel, find the **Data Collection** box and select the **Record Status Dashboard** link.

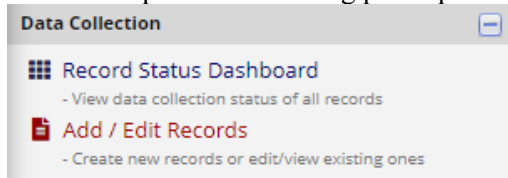


This dashboard displays the forms and form completion status for all participants. You can select an individual form to complete or select the ID number to go to the Record Home Page.

Displaying: [Instrument status only](#) | [Lock status only](#) | [All status types](#)

MESA ID	Participant Information	Study Group Assignment	Exam 7 Notes	Call Log	Clinic Reception	Anthropometry	Environmental Exposures Questionnaire	Medical History	Personal History	Ne Qu
3900001	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900002	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900003	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900004	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900005	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900006	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900007	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
3900008	<input checked="" type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

The other option for selecting participant records is from the **Add / Edit Records** in the **Data Collection** box.



To select a participant, either select the MESA Participant ID (Record ID) from the dropdown menu or enter their MESA Participant ID in the box and press the Enter key. This option takes you to the Record Home page that displays all forms (and their completion status) for the selected participant.

Total records: 4,275	
Choose an existing Record ID	-- select record -- ▾
Enter a new or existing Record ID	<input type="text"/>

The forms available to complete will show on the next screen. There are colored indicators for the completion status of each form. Select one of the circle buttons next to the form to open the desired form.

Record Home Page

The grid below displays the form-by-form progress of data entered for the currently selected record. You may click on the colored status icons to access that form/event.

 Choose action for record ▾

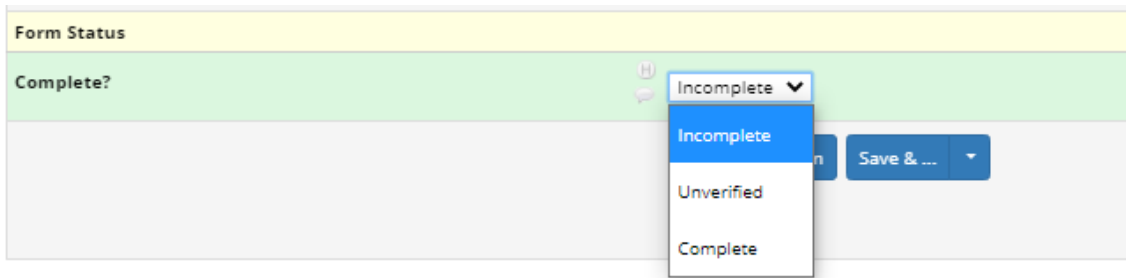
Legend for status icons:

- Incomplete Incomplete (no data saved) ?
- Unverified
- Complete

MESA ID **3900002**
3 Wake Forest

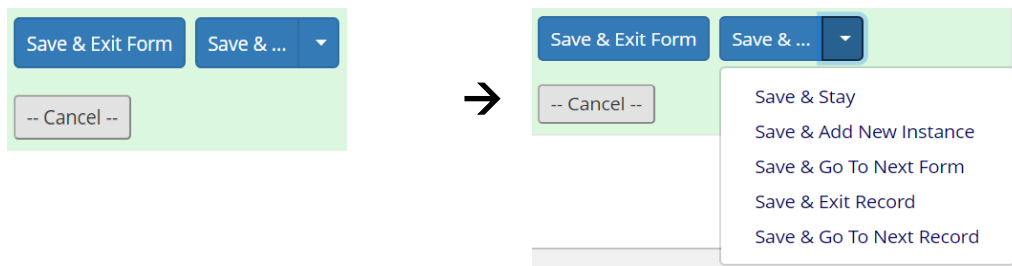
Data Collection Instrument	Status
Participant Information	●
Study Group Assignment	●
Exam 7 Notes	<input type="radio"/>
Call Log	<input type="radio"/>
Clinic Reception	<input type="radio"/>
Anthropometry	<input type="radio"/>
Environmental Exposures Questionnaire	<input type="radio"/>
Medical History	<input type="radio"/>
Personal History	<input type="radio"/>
Neighborhood Questionnaire	<input type="radio"/>

The completion status color code for each form is generated from the “Complete?” data entry field at the end of each form. Forms with status “Incomplete” are show in red. Those with “Unverified” display a yellow dot, and those marked as “Complete” display a green dot. If a form is started and you need to return to it later to add additional information, mark it as “Unverified,” which will display a yellow box, providing a visual cue in the Record Status Dashboard to return to the form later.

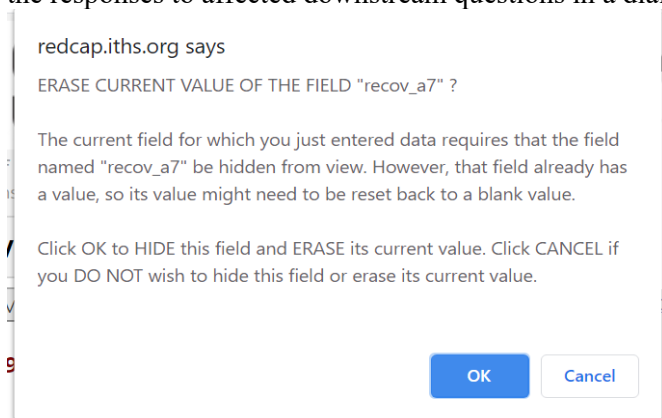


At the end of each form, there are several options to Cancel or Save the changes made. There are additional Save options available in the dropdown list (see image below).

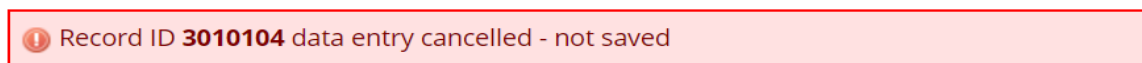
Selecting Cancel will return you to the home page for the record (ID) without saving any changes.



Skip patterns are programmed to appear automatically based on the answers to the root questions. If you change a previous response which effects downstream questions that have also already been answered, you may be asked to review the responses to affected downstream questions in a dialog box like the example below.



After exiting a form, a status bar will appear above the table of available forms indicating the action taken on the form. For example:



11.3.2 Data Entry Practice

The Exam 7 REDCap Data Collection Program includes test IDs that can be used to practice data entry. To access these “test IDs” use the “Dashboard displayed” filter to “Test Participant IDs”

Test Participant IDs

A list of only test Participant IDs

[Show legend](#)

Dashboard displayed: Test Participant IDs ▾
Displaying Data Access Group 5 Johns Hopkins ▾
Displaying record Page 1 of 1: "5900001" through "5900032" ▾ of **32** records ALL (32) ▾ records per page

Enter new record name + Create

Displaying: [Instrument status only](#) | [Lock status only](#) | [All status types](#)

MESA ID	Participant Information	Contact proxy reference	Health Care Provider reference	Follow-up 23 notes	Introduction script	Participant Tracking	Participant Tracking Spanish	Participant Tracking Chinese	General Health	General Health Spanish
5900001 (ARROKEM)	●	●	●	●	●	●	●	●	●	●
5900002 (ANDRRIM)	●	●	●	●	●	●	●	●	●	●
5900003 (MOORALF)	●	●	●	●	●	●	●	●	●	●
5900004 (JONEALF)	●	●	●	●	●	●	●	●	●	●
5900005 (ARROJOF)	●	●	●	●	●	●	●	●	●	●
5900006 (ARROJOM)	●	●	●	●	●	●	●	●	●	●
5900007 (RAMIMAM)	●	●	●	●	●	●	●	●	●	●

11.4 Data Transfer

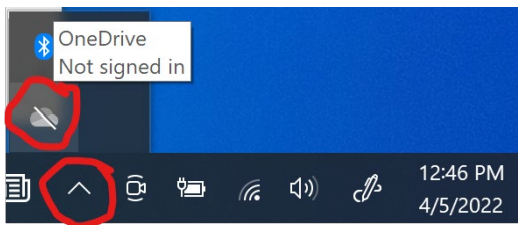
11.4.1 Transferring monitor data from devices to OneDrive

Monitor data files should be downloaded from the devices and into the shared Exam 7 OneDrive.

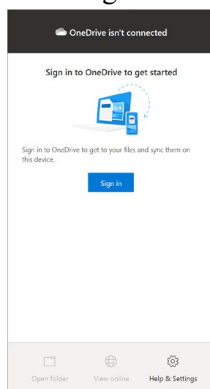
When downloading data from devices to the Surface tablet, always store the data files inside a OneDrive folder, so that the data is securely backed up to the cloud. These instructions will show you how to setup OneDrive.

1) Start OneDrive

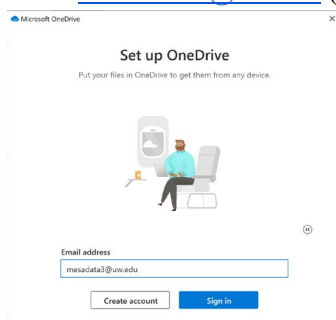
- In the lower-right of the Windows 10 taskbar, click on the up arrow to reveal the OneDrive icon.
- Click on the OneDrive icon



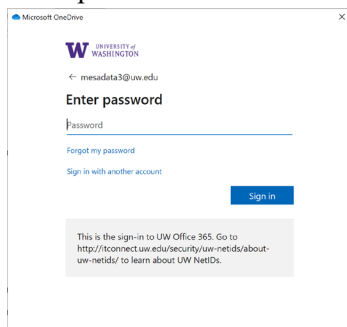
2) Click Sign In



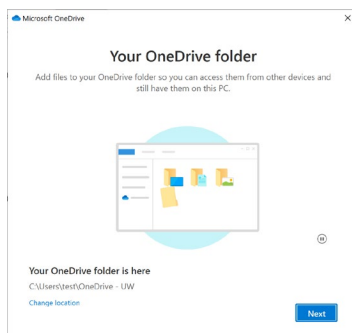
3) Enter mesadataX@uw.edu (where X is your MESA site number) and click "Sign In"



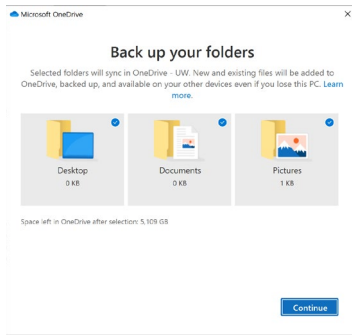
4) Enter password



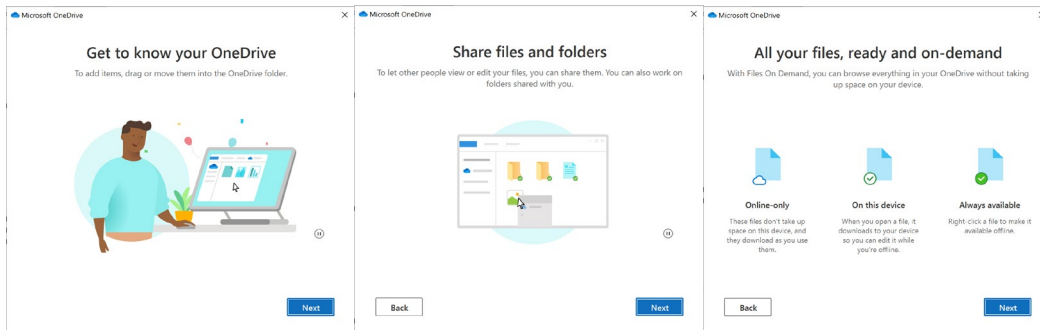
5) Click Next



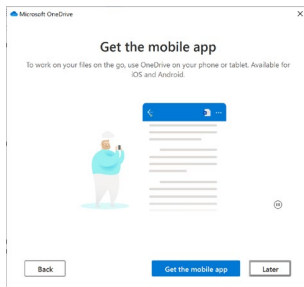
6) Click Continue



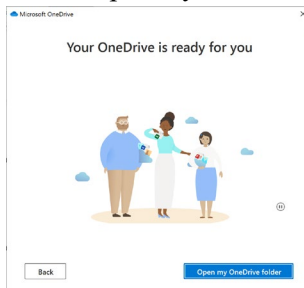
7) Click Next three times



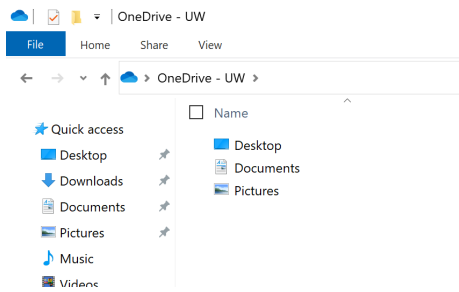
8) Click "Later"



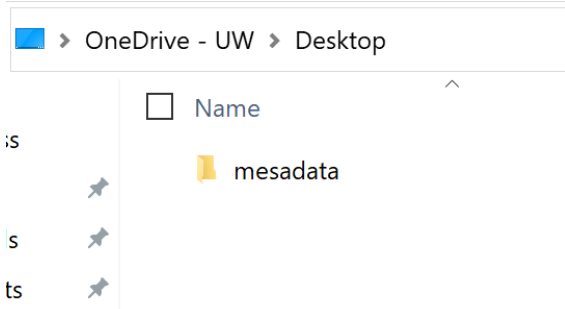
9) Click "Open my OneDrive folder"



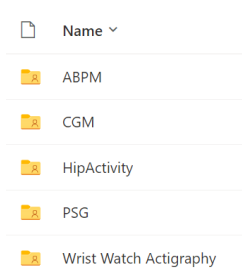
10) Double-click on the “Desktop” folder to open it



11) Open the folder "mesadataX" (where X is your site number)



12) In the metadata folder, there are subfolders for different types of device data



11.4.2 Transferring monitor data from OneDrive to the Coordinating Center

From OneDrive, upload the files to NextCloud (as they are received) into the following folders:

Deice	FC Data Transfer Process: NextCloud Folder “ Exam 7 Data Transfer ”	File Naming Requirements
Wrist Actigraphy	Copy data files to NextCloud here: https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20OFC%20Data%20Transfer/Sleep%20Wrist%20Actigraphy%20Monitor&fileid=379325	.zip folder The actigraphy zip folder is named "ParticipantID-YYYYMMDD" and the date is the visit date
ABPM	Copy data files to NextCloud here: https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20OFC%20Data%20Transfer/Sleep%2024H%20Blood%20Pressure%20Monitor&fileid=379326	.SNTL file The Sentinel software gives names to the data files. Please do NOT change the file names.

PSG	Copy data files to NextCloud here: https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20FC%20Data%20Transfer/Sleep%20PSG&fileid=379327	.zip folder The PSG zip folder is named "ParticipantID-YYYYMMDD" and the date is the visit date
Hip Actigraphy	Copy data files to NextCloud here: https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20FC%20Data%20Transfer/24H%20ACT%20Hip%20Activity%20Monitor&fileid=379324	.gt3x file File name must start with 7-digit MESA ID number
CGM	Copy data files to NextCloud here: https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20FC%20Data%20Transfer/Glucose%20CGM&fileid=379992	.PDF and .csv files File name "Field Center-PPT#" using [COLU, JOHNS, MINN, NWTN, UCLA, WAKE]
Arterial Stiffness	To transfer the data, log in to Box and open the Box folder specific to your institution that the Penn core lab has established. Drag and drop the appropriately named zipped file on your computer into Penn+Box. See FC MOP Section 7.8.7 for more details.	
Spirometry		

12 EVENTS SURVEILLANCE

12.1 Purpose

MESA’s official, scheduled “Follow-up Phone Calls” serve several purposes:

- To update participants' tracking data, including their address, phone number, and contact information
- To update participants' vital status
- To obtain information regarding participants' general health and health care treatment.
- To obtain detailed information about specific medical conditions diagnosed by a physician that the participants report have had since their last MESA Follow-up phone interview
- To obtain detailed information about any procedures or hospitalizations participants have had since their last MESA Follow-up phone interview
- To schedule the participant for an upcoming Exam Clinic Visit appointment, when necessary, including MESA CT/MRI appointments, when necessary.

12.2 Follow-up Call

The “Follow-up Call” is a telephone interview conducted with each participant. Calls are scheduled every twelve months. The 23rd and 24th follow-up calls should be linked to Exam 7 and are designed to allow for the scheduling of the exam during this call.

If the Exam staff needs to contact a participant (e.g., to schedule an Exam Visit after the Follow-up Call failed in scheduling the Exam Visit), the Exam staff should be aware of the participant's usual schedule of official Follow-up Calls. Unscheduled contact is not the same as a scheduled Follow-up Call used to collect data. If, during an unscheduled contact, the participant tells the Exam staff member about a condition, procedure, or hospital stay, the staff member should alert the Events Coordinator so that full information about the potential event can be collected.

The Follow-up 23 MOP is available on the MESA website at <https://www.mesa-nhlbi.org/MesaInternal/Manuals.aspx>

12.3 Continuing Participant Surveillance

If, during an Exam visit, a participant tells the Exam staff member about a condition, procedure, or hospital stay, the staff member should alert the Events Coordinator so that full information about the potential event can be collected.

At the end of the Exam, each participant is asked to notify the clinic should any changes occur in their health, especially involving a hospitalization, nursing home admission, or diagnosis of myocardial infarction (heart attack), angina (chest pain), heart failure (CHF), peripheral vascular disease (PVD), stroke, or transient ischemic attack (TIA).

Clinic staff should inform the participant they will be later be contacted for their scheduled Follow-up Call, which may include the scheduling of the next Exam Visit.

Let the participant know that we are attempting to keep the record as updated as possible to learn all that we can.

All Follow-up forms are interviewer-administered to MESA participants over the telephone. If the participant prefers to relay this information in person or, for some reason, is unable to complete the interview by phone, a home or clinic visit may be scheduled.

12.4 Use of Proxy

If a participant is not able to do the interview (e.g., due to a medical problem), a proxy may be used. A "proxy" is a relative or other knowledgeable contact. If the participant has died, the proxy may complete the questionnaire for the period between the last Follow-up Call and the date of death.

The proxy may or may not be someone previously designated as a contact by the participant. For example, the participant may have designated their spouse as a primary contact, but the participant's son or daughter ends up being the person to complete the questionnaire. This is fine, if the new person is knowledgeable regarding the participant's medical condition, procedures of interest, etc.

12.5 Administering and Processing Follow-up Forms

Please refer to the Events Manual of Operation for detailed information regarding the administration and processing of follow-up forms

13 CERTIFICATION

13.1 Standardization of Clinical Procedures

Ongoing studies at the Field Centers will result in data accumulated by study personnel and derived from adhering to multiple procedures in the course of their responsibilities. By standardizing study procedures and requiring such data-gathering individuals need to demonstrate the required level of procedural knowledge and competency, the opportunity for inconsistent data will be greatly reduced.

13.2 Responsibilities and Qualifications of Coordinators and Data Entry Personnel

Personnel are required to successfully demonstrate competency to the satisfaction of an authorized qualified individual following the completion of online and/or in-person training sessions. In the case of personnel turnover during the study, replacement personnel shall complete standard training and certification prior to their participation in MESA activities.

The Study Coordinator is responsible for all study operations of their respective Field Center. The Study Coordinator will share all information related to specific tests and procedures including manuals of operation (MOP), forms, and training materials related to the protocol with study personnel (clinic coordinator, technicians, data entry personnel) as appropriate.

13.3 Data Entry and Clinical Operations Training and Certification

Consistency in performing protocol-defined procedures and recording study data strengthens the ability to achieve scientifically accurate outcomes. Therefore, it is crucial that research staff are trained and certified in all MESA procedures. The CC designs sessions to train the Field Center Site staff in skills necessary to collect, record, and process data, such as using the secure MESA web site, recording data in the Exam 7 REDCap Program, and performing all MESA procedures. The CC will develop protocol training sessions as well as web-based or videoconference training presentations. When there is turnover in the Lead Study Coordinator position at a Field Center, the DCC will provide protocol and application training for the new Lead Study Coordinator. Replacement personnel will complete standard training and certification prior to their participation in MESA clinic activities.

13.4 Human Subjects Protection Training

NIH requires that MESA personnel complete Human Subjects Protection training. The original tutorial, exam, and certification documentation are available at <https://ohsr.od.nih.gov/>. Clinical staff follow training and certification guidelines their institutions' Human Subject Protection Office (HSPO) to ensure they meet their institutional requirements.

Site Visits

On-site reviews of Field Centers may be scheduled on an as-needed basis to:

- Assess the overall performance of the Field Center, and the conduct of the ongoing protocol training
- Assess the quality of data collection
- Provide consultation in identifying and solving problems
- Transfer effective approaches from one Field Center to another
- Components of the site visit will include:
 - Meeting with personnel.
 - Examining facilities
 - Review administrative organization within the center
 - Other activities proposed by the CC, the NHLBI, and the Observational Monitoring Board (OSMB).

The site visit team will include representatives from the Coordinating Center and possibly NHLBI, and Ancillary Study PI, or a representative from another Field Center. The CC will prepare site visit reports which will include specific recommendations for the Field Center. The report will be sent to the PI and Study Coordinator at the Field Center where the site visit was performed, NHLBI, and the Chair of the Steering and Operations Committees. If serious problems are

detected, the report will also be sent to the Steering Committee for review. Each Field Center will be site-visited, as necessary, during the project period.

13.5 Summary of Certification Requirements

Exam 7 Certification Requirements for new and returning technicians are outlined in the following table.

In addition to the detailed requirements listed in the table by examination component, the following certification requirements apply to all components:

- Trainees must thoroughly read the relevant section in the MOP.
- Appropriate supporting documents (e.g., checklists and tests) must be completed when required.
- All certification documentation should be sent to the CC and to designated RCs when specified.
- A copy of the supporting certification documents should be retained at the FC for local records in a designated binder.

Exam Component	Requirements	Certification Details
Interviewer-Administered Questionnaires	<p>Read the interviewing protocol in the Exam 7 MOP (Section 6.1)</p> <p>Practice the questionnaire to become familiar with the questions and responses</p> <p>Conduct and record 3 sets of interviews with 3 different volunteers.</p> <p>Use a test participant ID (third, fourth, and fifth digit is “9”) to enter practice interview data into the REDCap Exam 7 project.</p> <p>Send all 3 sets of recordings to CC for review. Use CC file sharing application NextCloud if the recording files are too large to email.</p> <p>Include the test IDs used to enter in data in the Exam 7 REDCap project.</p>	<p>Certification packet includes Medical History, Personal History, and Medications Form.</p> <p>Certified Field Center staff may train additional staff. Certification performed by Coordinating Center.</p> <p>Previously certified interviewers submit one interview packet (instead of 3)</p> <p>Questions? Contact Amy Hoffman ajulian@uw.edu</p>

Exam Component	Requirements	Certification Details
Anthropometry	<ul style="list-style-type: none"> • Read Section 7.1 in the Exam 7 MOP and practice the procedure according to the MOP with at least 5 volunteers. • For Certification, obtain height, weight, hip, waist, and neck circumference on 5* volunteers in accordance with the MESA Anthropometry Certification / Supervisor Checklist. The readings must not differ from the trainer's by more than the following: ± 1 cm for height, ± 1 pound for weight (both for balance beam and body composition scale), ± 2 cm for hip and waist girth, and 1cm for neck circumference. • Send checklists, completed by the trainer technician, to the CC. Include the test IDs used to enter data in the Exam 7 REDCap project. <p>* Exam 6 or MIND visit A certified techs submit data for 2 volunteers.</p>	<p>Certified Field Center staff may train and certify additional staff.</p> <p>Questions? Contact Amy Hoffman ajulian@uw.edu</p>
Seated Blood Pressure	<p>Read the blood pressure protocol in Section 7.2 of the Exam 7 MOP.</p> <p>Practice as necessary, depending on previous experience.</p> <p>Perform 5* blood pressure measurements in accordance with certification checklist under supervision of the lead staff person in the clinic.</p> <p>Send Seated Blood Pressure checklists, completed by the trainer technician, to the CC. Include the test IDs used to enter data in the Exam 7 REDCap project.</p> <p>* Exam 6 or MIND visit A certified techs submit data for 2 volunteers.</p>	<p>Certified Field Center staff may train and certify additional staff.</p> <p>Questions? Contact Amy Hoffman ajulian@uw.edu</p>

Exam Component	Requirements	Certification Details
Phlebotomy	<ol style="list-style-type: none"> 1. Read MESA’s Laboratory MOP. 2. Observe the process performed by a certified technician. 3. Successfully perform 1 phlebotomy on a volunteer as described in the protocol and in accordance with certification checklist under supervision of the lead person in the clinic. 4. Pass written examination prepared by CBAL. 5. Send exams and checklists to CBAL and CC. 	<p>Certified Field Center staff may train additional staff. Certification performed by Central Lab.</p> <p>Questions? Contact Jess Rooney jessica.lanzer@med.uvm.edu</p>
Blood Processing	<ol style="list-style-type: none"> 1. Read MESA’s Laboratory MOP. 2. Observe the process performed by a certified technician. 3. Successfully process blood samples from 1 volunteer as described in the protocol and in accordance with the laboratory processing certification checklist under supervision of the lead person. 4. Pass written examination prepared by LCBR. 5. Send exams and checklists to LCBR and CC. 	<p>Certified Field Center staff may train additional staff. Certification performed by Central Lab.</p> <p>Questions? Contact Jess Rooney jessica.lanzer@med.uvm.edu</p>
Nasal brushing and hair collection	<ol style="list-style-type: none"> 1. Read the MOP sections 7.10 and 7.11. 2. Perform twice observed in a satisfactory manner. <p>Sites can either request a Zoom call with Graham or Emilia or a submit a video performing the collection to the NextCloud certification folder so that Graham Barr and/or Emilia Hermann can review.</p>	<p>Questions? Contact Emilia Hermann eah2191@cumc.columbia.edu</p>

Exam Component	Requirements	Certification Details
SPPB	<ol style="list-style-type: none"> 1. Read the MOP sections 7.10 and 7.11. 2. Certification to administer the extended SPPB will be done with a volunteer who is not a study participant, either by video call with Michelle Gordon (Wake Forest, migordon@wakehealth.edu) or the administration can be video recorded and uploaded to the MESA-MIND OneDrive folder. 3. If the video file size is too large to be uploaded to the OneDrive folder, it can be uploaded to the NextCloud folder. Uploading to these folders requires a UW NetID. If you upload to the NextCloud folder, please also send an email to mesamind@uw.edu, notifying us of the upload. Issues with or questions about file uploading can be sent to mesamind@uw.edu. 	<p>Questions? Contact Michelle Gordon migordon@wakehealth.edu</p>
Sleep home visit	<ol style="list-style-type: none"> 1. Read the MOP section 8.6 2. Certification requires completion of the PSG Written and Practical Exams (see MOP Section 8.6.16) 	<p>Questions? Contact Dan Mobley dmobley@bwh.harvard.edu</p>
24H Blood Pressure Monitor	<ol style="list-style-type: none"> 1. Read section 8.5 of the Exam 7 MOP 2. Review training video 3. A practical exam, demonstrating ability to explain the procedure to participants, proper measurement of the arm and selection of cuff size, proper application of the device, checking comparability with a manual BP read, and completion of forms. A checklist will be used by the trainer to verify that all procedures are performed correctly by the RA 4. Complete and pass a written exam 5. Submit one acceptable practice study that records data over 24 hours on a volunteer-showing a minimal of 20 day and 7-night valid readings. TBD 	<p>Questions? Contact Dan Mobley dmobley@bwh.harvard.edu</p>

Exam Component	Requirements	Certification Details
Sleep Study Wrist Monitor	<ol style="list-style-type: none"> 1. Read MOP section 8.2. 2. Training under the direction of a member of the SRC or by a centrally trained staff member. 3. Submission of one (1) successful certification study demonstrating: <ol style="list-style-type: none"> a. Successful GENEActiv device initialization using the GENEActiv PC software. b. Collection of at least 24 hours of data recorded on a volunteer. c. Download of data from the GENEActiv device. 4. Successful transmission of study data to the CC. 	<p>Questions? Contact Emily Kaplan ekaplan1@bwh.harvard.edu</p>
24H-ACT Hip Monitor	<ol style="list-style-type: none"> 1. Read and understand the MESA 24H-ACT protocol in the MOP Section 8.1. 2. Review the MESA 24H-ACT recorded training video, staff documents, and participant forms, including take-home package materials. 3. Successfully initialize the hip monitor, prepare take-home package, and instruct the participant on placement and wear protocol on 2 volunteers as described in the protocol. 4. Prepare videotaped recording of participant instruction for the 2 pilot studies. 5. After the wear period, successfully download the data file to the appropriate computer directory for transmission to the Coordinating Center. 6. Upload the videotaped recording of the participant instruction and data files (.gt3x) to NextCloud for review by MESA 24H-ACT Investigators. 	<p>Training and certification for initialization and download completed at Central Training or as scheduled with MESA 24H-ACT Team.</p> <p>Training and certification for the remaining components completed and submitted via NextCloud.</p> <p>Questions? Contact Margaret Murdock mem2356@cumc.columbia.edu</p>

Exam Component	Requirements	Certification Details
Glucose monitor	<ol style="list-style-type: none"> 1. Read and understand the CGM protocol in Section 8.3 of the Exam 7 MOP. 2. Observe the CGM placement process in the training videos and handouts and read the FAQ document. 3. Successfully apply a CGM device with appropriate placement on 3 volunteers and activate the device as described in the protocol. Complete the check list for device placement, activation, removal, data download, and data saving, as well as reader cleaning (physical and data removal), CGM applicator disposal, and CGM sensor storage. If this was not done at central training, application must be videotaped and the video should be transmitted to Wake Forest. 	<p>Training and certification can be completed at Central Training or at individual field centers.</p> <p>Questions? Contact Lenore Crago lcrago@wakehealth.edu</p>
Heart Monitor Patch	<ol style="list-style-type: none"> 1. Read the Heart Monitor Patch Application section (Section 8.4) of the Exam 7 MOP. 2. Review the Central Training Presentation. 3. Review Cardea SOLO Training Slides and Video. 4. Pass Cardea SOLO Quiz. 5. Observe the process performed by a certified technician. 6. Successfully perform 1 patch application on a volunteer as described in the protocol. If this was not done at central training, application must be videotaped and final applied patch photographed and these should be transmitted to the CC. <p style="text-align: center;">-OR-</p> <ol style="list-style-type: none"> 7. Successfully perform patch application procedures as described in the protocol and in accordance with certification checklist under supervision of the lead person in the clinic. 8. Send checklist to CC. 	<p>Certified Field Center staff may train additional staff.</p> <p>Questions? Contact Lauren Hoffer lauren.hoffer@northwestern.edu</p>

Exam Component	Requirements	Certification Details
Cognitive Testing	<p>See certification details at https://www.mesa-nhlbi.org/MESAMind/Account/MESAMindInternal/TrainingMaterials</p> <p>Certification recordings are submitted to Ashley Morgan via the NextCloud folder for “E7 Certification Recordings.” See section 13.6.2.</p>	<p>Questions? Contact Ashley Morgan armorgan@wakehealth.edu</p>
Arterial Stiffness	<ol style="list-style-type: none"> 1. Participate in Central Training or watch training presentation video. 2. Read and review section 7.8 of the MOP, and contact the NUECL with any questions before performing the certification arterial stiffness recording. 3. Perform the certification recording on a non-study participant, making sure to include all required information. 4. Copy the study directly from VaSera device to the Penn Box MESA Exam 7 folder (See section 13.6). 5. Wait for confirmation of certification from the NUECL before submitting any arterial stiffness recordings performed on study participants. 	<p>For questions, contact Caroline Margo Caroline.Margo@Penmedicine.upenn.edu</p>
Brain MRI	TBD	<p>Questions? Contact Lisa Desiderio Lisa.Desiderio@penmedicine.upenn.edu</p>
Amyloid PET	TBD	
Lung CT	<ol style="list-style-type: none"> 1. Read and understand the CT MOP. 2. Schedule a Zoom training session with the Reading Center in which at least one coordinator and one technologist must attend. 3. Complete the certification phantom scans as detailed in the Phantom Training slides. 4. 	<p>Lung CT Reading Center will train and certify staff.</p> <p>Questions? Contact Jarron Atha jarron-atha@uiowa.edu</p>

Exam Component	Requirements	Certification Details
Spirometry	<ol style="list-style-type: none"> 1. Read and understand the Spirometry Protocol in section 7.9 of the Exam 7 MOP. 2. Practice the procedure (including albuterol inhalation) on at least 5 volunteers or as often as needed to become comfortable with the procedure. 3. Complete online training including answering all chapter questions. 4. Complete and pass final on-line test. 5. Perform and transmit 10 good quality tests (as determined by Spirometry RC staff). If any are of poor quality, additional practice and transmission of 5 additional tests will be required. <p>Note: techs that have performed MESA-related spirometry in the past 6 months submit 5 unobserved tests to the spirometry reading center.</p>	<p>A web-training account can be obtained from john@occspiro.com</p> <p>Slides from the spirometry training are on the MESA Lung website, http://www.uwchsc.org/MESALung/MesaLung2.aspx under the link, “Spirometry for MESA Lung Webinar - February 2010.”</p> <p>For questions, contact john@occspiro.com</p>
Oximetry	<ol style="list-style-type: none"> 1. Read and understand the Oximetry Protocol in the Section 7.3 in the Exam 7 MOP. 2. Practice the procedure on at least 5 volunteers* or as often as needed to become comfortable with the procedure. 3. Perform 5 oximetry measurements in accordance with certification checklist. 4. Send checklists, completed by the trainer technician, to the CC. Include the test ID used to enter data in the Exam 7 REDCap software. <p>* Exam 6 certified techs submit data for 2 volunteers.</p>	<p>Certified Field Center staff may train and certify additional staff.</p> <p>Questions? Contact Emilia Hermann eah219@cumc.columbia.edu</p>

13.6 Submitting Certification Materials for Review

13.6.1 MESA E7 Certification Recording Submission Form

When uploading certification materials to NextCloud, complete the Smartsheet form at <https://app.smartsheet.com/b/form/ff2ae5b613b74414b70d24b2430aead1>

Complete this form when uploading an E7 certification recording and documentation for review. Please name the recording file with "technician last name.procedure.number" (for example "Amy.anthropometry1 & Amy.anthropometry2").

13.6.2 NextCloud Certification Materials

From the NextCloud folder link below, add your MESA E7 certification recordings and certification checklists to the folder for your specific Field Center. Name the file with "Technician.procedure.number".

<https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/E7%20Certification%20Recordings&fileid=373397>

13.6.3 NextCloud Data Transfer

From the NextCloud link below, upload monitor data files that are necessary for certification activities.

<https://nextcloud.chscc.biostat.washington.edu/nextcloud/index.php/apps/files/?dir=/MESA/Exam%207%20FC%20Data%20Transfer&fileid=379323>

This includes data files from wrist actigraphy, hip activity, Sleep PSG, 24-hour blood pressure, continuous glucose monitor.

13.6.4 Arterial Stiffness Data Transfer

1. The trained VaSera device operator runs a procedure for a VaSera test session (standard CAVI “PW/PB Exam” as well as “Thigh test”) on a live volunteer (as opposed to using simulated data inputs) and in accordance with the test protocol defined in the latest MESA MIND MOP document. Care should be taken to obtain “clean” waveforms for the test session, avoiding artifacts. Test sessions may be repeated by the operator to improve waveform quality, if need be.
 2. The results of this test session are saved automatically to “USB3” flash drive and SD card in the front-panel of the device.
 3. Remove the USB3 media and plug it into a USB port on a PC.
 4. Browse to the “IMAGE” folder on the VaSera media (USB3 flash drive or SD card), which contains report files named according to the date and time they were created and by the subject ID# inputted for the test session. These files are PDF format files of VaSera test reports.
 5. Select the file that is to be used for the certification (i.e., the file created by the VaSera operator who is to be certified).
 6. Attached two report files for one selected test session to an email and email them to Caroline Margo (Caroline.Margo@Pennmedicine.upenn.edu) and to Hannah Maynard (Hannah.Maynard@Pennmedicine.upenn.edu) at the University of Pennsylvania. In this email, be sure to indicate which operator generated the attached report files so that there will be no confusion as to who is being certified.
 7. Return the VaSera media (USB3 flash drive or SD card) to its slot on the VaSera machine.
 8. Caroline Margo will review the waveform quality in the two report files she receives per VaSera operator. If the reports contain waveforms (from PCG or cuffs) that show obvious artifacts or corruption, Caroline will notify the sender to repeat the tests and send better quality reports. If the reports illustrate that good quality waveforms are represented, Caroline will notify the sender that the operator who created them is “certified” to use VaSera and will record this information.
-