

THE ADNI **DEPRESSION PROJECT**
Procedures Manual



Characterizing Cognitive Decline in
Late Life Depression

Version 1.1 April 6, 2015

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Protocol Summary

Title: The Alzheimer's Disease Neuroimaging Initiative (ADNI) Depression Project: Characterizing Cognitive Decline in Late Life Depression

Study Sponsor: National Institute of Mental Health

Overall Objective

The overall goal of this project is to characterize the mechanisms contributing to cognitive impairment and accelerated cognitive decline in Late Life Depression (LLD). Cognitive Impairment (CI) occurs in up to 60% of individuals with LLD and is most often characterized by deficits of executive functioning, memory, and expressive language. CI represents one of the most debilitating and costly aspects of LLD and determining the etiology of CI in LLD represents a significant avenue to improve health and disability outcomes for older adults through interventions and treatments. Existing data suggests that remission of depression is associated with focal improvements in executive function, whereas, deficits of memory and expressive language typically persist, and that LLD is associated with more rapid rates of cognitive decline across cognitive domains. Compelling evidence suggests that cerebral hypoperfusion represents a significant aspect of LLD that contributes to remediable deficits of executive function and that cortical atrophy is associated with memory and language deficits in LLD. Further, while understudied, accelerated cognitive decline in LLD is likely the result of multiple factors including hypoperfusion, amyloid deposition, cortical atrophy, white matter signal hyperintensities, and genetic susceptibility. In the past, determining the specific mechanisms contributing to CI in LLD has been challenging due to the co-occurrence of neurodegenerative disease and methodological limitations related to small sample sizes. With the advent of new imaging techniques, including measures of cerebral blood flow, radioligands to evaluate amyloid deposition in vivo, and the establishment of national research consortiums developed to identify neural substrates of CI in older adults, there is now a tremendous opportunity to leverage these resources to clarify the neurobiological substrates of CI in LLD.

Through dynamic partnerships with the Alzheimer's Disease Neuroimaging Initiative (ADNI-II) and industry sponsorship, the ADNI-D study is well positioned to successfully address the impact of reduced cerebral blood flow (hypoperfusion), cortical atrophy, and amyloid deposition on cognitive impairment and accelerated cognitive decline in LLD in the context of previously documented relationships between cognitive impairment and subcortical white matter abnormalities and genetic risk factors. ADNI-D is focused on establishing improved diagnostic approaches and targeted treatment trials aimed at LLD and CI associated with LLD, ultimately leading to improved health outcomes and reduced healthcare costs.

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Primary Objective

The study aims are focused on prediction of clinical outcomes, and fulfillment of these aims will add considerably to what is known about the basic neuroscience of Late Life Depression and disability in the geriatric community.

- **Aim 1:** To clarify neurobiological substrates of cognitive dysfunction in LLD.
- **Aim 2:** To clarify the impact of LLD on rate of cognitive decline over 2.5 years.
- **Aim 3:** Use biomarkers data employed in ADNI-2 and the NIA AD Genetics Consortium to determine the genotypes needed for the genome wide association study (GWAS) for pathways and candidate gene studies that investigators may wish to pursue in future studies. Data from participants will be entered into the NIH Genome-Wide database and made available to the scientific community.

Sample Size

This is a non-randomized non treatment study. This longitudinal study will enroll 120 participants who meet criteria for Major Depression or Late Life Depression (LLD) for the duration of 5 years. Participants will be recruited from 2 ADNI-II sites selected on the basis of established programs of research in LLD and the ability to obtain ASL perfusion MRI and amyloid PET scans. These sites are the University of California San Francisco and the University of Pittsburgh Medical Center. Clinical and cognitive assessments, collection of depression history, health information, and blood samples will be collected at 2 time points 2.5 years apart. Overall sample of consented, screened, eligible and enrolled participants will be 60 participants at each depression site (UCSF and UPITT) over a 2 year time period. Each site will be expected to enroll at least 30 participants per year.

Comparison subjects will consist of 300 non-depressed older adults from the ADNI-II study; 200 of which have mild cognitive impairment and 100 participants who are cognitively normal.

Procedures

After initial contact and telephone screening, all eligible participants will undergo a clinical psychological interview using the Structured Diagnostic Interview SCID-I for DSM IV-TR, and the Hamilton Depression Rating Scale to determine depression severity, conducted by the Late Life Depression locations at the University of California San Francisco Langley Porter Psychiatric Institute and the University of Pittsburgh medical center to determine eligibility.

At each psychiatry site, psychiatry PIs will identify eligible participants, screen for initial eligibility, and enroll participants into the study. If the participant meets criteria for a current Major Depressive Episode and all other inclusion/exclusion criteria, they will

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continue with the Depression Assessment visit and complete the cognitive portion of the interview.

The participant will then be referred to their closest ADNI clinic, i.e. University of Pittsburgh Medical Center or University of California, San Francisco Mission Bay, where they will complete a Baseline Assessment. The study participant will have clinical/cognitive assessments, biomarker and genetic sample collection, and imaging. A reduced battery of tests is allowable if the subject is not able/willing to complete the full battery. Specific eligibility criteria will be discussed with the participant at the baseline clinic visit as well to screen for physical, MRI, and/or PET specific exclusions. If at this point the participant is deemed ineligible, the ADNI site may drop them from the study.

All MRI and PET scans will be rapidly assessed for quality so that subjects may be rescanned if necessary. All clinical data will be collected and stored by the Coordinating Center at the University of California, San Diego. NCRAD will receive all samples for storage and process genetic samples. All raw and processed imaging data will be archived at LONI.

The psychiatry sites will be responsible for the mail effort, recruitment, telephone screeners and psychiatric interviews. ADCS will provide study recruitment materials, including targeted flyers, brochures, press releases, and presentations, and will provide additional consultations with recruitment strategies. Paid newspaper advertisements, direct mail and internet advertising will be used as needed to supplement recruitment.

Several steps will be taken to assure the high follow up rate that is essential to the validity of the study results. All staff members will be carefully instructed regarding the need for an expectation of full follow up participation and the process of removing barriers to participation. At entry, each participant will be queried regarding plans to change residence or leave the area. Frequent contact by telephone will be maintained with participants at twelve-month intervals. [OPTIONAL: Each participant will receive a thank you note following the clinical evaluation and a personalized greeting card on his or her birthday and/or on a major holiday. A personalized reminder notice will be sent on 6 month intervals to participants thanking them for their participation and reminding them of their next scheduled visit or telephone contact.]

Duration of Participation

This study is funded for five years, which involves about 6 months of start-up time, about 24 months of enrollment and about 30 months of follow up. Study participants will have an initial prescreening telephone interview, Depression Assessment at the participating psychiatry sites, Baseline Assessment at the ADNI clinic, and a 12 month and 24 month interim phone check. At the 30 month mark participants will be brought back in for a Follow Up Depression Assessment visit and a Follow Up ADNI Clinical Assessment visit.

ADNI Depression Project: Schedule of Events	Month 1		Month 12	Month 24	Month 30	
	Psych	ADNI	Psych	Psych	Psych	ADNI
Visit Type						
Explain Study	X	X				
Obtain Consent	X					
Study Partner Consent		X				
Demographics	X					
Inclusion and Exclusion Criteria	X					
Family History		X				
Depression History	X				X	
Structured Clinical Interview DSM-IV (SCID)	X				X	
Hamilton Rating Scale for Depression (HRDS)	X		X	X	X	
Generalized Anxiety Disorder -7 (GAD-7)	X				X	
Patient Health Questionnaire-9 (PHQ-9)	X				X	
Duke Social Support Index (DSSI)	X				X	
Stroop Color-Word	X				X	
Motor-Visual Perception Test-3 (MVPT-3)	X				X	
Brief Visuospatial Memory Test (BVMPT)	X				X	
Benton Judgment of Line Orientation (JLO)	X				X	
WAIS Digit Symbol	X				X	
WAIS Digit Span	X				X	
Follow Up Treatment Form			X	X	X	
Cognitive Change Index -20 Participant		X				X
Cognitive Change Index-20 Informant		X				X
Medical History, Hachinski		X				
Physical Exam, Neurological Exam		X				X
Vital Signs		X				X
Height		X				
DNA Sample Collection for ApoE Genotyping, GWAS, Differential, Hematology		X				
Cell Immortalization Sample Collection		X				
American National Adult Reading Test		X				
Mini Mental Status Examination	X				X	
Logical Memory I and II		X				X
Everyday Cognition (ECog)		X				X
Montreal Cognitive Assessment (MoCA)		X				X
Category Fluency (Animals)		X				X
Trails A & B		X				X
Boston Naming Test (30-item)		X				X
Auditory Verbal Learning Test		X				X
Geriatric Depression Scale		X				X
Clock Drawing		X				X
Neuropsychiatric Inventory		X				X
ADAS-Cog 13 (w/ Delayed Recall and Number Cancellation)		X				X
Clinical Dementia Rating Scale		X				X
Activities of Daily Living (FAQ)		X				X
Plasma and Serum Biomarker Collection		X				X
RNA Sample Collection		X				X
Telomere and "TBD" assays		X				X
Concomitant Medications		X	X	X		X
Serious Adverse Events		X	X	X		X
Diagnostic Summary		X				X
Telephone Check -Participant Status			X	X		
3T MRI Imaging		X				
Florbetapir Amyloid Imaging		X				

Start-Up and General Information

Personnel Requirements – Depression Site

At a minimum three staff roles (Site Principal Investigator, Study Coordinator, Psychometrician) will be required to conduct the protocol at each site. Additional roles are outlined below that are recommended in order to conduct the study successfully. These functions may be covered by one staff member at certain sites, for other sites there will be multiple staff assigned.

Site Protocol Principal Investigator (PI)

The PI should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial.

Responsibilities include, but not limited to:

- Protect the rights and well-being of study participants.
- Ensure the appropriate conduct for informed consent of study participants.
- Maintain appropriate staff qualifications including study specific training.
- Adequate staffing resources.
- Medical care of study participants.
- Supervision of study personnel, including:
 - Delegation of roles and duties to appropriately qualified study personnel.
 - Ensuring that all study personnel are informed about the protocol and their delegated duties.
 - Ensure that clinical raters maintain a high level of skill and accuracy.
- Conduct the study in accordance with Federal Regulations, Internal Conference on Harmonization (ICH) and Good Clinical Practices (GCP).
- Approved protocol.
- Communications with IRB.
- Compliance with study protocol.
- Maintenance of adequate and accurate source documents, study records and other study related reports.
- Safety Reporting.

Study Coordinator

Responsibilities include, but not limited to:

- Managing the day-to-day conduct of the trial.
- Ensuring accurate administration of all instruments at the site.
- Supervising accurate data collection and maintain case report forms.
- Regulatory: This person will be responsible for managing all regulatory related documents for the duration of the trial, including submitting all required regulatory documents to ADCS regulatory affairs.

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Project Interviewer/Psychometrist

Responsibilities include, but not limited to:

- This person will have at least a bachelor's degree in healthcare psychology, social work or a related field, and/or well-documented experience in administering interviews and neuropsychological tests.

The Study Coordinator may serve as the Interviewer/Psychometrician as long as he/she is properly trained.

Personnel Requirements– ADNI Clinic Site

Along with the Site Principal Investigator, three staff functions (Clinician, Psychometrist, Study Coordinator) will be required to conduct the protocol at the ADNI sites. Additional roles are outlined below that are recommended in order to conduct the study successfully. These functions may be covered by one staff member at certain sites, for other sites there will be multiple staff assigned.

Site Protocol Principal Investigator (PI)

The PI should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial.

Responsibilities include, but not limited to:

- Protect the rights and well-being of study participants.
- Ensure the conduct or supervise the described study.
- Maintain appropriate staff qualifications including study specific training.
- Adequate staffing resources.
- Medical care of study participants.
- Supervision of study personnel, including:
 - Delegation of roles and duties to appropriately qualified study personnel.
 - Ensuring that all study personnel are informed about the protocol and their delegated duties.
 - Ensure that clinical raters maintain a high level of skill and accuracy.
- Conduct the study in accordance with Federal Regulations, Internal Conference on Harmonization (ICH) and Good Clinical Practices (GCP).
- Approved protocol.
- Compliance with study protocol.
- Maintenance of adequate and accurate source documents, study records and other study related reports.
- Safety Reporting.

Study Physician/Site Clinician

Responsibilities include, but not limited to:

- Conducting or supervising the clinical evaluation of all participants including

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physical and neurological exams, reviewing serious adverse events, interpreting lab results, assessing diagnosis at all visits.

- Ensuring that biological samples (blood) are correctly processed.

Study Coordinator

Responsibilities include, but not limited to:

- Managing the day-to-day conduct of the trial.
- Ensuring accurate administration of all instruments at the site.
- Supervising accurate data collection.
- Preparing, handling, and processing of all laboratory samples.
- Coordinating clinic visits.
- Scheduling visits at MRI and PET centers and schedule assessments.

Below are other roles that may or may not be fulfilled by the study coordinator:

- Billing Remittance and Statement: This person will be responsible for reviewing and verifying payments from the ADCS are in alignment with procedures completed, along with accepting and processing payments from the ADCS for ADNI clinic site work only.
- MRI Contact: This person will be responsible for conducting phantom and human volunteer scans for site qualification purposes using the appropriate scanning sequence. As well as conducting participant and phantom MRI scans per protocol and ensuring the scans are uploaded to LONI in a timely manner.
- PET Contact: This person will be responsible for conducting phantom scans for site qualification purposes and as needed to assess for drift using the appropriate scanning sequence. As well as conducting participant PET scans per protocol and ensuring the scans are uploaded to LONI in a timely manner.

Project Interviewer/Psychometrist

Responsibilities include, but not limited to:

- This person will have at least a bachelor's degree in healthcare psychology, social work or a related field, and/or well-documented experience in administering interviews and neuropsychological tests.
- This person may be responsible for administering the ADAS-Cog and/or the CDR.

The Study Coordinator may serve as the Interviewer/Psychometrician as long as he/she is properly trained.

ADAS Administration

All individuals administering the ADAS must obtain ADAS certification. If an ADAS rater has already completed an ADCS certification for ADNI in the past 5 years, he/she is also certified to conduct the ADAS-Cog for ADNI-D. Certification is required for those who are ADAS- Naïve and for those certified more than 5 years ago. Certification is a simple process of completing an ADAS questionnaire and scoring better than 75%.

To request a certification questionnaire please email adcs-clinops@ucsd.edu. After being scored, the rater will receive ADAS certification by email from the ADCS. Certification is valid for ADNI and ADNI-related studies for 5 years; after this time the rater must recertify.

CDR Rater

All individuals administering the CDR for ADNI-D must be certified. Depending on previous CDR certification there are two separate requirements:

CDR Naïve: If a rater has never been CDR certified, full certification is required. The training includes nine (9) reliability tapes. The scores submitted will be compared to the Gold Standard and if the rater passes a certificate will be issued by Washington University.

CDR Certified: For those raters who have been previously certified a refresher is required. This refresher includes five (5) reliability tapes. The scores submitted will be compared to the Gold Standard and if the rater passes a certificate will be issued by Washington University.

CDR Certification and Refreshing can be found online at the following url:
<http://alzheimer.wustl.edu/cdr/application/step1.htm>.

It is important for the CDR rater to remain blinded to the ADAS-Cog data. If the CDR rater is also the PI, the CDR must be completed before viewing and approving the study data collected during the visit.

Signatures

“Wet” signatures on hard copy worksheets and electronic signatures on eCRFs serve to acknowledge that a clinician has reviewed each study visit and that the visit was conducted to his/her satisfaction.

Hard Copy (‘Wet’) Signatures

The following worksheets must be signed off by a clinician trained in the administration/review of these assessments (only credentials MD, PA, DO or NP).

- Neurological Exam
- Serious Adverse Events and Hospitalizations
- MRI Clinical Read
- Physical Exam

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Study Coordinators with these credentials are allowed to perform and sign off on these assessments.

Electronic Signatures

Some visits require a clinician to review and acknowledge that the visit was conducted to his/her satisfaction. The electronic signature is collected by unique user name and password and is the equivalent of a 'wet' signature.

The following eCRFs must be signed off by a clinician (only credentials MD, PA, DO or NP):

- Clinician Verification of Inclusion and Exclusion Criteria Form (Depression Assessment and Baseline Assessment)
- Clinician Review
- Protocol PI Approval (completed by Site Protocol PI at completion of Protocol)

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Site Approval to Begin Enrollment

Before screening begins, a site must meet requirements for ADCS start-up. Meeting site approval requirements to begin enrollment will require that you work closely with the ADCS Regulatory, Contracts, Recruitment, and Clinical Operations groups.

Sites must receive IRB approval within 3 months after the receiving the Final Protocol. In order to meet IRB approval and first screening visit deadlines, please follow Site Approval requirements checklist below.

Regulatory Requirements

- Consent form for ADCS review / approval
- IRB approval of Protocol and ICF(s) submitted to ADCS RA.
- Protocol Signature Sheets signed by both Depression Site PI and ADNI Clinic Site PI.
- Signed & Dated CV, Medical License and Human Subjects Certification for PI and all sub-investigators identified as “Key Personnel” on the ADNI-D Personnel Sheets.
- Certificate of Confidentiality submitted to NIA via email; ADCS RA should be cc’d with emailed submission to NIA.

NOTE: Original “wet” signatures required for Signature Sheets **ONLY**; CVs, Medical Licenses and Human Subject Certifications can be emailed to ADCS Regulatory Affairs.

Forms may be downloaded from **ADCS Admin Portal > Library > Regulatory Affairs.**

Originals can be FedEx’d to:
ADCS Regulatory Affairs
8950 Villa La Jolla Drive, C227
La Jolla, CA 92037
Tel: 858-246-1320
Reference: ADNI-D / FedEx Acct # 159505316

All other documentation can be faxed or emailed:

Fax: 858-246-1413 | Email: adcsra@ucsd.edu

Contract Requirements

- Master Contract
- Signed Study Agreement

Certification and Other Administrative Requirements

- Completed Set of Personnel Sheets (please see section below for more details)
- Enter Contact Information for new personnel (via ADCS Admin Portal)

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- ADAS-Cog Certification (through ADCS)
- CDR Certification (through Washington University, St. Louis)
- MRI Certification
- PET Certification
- Trained Psychometrist and Raters for Neuropsychometric Testing Battery and other assessments

Personnel Sheets

The Personnel Sheets detail study staff to whom significant study-related tasks have been delegated as well as each individual's dates of involvement in the trial. The form will also document that the PI is responsible for, accountable for, and has approved such delegation of duties. In addition, the full legal signature and initials of all study personnel will be captured.

The Personnel Sheets should be completed prior to beginning trial-related activities and updates as needed to reflect changes in staff, role assignments and/or the delegation of responsibilities. Any changes to the forms must be documented using a blue or black ink pen.

The Study Coordinator can complete the forms; however, the PI must review and acknowledge approval of the duties being delegated by providing his/her initials and the date for each personnel. Similarly, if any changes are made to the Personnel Sheet during the course of the study the PI must review and acknowledge approval of the changes by providing his/her initials and the date next to the change.

For detailed instructions on how to complete the form, please refer to the "Personnel Sheet Instructions" posted in the document repository.

MRI Scan Certification

Any new participating site for ADNI-D must complete the scanner certification process for 3T MRI. Sites that have been previously certified for ADNI-2 do **NOT** require recertification unless there has been a change in the 3T MRI scanner or significant software upgrade. The same protocol sequences loaded for ADNI-2 will be used in ADNI-D with some minor modifications. *See the ADNI-D MRI Protocol for more information on sequence modifications.* Site MRI qualification requires a phantom scan and a volunteer scan. See MRI section for further details.

PET Scan Certification

Any new participating sites for ADNI-D must complete the PET scanner certification process. Sites that have been certified previously for ADNI-2 do **NOT** require recertification unless there has been a change in PET scanner or change in software platform.

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Study Supplies

Once your site receives a 'Site Approval' notification email from adcsra@ad.ucsd.edu to begin enrollment, you will be contacted by ADCS Clinical Operations confirming the supplies needed by your site. The supplies you need will depend on the number of participants you have identified to screen for ADNI-D. Study supplies will be sent to the Study Coordinator. Please keep your Protocol Personnel Log updated so that supplies are sent to the appropriate person.

- **There are no auto shipments after the initial set of supplies are shipped.**
- Please be sure to order supplies far enough in advance of scheduled visits (at least 10 days prior).

The ADNI Coordinating Center at the ADCS will provide the following supplies for the ADNI-D study:

- DNA, APOE, Cell Immortalization, PBMC Banking and RNA Collection, Labels and Shipping Supplies.
- Biomarker Collection, Labels and Shipping Supplies.
- Additional blood draw supplies (for Telomeres and "TBD" assay sample collection).
- Buffy Coat supplies.
- Neuropsychometric Testing Supplies (ADAS Kits, Boston Naming Testing Booklet).
- Subject binder inserts/tabs, spine and covers. (Actual binders are not being provided by ADCS, rather all sites were provided a startup fund at the start of ADNI-D from the ADCS which is to be used to cover the cost of binders.
- Worksheets and Procedures Manuals will not be printed for sites. If a paper copy is needed, print the most recent version which is located in the document repository.

ADAS Kits and Boston Naming Testing Booklet are the same supplies provided and used in ADNI2. Neuropsychometric supplies will NOT routinely be provided to each site as it is expected to use one set across ADNI2 and ADNI-D.

- Hard copies of the cognitive assessment record forms (including MMSE Worksheet and record forms for the Depression Assessment)
 - Due to copyright restrictions, some cognitive measures (including MMSE) will no longer be included in the source document packets posted in the document repository. The number of hard copies of these measures included in the initial shipment from the ADCS will be based on the number of potential participants prescreened in your area. The order form posted in the document repository will need to be used to order additional copies of the record forms.

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- DO NOT make photocopies of the hard copies provided by ADCS at any time. Hard copies should be ordered directly from the ADCS.

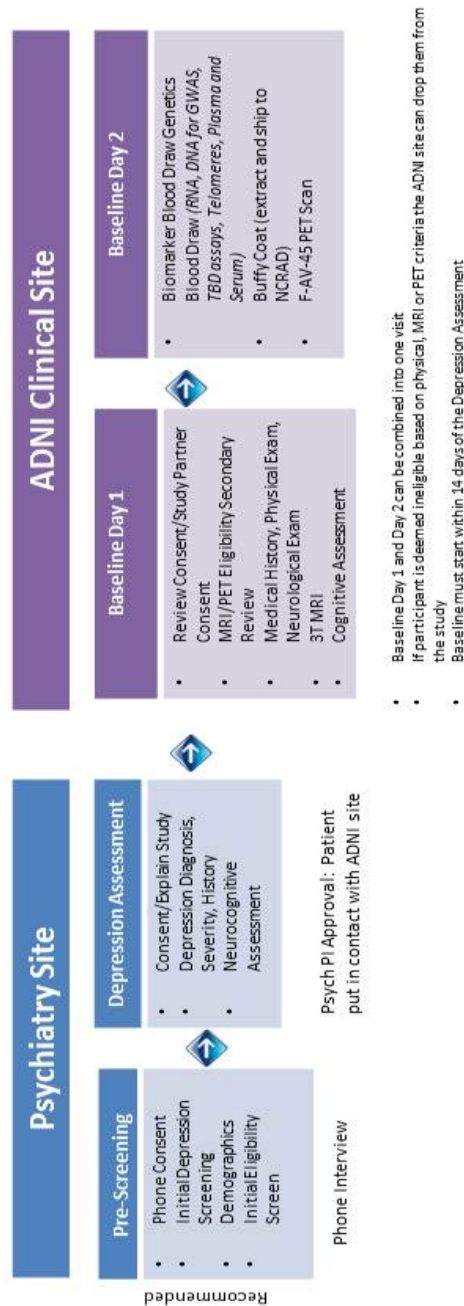
NOTE: Spanish testing supplies will NOT be offered for this study, as all participants must be fluent in English.

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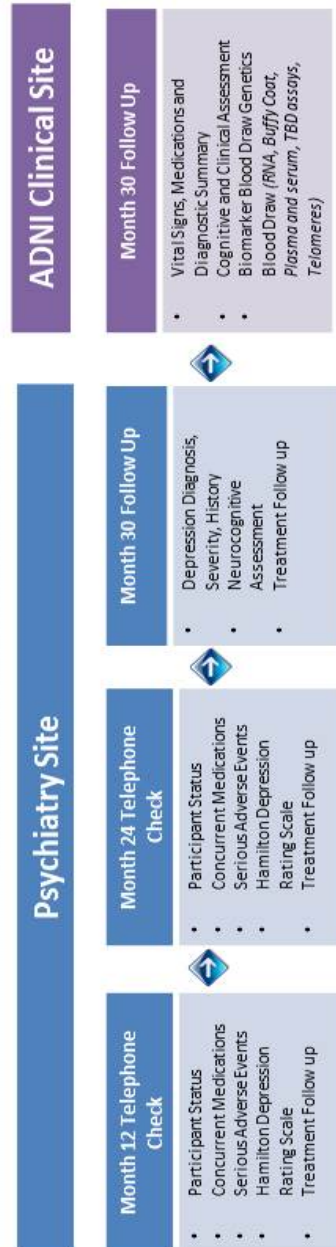
ADNI-D Scheduling Guidelines

Below are the general guidelines for scheduling visits for ADNI-D. More detailed instructions for each visit are in the Visit Procedures Section. In order to ensure standardized outcomes it is important the ADNI-D guidelines for scheduling participant visits are followed

ADNI-D Visit Schedule (Screening and Baseline)



ADNI-D Visit Schedule (Follow Ups)



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Data Management

Overview

There are three locations for the management of data for the ADNI-D Study.

1. **ADNI-D Clinical Data Portal:** The electronic data capture (EDC) is the primary point of registering a new participant or follow up subject, entering clinical data, signing off on eligibility, obtaining worksheets and procedures manuals. Additionally, the Query and Support tool is available through the EDC for sites to pose questions, review and respond to data queries from Coordinating Center.
2. **ADNI LONI Imaging Database:** LONI is the primary interface for imaging data upload. All MRI scans and florbetapir F 18 PET scans are uploaded to LONI.
3. **ADCS Administration Portal:** This site is the location where contact information is entered and payment invoices for the ADNI clinical site can be retrieved.

Accounts for each of these online databases are separate. Once an account is issued, access to any of these online databases can take place at any time and from any place internet access is available.

Never share your password with another person. Every interaction with ADNI online data management tools is time and date stamped and is traceable to the user who completed the transaction.

ADNI-D data is managed on a different data portal than the ADNI-2 protocol, and all data entry should be kept current on an ongoing basis. This is also important because of the public access to all ADNI data on an ongoing basis.

To access the websites described in this section, go to <http://adcs.org>. **Select ADCS Investigators>Study Resources>**

- If you forgot your username or password, use the “forgot password” feature on the individual site of interest.

ADNI-D Clinical Data Portal / EDC

Activities on the ADNI-D Clinical Data Portal:

- Assign Participant ID
- Enter Visit Data and upload source documents
- Sign off on Eligibility
- Study Docs: Print Visit Packets, Access Procedures Manuals, SAE Reports, Study Memorandums, and Supply Order Forms
- Queries tool

Accounts

After Site Approval is received, online accounts will be generated according to the access levels requested on the Personnel Sheets. Complete/Update the Personnel Sheet

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and enter Contact Information if new personnel at your site need online accounts or to remove access for this protocol.

Send all updates and questions on access to: adcs-clinops@ucsd.edu.

Data Access Level:

View eCRFs: Allows view access only to site-specific study database.

Enter and update eCRFs: Allows user to enter and update data to site-specific study database.

Sign Off on Participant Eligibility: Provides access to approval forms. Credentials required are: MD, PA, DO, or NP. The electronic signature is a binding legal signature.

The following forms require electronic signature:

- Clinician Verification of Inclusion and Exclusion Criteria Form
- Clinician Review
- Site PI Approval (only Site PI can complete this form)

Timeliness of Data Entry

- Data collected must be entered **promptly** on the ADNI-D online database
- For all visits, data must be submitted online within 1-2 business days.

ADNI LONI

Activities on the ADNI LONI Site:

- MRI Image and Phantom Upload
- PET Image and Phantom Upload

Details on accessing and uploading images for ADNI are part of the MRI and PET Technical Manuals. LONI is also the location where publicly-available datasets may be downloaded by users. A guide for registering on the LONI website is available on the data portal under Docs > studydocs > Procedures Manuals. Please send any questions to: dba@loni.usc.edu. Navigate to ADNI LONI database using this url:

<https://ida.loni.usc.edu>

ADCS Administration Website:

Activities on the ADCS Administration Site:

- Payment Invoices for ADNI Clinical Site
- Entry of Contact Information (see instructions posted on the data portal under Docs > studydocs > site-personnel-forms)

Please note that the ADCS Administration Website is a separate URL from the ADNI-D EDC web portal and is a separate login.

If you have difficulties logging in to the ADCS Administration Website, email: adcs-sd@ucsd.edu.

Use of Multiple Locations at a Single Center

Some ADNI sites will use more than one location using the same personnel. The following guidelines have been developed to aid in the decision concerning the use of additional locations at a single center.

Any plan to use more than one location to conduct the ADNI must be approved by Dr. Weiner and Dr. Aisen. The Site Principal Investigator must take responsibility for any additional locations. Also, a single contract will be filed for each center; any exceptions must be approved by both Dr. Aisen and Dr. Weiner.

- Study Coordinators must be available to answer questions about data entered on the ADNI EDC from all locations. The ADNI Coordinating Center at the ADCS should be immediately notified if there are any changes in the study coordinator.

Study Closeout

Important Note

Do not close out any study with your IRB until you are officially notified by the ADCS that the trial has been completed and it is appropriate to do so. Until such time, it is essential that all study documents and information are easily retrievable and continue to be stored in a secure location.

If the investigator becomes unable to maintain the study records that he/she should notify ADCS of the location of the records and the person responsible for retention

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Recruitment and Retention

The ADNI Depression Project will differ from the current ADNI projects, in that all recruitment will be done through the established geriatric psychiatry research sites (i.e., UCSF Langley Porter Psychiatric Institute and University of Pittsburgh Medical Center).

The psychiatry research sites will be identifying possible participants through ADCS provided recruitment materials, be responsible for the mail effort for potential participants, conducting a prescreening telephone interview, as well as psychiatric interviews to confirm eligibility.

The ADCS Recruitment and Retention Team has a host of ADNI-D recruitment materials available to assist with site efforts. These include:

- Flyer
- Trifold Brochure
- Postcard
- Physician Pocket Cards (also known as Doc Cards)
- Informational PET Pamphlet
- Informational MRI Pamphlet
- Newspaper Advertisement
- Dear Colleague Letter
- Letter to the Editor
- Press Release
- Study information page on ADCS.org website that features contact information for all sites participating in ADNI2.
- Blurb placed in the Alzheimer's Disease Information Network E-Newsletter distributed to over 3,000 subscribers.

All patient data and telephone calls conducted for prescreening will not be entered into the EDC portal with the exception of the Hamilton Depression Rating Scale. Pertinent Data (i.e., Medical History, Psychiatric History, and Concomitant Medications) will be used for initial eligibility pre-screening and will be reassessed at the Depression Assessment visit.

Contact Us

Please contact the Late Life Depression Program for any requests, questions, comments or suggestions. Attn: David Bickford, David.bickford@ucsf.edu (415) 476-7046

New Enrollees: Baseline and Follow Up Procedure

Phone Screen Procedures

Summary

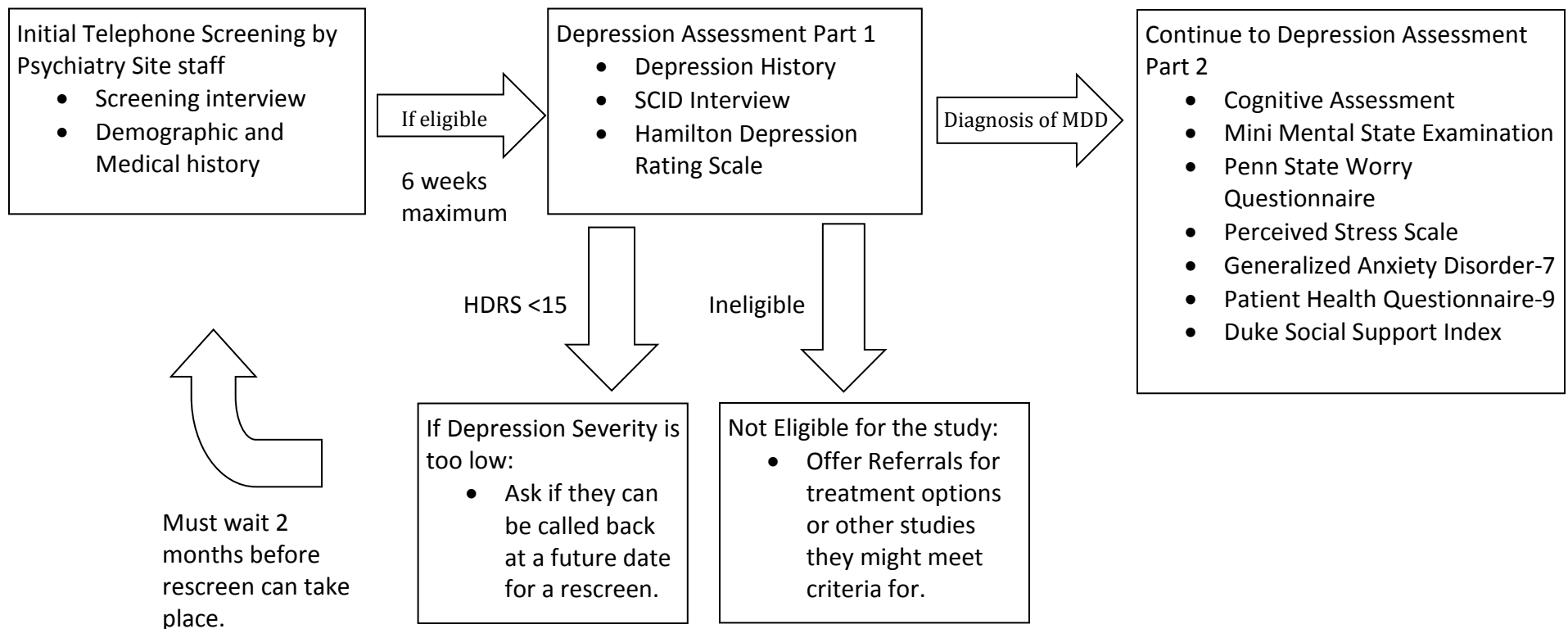
The purpose of the ADNI-D phone screening is to determine eligibility and gather a rating of current depression severity. It is recommended that all new participants have a phone screen. Phone screenings will involve a phone interview briefly explaining the nature of the study as well as acquiring basic demographic information. Verbal consent will be obtained before any portion of the phone screen is initiated. Depression severity will be assessed after demographic history (including medical history, medication, alcohol use and drug use) and publicity tracking data has been collected. Demographic information gathered during this initial phone screen will be used to help determine initial eligibility but will not be entered into the EDC portal until after the participant has come in for their Depression Assessment. Participant demographic information for potential participants deemed ineligible will not be entered into the portal.

Eligibility will be determined according to the inclusion/exclusion criteria outlined later in this section. If the participant is deemed potentially eligible they can be brought in for an in person assessment at the depression sites. *Note: Participants are not considered officially eligible until a diagnosis of Major Depressive Disorder has been confirmed by the Structured Clinical Interview of the DSM-IV.*

Key Reminders

- The window from phone screening to Depression Assessment is 6 weeks.
- Participants must meet all inclusion/exclusion criteria.
- Complete Data Entry within 1-2 business days of the Depression Assessment.
- The Hamilton Depression Rating Scale only rates depression severity for the previous 7 days. The sooner the participant can be scheduled for a Depression Assessment the more reliable the phone screen Hamilton Depression Rating Scale score.

Study Eligibility Flow Chart



The psychiatry site study coordinator will give the participant's information to the ADNI clinical site. The Baseline Assessment should be scheduled within 14 days of completing the Depression Assessment.

Participant Eligibility Procedures

Summary

A standardized evaluation will be performed at each site with a time interval no later than 6 weeks between the phone screen and Depression Assessment. If the participant is not brought in for an assessment by the 6 week cut off a second pre-screening phone interview is required to re-assess depression severity and eligibility criteria.

Consent will be obtained before any further portion of the Depression Assessment is initiated.

Eligibility will be determined according to the inclusion/exclusion criteria outlined later in this section and confirmed by the psychiatry site PI before the subject can be brought back for a Baseline Assessment.

Key Reminders

- The window from to Depression Assessment to Baseline Assessment is 14 days.
- Participants must meet all inclusion/exclusion criteria and must be confirmed by the psychiatry site PI.
- Complete data entry within 1-2 business days of the Depression Assessment.

Participant Identifiers

The ADNI Participant ID (PTID) consists of the ADCS 3-digit site number, a single character identifier (D for 'Depression Subject'), followed by a sequential 4-digit subject number reflecting the chronological order in which the ID's are assigned across sites. Participants from ADNI1 began at 0001, EMCI participants enrolled into ADNIGO began at 2001, ADNI 2 participants began at 4001, and participants enrolled into ADNI-D will begin at 3001.

Example: A participant from site 900 who is the third subject assigned for ADNI D is 900_D_3003.

Use the Participant ID for all study documents, source documents, MRI/PET scans and biological samples. Phantom IDs are not assigned on the ADNI Clinical Data Portal. Assign Phantom IDs following instructions in the MRI and PET Technical Manuals, while uploading to the LONI database.

TO ASSIGN AN ADNI PTID FOR NEW PARTICIPANTS:


- Log on to the ADNI-D Data Portal: adcs.org > **ADCS Investigators > Study**

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE


Resources > ADNI-D EDC

- From 'EDC', click on 'Add a New Participant'.
- The new participant ID will be displayed on the following screen.

ADNIGO > TEST > Participant Menu

 Add a New Participant

Please select a participant from the following list:

Participant	Status	Last Visit
TST_S_9002		

Register Participant

New participant registered: TST_S_9509

Please click [here](#) to start entering data.

(Example from ADNIGO, the same procedure will be used for ADNI-D)

Enter Registry as soon as possible after a visit is initiated

1. Indicate participant status as active (even for participants who are deemed ineligible at Depression Assessment).
2. Visit type as standard for those that complete their first ADNI-D Depression Assessment (even if the participant is deemed ineligible).
3. The examination date is the date the ADNI-D Depression Assessment visit was completed.
4. If a participant is a Depression Assessment rescreen, indicate "yes" for "Is this a rescreen" and enter the previous participant ID in the subsequent field.

Please remember any participant who is a rescreen requires prior approval and at a minimum 2 months between original Depression Assessment screen and Depression Assessment rescreen.

REMINDER: In the registry eCRF a 'standard' visit should be selected when most all primary outcome measures were conducted. A 'nonstandard' visit should be selected when most of the primary measures were NOT conducted.

Data Flow

Phone Screening:

- Review participant's medical history, medications, demographics and any past diagnoses for eligibility.
- Perform Hamilton Depression Rating Scale assessment to assess participant depression severity.

Note: The Hamilton phone screen score and participant demographics are entered with the Depression Assessment visit.

Depression Assessment Visit:

- Consent must be obtained prior to assigning a Participant ID.
- Enter all data in the ADNI-D Data Portal within 3 business days of Depression Assessment: adcs.org > **ADCS Investigators** > **Study Resources** > **ADNI-D EDC**
- Scan and upload worksheets to the Source Doc Upload eCRF in the ADNI-D EDC system.
- Enter Clinician Verification after completing review of all required assessments.

Please Note:

Although participant demographics are collected at the Depression Assessment visit, the ADNI clinical sites will verify the information entered at the Baseline Assessment visit. The ADNI clinical sites will check this information in the portal and submit/report any discrepancies found.

3T MRI Scan:

- Unlike ADNI-2 procedure, the 3T MRI scan will not be used for eligibility criteria. Once the participant has been deemed eligible by the psychiatry site, and MRI and PET safety is confirmed with the ADNI Clinic site the participant is eligible for an MRI scan and Baseline visit.
- Conduct along with the Baseline Clinical Assessment.
- Ensure participant and study partner have the MRI pamphlet with appointment reminder and directions.
- Ensure MRI Center has current ADNI-D MRI Technologist Manual and MRI Scan Information form for this participant.
- Upload Scan to LONI day of scan (see MRI Training Manual for details.)
- Enter MRI Scan Information form in EDC on day of scan: adcs.org > **ADCS Investigators** > **Study Resources** > **ADNI-D EDC**
- Upload copy of de-identified Radiology Report/Clinical Read as soon as it has been reviewed/signed off by Study Clinician via the Source Doc Upload eCRF in the data portal.

Ensure any identifiers are blacked out on the copy uploaded to the ADCS including Medical Record numbers, telephone numbers, and date of birth.

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

MRI QC Review:

MRI Quality Control at Mayo Clinic (MRI QC) will review the scan for quality confirmation. In order for Mayo to QC the scan, it is imperative that the MRI Scan Information form is entered online and that the scan date entered is accurate. If either of these are not complete or not correct, the QC results will not make it in the EDC system.

Important Reminders:

- Baseline will be conducted with 3T MRI scans. These scans will not need to be approved by Mayo MRI QC group or clinician to schedule the Baseline Assessment.
- Baseline visit (in-clinic assessment) must start within 14 days of the Depression Assessment visit. There is an additional 2 weeks to complete other Baseline procedures (e.g. PET, Neuropsych).

Screen Failures and Rescreens

All participants who sign consent must be assigned an ADNI-D ID, even if a Depression Assessment visit is not fully completed. Indicate whether a participant is a screen fail on the Clinician Verification form. The Depression Assessment visit is split into two sections; the first section determines eligibility and whether a diagnosis of Major Depressive Disorder is present based on SCID criteria. If the participant meets eligibility criteria and has a positive Diagnosis of Major Depressive Disorder the second section will be conducted including the cognitive testing and self-reports.

Enter all data collected for screen fails. At a minimum these forms are required:

1. Registry (Reminder: For all participants, even those who screen fail, the participant status should be 'active,' and visit type as 'standard').
2. Eligibility Criteria
3. Clinician Verification
4. Publicity Tracking
5. Depression Severity Score (Hamilton Depression Rating Scale)
6. Structured Clinical Interview Diagnosis

Before scheduling a rescreen, contact your site PI for approval. There is a minimum of 2 months required before a rescreen can be scheduled. Rescreens must be assigned a new ADNI-D Participant ID (PTID). Ensure Clinician Verification for initial screen is entered as 'ineligible'.

- All rescreen data must be entered under the new subject ID number.

Inclusion Criteria

1. Current DSM–IV diagnosis of Major Depressive Disorder, unipolar type, without psychotic features and six week minimum duration of current depressive episode.
2. English Speaking
3. 65+ years of age
4. Able to give informed consent
5. Hamilton Depression Rating Scale score ≥ 15
6. Willing to undergo one MRI (3 Tesla) and one PET scan (Amyloid imaging)
7. Able to fit in an MRI machine comfortably (BMI \leq 38)
8. Agrees to collection of blood for GWAS, APOE testing and DNA and RNA testing
9. Agrees to collection of blood for biomarker testing
10. Agrees to collection of additional blood for future testing (telomere and “TBD” assay sample collection)
11. Visual and auditory acuity adequate for neuropsychological testing
12. Good general health with no diseases expected to interfere with study outcomes
13. Stability of permitted antidepressant medications for 4 weeks (if applicable)
14. Stability of psychotherapy treatment for 4 weeks (if applicable)
15. Completed six grades of education or has an established work history (sufficient to exclude mental retardation)
16. Study partner is available who has frequent contact with the subject (e.g. an average of 10 hours per week or more), and can accompany the subject to clinical visits for the duration of the protocol

Exclusion Criteria

The following exclusion criteria apply to all participants:

1. Current diagnosis of other axis 1 psychiatric disorders (with the exception of Simple Phobias and Generalized Anxiety Disorder)
2. Evidence of Dementia (MMSE < 25)
3. Any electroconvulsive therapy within the past 6 months
4. Undergoing antidepressant or psychotherapy treatment (exceptions listed 4.3. Treatment Exclusion Exceptions)
5. Any significant neurological diseases (i.e. Parkinson’s disease, epilepsy, cortical stroke, traumatic brain injury, HIV+, multiple sclerosis)
6. History of alcohol or substance abuse or dependence within the past 2 years (DSM-IV criteria)

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

7. Any active and serious suicidal ideation, including ideation, plan and intent to carry out that plan, as assessed by the HDRS
8. Any significant systemic illness or unstable medical condition which could lead to difficulty complying with the protocol
9. History of surgical procedures effecting study outcomes
10. Residence in skilled nursing facility
11. Participation in clinical studies involving the same neuropsychological measures used for ADNI-D that may impact study outcomes
12. Investigational agents are prohibited one month prior to entry and for the duration of the trial
13. Exclusion for amyloid imaging with ^{18}F –AV-45: Current or recent participation in any procedures involving radioactive agents such that the total radiation dose exposure to the subject in any given year would exceed the limits of annual and total dose commitment set forth in the US Code of Federal Regulations (CFR) Title 21 Section 361.1
14. Known history of MRI scans with evidence of infection, infarction, or other focal lesions. Subjects with multiple lacunes or lacunes in a critical memory structure are excluded
15. Presence of pacemakers, aneurysm clips, artificial heart valves, ear implants, metal fragments or foreign objects in the eyes, skin or body, claustrophobia
16. Pregnant, lactating, or of childbearing potential (i.e. women must be two years post-menopausal or surgically sterile)

GENERAL RULE: Any history of cancer five years prior to screening is exclusionary (history of skin melanoma is not exclusionary)

Treatment Exclusion Exceptions:

1. Anti-depressant medication treatment is allowed only if the medication dose is stable for 4 weeks prior to the MRI scan
2. Psychotherapy interventions is allowed only if they have completed at least 4 weeks of individual or group psychotherapy intervention
3. Participant taking cognitive enhancing medication will be able to enter the study. (i.e.: Namenda, Aricept, etc.)

Excluded Medications

Please Note:

This is not a complete list of all excluded medications. For drugs not included here, please bring to the attention of your site PI.

1. Current use of Pradaxa (Dabigatran) or Heparin.
2. Regular use of narcotic analgesics (>2 doses per week) within 4 weeks of screening.
3. Use of neuroleptics with anticholinergic properties (e.g., chlorpromazine, thioridazine) within 4 weeks of screening.
4. Chronic use of other medications with significant central nervous system anticholinergic activity within 4 weeks of screening (e.g., diphenhydramine).
5. Use of Anti-Parkinsonian medications (including Sinemet, amantadine, bromocriptine, pergolide, selegeline) within 4 weeks of screening.
6. Participation in any other investigational drug study within 4 weeks of screening (individuals may not participate in any drug study while participating in this protocol).
7. Diuretic drugs should not be started or discontinued within 4 weeks prior to screening.

Any change in diuretic medication during the study should be reported.

EXPANDED LIST ON FOLLOWING PAGES

NARCOTIC ANALGESICS: Not allowed within 4 weeks prior to screening	
GENERIC NAME	BRAND NAME
Hydromorphone	Dilaudid
Oxycodone/Acetaminophen	Percocet
Oxycodone/Aspirin	Percodan
Propoxyphene/Darvon and its variations	
Narcotics that contain codeine or morphine	
NEUROLEPTICS: Not allowed within 4 weeks prior to screening	
Chlorpromazine	Thorazine
Fluphenazine	Prolixin
Loxapine	Loxitane
Perphenazine	Etrafon, Trilafon
Thioridazine	Mellaril
Thiothixene	Navane
Trifluoperazine	Stelazine
Clozapine	Clozaril
Haloperidol	Haldol
Use of the following is permitted if dose is stable for 4 weeks prior to screening:	
Aripiprazole	Abilify

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

Olanzapine	Zyprexa
Quetiapine	Seroquel
Risperidone	Risperdal (up to 2mg/day)
Ziprasidone	Geodon

ANTICHOLINERGIC AGENTS: Not allowed within 4 weeks prior to screening

Amantadine	Symmetrel
Benztropine	Cogentin
Cyproheptadine	Periactin
Dicyclomine	Bentyl
Diphenhydramine	Benadryl, Sominex 2
Diphenoxylate with Atropine	Lomotil
Hydroxyzine	Vistaril, Atarax
Hyoscyamine	Levsin
Meclizine	Antivert, Bonine
Prochlorperazine	Compazine
Trihexyphenidyl	Artane
Trimethobenzamide	Tigan

ANTIPARKINSONIAN MEDICATIONS: Not allowed within 4 weeks prior to screening

GENERIC NAME	BRAND NAME
Bromocriptine	Parlodel
Deprenyl/Selegilene	Eldepry
Levodopa	Sinemet
Pergolide	Permax
Pramipexole	Mirapex

SEDATIVES/BENZODIAZEPINES: Not allowed within 4 weeks of screening

Chlordiazepoxide	Librium
Clonazepam	Klonopin
Diazepam	Valium
Flurazepam	Dalmane
Meprobamate	Miltown
Triazolam	Halcion

Allowed if on stable doses 4 weeks prior to screening:

Alprazolam	Xanax
Buspirone	Buspar
Chloral Hydrate	Noctec
Lorazepam	Ativan
Oxazepam	Serax
Temazepam	Restoril
Trazodone	Desyrel
Zaleplon	Sonata
Zolpidem	Ambien

ANTIHYPERTENSIVE AGENTS WITH FREQUENT CNS SIDE-EFFECTS: Not allowed within 4 weeks of screening

Clonidine	Catapres
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Permitted Medications

1. Cholinesterase inhibitors and Memantine are permitted if the dose is stable for 12 weeks prior to screening.
2. Use of estrogen and estrogen-like compounds is allowed if the dose has been stable for 4 weeks prior to screening.
3. Use of vitamin E is allowed if the dose has been stable for 4 weeks prior to screening (no cap on amount allowed).

Exceptions to these criteria may be considered on a case-by-case basis at the discretion of the Protocol PI

Psychiatric Medications to Review

Below is a list of commonly prescribed psychiatric medications that may be used for depression or other psychiatric disorders. Check this list if the participant is taking/or has taken any psychiatric medication to assist in an accurate diagnosis.

TCAs/ Tetracyclics		
GENERIC NAME	BRAND NAME	COMMON USE
Desipramine	Norpramin	Tricyclic antidepressants used for treating depression. Not as common.
Amoxapine	Asendin, Asendis, Defanyl, Demolox	
Doxepin	Silenor, Zonalon, Prudoxin	
Imipramine	Tofranil-pm, Trofanil	
Amitriptyline	Elavil	
Nortriptyline	Pamelor	
Trimipramine	Surmontil	
Maprotiline	Ludiomil	
Protriptyline	Vivactil	
Clomipramine	Anafranil	Usually used in OCD, can be used in depression.
MAOIs/ Monoamine Oxidase Inhibitors		
Phenelzine	Nardil	Older antidepressants used in depression.
Tranycypromine	Parnate	
Selegiline	Emsam, Eldepryl, Zelapar	
Isocarboxazid	Marplan	
SSRIs/ Selective Serotonin Reuptake Inhibitors		
Citalopram	Celexa	Common SSRI's used for depression.
Paroxetine	Paxil	

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

Sertraline	Zoloft	Commonly used for OCD but can be used for depression.
Fluoxetine	Sarafem, Prozac	
Escitalopram	Lexapro	
Vortioxetine	Brintellix	
Vilazodone	Viibryd	
Fluvoxamine	Luvox	
SNRIs/ Serotonin-Norepinephrine Reuptake Inhibitors		
Venlafaxine	Effexor	SNRI's: used in depression and sometimes pain management. Milnacipran is not approved for use in depression in the US.
Desvenlafaxine	Khedeza, Pristiq	
Duloxetine	Cymbalta	
Levomilnacipran	Fetzima	
Milnacipran	Savella	
Other Antidepressants		
Bupropion	Wellbutrin	Various antidepressants used for depression. Trazodone is often used for sleep but is an antidepressant at higher doses (e.g. ≥ 300 mg/day)
Nefazodone	Serzone	
Mirtazapine	Remeron	
Trazodone	Oleptro	
Atypical Antipsychotics		
Quetiapine	Seroquel	Atypical Antipsychotic Drugs: Can be used in depression but are more commonly used in schizophrenia and bipolar disorder. If participant is taking these be sure to thoroughly investigate their symptoms in the SCID.
Olanzapine	Zyprexa	
Risperidone	Risperdal	
Lurasidone	Latuda	
Arpiprazole	Abilify	
Mood Stabilizers		
Lithium	Lithane, Lithobid	Mood Stabilizers: Not often used in unipolar depression. Should check for bipolar illness.
Valproic acid	Depakene, Depacon, Stavzor, Valproic	
Carbamazepine	Tagretol, Carbotrol, Equetro, Eptol	
Oxcarbazepine	Trileptal	
Lamotrigine	Lamictal	
Other Medications		
Gabapentin	Gralise, Neurontin, Horizant, Fanatex	Various agents used for anxiety. Can be used in anxious depressed patients.
Benzodiazepines	Xanax, Klonopin, Valium, Halcion, etc.	
Pregabalin	Lyrica	
Buspirone	Buspar	
Combination Drugs		
Perphenazine/amitriptyline	Etrafon/Elavil	Combination agents: can be used for depression but may suggest bipolar illness or psychotic disorder.
Olanzapine/Fluoxetine	Zyprexa/Sarafem, Prozac	

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

Change in Medication after Enrollment

Record any change in medication (including dose or frequency) on the Concurrent Medications Log for the visit the change is reported. If a participant begins an excluded medication, report this as a protocol deviation.

If a participant begins a cholinesterase inhibitor or Memantine after being approved for enrollment into the study, this should be documented by completing the Protocol Deviation Form.

Depression Assessment – Psychiatry Site

Summary

The purpose of the Depression Assessment is to determine eligibility for the study as well as collect measures that will be used as a reference to assess change. A combined Informed Consent form will be used at the Depression Assessment visit to consent the participant for all ADNI-D study procedures. The ADNI clinical site will also explain the study and review the Informed Consent form to ensure there are no additional questions about the specific procedures being conducted at the Baseline Assessment visit. One major component of eligibility is a diagnosis of a current Major Depressive Episode which will be assessed using the Structured Clinical Interview of the DSM-IV. If criteria for a current Major Depressive Episode are not met, the participant will be thanked for their time and the remainder of the Depression Assessment visit will not be conducted.

- Explain study
- Obtain consent
- Demographics (Participant) **Demographic information collected at the Depression Assessment visit will be used for eligibility purposes and will be verified at the ADNI Baseline Assessment**
- Inclusion and Exclusion Criteria
- Publicity Tracking **This only needs to be completed if information was not gathered during the phone screen**
- Hamilton Depression Rating Scale (HDRS)
- Structured Clinical Interview of the DSM-IV (SCID-IV)
- Depression History
- Mini Mental State Examination

If by this point in the assessment the participant does not meet criteria for Major Depressive Disorder and is deemed ineligible, the Depression Assessment visit will be stopped.

- Brief Visuospatial Memory Test
- Controlled Oral Word Association Test
- Hopkins Verbal Learning Test
- Generalized Anxiety Disorder-7
- Patient Health Questionnaire-9
- Duke Social Support Index
- Penn State Worry Questionnaire
- Perceived Stress Scale
- Geriatric Suicide Ideation Scale
- Pittsburgh Sleep Quality Index
- Stroop Color Word

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

- WAIS Digit Span
- WAIS Digit Symbol
- Benton Judgment of Line Orientation – Form H
- Motor-Free Visual Perception Test-3
- Grip Strength Test
- Grooved Pegboard Test

Baseline Assessment – ADNI Clinic

Key Reminders

- The ideal window from Depression Assessment to Baseline is 14 days.
- Participants must meet all inclusion/exclusion criteria.
- Complete data entry within 5 business days of the visit.
- Once the Baseline visit begins, you have 2 weeks to complete all Baseline procedures.
- Since this will be the first visit for the study partner, consent will need to be obtained. Study partner consent is obtained on the last page of the participant's Informed Consent form.

Keep in mind that the plasma and serum collection for biomarker analysis and “TBD” assays, as well as Telomere sample collection must occur after **at least a 6 hour fast**. Buffy Coat is extracted from plasma tubes and shipped frozen to NCRAD.

Important Note:

Cognitive assessments should NOT be scheduled while the participant is fasting, or immediately after an imaging session.

Scan and Upload worksheets to the Source Doc Upload eCRF in the EDC system.

Baseline Assessment

- Explain study/Review consent
- Obtain Study Partner consent
- Demographics (participant verified and study partner obtained)
- Family History
- Physical, MRI or PET Exclusionary Criteria **Eligibility will be verified at the ADNI Baseline Assessment to ensure there were no additional exclusion criteria found.**
- Medical History
- Physical Exam
- Neurological Exam
- Modified Hachinski
- Height
- Logical Memory I and II

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

- Geriatric Depression Scale
- Clinical Dementia Rating Scale
- Vital Signs
- American National Adult Reading Test
- Everyday Cognition (ECog)
- Montreal Cognitive Assessment (MoCA)
- Category Fluency (Animals)
- Trails A & B
- Boston Naming Test (30-item)
- Auditory Verbal Learning Test
- Clock drawing
- Neuropsychiatric Inventory
- Cognitive Change Index 20 Participant
- Cognitive Change Index 20 Study Partner
- ADAS-Cog 13 (with Delayed Word Recall and Number Cancellation)
- Activities of Daily Living (FAQ)
- Plasma and Serum Biomarkers Collection*
- Genetic Sample Collection (DNA, RNA, Cell Immortalization, PBMC Banking)
- Telomere and “TBD” Assay Sample Collection*
- Concomitant Medications / Key Background Medications
- MRI (3T) – Baseline MRI only to be conducted after confirmation that the subject has met all other inclusion/exclusion criteria.
- Serious Adverse Events
- Diagnostic Summary / Clinical Status Form
- ¹⁸F-AV-45 Amyloid Imaging
- Florbetapir F 18 Pre and Post Injection Vitals

* Fasting

General Sample Guidelines

- All blood draws are completed on the same day
- RNA sample should be taken last
- If RNA blood draw occurs separate from the other blood draws, the red topped evacuation tube should be used to capture the initial blood flow and discarded
- Buffy Coat is extracted from the Biomarker Plasma Sample and the “TBD” Assay Plasma Sample and shipped to NCRAD
- Cognitive assessments should not be done immediately after blood draws, as this may affect the results
- Once participants start Baseline they have two weeks to complete all Baseline procedures.

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

12 & 24 Month Interim Phone Check/In Person Visit

The 12 month interim telephone visits or in person visit (site depending) will be timed at 12 and 24 months from Baseline visit day 1. The purpose of these visits is to retain contact with the participant and study partner to assess change in cognition, depression severity and address possible Serious Adverse Events that may have occurred since the last in-clinic visit. This visit will NOT be screening anyone out of the study, but will help determine whether anything has changed since the last clinic visit that may make a particular procedure unsafe, and to determine that the participant is still willing and able to participate.

12/24 Month Assessments

1. Concomitant Medications
2. Serious Adverse Events
3. Participant Status
4. Hamilton Depression Rating Scale (HDRS)
5. Follow up Treatment Form

Data Flow



Complete Data entry within 5 business days of the visit. Scan and upload worksheets to the Source Doc Upload eCRF in the EDC system.

Month 30 Follow Up Visit Procedure

Summary

Every attempt should be made to retain participants for longitudinal follow-up as long as possible. If subjects are not willing or able to complete the full schedule of assessments at the last visit, those assessments or procedures they are willing to complete should be conducted. If subjects are no longer willing or able to travel to the clinic for the follow-up visit, as much information should be collected via telephone as possible.

Month 30 visits will be conducted 2.5 years after completion of the ADNI-D Baseline visit. Visits will be scheduled based on the original Baseline date and should be completed within a 1 month window.

Month 30 Depression Follow Up Assessment – Psychiatry Site

- Hamilton Depression Rating Scale (HDRS)
- Structured Clinical Interview of the DSM-IV (SCID-IV)
- Follow up Treatment Form

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

- Mini Mental State Examination
- Brief Visuospatial Memory Test
- Controlled Oral Word Association Test
- Hopkins Verbal Learning Test
- Generalized Anxiety Disorder-7
- Patient Health Questionnaire-9
- Duke Social Support Index
- Penn State Worry Questionnaire
- Perceived Stress Scale
- Geriatric Suicide Ideation Scale
- Pittsburgh Sleep Quality Index
- Stroop Color Word
- WAIS Digit Span
- WAIS Digit Symbol
- Benton Judgment of Line Orientation – Form H
- Motor-Free Visual Perception Test-3
- Grip Strength Test
- Grooved Pegboard Test

Month 30 Follow Up Assessment – ADNI Clinic

Key Reminders

- The window from Depression Follow Up assessment to the ADNI Follow Up assessment is 14 days.
- Complete data entry within 5 business days of the visit.
- Once the ADNI Follow up visit begins, you have 2 weeks to complete all follow up procedures.

Keep in mind that the plasma and serum collection for biomarker analysis and “TBD” assays, as well as Telomere sample collection must occur after **at least a 6 hour fast**. Buffy Coat is extracted from plasma tubes and shipped frozen to NCRAD.

Important Note:

Cognitive assessments should NOT be scheduled while the participant is fasting.

Scan and Upload worksheets to the Source Doc Upload eCRF in the EDC system.

- Physical Exam
- Neurological Exam
- Logical Memory I and II
- Geriatric Depression Scale
- Clinical Dementia Rating Scale

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

- Vital Signs
- Everyday Cognition (ECog)
- Montreal Cognitive Assessment (MoCA)
- Category Fluency (Animals)
- Trails A & B
- Boston Naming Test (30-item)
- Auditory Verbal Learning Test
- Clock drawing
- Neuropsychiatric Inventory
- Cognitive Change Index 20 Participant
- Cognitive Change Index 20 Study Partner
- ADAS-Cog 13 (with Delayed Word Recall and Number Cancellation)
- Activities of Daily Living (FAQ)
- Plasma and Serum Biomarkers Collection*
- Genetic Sample Collection (DNA, RNA, Cell Immortalization)
- Telomere and “TBD” Assay Sample Collection*
- Concomitant Medications / Key Background Medications
- Serious Adverse Events
- Diagnostic Summary / Clinical Status Form

* Fasting

General Sample Guidelines

- All blood draws are completed at the same visit
- RNA sample should be taken last
- If RNA blood draw occurs separate from the other blood draws, the red topped evacuation tube should be used to capture the initial blood flow and discarded
- Buffy Coat is extracted from the Biomarker Plasma Sample and the “TBD” Assay Plasma Sample and shipped to NCRAD
- Cognitive assessments should not be done immediately after blood draws, as this may affect the results
- Once participants start the ADNI Follow Up assessment they have two weeks to complete all follow up procedures.

Telephone Visit Option

The following participants are eligible for telephone-only follow-up:

- ADNI-D enrollees who have completed all Baseline assessments under ADNI-D but then after this visit, are only available by phone.

The intent of the phone visit is to obtain as much information as possible over the phone in cases where the participant is unable or unwilling to come into the clinic. We are offering this information because the longitudinal data on such participants are extremely valuable. You should offer the phone visit option to any eligible participant who is no longer able to come to the clinic for their Month 30 Follow Up visits.

PLEASE NOTE: These phone visits are in replacement of the Month 30 Follow Up visits and are separate from the interim phone checks.

For these visits please select “non standard” visit on the registry form online.

Telephone Visit (Replacement of Depression Follow Up Assessments)

- Hamilton Depression Rating Scale
- Generalized Anxiety Disorder – 7 item¹
- Patient Health Questionnaire 9¹
- Duke Social Support Index¹
- Penn State Worry Questionnaire¹
- Perceived Stress Scale¹
- Follow Up Treatment Form
- Serious Adverse Events Review

¹Some of the Depression Follow Up Assessment forms (when not done at the site), should be mailed to participant to be done at home and returned by mail. If participant is not able to return by mail, the interview may be done on the phone, but the participant must be looking at the worksheet during the phone visit

Telephone Visit (Replacement of In-Clinic Visits) Assessments

- Clinical Dementia Rating Version 2 ¹
- Geriatric Depression Scale
- Neuropsychiatric Inventory
- Activities of Daily Living
- Everyday Cognition - Participant and Study Partner Self Report ²
- Concurrent Medication Review
- Pre-Existing Symptoms Checklist and Log³
- Medical History Review³
- Serious Adverse Event Review

NEW ENROLLEES: BASELINE AND FOLLOW UP PROCEDURE

¹ Full interview with only informant. Used in cases where a telephone visit is being conducted in replace of the in person clinic visit. ² Everyday Cognition Assessment (when not done in clinic), should be mailed to participant and study partner to be done at home and returned by mail. If participant and partner are not able to return by mail, the interview may be done on the phone, but the participant and study partner must be looking at the worksheet during the phone visit. ³ Applicable for continuing participants where their initial visit in ADNI-D is conducted over the phone.

If a change in cognitive status is apparent during the phone visit, this should be documented in the visit comment form. The diagnosis summary and diagnosis summary clinical status forms cannot be completed with a telephone visit.

Pre-Existing Symptoms Checklist and Log

The Pre-Existing Symptoms Checklist is completed at Baseline. Any symptom present must be entered in the Pre-Existing Symptoms Log which is then reviewed and updated at every visit.

Details about the symptoms should be captured on the Pre-Existing Symptoms Log under “Description of Symptom.” If episodic symptoms associated with the medical conditions listed on the Medical History form have occurred during the three months prior to the initial visit, these symptoms should also be captured on both the Pre-Existing Symptoms Checklist and the Pre-Existing Symptoms Log. The actual medical condition/diagnosis would be captured only on the Medical History form.

EXAMPLE: The participant reports knee pain at the Baseline visit, which the study partner states is due to osteoarthritis. Record this on the Medical History form as ‘Osteoarthritis’ and on the Pre-Existing Checklist select ‘present’ to musculoskeletal pain, with details of this pain recorded on the Pre-Existing Symptoms Log.

Wherever possible, use medical terminology for documenting symptoms. Enter details for all symptoms marked “Present” on the Pre-Existing Symptoms Checklist on the Pre-Existing Symptoms Log.

- Enter both the symptom number and name on the Pre-Existing Symptoms Log.
- Date of onset may be estimated if necessary. An estimated month is required if the symptom began within the same calendar year.

EXAMPLE: If participant reports pain, elaborate on location of pain – “Pain in right foot”.

At each subsequent visit, review the Pre-Existing Symptoms Checklist with the participant and study partner and:

- If the symptom has ceased, enter the date the symptom ceased on the Pre-Existing Symptoms Log.
- If the symptom has seriously worsened in chronicity or severity from the participant’s initial visit under ADNI-D, enter the date the symptom changed in the “Date Ceased” box on the Pre-Existing Symptoms Log and create a new Serious Adverse Event on the SAE / Hospitalization Log and **NOT** an entry on the pre-existing symptoms checklist /log.
- If the symptom is still present at the end of the study, check the box on the Pre-Existing Symptoms Log under “CONTINUING AT FINAL FOLLOW UP.”

NOTE: If a symptom has improved in chronicity or severity from Baseline, do not create a new entry.

All new symptoms and Pre-Existing symptoms that have seriously worsened in chronicity or severity *MUST* be recorded as a Serious Adverse Event, and *SHOULD NOT* be added to the Pre-Existing Symptoms Log.

PRE-EXISTING SYMPTOMS CHECKLIST AND LOG

If, after the initial Baseline visit under ADNI-D, a participant and/or study partner reports a symptom that should have been recorded at the Baseline visit, but was overlooked at the time, then record the symptom as a Pre-Existing symptom, not a Serious Adverse Event. Upon determination that this symptom was clearly in existence prior to consent, site personnel should then update the following worksheets:

1. Pre-Existing Symptoms Checklist: Any symptom that was previously recorded as “absent” should be checked as “present”.
2. Pre-Existing Symptoms Log: Any missed symptom(s) should be added to the form with all the necessary information such as; symptom number, description, severity, chronicity, date of onset and date ceased (if applicable).
3. If the participant or study partner is unsure (or if the symptom began after consent but they forgot to report it), and the symptom is deemed serious, then it should be reported as a Serious Adverse Event (SAE).

Medical History: Review the participant’s medical history during the initial ADNI-D Baseline visit. All significant/relevant medical history will need to be documented in the source worksheets and/or research chart, as well as entered in the ADNI-D EDC.

Adverse Events: Unlike ADNI2 procedure, ADNI-D will **NOT** be recording AE’s and instead will only be reporting SAE’s.

Symptoms of Potential Concern

Some symptoms on the checklist may be particularly difficult to interpret. Other complaints are commonly voiced in vague language. When recording symptoms under “Description of Symptom” on the Pre-Existing Symptoms Log use the Symptoms of Potential Concern below as a guide to defining the symptoms in terminology that is as specific as possible.

SYMPTOMS OF POTENTIAL CONCERN	
Abdominal Discomfort	Describe discomfort: epigastric burning; lower abdominal fullness; cramping, etc.
Dizziness	If you can determine that the participant is actually experiencing light-headedness, vertigo, drowsiness, palpitations, confusion, poor concentration, etc., report the more specific symptom. If you cannot obtain a better understanding of this symptom and do not feel that it requires further investigation, please add NOS (or “not otherwise specified”) to your comments. If the dizziness is part of a symptom complex that requires further investigation, add this information in a comment.
Chest Pain	This complaint should always elicit further questions to determine if further investigation is needed. Please indicate if you feel the etiology is most likely cardiac, pulmonary, gastrointestinal or musculoskeletal.

PRE-EXISTING SYMPTOMS CHECKLIST AND LOG

Fall	<p>Anytime you record a fall, please comment on the circumstance, when possible, i.e., tripped on rug; stood up, felt faint and fell; worsening gait apraxia; attempted to walk without cane.</p> <p>Also, if you have recorded a wrist fracture or other such trauma, ask if it was associated with a fall.</p>
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It will not be possible to reliably determine whether adverse symptoms that occur during the study are attributable to study procedures, other causes, or a combination of these. For the purpose of study monitoring, only symptoms that are deemed serious or which lead to hospitalization will be reported as a Serious Adverse Event.

Serious Adverse Events and Hospitalizations

Serious Adverse Events will be collected from the time of informed consent until the end of the study. A Serious Adverse Event (SAE) is any unfavorable medical events that occurs in a study participant and results in any of the following outcomes:

- Death
- Immediately life threatening
- Hospitalization or prolongation of existing hospitalization
- Disability or permanent damage
- Congenital anomaly or birth defect
- A medically important event
- Suggests any significant hazard, contraindication, side effect or precaution that may be associated with the use of a study procedure

The event **does not** need to have a causal relationship with study procedures to be considered a Serious Adverse Event.

Death

Death is an **OUTCOME** of an event, not an event term or diagnosis. It is necessary to find out the cause of death. When the cause of death is unknown at first reporting, this must be updated once cause is known. When death is the only information available then death can be documented as the event with an additional comment indicating that no qualifying information is available. There should only be one SAE with an outcome of death for each Participant.

Example: “Death due to myocardial infarction” is reported

Event: Myocardial infarction

Outcome: Death

Life-Threatening Event

An event is considered life-threatening if, in the opinion of the Investigator or the Sponsor, the participant was at immediate risk of death at the time of the event; it does not refer to an event which might have caused death if the event was more severe.

Examples:

- Pacemaker failure
- Hepatitis – resolved without hepatic failure
- Bone marrow suppression

Hospitalization or Prolongation of Existing Hospitalization

Hospitalization is any event resulting in admission to a healthcare facility that requires an overnight stay. **Hospitalization for pre-planned treatments, such as cosmetic**

SERIOUS ADVERSE EVENTS AND HOSPITALIZATION

surgery or elective surgeries for stable pre-existing conditions (e.g. total knee replacement), are considered Serious Adverse Events and should be recorded appropriately. Prolongation of existing hospitalization would be any event that extends a hospital stay beyond the normal expected time. Any hospitalization or prolongation of hospitalization is considered serious. Hospitalization or prolongation is used when admission to the hospital was a result of the event and should not be used as the event term itself.

Hospitalization does NOT include:

- Rehabilitation facilities
- Hospice
- Respite care
- Skilled nursing facilities
- Nursing homes
- Same day surgeries (i.e., outpatient and ambulatory procedures)

The following hospitalizations are NOT considered serious:

- Social admission (i.e., Participant has no place to sleep)
- Administrative admission (i.e., yearly physical exam)
- Protocol-specified admission (i.e., for a procedure required by the study protocol)

Disability or Permanent Damage

Event(s) that causes disability or permanent damage are those that result in substantial or permanent disruption of a person's ability to conduct normal life functions (i.e., AE resulted in significant, persistent, or permanent change, impairment, or disruption in the person's body function/structure, physical activities, and/or quality of life).

Congenital Anomaly/Birth Defect

Congenital anomaly/birth defects(s) are considered SAE(s) if it is suspected that exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.

Medically Important Event

A medically important event is any event that the Investigator regards as potentially jeopardizing to the participant and may require medical or surgical intervention/treatment in order to prevent one of the other serious outcomes.

Examples:

- Allergic bronchospasm that required treatment in an emergency room
- Seizures/convulsions that do not result in hospitalization

Additionally any experiences which the Investigator regards as serious, or which would

SERIOUS ADVERSE EVENTS AND HOSPITALIZATION

suggest significant hazard, contraindication, side effects, or precaution associated with participation in the study should be reported as a Serious Adverse Event.

Collection and Documentation of Serious Adverse Events

Any such experience due to any cause, which occurs after verbal consent and up to 30 days after the last study visit, must be reported to the Project Director within 24 hours after learning of the event.

The same guidelines for collecting and documenting AEs in ADNI2 should be followed when collecting and documenting SAEs. An event is considered serious if it resulted in one of the outcomes described earlier in this section of the procedures manual (i.e., death, life-threatening, hospitalization or prolongation of existing hospitalization, disability or permanent damage, congenital anomaly/birth defect, important medical events).

The reporting Investigator must follow all SAEs to resolution based upon the information that is available and approved via the Informed Consent. Resolution of an event occurs when one of the following criteria are met:

- Health has returned to baseline status or applicable variables have returned to normal
- The event has stabilized and the Investigator expects no further improvement or worsening of the event

Over time some events may resolve such that the original symptoms are no longer present. In these circumstances the outcome would probably best be described as “resolved.”

By contrast some events may resolve such that the original symptoms are no longer present, but other related symptoms may be present. In these circumstances the outcome would probably best be described as “resolved with sequelae.”

Comments/Narrative

Use the Comments/Narrative section on the **last page** of the Serious Adverse Events worksheet to provide a clear, concise, chronology, and comprehensive description of the event. The information provided should be detailed and descriptive enough to assess the event remotely. You do not need to repeat information in the Comments/Narrative section that was previously reported on the Serious Adverse Events worksheet.

A detailed, descriptive and relevant history may include, but is not limited to, the following:

- Underlying medical conditions
- Significant medical history

SERIOUS ADVERSE EVENTS AND HOSPITALIZATION

- Precipitating events that may be a factor in the current event
- Concomitant medications
- Laboratory, radiological, or other diagnostic results

All entries should begin with the date and the initials of the person writing the narrative. For example, if the Serious Adverse Event worksheet was being completed on Jun 15, 2014 by a Study Coordinator then the Comments/Narrative section might begin with something like, "(06-15-2014) SC."

Other Relevant History

Provide a description of relevant medical history or pre-existing symptoms in the Other Relevant History section on the last page of the Serious Adverse Events worksheet. If applicable, also comment on how the event might be related to other pre-existing symptoms or SAE's.

Concurrent Medications

It is important that the Project Director and the ADCS Medical and Safety Core are provided with the most up-to-date information about concurrent medications when they are reviewing SAE's. The Project Director will be provided with a summary of the medications present in the Concurrent Medications eCRF at the time the SAE report is submitted so please review and update that eCRF immediately prior to submitting the SAE report.

Follow Up Reports

The site is responsible for following up on events that occurred after signed consent at the psychiatry sites. Whenever new information is obtained for an event that is the responsibility of the Site Investigator to follow up on it must be reported to the ADCS as soon as it becomes available. Examples of reports that may require follow up:

- An SAE for which complete information was not available at the time of the report.
- Updates of new information related to an event that was previously reported.
- Resolution of a previously unresolved event.

Once the initial SAE has been reported any new information or changes to previously reported information should be appended onto the initial comments/narrative field of the Serious Adverse Events worksheet. Be sure to include the SAE number from the initial SAE report and assign a follow up report number (i.e. F/U 1 for the first follow up report, the F/U 2 for the second follow up report and so on).

As with the initial report, all follow up narratives should have the date and the initials of the person writing the narrative. **Please email an update in order to ensure the Medical and Safety Core is apprised of the update and a follow up SAE report is created by the ADCS Medical and Safety Core.**

IMPORTANT: Do NOT delete previous entries in the narrative field. New entries and/or updates to the narrative should be appended.

SAE Reporting Procedures

1. Screen for potential SAEs at every study visit.
2. Confirm that the event should be considered serious based on the fact that the event results in one of the following outcomes:
 - Death
 - Immediately life-threatening
 - Hospitalization or prolongation of existing hospitalization
 - Disability or permanent damage
 - Congenital anomaly/birth defect
 - Important medical event
3. Report Serious Adverse Events (SAE) by completing the Serious Adverse Events and Hospitalizations eCRF within 24 hours.
4. Complete the form to the best of your ability with the information currently available. If all the information requested on the form is not known, just complete what you can and submit within 24 hours. BE SURE to mark the “Serious” box in the online form.
5. Submit the online form using the “Submit” button. Submission of this online form will trigger an automatic email notification to the Project Director who will immediately review the information you have entered on the Serious Adverse Events and Hospitalizations form.
6. Fulfill the SAE reporting requirements of your IRB as soon as possible (sites should check with their IRB for SAE reporting deadlines).
7. Be sure to update and complete any parts of the Serious Adverse Events and Hospitalizations form that were left blank for the initial submission as soon as the information becomes available.
8. Do not delete text entered in the ‘Comments’ Field. If updates are made to the comments include date and your initials.

SITES MUST REPORT ANY SERIOUS OR LIFE-THREATENING ADVERSE EVENT WHETHER OR NOT IT IS RELATED TO STUDY PROCEDURES.

Any Serious Adverse Event (including death) due to any cause, which occurs after informed consent has been signed, or within 30 days after the last study procedure, must be reported immediately to the Site Investigator by completion of the online form.

It is imperative that the online form be submitted within 24 hours of a serious adverse experience.

SERIOUS ADVERSE EVENTS AND HOSPITALIZATION

Severity

Severity is not the same as seriousness. **Severity** is used to describe the intensity of an event (e.g., mild, moderate, or severe myocardial infarction). The event itself may be of relatively minor medical significance (e.g., severe headache) and would not be considered serious unless it resulted in one of the SAE outcomes. **Seriousness** is based on patient and/or event outcome, and is used to define regulatory reporting requirements.

Mild: Awareness of signs or symptoms but no disruption of normal daily activities. Signs and symptoms are transient. Event resolved without intervention.

Moderate: Discomfort sufficient to reduce or affect normal daily life.

Severe: Incapacitating with inability to perform normal daily activities.

Reporting a Change in Severity

If a previously reported SAE increases in severity or frequency, note this in the original worksheet and eCRF and report as a new SAE at the higher severity grade (i.e. worsening of osteoarthritis). The onset date will be the date that the severity or frequency increased. A decrease in severity should **NOT** be reported as a new SAE.

Relatedness

The Investigator is responsible for determining whether or not an event is related to imaging or other study procedure(s).

Note: Other Study Procedure(s) refer to any procedure other than imaging that may be deemed a causal relationship to the Serious Adverse Event.

Not Related: There is no evidence of a causal relationship and a causal relationship cannot be reasonably attributed to study procedure.

Possibly Related: A relationship cannot be ruled out with certainty and the event may be related. There is some evidence to suggest a causal relationship but the influence of other factors may have contributed to the event, such as the participant's clinical condition or concomitant treatments.

Probably Related: The event is likely related to the study. There is evidence to suggest a causal relationship, such as a reasonable temporal sequence from procedure. The influence of other factors is unlikely.

Definitely Related: The event is clearly related to the study and there is clear evidence to suggest a causal relationship. The influence of other factors can be ruled out.

SERIOUS ADVERSE EVENTS AND HOSPITALIZATION

Event Outcome

Event outcome is captured in order to provide a complete picture of each event that occurred during the trial. Outcome must be answered for each individual event. For example, if there is a compound event (stroke, hip fracture, pneumonia) in which death occurred as a direct result of one of those events (pneumonia), only that event (pneumonia) should have an outcome of Fatal. The other related events (stroke, hip fracture) cannot have Fatal as an event outcome nor can they have Recovering/Resolving as an outcome.

Events that are not resolved prior to death or by the end of the study cannot be Recovering/Resolving; they must be either Not Resolved/Not Recovered or Unknown. The cease date must be the same as the date of death or the same as the last study visit date. Again each participant should only have one SAE with an outcome of Fatal.

Downgrading or Correcting an SAE to an AE

If it is determined that an event initially recorded as an SAE does not meet the criteria to be considered serious; then complete a follow-up report and in the Comments/Narrative field explain why the event was determined not to be serious. Also be sure to uncheck the serious box on the SAE eCRF.

If a symptom has improved in frequency or severity do not create a new entry. Only record new or worsening of symptoms.

MRI Procedures

Summary

Magnetic Resonance Imaging (MRI) is a principle component of the Alzheimer's Disease Neuroimaging Initiative Depression Project (ADNI-D). All participants enrolled into ADNI-D will be scanned using protocol sequences specific to the ADNI-D study. **The protocol sequences installed for ADNI 1 or ADNI GO/2 should NOT be used for this study.** The study participant will be scanned at the Baseline Assessment only.

For details on the MR protocol sequences for the ADNI-D study, please refer to the MRI Technical Manual posted in the document repository. It is your responsibility to ensure your MRI Technician has a current copy at all times.

Remember the collection of these images is central to meeting the ADNI Depression objective of characterizing the underlying pathology of Late Life Depression.

Goals

The specific objectives of the MRI core include:

1. Obtaining high quality multi-site data that is consistent over time.
2. Perform appropriate image quality control throughout the study.
3. Qualify (and re-qualify after upgrades) each scanner on the ADNI Depression MRI Protocol
4. Correct specific classes of image artifacts in each image acquired; imaging intensity nonuniformity, image warping due to gradient nonlinearity, and scaling changes over time.
5. Monitor each scanner longitudinally in the study using the ADNI phantom.
6. Perform quantitative measurements of all images.

MRI Qualification Scan

Each site must be qualified for MRI. If the machine being used has already been certified by the ADNI MRI Core under ADNI 2 and has not experienced any software upgrades, requalification will **NOT** be required.

If the machine has not already been certified by the ADNI MRI Core under ADNI 2 site qualification will include two different exams.

- The first, being the quality control phantom scans on the specially designed ADNI phantom using the ADNI Depression Phantom QC sequence loaded by your local service engineer.
- Secondly, your site will be asked to scan a human volunteer with the approved ADNI Depression human sequences loaded by your local service engineer, **AFTER your site has received IRB approval for the ADNI-D protocol.** In terms of human scanning, each site will image a volunteer subject with the protocol and send the

MRI PROCEDURES

images to LONI. Each parameter in each of the pulse sequences in the protocol will be checked at MAYO.

In the event that the protocol has NOT been performed according to protocol, the site will be asked to perform another human volunteer scan. This will be repeated as many times as necessary until the site has demonstrated exact execution of the MR protocol in a volunteer subject, at which point they will have passed the human scanning portion of the MR site qualification. The volunteers do not need to be elderly controls; in fact scanning for site qualification may be more easily performed with normal younger volunteers. In the event that repeat attempts are needed, repeat scans need not be on the same volunteer subject. Once a site has demonstrated perfect execution of the protocol, the protocol will be stored permanently on the scanner at that site that will be used in the study.

Anticipation of Hardware Upgrades:

The MAYO QC Team required notification prior to any software and/or hardware upgrades for any scanner involved in the ADNI Depression study. At least 2 months' notice is preferred. ADNIMRI@MAYO.EDU

Depending on the impact of the upgrade the site may be required to scan a phantom and/or volunteer prior to continued scanning.

For more information on the MRI scanner certification process and the phantom and human scan protocols to be used, please refer to the ADNI-D MRI Technical Manual posted to the document repository.

Data Flow

Please refer to the MRI Data Flow chart (later in this section) for an illustration of this data flow. Every MRI scan completed for ADNI-D will follow this flow of data. Ensure the MRI technician has a copy of the MRI Scan Information form for every scan scheduled (this file can be found in the document repository, and is also included in the worksheet packets). A process should be established for transferring this form back to the study coordinator. The study coordinator will then need to ensure the appropriate data is entered online within 24 hours of the scan.

The MRI center will typically be responsible for uploading each MRI scan to the Laboratory of Neuroimaging (LONI). In some institutions, the study coordinator may be asked to do this uploading. There are instructions for uploading the scans in the MRI Technical Manual (this can be found in the document repository), if you require additional help or training, please email: dba@loni.usc.edu.

MRI PROCEDURES

After the scan is uploaded into LONI, QC will be completed by the MRI core. If the participant requires a rescan, it must be completed within 4 weeks of the original scan.

Each MRI scan requires a local radiologist interpretation. The clinical read should follow standard practice. The site clinician is responsible to review the local radiological interpretation of the MRI scan, as well as upload the local read to the Source Doc Upload eCRF in the EDC system.

Quality Review of Scans

The ADNI MRI QC team at MAYO will review each scan (acquired from LONI). The QC team will check whether the scan meets protocol specifications and identify any clinically significant findings. A phantom must also be scanned each day a participant is scanned. If multiple participants are scanned on a single day, only one phantom scan needs to be acquired.

1. Clinically Significant Findings

If a significant abnormality is seen (e.g. hemispheric infarction) on the MRI scan, the participant will be notified about the finding by phone by the study coordinator. In the event that a radiological finding that is not normal for the participant's age is identified by MRI QC, the site will be informed of this result by email. If abnormality is considered too severe based on committee discussion and may affect study outcomes, the participant may be excluded from the rest of the study.

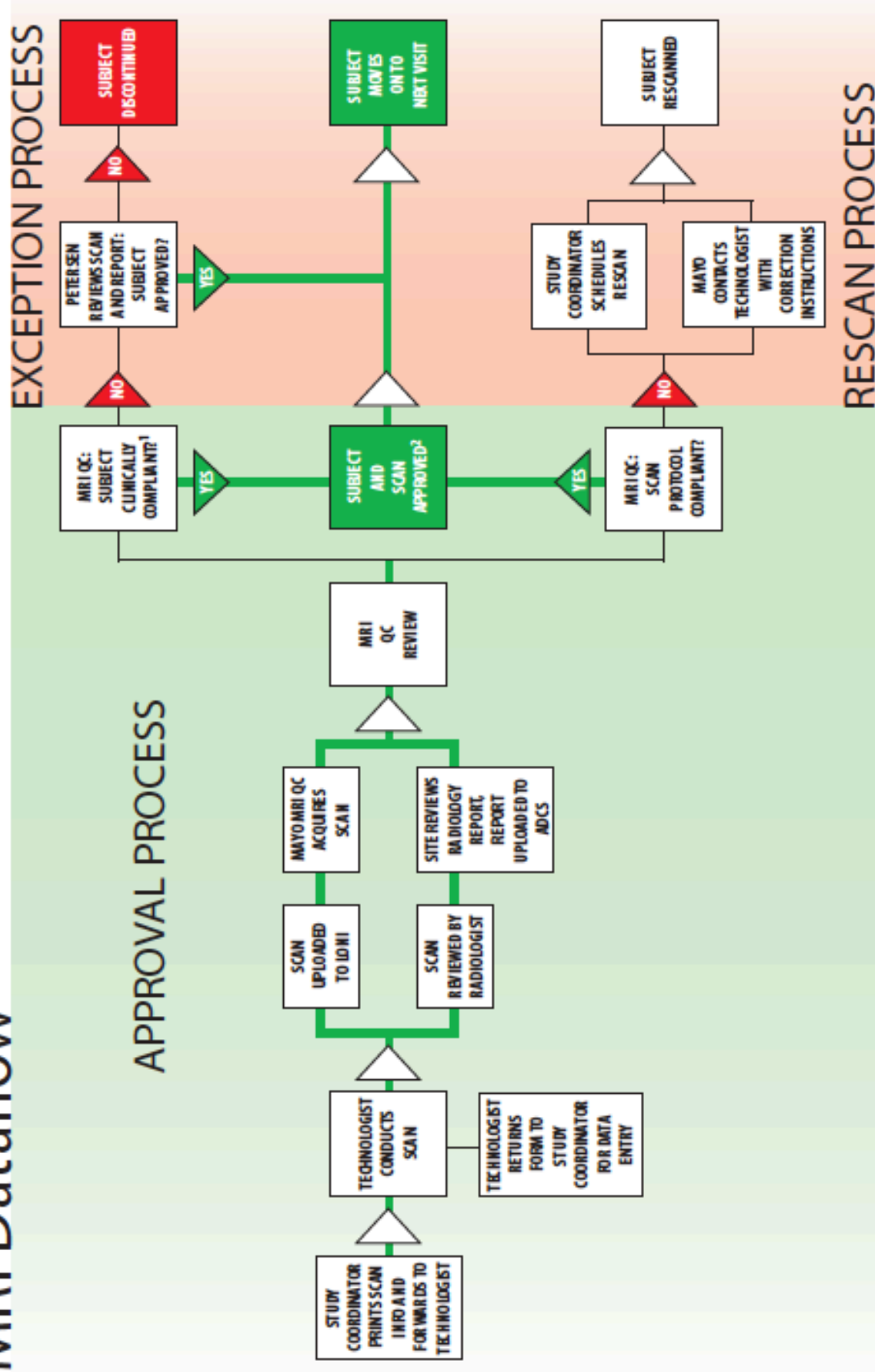
2. Protocol Compliance of Scan

If a problem is found with the way the scan was conducted the MRI QC team will contact the technologist directly to provide further instructions. The study coordinator and site PI will also receive email notification of the scan fail. When requested, a repeat scan will need to be scheduled within four weeks of the original scanning date. If the scan occurs out of window, this protocol deviation must be logged online.

For Technical Questions or Concerns about MRI scanning related issues or site qualification scans, please email the MRI technologist help desk: ADNIMRI@mayo.edu

If a scan is not usable (fails MRI QC) due to participant motion or non-compliance with scanning, the reason for the motion and non-compliance should be documented on the MRI Scan Information form. A rescan should be scheduled if the participant motion is believed to be correctable, and not due to chronic illness or deteriorated cognitive ability. If the rescan also fails due to participant motion or non-compliance the participant may be requested to complete another MRI scan, or continue in the study without the Baseline MRI scan being conducted.

MRI Dataflow



MRI PROCEDURES

Required Phantom Scanning at the Site

The radiology center for each site will be required to scan a phantom when scanning ADNI-D participants in order to ensure that the scanners are in compliance with ADNI-D requirements. When the MRI of the participant is uploaded to LONI, the MRI of the phantom should accompany it. Failure to comply with this could prevent the sites from enrolling for ADNI-D. Detailed instructions are provided in the MRI Technical Manual (available in the document repository).

The phantom must be scanned on the same day as the participant. If multiple participants are imaged on the same day, only a single phantom is required.

Guidelines for Scheduling MRI Scans

Baseline 3T MRI

The Baseline MRI cannot be conducted until both the psychiatry site and the ADNI Clinical site indicate that the participant meets inclusion/exclusion criteria for ADNI-D. Documentation of approval is done via the ADNI-D EDC system on the clinician verification eCRF. Once both confirm the participant meets eligibility criteria the participant may proceed to have their Baseline MRI conducted.

PLEASE NOTE: Most sites will need more than 2 weeks in order to obtain an imaging slot at their local MRI center. Please ensure to upload all source document worksheets in a timely manner to the Source Doc Upload eCRF in the EDC system. It is recommended that a tentatively scheduled scan date with the MRI center be scheduled 10-14 days before or after the Baseline Assessment.

Although the initial screening for inclusion/exclusion criteria for ADNI-D enrollment will be performed at the Depression Assessment visit with the psychiatry site, it is requested that the ADNI Clinical site performs a secondary inclusion/exclusion assessment focusing on Physical, MRI and PET specific criteria.

Checklist for Scheduling MRI Scanning Appointments:

- MRI Screening Form completed/reviewed for changes.
- Participant is given pamphlet with appointment time.
- Participant and study partner have directions and information for parking.
- MRI Technologist has copy of MRI data form.
- Scan is uploaded to LONI (by radiologist if possible).
- MRI scan information form received from technologist and data entered within 24 hours.

On the day of each appointment the study coordinator should phone the radiology center, confirm the appointment, and remind the radiologist which ADNI-D MRI protocol should be used in scanning this participant.

MRI PROCEDURES

MRI Pre-Screening

It is important to know when participants have ferrous (magnetic) metal objects in their body because MRI involves a strong magnetic field that may disrupt or dislodge these objects. The Pre-Screening Form will assess whether or not the participant has any metal in their body and will help to determine whether or not participants are eligible to have an MRI scan.

- **The Pre-Screening Form should be completed *during the Baseline visit*.**

The participant, the caretaker, or the study partner may fill out either of the screening forms, but anyone completing the form should have a firm understanding of the participant's medical history. Initial MRI screening will be performed at the Depression Assessment to determine eligibility but a **Formal** screening will be necessary at the Baseline Assessment.

First, write in the date and the participant's ADNI-D number at the top of the form. **Then** indicate whether or not the participant has any of the items listed in the left hand column of the Pre-Screening Form by placing a check in the appropriate box.

If the participant or study partner answers yes to any of the questions on the Pre-Screening Form under the heading **"Exclusionary Items"** the participant must be excluded from the study. The participant will not be able to participate in MRI scans because the metal object in question is not allowed in MRI scanners.

If the participant answers yes to any of the questions on the Pre-Screening Form under the heading **"Please Inform MRI Center,"** please do not exclude the participant. Instead, please contact your MRI center and let them know about the particular metal item in question. Try to get as much information as possible from the participant regarding the metal object so your radiology site may best assess whether or not a MRI would be safe for the participant.

In addition, if a participant indicates they are claustrophobic please try to discuss the level of discomfort a MRI may pose. Some participants might indicate they are claustrophobic, but are willing to undergo an MRI. **Please keep in mind that participants requiring sedation for the MRI should not be enrolled in ADNI-D.**

Sedation for the Baseline MRI scan is not offered for this protocol.

If the participant has worked extensively with metal, please ask if he/she is aware of any fragments that have been lodged in the body as a result.

This form is for screening purposes only; it should be kept with the participant's file. Please do not submit the Pre-Screening Form to the ADCS. Please note this screening form does not substitute for a pre-screen at the radiology site immediately prior to the MRI scan.

MRI PROCEDURES

Metal Safety Issues

Generally, metal implants that are anchored into bone are safe to scan, regardless of metallic composition. The older the implant, the better; Implants placed less than six to eight weeks prior are contraindications.

Any implant that is located in soft tissue (vessels, organs) presents the risk of dislocating when exposed to the magnetic force of the MRI.

Certain materials do not create this problem; many implants now use titanium, which is non-ferromagnetic metal. If you know of a questionable implant, it is essential to determine composition; alloys are also commonly used and those often have different ferromagnetic properties.

Magnetic implants of any sort are exclusionary, regardless of where they are located on the body. Aside from the risk of dislocation, they also run the risk of demagnetization, which would render them useless. Examples of these types of implants include magnetic sphincters, stoma plugs, and some dental implants. You should also be aware that the magnet will demagnetize credit cards; remember to check your pockets before approaching the magnet. Other implants for which function can be affected by the magnetic field include cardiac pacemakers, neurostimulators, and cochlear implants.

The Radio Frequency waves (RF) can also create heating in certain circumstances, which is another safety issue to be aware of. Certain implants have the potential to create a conducting loop, which occurs when the RF pulses used in MR imaging enter an object that does not have a current path allowing the energy to exit. This results in a concentration of electrical currents within the object, which can then cause burns to the surrounding tissue.

Most implants are carefully designed to have specific current pathways to eliminate this problem. Some implants, however, are not simply placed in the body; for example, sternal wires, used to close the ribcage after certain surgical procedures, can be wrapped in such a way that they loop back on themselves. This creates a heightened risk of forming a conducting loop, and special consideration should be given to participants who have undergone any surgical procedures involving a median sternotomy.

Cardiac pacing wires also carry an increased risk of generating a conducting loop and are a contraindication unless proven to be removed by implanter care notes. These are very tricky to verify removal of, and if the patient cannot obtain reports, the patient is not an MRI candidate. Heating (and burns) can also occur with tattoos and transdermal patches; medicated patches should be removed during the scan, and tattoos on the head and neck are exclusionary for our purposes. Pregnancy is a contraindication; the FDA has not yet established guidelines for MR imaging during pregnancy.

MRI PROCEDURES

TheraSeed Radioactive Seed Implants: The TheraSeed radioactive seed implant is used to deliver low-level radiation to the prostate to treat cancer. Palladium-103 is the isotope contained in TheraSeed implant. Because the radiation is so low and the seeds are placed so precisely, virtually all the radiation is absorbed by the prostate.

This relatively small implant is comprised of a titanium tube with two graphite pellets and a lead marker inside. Importantly, these seeds are implanted with spacers between them and placed according to treatment plans so that they do not touch during their intended “in vivo” use. Magnetic resonance tests (magnetic field interactions, heating, induced currents, and artifacts) conducted on the TheraSeed revealed that this implant is acceptable for patients undergoing MR procedures at 3-Tesla or less.

Stents: Some are only safe for 1.5T MRIs but not 3T MRIs. Unfortunately, most participants do not know what strength their previous MRIs were. Oftentimes, participants with stents are given a card to carry that will explicitly state what strength of magnet they are safe for. If screening someone with a stent, ask if they are carrying such a card, and have them bring it to their appointment with them.

MRI Screening Form
Alzheimer's Disease Neuroimaging Initiative MRI Study
Alzheimer's Disease Cooperative Study

Date: ____/____/____ **Participant ID** _____

Please check Yes/No for each of the following:

☐ Yes ☐ No Previous MRI scan

Exclusionary Items:

☐ Yes ☐ No Cardiac pacemaker/defibrillator

☐ Yes ☐ No Aneurysm or aortic clip(s)

☐ Yes ☐ No Neurostimulator

☐ Yes ☐ No Cochlear, otologic, or ear implant

Please Inform MRI Center:

☐ Yes ☐ No Prosthesis or implant

☐ Yes ☐ No Artificial limb or joint

☐ Yes ☐ No Insulin or infusion pump

☐ Yes ☐ No Bone growth/fusion stimulator

☐ Yes ☐ No Carotid artery vascular clamp

☐ Yes ☐ No Electrodes (on body, head, or brain)

☐ Yes ☐ No Stents, filters or coils (intravascular)

☐ Yes ☐ No Shunt (spinal or intraventricular)

☐ Yes ☐ No Vascular access port and/or catheter

☐ Yes ☐ No Tattooed makeup (eyeliner, lips, etc.)

☐ Yes ☐ No Body piercing(s)

☐ Yes ☐ No Any metal fragments or shrapnel (current or removed)

☐ Yes ☐ No Internal pacing wires

☐ Yes ☐ No Metal or wire mesh implants

☐ Yes ☐ No Bone/joint pin, screw, nail, wire, plate

☐ Yes ☐ No Breathing disorder

☐ Yes ☐ No Claustrophobia

☐ Yes ☐ No Hearing aid (Remove before MRI)

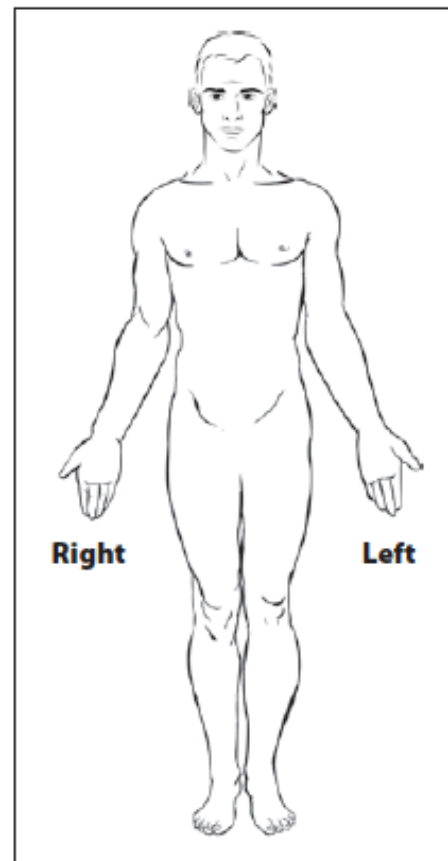
☐ Yes ☐ No Dentures (Remove before MRI)

If answers below are Yes, please explain below:

☐ Yes ☐ No Worked extensively with metal (grinding, etc.)

☐ Yes ☐ No A history of seizures continuing to present

Please mark on the figure below the location of any implant or metal inside your body



Remove all metal objects prior to your MRI examination

Explanation: _____

Signature of participant or participant's representative

Name of representative

Signature of person administering screening form

Date: ____/____/____

MRI PAMPHLET

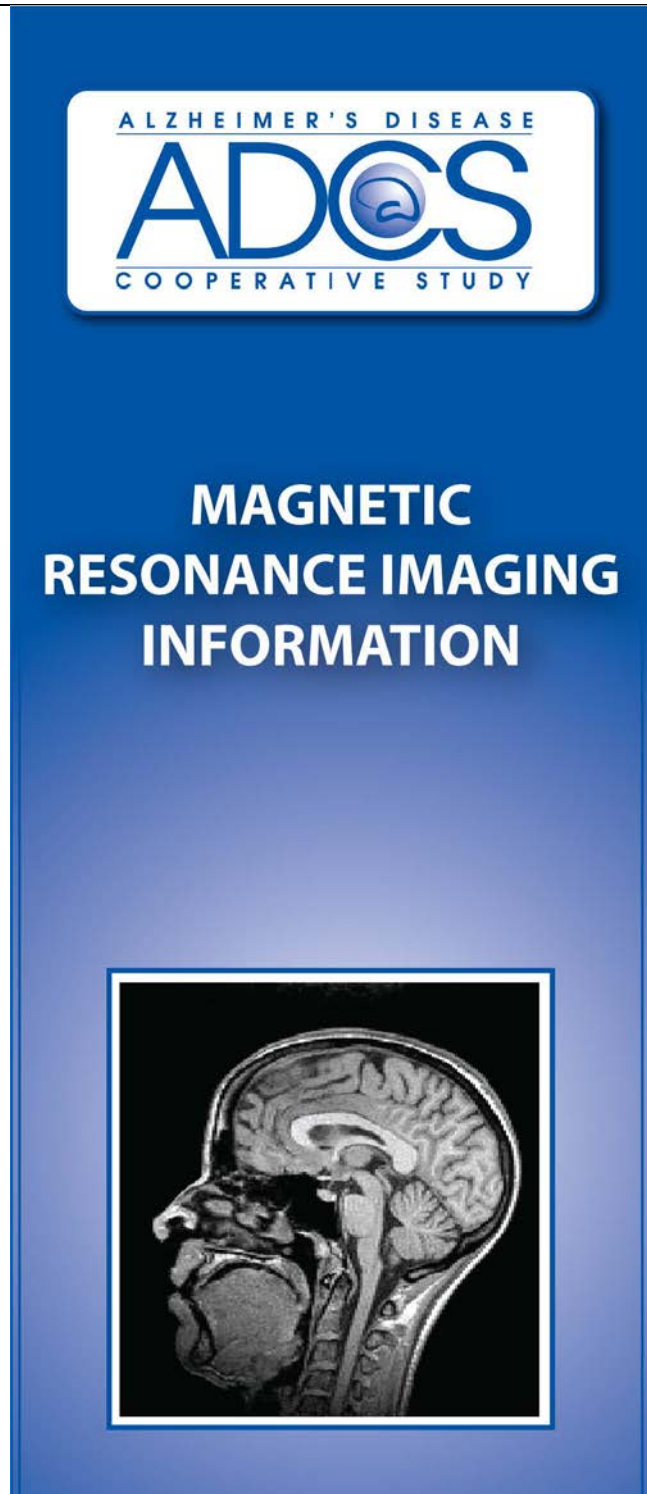
The MRI pamphlet should be distributed to participants in the Alzheimer's Disease Neuroimaging Initiative Depression study (ADNI-D).

The MRI pamphlet includes basic information regarding the details of a MRI scan. It briefly describes how participants can best prepare for their MRI and outlines ways participants can reduce anxiety during the procedure.

Participants should have plenty of time to review this information before their MRI appointment so the pamphlet should be distributed to participants when they are scheduled for their MRI scan.

When giving out the pamphlet please be sure to fill out the back page. Use the space provided to write in the specifics of the participant's MRI appointment (date, day of the week, time, and place). If the MRI scan is at a different facility than their clinical appointments, detailed directions to the radiology site should be provided to the participant or the study partner.

In addition, participants should be reminded to bring the pamphlet with them to their MRI appointment and display it when they check in to assure that they are scanned with the appropriate protocol sequence.



IRB approval will be required for the pamphlet.

To request a draft, please email

brainlink@ucsd.edu

PET Procedures

Summary

One of the major goals of the Alzheimer's Disease Neuroimaging Initiative Depression Project is to perform florbetapir F 18 amyloid imaging on all enrolled participants. This establishes a national network for florbetapir F 18 amyloid imaging, and will test hypotheses concerning the prevalence and severity of brain amyloid accumulation and its relationship to current and previous changes of clinical state in Late Life Depression.

Florbetapir F 18 imaging will be performed on all enrolled participants during the Baseline Assessment ADNI clinic visit and must be completed within 2 weeks before or 2 weeks after the in-clinic assessment at Baseline. Currently, the Florbetapir F18 PET scan is only conducted at Baseline and NOT at the Month 30 Follow Up visit.

Site Qualification

PET Scanner Certification

It is preferable for sites to use existing qualified ADNI scanners for the Florbetapir F 18 imaging. If a new scanner must be introduced it will need to be qualified using standard ADNI scanner qualification before imaging can be performed for ADNI-D.

Ideally, no hardware or software upgrades of the PET imaging system should occur during the duration of the study. In the event of such an upgrade, we ask that you inform the PET core **prior** to the anticipated upgrade. Depending on the nature of the upgrade the site may be asked to repeat the phantom scans prior to scanning any additional participants.

Contact adnipet@ucsd.edu prior to imaging if a new scanner will be used for ADNI-D or if hardware/software upgrades have occurred.

Exclusionary to PET Scans

All participants who consented to receive PET scans must be queried to assure that they do not have specific exclusions to PET. These are:

- received an investigational medication within 30 days of the scheduled florbetapir F18 scan
- received a radiopharmaceutical for imaging or therapy within the past 24 hours prior to the imaging session for ADNI-D
- pregnancy or risk of pregnancy
- a history of radiation therapy within the past year, or a history of receiving radiation for research purposes within the past year that would exceeds the limits of annual and total dose commitment set forth in the US Code of Federal Regulations (CFR) Title 21 Section 361.1
- participants taking a prohibited medication (i.e. immunotherapy, secretase inhibitor, selective amyloid lowering agents, experimental study with an amyloid targeting therapy)

PET PROCEDURES

PET Pre-Screening Checklist

This is to be completed by interview if the information is not in clinic records. If the answer to any of these is 'Yes' please consult with a technologist before consenting the participant to PET imaging for ADNI-D.

- ☐ Yes ☐ No Is there a history of radiation therapy in the past year?
- ☐ Yes ☐ No Is there a history of having radiation for research in the past year?
- ☐ Yes ☐ No Is the participant taking any prohibited medications?
- ☐ Yes ☐ No Is the participant pregnant or of child bearing potential?
- (if yes, a pregnancy test would need to be conducted to confirm/rule out pregnancy)
- ☐ Yes ☐ No Would there be problems with the participant's ability to cooperate with scan?

Florbetapir F 18 PET Scan Process: Standard Protocol Scan

Each participant will receive a single i.v. bolus (370 MBq (10 mCi +/- 10%) of florbetapir F18 prior to florbetapir PET imaging. Do not q.s. (add saline) to the dose prior to administration. Adding saline could potentially lead to precipitation out of solution form. After injection, rinse the syringe and flush the line with at least 10 cc of normal saline.

The brain florbetapir PET imaging for the standard protocol scan will be a 20 minutes duration (as four 5-minute frames), starting 50 minutes post-dose injection. Serious Adverse Events will be continuously monitored during the imaging session. Participants who experience a Serious Adverse Event will not be discharged until the event has been resolved or stabilized.

All Serious Adverse Events related to the florbetapir PET imaging procedure need to be reported within 24 hours to AVID.

A physician or person designated by the physician, with appropriate training and experience should be present during the florbetapir F18 injection and for approval to discharge the participant from the PET suite.

PET PROCEDURES

For detailed information on the florbetapir F 18 scan process please refer to the PET Technical Manual posted in the document repository.

Data Flow: Florbetapir F 18 Scans

Please refer to the PET Data Flow Charts for an illustration of this process. Study coordinators are responsible for collecting some basic information on each PET scan from the PET center conducting the scan. In general, this will involve interacting with the PET technologist who will usually be the individual conducting the PET Scans. The study coordinator must ensure the PET technologist has a copy of the florbetapir F 18 PET Scan Information Forms prior to each scan session. The study coordinator should ensure a process has been worked out with the radiology center on how to transfer this information immediately after the scan is completed. The study coordinator is responsible for entering scan data in the ADNI-D EDC system **within 24 hours of the scan**. All PET scans will be uploaded by your radiology center to the Laboratory of Neuroimaging (LONI). These procedures are outlined in the PET Technical Manual posted in the document repository. If your radiology center is unable to upload scans to LONI, please request training for uploading by emailing: dba@loni.usc.edu.

IMPORTANT: Data uploaded to LONI should be performed as soon as the images have been acquired & reconstructed as it will be important to promptly QC the data to identify if the scan needs to be repeated. The timeframe should be 1-2 business days from acquisition.

Quality Review of Florbetapir F 18 PET Scans

- Every florbetapir F 18 PET scan will be reviewed for protocol compliance by the ADNI PET QC team.
- If a problem is found with the way the scan was done and it can be fixed, the PET QC team will contact the PET technologist directly.
- If the problem with the scan is not fixable, the PET QC team will provide the PET technologist with protocol guidance to apply to future PET scans.

Before requesting the site to schedule a rescan for PET, the participant will be assessed for overall radiation exposure. If an additional scan would not exceed limits on exposure, study coordinators and site PIs will be emailed a request for a repeat scan. When requested, a repeat scan should be scheduled **within two weeks** of the original scanning date. If a scan or rescan is conducted outside of the allotted window document the date of imaging and reason for deviation on the protocol deviation log.

If a scan is not usable (fails PET QC) due to participant motion or non-compliance with scanning, the reason for the motion and non-compliance should be documented on the corresponding PET Scan Information Form. If a rescan is requested, it should only be scheduled if the participant motion is believed to be correctable, and not due to chronic

illness or deteriorated cognitive ability.

Questions on PET technical issues should be directed to:
adnipet@ucsd.edu

Guidelines for Scheduling Florbetapir F18 Scans

Most sites will need more than 2 weeks in order to obtain an imaging slot at their local radiology center. The PET scan for newly enrolled participants in ADNI-D should be scheduled after the Depression Assessment is finished and the participant has been in contact with the ADNI clinic study coordinator. If scans take place outside of the allowed window, provide the date of imaging and reason for the deviation of the protocol deviation log.

It is recommended that the ADNI-D study coordinator attend the first few PET scan sessions to ensure that he or she understands what is involved in scanning and to create a relationship with the PET technologists.

Florbetapir F18 Delivery of Investigational Product

Avid manufacturing will provide florbetapir F18 injection to all approved imaging facilities. As soon as a participant is scheduled for the florbetapir F 18 PET scan the study coordinator must notify (by phone and/or by email) the AVID Operations Lead of the date and time for imaging.

IMPORTANT: Avid will need at least 5 days' notice prior to the scheduled florbetapir F18 Pet Scan.

Phone: (215) 298-0731

Fax: (215) 689-4804

Email: payne@avidrp.com

Next the study coordinator will complete the top portion of the **Avid Dose Request Form** (located in the visit packet and Avid Clinical Supplies Guidance Document posted in the document repository) and email or fax to Avid Operations lead to confirm imaging date and time.

Please refer to the **Avid Clinical Supplies Guidance Document** posted in the document repository for specific details on ordering, shipping and receiving Florbetapir F18 unit doses for injection and the process for usage of clinical supplies.

Changes to the scheduling or deviations from the **Avid Clinical Supplies Guidance Document** may be possible (e.g. scheduling a participant with only 3 days' notice), but if they are required, the site should contact Avid as soon as possible to work with the manufacturing team on the logistics.

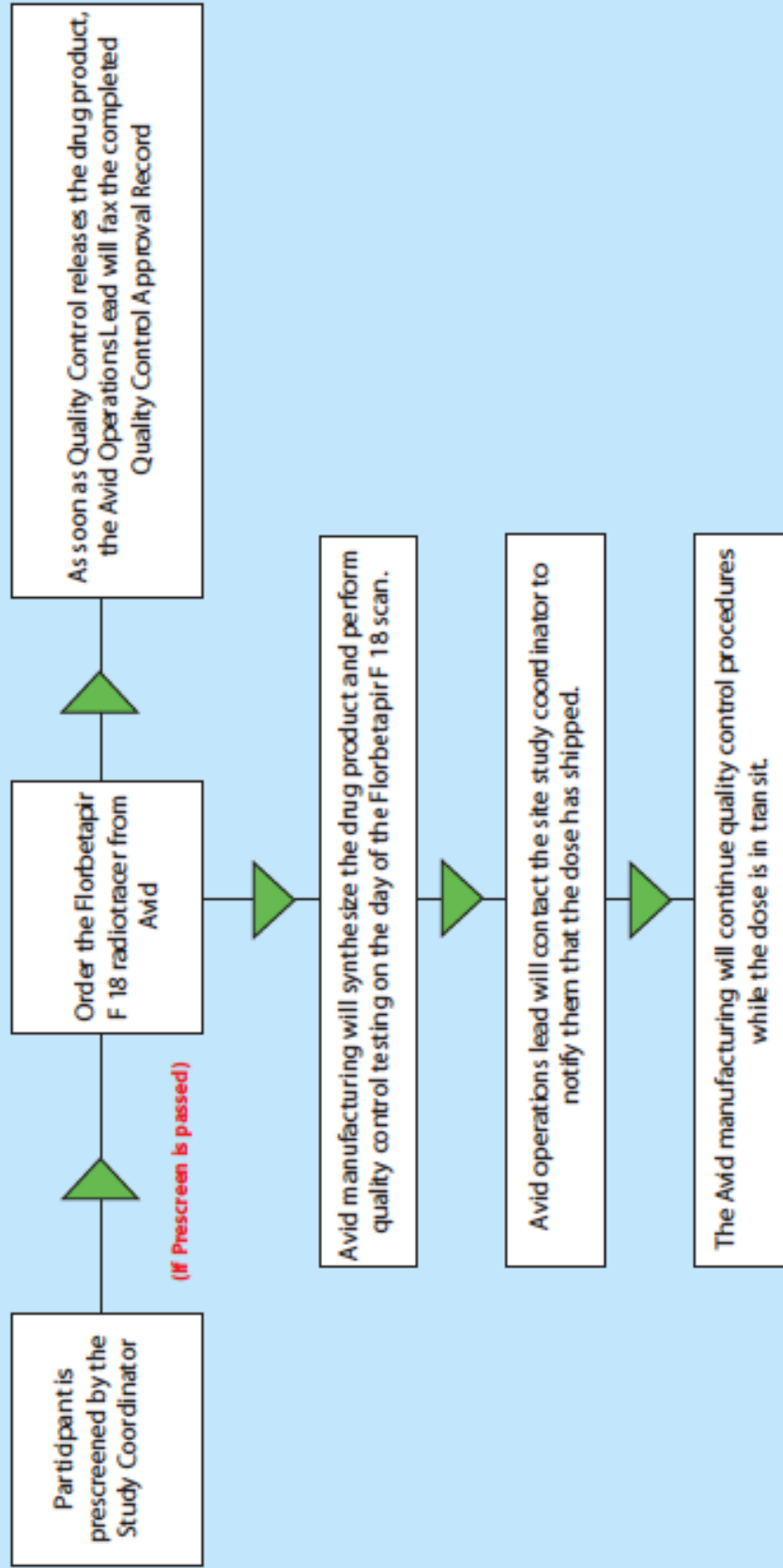
PET PROCEDURES

Checklist for Scheduling PET Scanning Appointments

- ☐ PET pre-screening checklist completed/reviewed for changes.
- ☐ Participant is given pamphlet with appointment information.
- ☐ Participant and study partner have directions and information for parking.
- ☐ PET technologist has copy of appropriate PET Scan Information Form
- ☐ Scan uploaded to LONI (by technologist if possible).
- ☐ Appropriate PET Scan Information form (florbetapir) received and data entered in ADCS data system within 24 hours of scan.

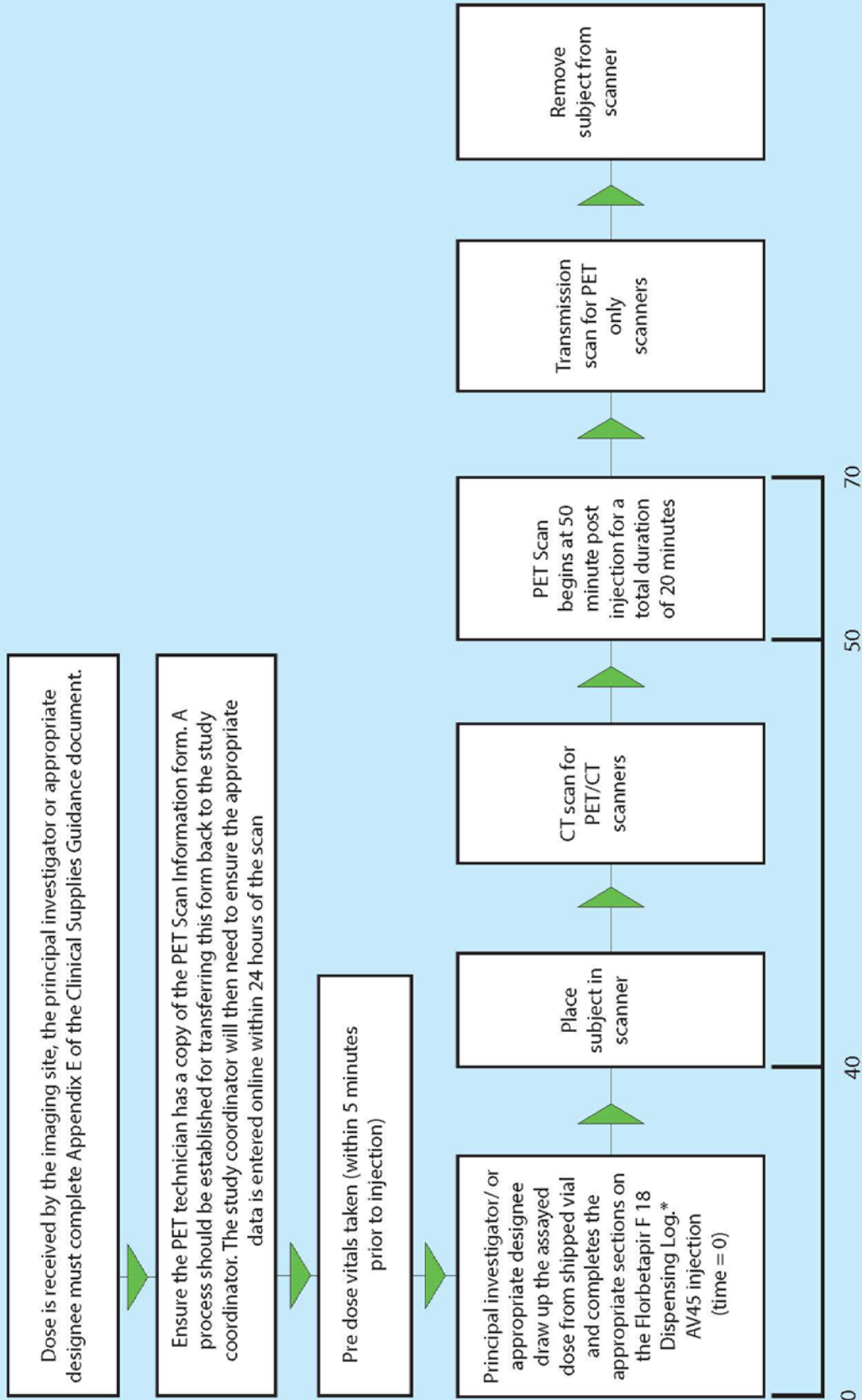
On the day of each appointment the study coordinator should phone the radiology center, confirm the appointment, and remind the radiologist to upload the PET Scan to LONI within 24 hours of the scan.

Prior to Florbetapir F 18 Scan



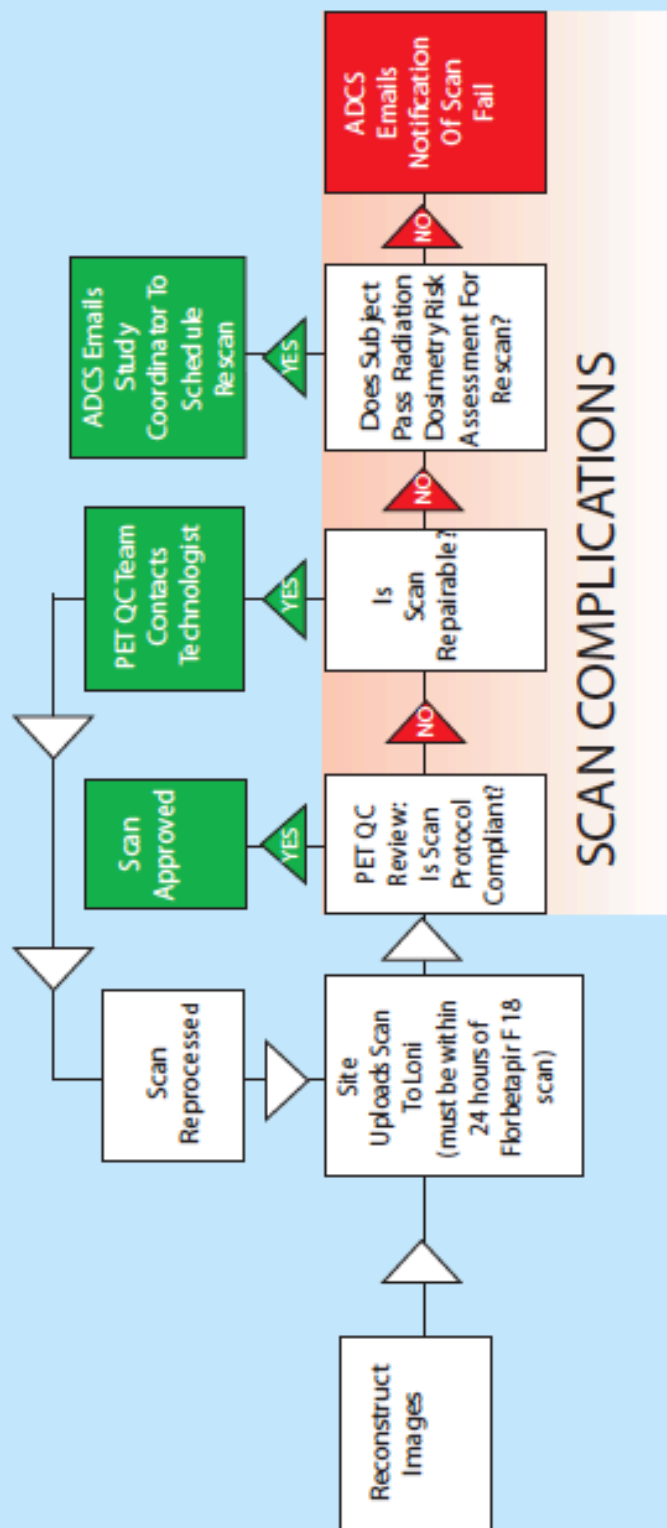
NOTE: Complete Appendix A of the Clinical Supplies Guidance Document located in the document repository when ordering the Florbetapir F 18 radiotracer.

Conducting the Florbetapir F 18 Scan



* Florbetapir F 18 Dispensing Log is Appendix B of the Clinical Supplies Guidance Document

Post Florbetapir F 18 Scan



PET PAMPHLET

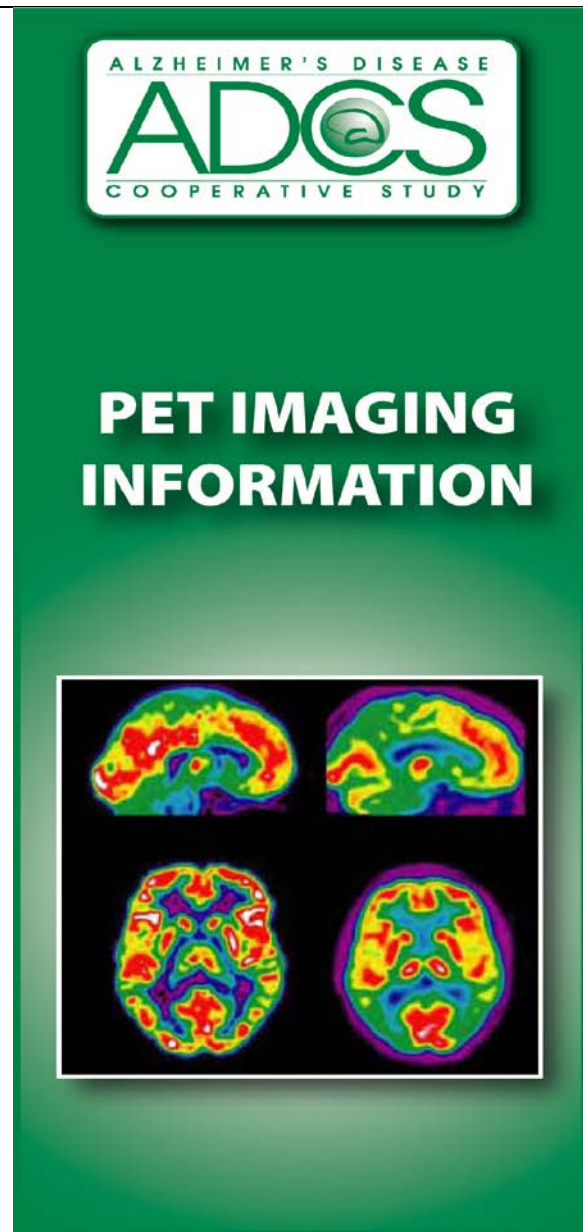
The PET pamphlet should be distributed to any participant undergoing a PET scan for the ADNI-D study.

The PET pamphlet includes basic information regarding the details of the florbetapir F 18 scan. It briefly describes how participants can best prepare for their PET scans and outlines ways participants can reduce anxiety during the procedure.

Participants should have plenty of time to review this information before their first PET appointment so the pamphlet should be distributed to participants when they are scheduled for their first PET scan.

When giving out the pamphlet please be sure to fill out the back page. Use the space provided to write in the specifics of the participants PET appointments (date, day of the week, time, and place). If the PET scan is at a different facility than their clinical appointments, detailed directions to the radiology site should be provided to the participant or the caretaker.

In addition, participants should be reminded to bring the pamphlet with them to their PET appointments and display it when they check in to assure that they are scanned with the appropriate PET protocol.



**IRB approval is required for the pamphlet.
To request a draft, please email:
brainlink@ucsd.edu**

Biofluids: Collection, Processing and Shipment

Summary

The collection of biofluids is central to the goals of the Alzheimer's Disease Neuroimaging Initiative Depression Project. The development of valid and reliable biomarkers for AD is needed to:

- Aid in the recognition of the illness at its earliest clinically recognizable stages
- Detect the disease before dementia or other symptoms appear
- Distinguish AD from other causes of dementia

Biomarkers, together with imaging tests, will be especially valuable in the evaluation of disease-modifying therapies.

Promising biomarkers that will be measured in ADNI-D fluids:

- A β 40 and A β 42 in Plasma
- ApoE genotyping-blood
- DNA from blood cells
- RNA from blood cells
- Other promising plasma biomarkers may be added based on ongoing multiplex immunoassay studies and mass spectrometry MRM studies as well

The following topics will be covered in this section:

- **Biofluids Collection Schedule**
- **Sample Identification and Tracking**
- **Ambient Samples – Collection Procedure**
 - DNA Sample Collection for GWAS and ApoE Genotyping
 - Cells for Immortalization and PBMC Banking
- **Ambient Samples Supplies and Shipping**
- **Frozen Samples – Collection Procedure**
 - Biomarker Plasma and Serum Samples
 - “TBD” Assays Plasma and Serum Samples
 - Buffy Coat Sample
 - RNA sample collection
 - Telomere sample collection
- **Frozen Samples Supplies and Shipping**

A glossary of terms is at the end of this section.

ADNI-D | Laboratory Specifications

Procedure	Analysis Analyte	Specimen	Fasting Required?	Optional?	Banked Future Research	Research Labs	Vacutainer Tube	# of Tubes	Sample Volume (mL)	TTL Volume	# of Aliquots	Protocol Reference s	Ship To	Notes
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BASELINE

Blood Draw	RNA	BLD	NO	NO			PAX	3	2.5	7.5		NCRAD	3 x 2.5 mL PAXgene Blood RNA tubes
	ApoE Genotyping		NO	NO								NCRAD	
	DNA Banking		NO	YES								NCRAD	
Blood Draw	GWAS	BLD	NO	NO			LTT	1	10	10		NCRAD	1 x 10 mL LTT
	Differential		NO	NO								NCRAD	
	Hematology		NO	NO								NCRAD	
Blood Draw	Biomarkers Banking	PL	YES	NO			LTT	2	10	20	20	NCRAD	2 x 10 mL LTT for Plasma Sample
		SER	YES	NO			RTT	2	10	20	20		2 x 10 mL RTT for Serum Sample
Blood Draw	Immortalized Cell Lines	BLD	YES	NO			ACD-A	1	8.5	8.5		NCRAD	1 x 8.5 mL ACD-A (yellow top) tube
	PBMC Banking	BLD	YES	YES			GTT	1	10	10			1 x 10 mL Green Top Tube
Blood Draw	Banked for Future "TBD" Assays	PL	YES	YES			LTT	3	10	30	30	NCRAD	3 x 10 mL LTT for Plasma Sample
		SER	YES	YES			RTT	3	10	30	30		3 x 10 mL RTT for Serum Sample
Blood Draw	Telomeres	BLD	YES	NO			LTT	1	4	4	5	NCRAD	1 x 4 mL LTT for Telomeres

8-hour overnight fast for blood collection. NCRAD requested 8-10 aliquots of (0.5mL) for each blood tube for serum and plasma. Buffy coat will be extracted from the 5 lavender-top EDTA tubes used for the biomarker/"TBD" lab blood draw.

MONTH 30

Blood Draw	RNA	BLD	NO	NO			PAX	3	2.5	7.5		NCRAD	3 x 2.5 mL PAXgene Blood RNA tubes
Blood Draw	Biomarkers Banking	PL	YES	NO			LTT	2	10	20	20		2 x 10 mL LTT for Plasma Sample
		SER	YES	NO			RTT	2	10	20	20		2 x 10 mL RTT for Serum Sample
Blood Draw	Banked for Future "TBD" Assays	PL	YES	YES			LTT	3	10	30	30	NCRAD	3 x 10 mL LTT for Plasma Sample
		SER	YES	YES			RTT	3	10	30	30		3 x 10 mL RTT for Serum Sample
Blood Draw	Telomeres	BLD	YES	NO			LTT	1	4	4	5	NCRAD	1 x 4 mL LTT for Telomeres

8-hour overnight fast for blood collection. NCRAD requested 8-10 aliquots of (0.5mL) for each blood tube for serum and plasma. Buffy coat will be extracted from the 5 lavender-top EDTA tubes used for the biomarker/"TBD" lab blood draw.

NOTES: RESEARCH LABS should outline what samples will be banked for future research and any such delineations must cross-check and match study ICFs.

BLOOD VOLUME TOTALS	mL	TBSP	tsp	# of Tubes
Baseline Visit (TTL)	140	9.3	28.0	17
Month 30 Visit (TTL)	111.5	7.4	22.3	14
All Study Visits (TTL)	251.5	16.8	50.3	

BLD	Blood (Whole)
GT SST	Gold Top Serum Separator Tube
HCY	Homocysteine
LTT	Lavendar Top Tube (EDTA)
PL	Plasma
SER	Serum
SST	Serum Separator Tube
RTT	Red Top Tubes
GTT	Green Top Tube

Note: 8 hour fast is no longer necessary, participants are now recommended to fast for 6 hours.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Sample Identification and Tracking

Please confirm you have labels for each visit BEFORE scheduling the visit.

- ApoE, GWAS, RNA, Cell Immortalization, PBMC Banking, and Buffy Coat must be identified using the NCRAD Sample Identification label provided by the ADCS.

NCRAD SAMPLE LABEL

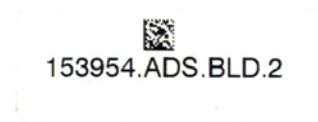
Participant ID ____ -D- ____
 Protocol ADNI-D
 Year of Birth ____ Gender: M / F
 Collection Date: ____ / ____ / ____
 Baseline Month30 D/C

- All biomarker samples** (plasma, serum, and telomeres) must be identified using the NCRAD micro tube identification label provided by the ADCS. These samples should **NOT** have any identifiable information on them.

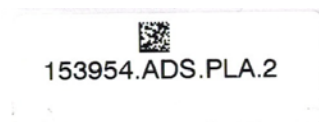
NCRAD MICROTUBE SAMPLE LABEL



Kit Number Label: Place on the Sample Forms and the bag/envelope that the cryobox goes in.



Telomere Label



Plasma Label



Serum Label

Note: The first six digits on the sample labels are the kit number and should be the same on all tubes for an individual participant.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT**Sample Tracking**

All samples will be tracked online using the FedEx Tracking number.

- Biomarker samples (serum and plasma) will also be tracked at NCRAD using the sample label.

The Genetic Sample Collection worksheet, Biomarker Sample Collection worksheet, Telomere Sample Collection worksheet and Buffy Coat Sample Collection worksheet (located in the worksheet packets posted in the document repository) must be completed **on the day of each visit**. These forms include information used to track the sample, confirm receipt of the sample, and collect information essential to processing and analysis. Additionally, the corresponding eCRF in the ADNI-D web portal must be completed on the day of each visit.

Extra labels will be provided by NCRAD to be placed on sample collection worksheets and cryovial shipping bags/envelopes for identification accuracy.

For all samples and shipping, please email or fax a copy of the sample form to NCRAD **BEFORE** shipping so the lab knows to expect the sample.

NCRAD email: alzstudy@iupui.edu

NCRAD fax: 317-278-1100

In addition to being tracked online in the ADNI-D web portal, the condition and amount of samples received will be tracked by NCRAD.

- Sites are responsible to ensure the requested amounts of each fluid are collected, to the best of their ability.
- If a sample is not obtained at a particular visit, this should be recorded on the appropriate form (Sample Collection: Biomarker Samples; Sample Collection: Genetic Samples, and/or Sample Collection: Buffy Coat) in the worksheet packet and eCRF in the ADNI-D web portal. Please ensure the reason why the sample was not obtained is provided.

IMPORTANT: Please ensure to use the appropriate sample labels for each sample type. NCRAD whole blood labels for Cell Immortalization sample, PBMC Banking sample, APOE/GWAS sample, RNA sample, and Buffy Coat sample. Plasma samples, serum samples, and telomere samples will use a separate micro tube label also provided by NCRAD.

Ambient Samples - Collection Procedure

DNA Sample Collection for GWAS and ApoE Genotyping

Blood samples will be collected for DNA/GWAS, ApoE genotyping, differential panel and hematology slide creation at Baseline for all study participants after passing eligibility criteria for this study. Whole blood will be collected in a single 10 mL EDTA (lavender top) tube.

ApoE genotyping, differential panel, and hematology slides will be done using the same 10 mL whole blood sample.

Begin by confirming the subject consented to DNA testing and sample storage per their informed consent.

Next, complete the information on the genetic label for the EDTA (lavender top) tube.

- Securely place the label onto the EDTA (lavender top) tube **BEFORE** the blood draw.

Participant ID ____ -D- ____
 Protocol ADNI-D
 Year of Birth ____ Gender: M / F
 Collection Date: ____ / ____ / ____
 Baseline Month 30 D/C

Blood Collection:

1 x 10 mL EDTA (lavender top) tube of whole blood will be collected; gently mix by inversion, 10 -12 times, to assure that the EDTA anticoagulant is well-mixed with the whole blood sample.

Completion of Sample Collection – Genetic Worksheet:

Ensure all fields on the sample collection worksheet located in the visit packet are complete. Pay particular attention to questions regarding the subjects consent to DNA testing and sample storage. Ensure the name of the individual who packaged and shipped the blood specimen, along with their phone number and email is listed on the worksheet. Additionally, please list in the comments section of the worksheet any issues that occurred during the blood draw with packaging or any temperature excursions.

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the whole blood sample within 24 hours of collection. The whole blood sample is maintained at room temperature (20-25 degrees Celsius) and shipped at ambient temperature.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Shipping:

The whole blood samples must be maintained at room temperature and shipped by Federal Express – **Priority Overnight** (Monday – Thursday) at ambient temperature to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and ambient shippers will be provided by ADCS. If your site needs additional air waybills or ambient shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber
National Cell Repository for AD
980 W Walnut St R3 C158
Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu
Tel: (800) 526-2839
Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the EDTA (lavender top) tube needs to be stored at room temperature (20-25 degrees Celsius) from Friday until Monday and must be shipped out no later than Monday to NCRAD.

Notifying the National Cell Repository for AD (NCRAD):

The day the blood sample is shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Genetic Sample Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the Genetic Sample electronic case report form located in the ADNI-D web portal immediately after sample collection. Remember to include any issues that occurred during the sample collection, with packaging or temperature excursions on the Visit Comment electronic case report form.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Cells for Immortalization and PBMC Banking

Blood samples will be collected for Cell Immortalization and PBMC banking at Baseline for all enrolled participants after passing eligibility criteria for this study. Whole blood will be collected in one 8.5 mL ACD-A (yellow top) tube for Cell Immortalization and one 10 mL green top tube for PBMC banking.

Begin by confirming the participant consented to DNA testing and sample storage per their informed consent.

Next, complete the information on the genetic label for the ACD-A (yellow top) tube and Sodium Heparin (green top) tube.

- Securely place the label onto each tube before the blood draw.

Participant ID ____ -D- ____
 Protocol ADNI-D
 Year of Birth ____ Gender: M / F
 Collection Date: ____ / ____ / ____
 Baseline Month 30 D/C

Blood Collection:

1 x 8.5 mL ACD-A (yellow top) tube of whole blood will be collected for Cell Immortalization; gently mix by inversion, 6-10 times, to assure complete mixing of the blood sample with the anticoagulant Acid Citrate Dextrose.

1 x 10 mL Sodium Heparin (green top) tube of whole blood will be collected for PBMC banking; gently mix by inversion, 6-10 times, to assure complete mixing of the blood sample.

Completion of Sample Collection – Cell for Immortalization Worksheet:

Ensure all fields on the sample collection worksheet located in the visit packet are complete. Include the name of the individual who packaged and shipped the blood specimen, along with their phone number and email. Additionally, in the comments section of the worksheet, please list any issues that occurred during the blood draw, packaging or any temperature excursions.

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the whole blood sample within 24 hours of collection. The whole blood sample is maintained at room temperature (20-25 degrees Celsius) and shipped at ambient temperature.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT**Shipping:**

The whole blood samples must be maintained at room temperature and shipped by Federal Express – **Priority Overnight** (Monday – Thursday) at ambient temperature to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and ambient shippers will be provided by ADCS. If your site needs additional air waybills or ambient shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber

National Cell Repository for AD

980 W Walnut St R3 C158

Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu

Tel: (800) 526-2839

Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the ACD-A (yellow top) tube needs to be stored at room temperature (20-25 degrees Celsius) from Friday until Monday and must be shipped out no later than Monday to NCRAD. The Sodium Heparin (green top) tubes cannot be held until Monday for shipment. Do not collect Sodium Heparin (green top) tubes on a Friday.

IMPORTANT NOTE: It is crucial that the ACD-A tube and Sodium Heparin tube are NOT refrigerated, as they must stay at room temperature.

Notifying the National Cell Repository for AD (NCRAD):

The day the blood sample is shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Cell for Immortalization Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the Cell for Immortalization electronic case report form located in the ADNI-D web portal immediately after sample collection. Remember to include any issues that occurred during the sample collection, with packaging or temperature excursions on the Visit Comment electronic case report form.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Ambient Samples Collection Supplies (GWAS/ApoE, Cell Immortalization, and PBMC Banking)

1. General Supplies for Processing and Shipment of Ambient Samples

- ☐ 1 BD Vacutainer safety-Lok blood collection set (with butterfly needle)
- ☐ 1 BD Vacutainer Tube Holder
- ☐ 1 Therapak Ambient Shipper (small canister, fits 4 tubes)
- ☐ 1 Federal Express priority overnight ambient airbill
- ☐ 1 sheet Specimen Labels (30) for RNA, buffy coat, telomeres, cell immortalization, DNA, and PBMC Banking

2. DNA / GWAS / ApoE / Hematology / Differential

- ☐ 1 BD Vacutainer Lavender-Topped Blood Collection Tube (EDTA, 10 cc)

3. Cell Immortalization and PBMC Banking

- ☐ 1 BD Vacutainer Yellow-Topped Blood Collection Tube (ACD-A, 8.5 cc)
- ☐ 1 BD Vacutainer Sodium Heparin Green-Topped Blood Collection Tube (10 cc)

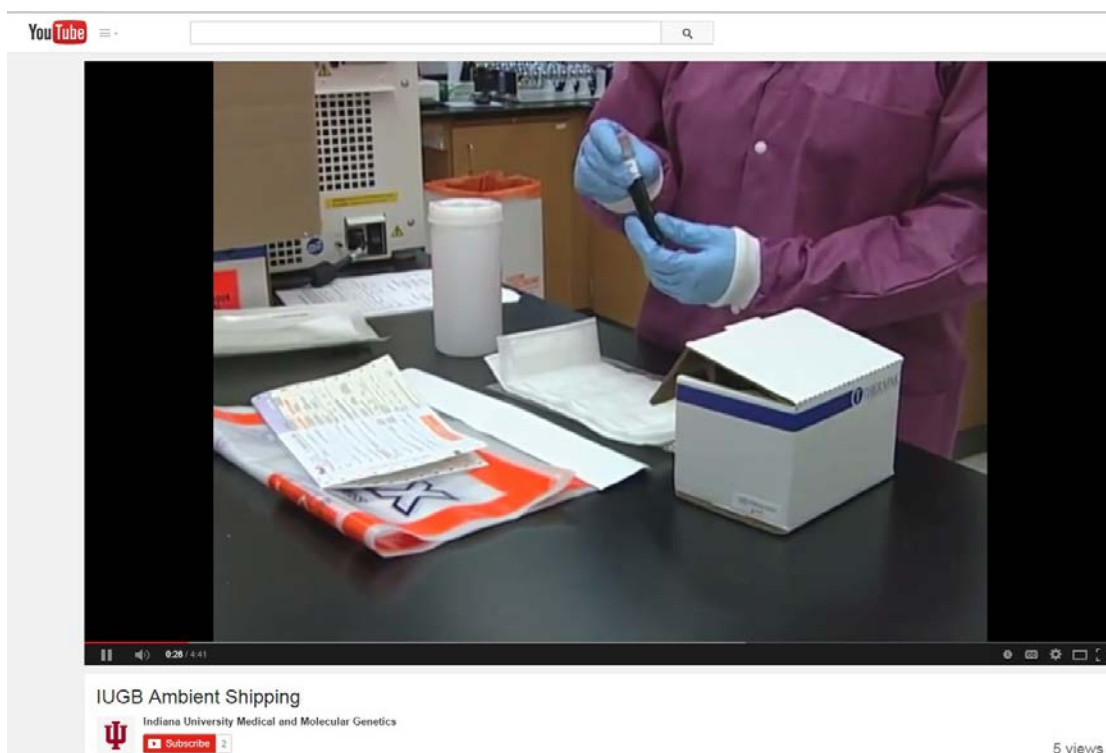


Shipping Ambient Samples to NCRAD

There are a number of requirements for the shipment of biohazard material including blood and blood products. The first requirement is the materials are contained in a leak proof vessel such as a blood collection tube, cryovial or centrifuge tube. An absorbent material capable of absorbing all the liquid in the shipment must be included. That absorbent material, along with the primary vessel such as the collection tube must be placed in a secondary leak proof container. The secondary container may be a sealable poly bag or an airtight canister. These should then be placed in a rigid container like a cardboard box for shipment. Also many times shippers come as a complete kit. The exterior of the shipping container must be labeled with the UN code and biological substance category label. The UN code and category label for shipments of blood, tissue, and other potential infectious human biologicals is code UN3373 category B.

For more in depth information on shipping guidelines please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=9wIAa2m9VI4>



BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

1. Fill out NCRAD label and attach to each tube prior to collecting sample.

2. Ambient samples shipping supplies



INCLUDES:

- ➔ 1 medium 95kPa canister,
- ➔ Aqui-Pak segmented absorbent pouch
- ➔ Cushioning material
- ➔ List of contents card
- ➔ Biohazard symbol label
- ➔ Biological Substance Category B label
- ➔ Shipping box



3. Insert the tubes for Cell Immortalization, DNA, and PBMC Banking into the absorbent sleeve.



4. Carefully roll up sleeve, insert into canister and wrap **OUTSIDE** canister in bubble wrap. Be sure to seal the canister tightly. Bubble wrap or other packing material is used to prevent the canister from excess shifting in the box.

List of Contents	
This item list must be placed between the secondary receptacle(s) and outer packaging in accordance with IATA Packing Instruction 650.	
<input checked="" type="checkbox"/> Diagnostic Specimens	<input type="checkbox"/> Absorbent Pad(s)
<input checked="" type="checkbox"/> (Human, No Animal Matter)	<input type="checkbox"/> Requisition
<input checked="" type="checkbox"/> Glass and/or Plastic Tubes	<input type="checkbox"/> Instruction Sheet
<input type="checkbox"/> Glass Slides/Slide Mailer	<input type="checkbox"/> Transport Media or Preservative
<input checked="" type="checkbox"/> Tube Separator Bag(s)	<input type="checkbox"/> Dry Ice
<input checked="" type="checkbox"/> Secondary Container/Canister	<input type="checkbox"/> Gel Pack/Refrigerant
<input type="checkbox"/> Other	
Therapak Corporation	54765

5. Fill out the list of contents card.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT



6. Place card and canister into shipping box. Paperwork corresponding to the sample, such as blood collection forms or case report forms should be included in the shipping box.



7. Please see note below, otherwise affix both biohazard labels to box. Complete the shipper's waybill with the sender and destination address. Retain a copy of the waybill or tracking number for your records and notify the recipient of the shipment.

NOTE: In order to be able to reuse the shipping box it is recommended to place the shipping box into a FedEx Clinical Pak and affix both biohazard labels/FedEx airbill to Clinical Pak. FedEx Clinical Paks can be ordered for free directly from FedEx at

www.fedex.com/us

Frozen Samples - Collection Procedure

Biomarker Plasma and Serum Samples

Plasma and serum for biomarkers will be collected at Baseline and Month 30 Follow Up visits for all enrolled participants.

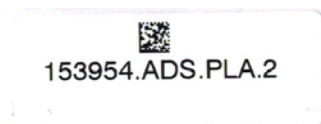
Fasting overnight (minimum 6 hours) is required for plasma and serum sample collection.

- Only water is permitted until blood draws are completed

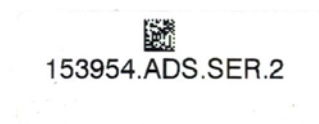
Begin by confirming the subject consented to biomarker collection per their informed consent.

Next, securely place the label onto the 0.5 mL aliquot tubes PRIOR to transfer of biomarker samples.

The Sample Identification label must be placed on the aliquot tubes prior to freezing!



Plasma Label



Serum Label

Make sure the microtube labels contain matching kit numbers for an individual participant.

Blood Collection:

TUBES 1 AND 2: 10 mL PLAIN RED-TOP TUBES FOR SERUM SAMPLES

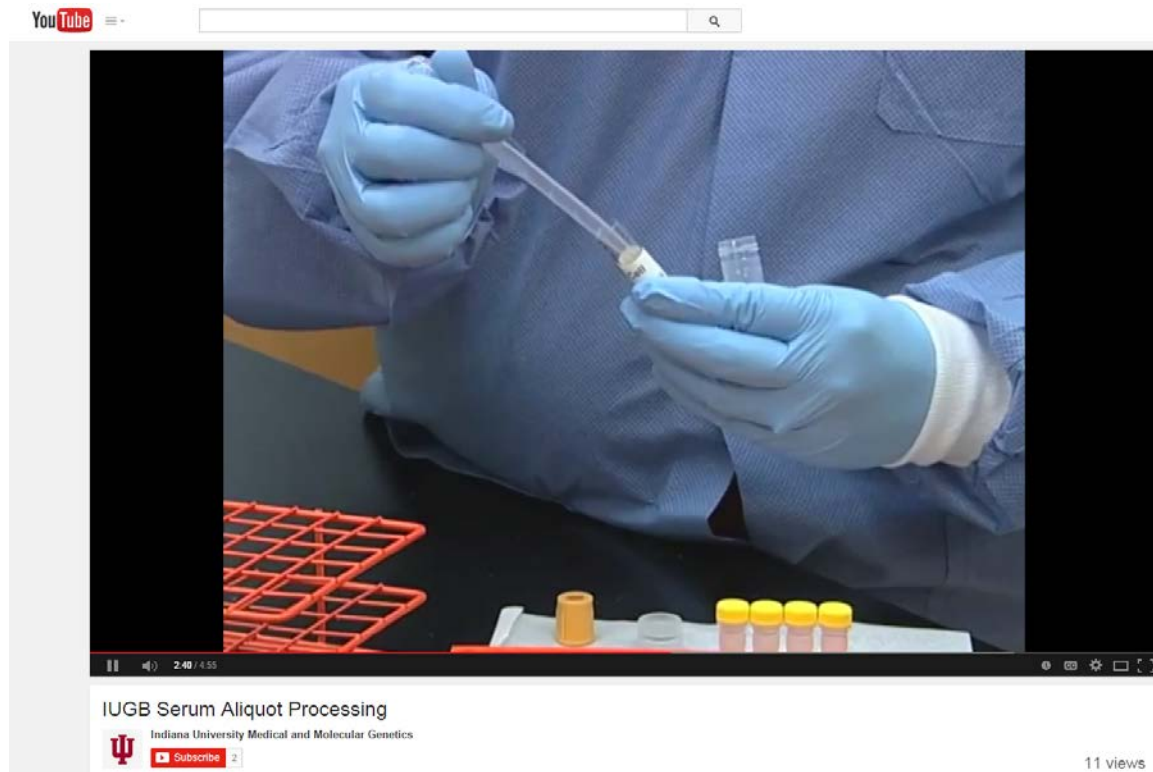
1. Write the Subject Identification Number on the side of the collection tubes **ONLY**, prior to drawing blood. Do not write Subject ID on microtubes.
2. Collect blood until each tube is full.
3. Estimate blood volume and record on the ADNI Biomarker Samples form.
4. Allow the blood to clot for 30 minutes at room temperature in a vertical position.
5. Centrifuge the tube at room temperature within one (1) hour of collection. Spin for 15 minutes using the Sorvall T 6000D Centrifuge (rotor H-1000B swinging bucket rotor) at 3000 rpm (1500 rcf) with the brake on, or in another centrifuge at a comparable rcf.
6. Place bar code labels on the 0.5 mL plastic aliquots.
7. Using a **STERILE** pipette carefully transfer serum from each of the two red-top tubes into the bar code-labeled 0.5 mL aliquots, then firmly cap. Each red-top tube should fill approximately 8-10 0.5 mL aliquots.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

8. After the serum has been transferred to the plastic bar-code labeled aliquots and capped (red cap), place the aliquots in dry ice and allow to completely freeze.

For more in depth information on serum aliquot processing please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=uMVI8-vK0m8>



TUBES 3 AND 4: 10 mL LAVENDER-TOP TUBES FOR PLASMA SAMPLES

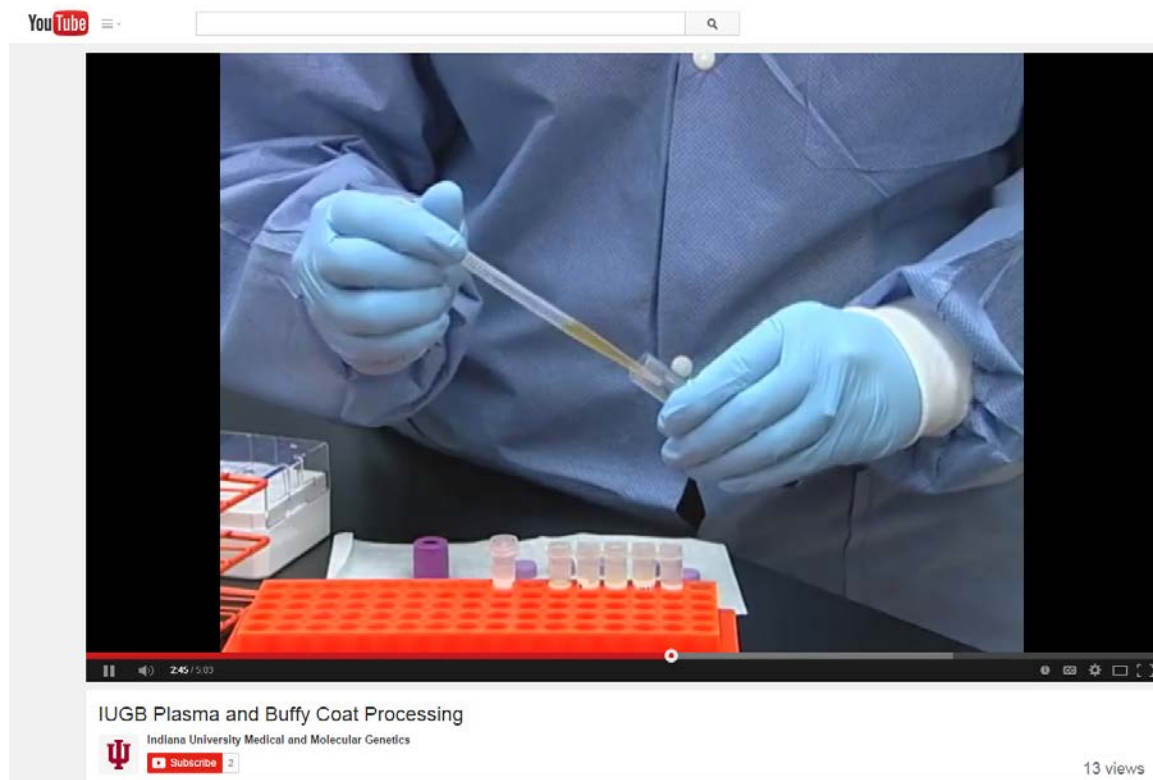
1. Write the Subject Identification Number on the side of the collection tubes **ONLY**, prior to drawing blood. Do not write Subject ID on microtubes.
2. Collect blood until each tube is full; gently mix by inversion, 10-12 times.
3. Estimate blood volume and record on the ADNI Biomarker Samples form.
4. Centrifuge the tube at room temperature within one (1) hour of collection. Spin for 15 minutes using the Sorvall T 6000D Centrifuge (rotor H-1000B swinging bucket rotor) at 3000 rpm (1500 rcf) with the brake on, or in another centrifuge and rotor at a comparable rcf.
5. Place bar code labels on the 0.5 mL plastic aliquots.
6. Using a **STERILE** pipette carefully transfer plasma from each of the two lavender top blood tubes into the bar code-labeled 0.5 mL plastic aliquots. Then firmly cap with the screw cap. Each lavender-top tube should fill approximately 8-10 0.5 mL aliquots.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

7. After the plasma has been transferred to the plastic labeled aliquots and capped (lavender cap), place the screw-capped aliquots in dry ice and allow it to completely freeze.
8. **Do not discard the lavender-top tubes.** Refer to the Biomarkers: Buffy Coat sample collection section for more information.

For more in depth information on Plasma and Buffy Coat Processing please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=O9XIYDotFEM>



Completion of Sample Collection: Biomarkers Worksheet

Ensure all fields on the sample collection worksheet located in the visit packet are complete. A copy of the worksheet should be included with the shipment, original remains onsite. **Be sure to put a kit number label on the worksheet before sending to NCRAD.**

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the plasma and serum samples within 24 hours of collection. The plasma and serum is frozen on dry ice before shipment to NCRAD.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT**Shipping:**

The plasma and serum samples must be frozen on dry ice and shipped by Federal Express—**Priority Overnight (Monday – Wednesday)** to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and Therapak Frozen Biological Substance shippers will be provided by ADCS. If your site needs additional air waybills or Therapak Frozen Biological Substance shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber
National Cell Repository for AD
980 W Walnut St R3 C158
Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu
Tel: (800) 526-2839
Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the plasma and serum samples should be placed in a -80 or –20 degree Celsius freezer over the weekend and shipped frozen (on dry ice) on Monday to NCRAD.

Notifying the National Cell Repository for AD (NCRAD):

The day the plasma and serum samples are extracted and shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Biomarkers Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the biomarkers electronic case report form located in the ADNI-D web portal immediately after the visit. Remember to include any issues that occurred during the extraction procedure, with packaging or temperature excursions on the visit comment electronic case report form.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Biomarkers: Banked for Future “TBD” Assays

Additional plasma and serum will be collected at Baseline and Month 30 Follow Up visits to be banked for future “to be determined” assays for all enrolled participants.

Fasting overnight (minimum 6 hours) is required for “TBD” plasma and serum sample collection.

- Only water is permitted until blood draws are completed

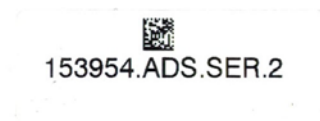
Begin by confirming the subject consented to additional blood sample collection per their informed consent.

Next, securely place the labels onto the 0.5 mL aliquot tubes PRIOR to transfer of plasma and serum samples.

The Sample label must be placed on the aliquot tubes prior to freezing!



Plasma Label



Serum Label

Make sure the microtube labels contain matching kit numbers for an individual participant.

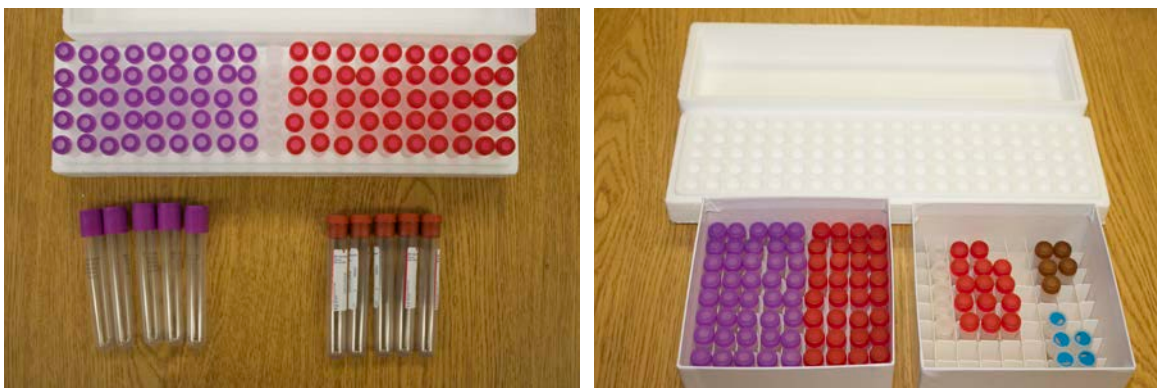
Blood Collection:

TUBES 1-3: 10 mL PLAIN RED-TOP TUBES FOR “TBD” SERUM SAMPLES

1. Write the Subject Identification Number on the side of the collection tubes **ONLY**, prior to drawing blood. Do not write Subject ID on microtubes.
2. Collect blood until each tube is full
3. Estimate blood volume and record on the ADNI Biomarker Samples form.
4. Allow the blood to clot for 30 minutes at room temperature in a vertical position.
5. Centrifuge the tube at room temperature within one (1) hour of collection. Spin for 15 minutes using the Sorvall T 6000D Centrifuge (rotor H-1000B swinging bucket rotor) at 3000 rpm (1500 rcf) with the brake on, or in another centrifuge at a comparable rcf.
6. Place bar code labels on the 0.5 mL plastic aliquots.
7. Using a **STERILE** pipette carefully transfer serum from each of the three red-top tubes into the bar code-labeled 0.5 mL aliquots, then firmly cap. Each red-top tube should fill approximately 8-10 0.5 mL aliquots.
8. After the serum has been transferred to the plastic bar-code labeled aliquots and capped (red caps), place the aliquots in dry ice and allow it to completely freeze.

TUBES 4-6: 10 mL LAVENDER-TOP TUBES FOR “TBD” PLASMA SAMPLES

1. Write the Subject Identification Number on the side of the collection tubes **ONLY**, prior to drawing blood. Do not write Subject ID on microtubes.
2. Collect blood until each tube is full; gently mix by inversion, 10-12 times.
3. Estimate blood volume and record on the ADNI Biomarker Samples form.
4. Centrifuge the tube at room temperature within one (1) hour of collection. Spin for 15 minutes using the Sorvall T 6000D Centrifuge (rotor H-1000B swinging bucket rotor) at 3000 rpm (1500 rcf) with the brake on, or in another centrifuge and rotor at a comparable rcf.
5. Place bar code labels on the 0.5 mL plastic aliquots.
6. Using a **STERILE** pipette carefully transfer plasma from each of the three lavender top blood tubes into the bar code-labeled 0.5 mL plastic aliquots. Then firmly cap with the screw cap (lavender cap). Each lavender-top tube should fill approximately 8-10 0.5 mL aliquots.
7. After the plasma has been transferred to the plastic labeled aliquots and capped, place the screw-capped aliquots in dry ice and allow it to completely freeze.
8. **Do not discard the lavender-top tubes.** Refer to the Biomarkers: Buffy Coat sample collection section for more information.

**Completion of Sample Collection: Biomarkers Worksheet**

Ensure all fields on the sample collection worksheet located in the visit packet are complete. A copy of the worksheet should be included with the shipment, original remains onsite. **Be sure to put a kit number label on the worksheet before sending to NCRAD.**

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the plasma and serum samples within 24 hours of collection. The plasma and serum is frozen on dry ice before shipment to NCRAD.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT**Shipping:**

The plasma and serum samples must be frozen on dry ice and shipped by Federal Express—**Priority Overnight (Monday – Wednesday)** to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and Therapak Frozen Biological Substance shippers will be provided by ADCS. If your site needs additional air waybills or Therapak Frozen Biological Substance shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber
National Cell Repository for AD
980 W Walnut St R3 C158
Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu
Tel: (800) 526-2839
Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the “TBD” plasma and serum samples should be placed in a -80 or -20 degree Celsius freezer over the weekend and shipped frozen (on dry ice) on Monday to NCRAD.

Notifying the National Cell Repository for AD (NCRAD):

The day the “TBD” plasma and serum samples are extracted and shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Biomarkers Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at **alzstudy@iupui.edu**. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

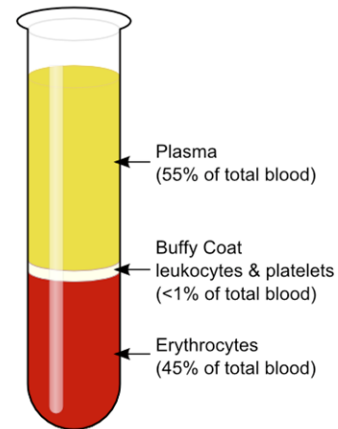
Complete the biomarkers electronic case report form located in the ADNI-D web portal immediately after the visit. Remember to include any issues that occurred during the extraction procedure, with packaging or temperature excursions on the Visit Comment electronic case report form.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Biomarkers: Buffy Coat Sample Collection

The buffy coat is the thin layer in between the red blood cells and plasma after centrifugation of the lavender-top tubes used for plasma sample collection during the biomarker/TBD lab procedures.

Buffy coat extraction should follow each biomarker lab blood draw at Baseline and Month 30 Follow Up. Extract the buffy coat from the 2 lavender-top EDTA tubes that are used for the biomarker lab blood draw and the 3 lavender-top EDTA tubes that are used for the “TBD” assay lab blood draw as follows:



1. After the lavender-top EDTA tubes have been centrifuged at 3000 rpm transfer the plasma into the 0.5 mL plastic aliquots, which will be sent to NCRAD.
2. Using sterile gloves and a sterile pipette, extract the buffy coat from one of the lavender-top EDTA tubes and aliquot it into one of the 2mL cryogenic vials. Move the pipette tip in a circular fashion collecting the buffy coat layer. Repeat this process for the other lavender-top EDTA tubes and the remaining, empty 2mL cryogenic vials. **It is very normal to get some of the red blood cells when pulling off the buffy coat. Generally, if you don't see red then you haven't gone far enough down the tube. After extracting the buffy coat, the remaining cells can be discarded.** Then firmly cap with the screw cap (blue cap).
3. Complete the information on the genetic label. Ensure all fields on the label are complete using a ball-point pen or permanent marker. Securely place the label onto each cryogenic vial.

Participant ID _____ -D- _____
 Protocol ADNI-D
 Year of Birth _____ Gender: M / F
 Collection Date: ____ / ____ / ____
 Baseline Month30 D/C

4. The label will be larger than the vial and should be dovetailed rather than wrapped around the tube in order to view all the information on the label.

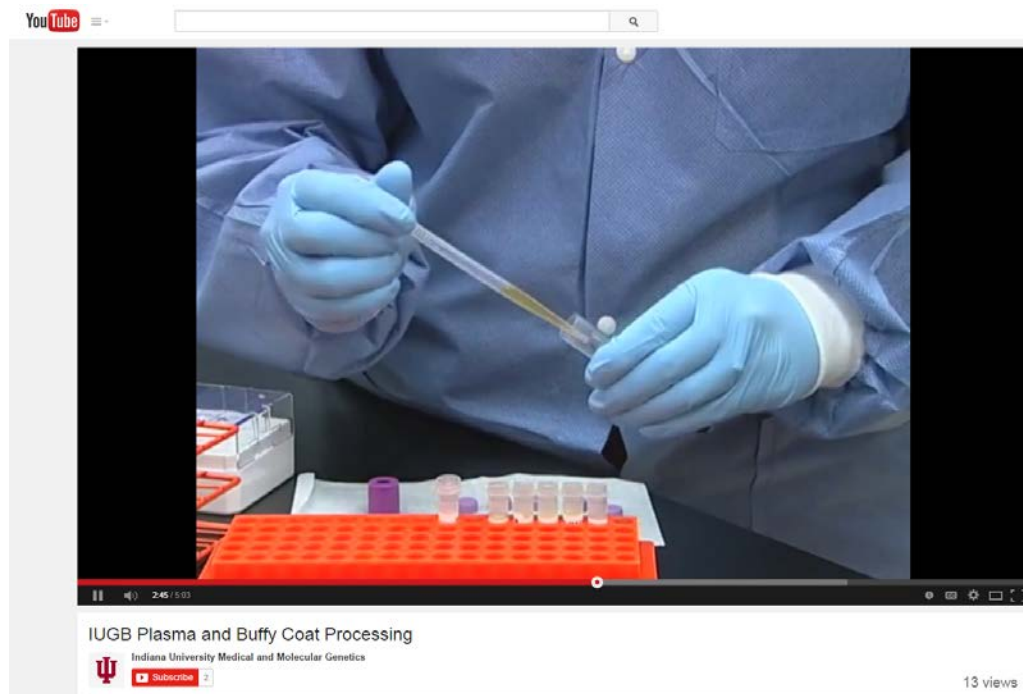
BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

For more in depth information on Buffy Coat Sample Collection please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=O9XIYDOtFEM>

&

<http://www.preanalytix.com/videos/rna-tube-collection-video/>



Completion of Sample Collection: Buffy Coat Worksheet

Ensure all fields on the sample collection worksheet located in the visit packet are complete. A copy of the worksheet should be included with the shipment, original remains onsite.

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the buffy coat samples within 24 hours of collection. The buffy coat is frozen on dry ice before shipment to NCRAD.

Shipping:

The buffy coat samples must be frozen on dry ice and shipped by Federal Express—**Priority Overnight (Monday – Wednesday)** to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and Therapak Frozen Biological Substance shippers will be provided by ADCS. If your site needs additional air waybills or Therapak Frozen Biological Substance shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber
National Cell Repository for AD
980 W Walnut St R3 C158
Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu
Tel: (800) 526-2839
Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the buffy coat should be placed in a -80 or -20 degree Celsius freezer over the weekend and shipped frozen (on dry ice) on Monday to NCRAD.

Notifying the National Cell Repository for AD (NCRAD):

The day the buffy coat is extracted and shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Buffy Coat Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the Buffy Coat electronic case report form located in the ADNI-D web portal immediately after the visit. Remember to include any issues that occurred during the extraction of the buffy coat, with packaging or temperature excursions on the Visit Comment electronic case report form.

NOTE: Buffy coat extracted from each of the lavender-top biomarker tubes must be placed in separate cryogenic vials, for a total of 5 cryogenic vials being shipped to NCRAD.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

RNA Sample Collection

In order to measure gene expression across time, an RNA sample will be collected at Baseline and Month 30 Follow Up for all enrolled participants. Whole blood will be collected in three 2.5 mL PAXgene Blood RNA tubes.

IMPORTANT NOTE: If possible, RNA samples should be drawn last.

Begin by confirming the subject consented to RNA testing and sample storage per their informed consent.

Next, complete the information on the genetic label for each of the PAXgene Blood RNA tubes.

- Securely place the label onto each tube before the blood draw.

Participant ID ____ -D- ____
 Protocol ADNI-D
 Year of Birth ____ Gender: M / F
 Collection Date: ____ / ____ / ____
 Baseline Month30 D/C

Blood Collection:

3 x 2.5 mL PAXgene Blood RNA tubes will be collected at Baseline and Month 30 Follow Up visits for enrolled participants using the RNA sample collection kit provided by the ADCS.

1a. Ensure that the PAXgene Blood RNA tube is at room temperature prior to use.

1b. If the PAXgene Blood RNA tube is the only tube to be drawn, a small amount of blood should be drawn into a “discard tube” prior to drawing blood into the PAXgene Blood RNA tube. Otherwise, the PAXgene Blood RNA tube should be the LAST tube drawn in the phlebotomy procedure. (Discard tube is included in the RNA collection kit provided by ADCS)

2. Using a BD (Becton, Dickinson and Company) Vacutainer Safety-Lok Blood Collection Set, collect blood into the PAXgene Blood RNA tube using your institution’s recommended standard procedure for venipuncture.

3a. Hold the PAXgene Blood RNA tube vertically, below the blood donor’s arm, during blood collection.

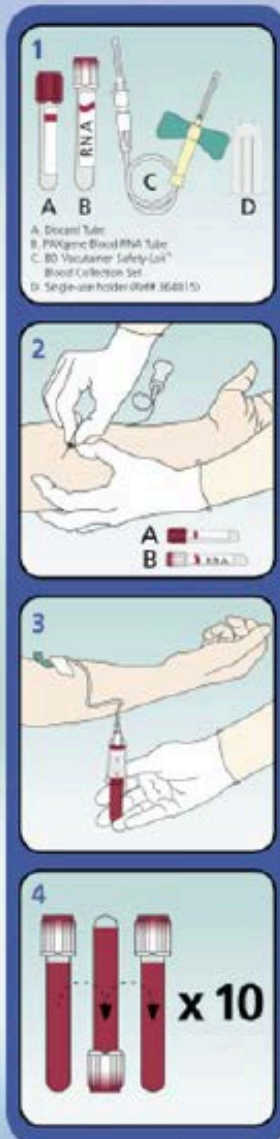
3b. Allow at least 10 seconds for a complete blood draw to take place. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder.

4a. Gently invert the PAXgene Blood RNA tube 8 to 10 times.

4b. Store the PAXgene Blood RNA tube upright at room temperature for 2 hours.

How to Collect Blood Using the PAXgene™ Blood RNA Tube

For Molecular Diagnostic Testing



Required Items:

- 1a. Ensure that the PAXgene Blood RNA Tube (B) is at room temperature (18°C-25°C) prior to use and properly labeled with patient identification.
- 1b. If the PAXgene Blood RNA Tube is the only tube to be drawn, a small amount of blood should be drawn into a "Discard Tube" (A) prior to drawing blood into the PAXgene Blood RNA Tube. Otherwise, the PAXgene Blood RNA Tube should be the last tube drawn in the phlebotomy procedure.

Venipuncture:

2. Using a BD Vacutainer® Safety-Lok™ Blood Collection Set (C), collect blood into the PAXgene Blood RNA Tube using your institution's recommended standard procedure for venipuncture.

Blood Collection:

- 3a. Hold the PAXgene Blood RNA Tube vertically, below the blood donor's arm, during blood collection.
- 3b. Allow at least 10 seconds for a complete blood draw to take place. Ensure that the blood has stopped flowing into the tube before removing the tube from the holder. (See Figure 1)

After Blood Collection:

- 4a. Gently invert the PAXgene Blood RNA Tube 8 to 10 times.
- 4b. Store the PAXgene Blood RNA Tube upright at room temperature (18°C-25°C) or at 4°C.*



BD Customer Service/Orders:
888.237.2762 (North America)
32.53.720.337 (Europe)

PreAnalytiX
A QIAGEN / BD Company

www.PreAnalytiX.com

CE

*Refer to PAXgene® Blood RNA Tube handbook.
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BD and all other trademarks are the property of Becton, Dickinson and Company. ©2015 BD
Printed in USA: 15/015 150213-1

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

For more in depth information on RNA PAXGene Processing please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=Jw1Dma-i83o>



Completion of Sample Collection: Genetics Worksheet

Ensure all fields on the sample collection worksheet located in the visit packet are complete. Pay close attention to questions regarding the subjects consent to RNA testing and sample storage. Ensure the name of the individual who packaged and shipped the blood specimen, along with their phone number and email is listed on the worksheet. Additionally, please list in the comments section of the worksheet any issues that occurred during the blood draw with packaging or any temperature excursions.

Temperature Requirements

The National Cell Repository must receive the whole blood sample for AD (NCRAD) within 24 hours of collection. The whole blood samples are frozen on dry ice before shipment to NCRAD.

Shipping:

The whole blood samples must be frozen on dry ice and shipped by Federal Express—**Priority Overnight (Monday – Wednesday)** to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and Therapak Frozen Biological Substance shippers

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

will be provided by ADCS. If your site needs additional air waybills or Therapak Frozen Biological Substance shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber

National Cell Repository for AD

980 W Walnut St R3 C158

Indianapolis, IN 46202

NCRAD Helpdesk:alzstudy@iupui.edu

Tel: (800) 526-2839

Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the PAXgene Blood RNA tubes **will need to be held at room temperature for 2 hours and then placed in -20° or -80° Celsius freezer over the weekend** and then shipped frozen (on dry ice) to NCRAD on Monday. Buffy coat can be shipped with the plasma and serum samples, since all need to be shipped on dry ice.

Notifying the National Cell Repository for AD (NCRAD):

The day the blood sample is shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection Genetics Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the Genetics worksheet electronic case report form located in the ADNI-D web portal immediately after sample collection. If any issues occurred during sample collection with packaging or temperature, include them on the visit comment section.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Telomere Length Measurement Sample Collection

Blood samples will be collected for telomere length measurement at Baseline and Month 30 for all study participants after passing screening criteria for this study. Whole blood will be collected in a single 4 mL EDTA (lavender top) tube.

Something to Consider:

Collecting blood for telomeres should not be sensitive to time of day, fasting state, menstrual status, etc. However, bulk telomere length in blood is dependent on the types of immune cells present at any one moment and site of blood draw. Therefore, since blood cell composition can change based on diurnal rhythm, and when someone has an active infection, it is best to follow these guidelines when possible.

- **Time of day:** Sample at the same time of day for all subjects, and especially for repeated measures for the same subjects. It is best to take a fasting morning blood draw, in the case that meal content affects distribution of leukocytes.
- **Health Status:** Never sample blood for telomere collection if the participant is showing signs of illness or has a major injury. It is prudent to call participants the night beforehand or to check by email to see if they have any symptoms including upper respiratory infections.

Fasting overnight (minimum 6 hours) is recommended for telomere length measurement sample collection.

Begin by confirming the subject consented to telomere testing and sample storage per their informed consent.

Next, complete the information on the genetic label for the EDTA (lavender top) tube.

- Securely place the label onto the EDTA (lavender top) tube **BEFORE** the blood draw.



Telomere Label

Make sure the microtube labels contain matching kit numbers for an individual participant.

Blood Collection:

1. 1 x 4 mL EDTA (lavender top) tube of whole blood will be collected; gently mix by inversion, 30 - 40 times, to assure that the EDTA anticoagulant is well-mixed with the whole blood sample.
2. Pipette 700 ul of whole blood into each of the five (5) 2 mL screw cap (brown caps) tubes within **4 hours** of the blood draw and allow to freeze on dry ice.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT**Completion of Sample Collection: Genetics Worksheet**

Ensure all fields on the sample collection worksheet located in the visit packet are complete. A copy of the worksheet should be included with the shipment, original remains onsite.

Temperature Requirements:

The National Cell Repository for AD (NCRAD) must receive the telomere samples within 24 hours of collection. The telomere whole blood samples are frozen on dry ice before shipment to NCRAD.

Shipping:

The telomere whole blood samples must be frozen on dry ice and shipped by Federal Express—**Priority Overnight (Monday – Wednesday)** to NCRAD.

- NCRAD will **NOT** be able to accept any shipment on Saturday or Sunday.

Pre-Paid Federal Express Air waybills and Therapak Frozen Biological Substance shippers will be provided by ADCS. If your site needs additional air waybills or Therapak Frozen Biological Substance shippers please complete the Supply Order Form located in the document repository.

NCRAD Shipping Address:

Kelley Faber
National Cell Repository for AD
980 W Walnut St R3 C158
Indianapolis, IN 46202

NCRAD Helpdesk:

alzstudy@iupui.edu
Tel: (800) 526-2839
Fax: 317-278-1100

For those instances in which a Friday study visit is necessary, the telomere samples should be placed in a -80 or -20 degree Celsius freezer over the weekend and shipped frozen (on dry ice) on Monday to NCRAD.

Notifying the National Cell Repository for AD (NCRAD):

The day the telomere samples are collected and shipped to NCRAD you must **FIRST** fax a copy of the completed **Sample Collection: Genetics Worksheet** to **(317) 278-1100** or email a copy of the completed worksheet to NCRAD at alzstudy@iupui.edu. **Also be sure to include a copy of this worksheet with the shipment.**

Sample Tracking:

Complete the telomere electronic case report form located in the ADNI-D web portal immediately after the visit. Remember to include any issues that occurred during the extraction procedure, with packaging or temperature excursions on the visit comment electronic case report form.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

Supplies for Frozen Sample Collection & Shipping:

There is no auto-shipment of initial supplies for ADNI-D. Once a site is approved by ADCS Regulatory Affairs, ADCS operations will contact the site coordinator to assess the number of potential subjects identified for assessment so that ADCS operations and the site coordinator can determine the amount of supplies needed. Sites will use the order form available on the document repository to request resupply.

1. General Supplies for Processing and Shipment of Frozen Samples

- ☐ 1 BD Vacutainer safety-Lok blood collection set (with butterfly needle)
- ☐ 1 BD Vacutainer Tube Holder
- ☐ 1 Styrofoam container for securing micro tubes (100 apertures)
- ☐ 2 Therapak Frozen Substance Shipping System (81 micro tubes)
- ☐ 2 (NCRAD) Federal Express Priority Overnight Frozen/Dry Ice Airbill
- ☐ 1 roll/100 labels: plasma and serum specimen micro tube labels
- ☐ 1 sheet Specimen Labels (30) for RNA, buffy coat, telomeres, cell immortalization, DNA, and PBMC Banking

If all samples are NOT drawn on the same day an additional blood collection kit and BD Vacutainer Tube Holder will need to be ordered.

2. Biomarkers Plasma and Serum

- ☐ 2 BD Vacutainer Lavender-Topped Blood Collection Tubes (EDTA, 10 cc) for plasma
- ☐ 2 BD Vacutainer Red-Topped Blood Collection Plastic Tubes (ACD-A, 10 cc) for serum
- ☐ 40 Sarstedt 0.5 mL Screw Cap Tubes (0.5 cc): 20 for plasma & 20 for serum
- ☐ 20 Sarstedt Lavender Lid for Screw Cap Tubes for plasma
- ☐ 20 Sarstedt Red Lid for Screw Cap Tubes for serum
- ☐ 2 Fisher Disposable Pipettes (1 for plasma, 1 for serum)

3. "TBD" Assay Plasma and Serum

- ☐ 3 BD Vacutainer Lavender-Topped Blood Collection Tubes (EDTA, 10 cc) for plasma
- ☐ 3 BD Vacutainer Red-Topped Blood Collection Plastic Tubes (ACD-A, 10 cc) for serum
- ☐ 60 Sarstedt 0.5 mL Screw Cap Tubes (0.5 cc) 30 for plasma & 30 for serum
- ☐ 30 Sarstedt Lavender Lid for Screw Cap Tubes – for plasma
- ☐ 30 Sarstedt Red Lid for Screw Cap Tubes – for serum
- ☐ 2 Fisher Disposable Pipettes (1 for plasma, 1 for serum)

4. Buffy Coat

- ☐ 5 Fisher 2 mL Cryogenic Vial (2 cc)

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

- ☐ 5 Fisherbrand Color Coders Blue for Cryogenic Vials
- ☐ 2 Fisher STERILE Disposable Pipettes

5. RNA Sample

- ☐ 3 PAXgene Blood RNA Tubes (2.5 cc)
- ☐ 1 BD Vacutainer Discard Tube (4 cc) (only needed if RNA drawn before serum, this will be discarded)
- ☐ 1 protective canister and absorbent sleeve for shipping.

6. Telomere Length Measurement

- ☐ 1 BD Vacutainer Lavender-Topped Blood Collection Tube (EDTA, 4 cc)
- ☐ 5 Sarstedt 2 mL Screw Cap Tubes (2 cc)
- ☐ 5 Sarstedt Brown Lids for 2 mL Screw Cap Tubes
- ☐ 1 Fisher Disposable Pipettes

To order additional Biomarker kits, please fill out the Supply order form located in the document repository and send to: adcs-clinops@ucsd.edu.

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

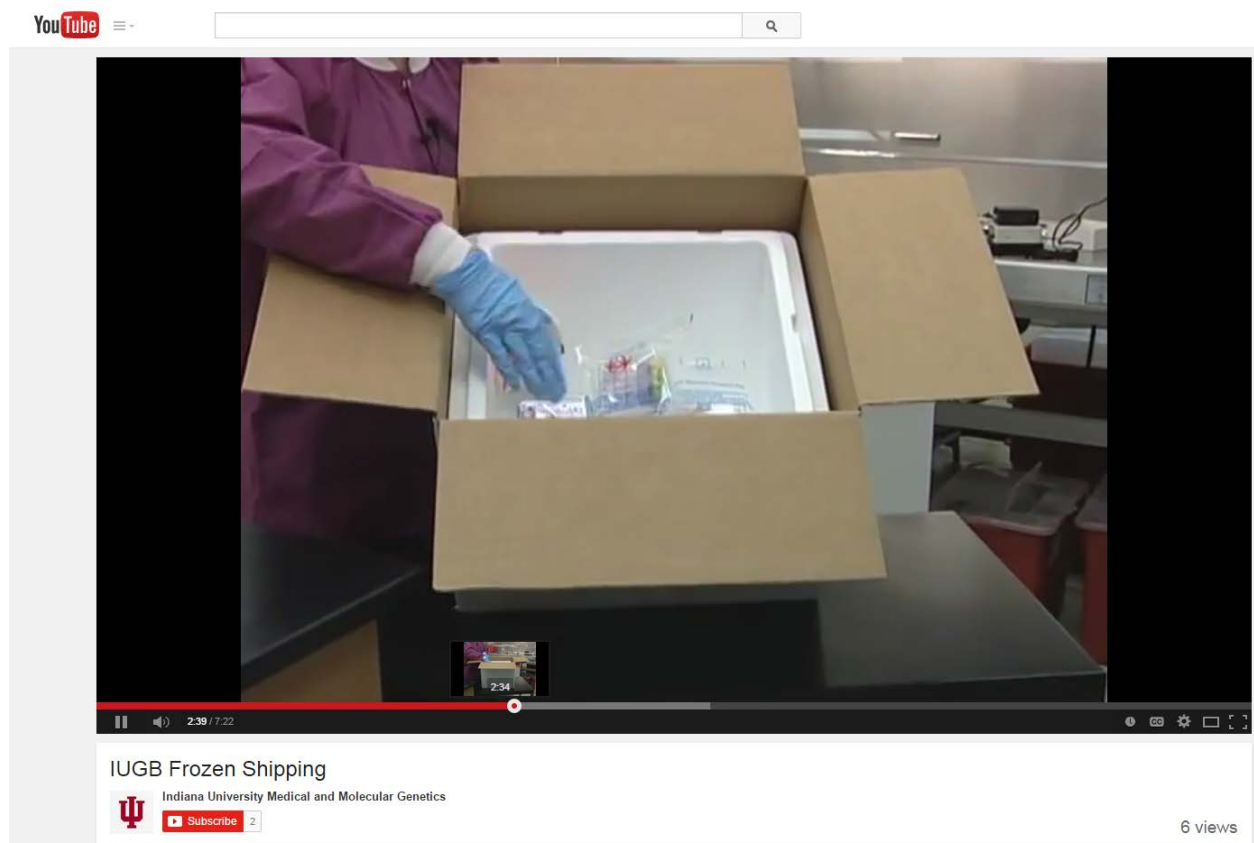
Shipping Frozen Samples to NCRAD

There are a number of requirements for the shipment of biohazard materials including blood and blood products. The first requirement is that all materials are contained in a leak proof vessel such as a blood collection tube, cryovials or centrifuge tubes.

Absorbent materials capable of absorbing all the liquid in the shipment must also be included with the specimen. This absorbent material can be in the form of a sleeve (for blood collection tubes) or an absorbent sheet. The secondary container may be an airtight canister or a sealable poly bag. The container can then be placed directly on a layer of dry ice in the shipping box. Ensure all proper requirements provided below have been fulfilled before shipping. The following steps (with the exception of RNA which will only be shipped in one container) should be followed for both Therapak Insulated Shippers.

For more in depth information on shipping guidelines please refer to the YouTube videos provided by Indiana University.

Link: <https://www.youtube.com/watch?v=zzQgf7-ASxw>



BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT

1. Place all the aliquots upright in dry ice and allow to completely freeze.
2. Once samples are ready for shipment and frozen, prepare the Therapak insulated shipper by placing a base layer of dry ice to the bottom of the Styrofoam insulation box.
3. When shipping multiple aliquots in a sample or multiple samples, they may remain in the cryobox in which they were stored in the freezer.



4. Before shipment, the cryobox must be placed in a secondary leak proof container such as a bag containing an absorbent sheet. Then seal the bag.



5. Once the bag is sealed, this can be placed directly on the dry ice in the shipping box. (Repeat steps for the second cryobox. One box per Therapak shipping container) **A kit number label should be placed on the outside of the bag before placing in shipping box.**

BIOFLUIDS: COLLECTION, PROCESSING AND SHIPMENT



6. Next prepare the RNA samples for shipment in one of the two Therapak boxes.
 - a. RNA samples will be shipped along with plasma and serum on dry ice. As required for biohazard material shipment, RNA samples will be stored in 3 x 2.5 mL leak proof PAXgene tubes.
 - b. Insert all three RNA tubes into absorbent tube sleeve.
 - c. Carefully roll up sleeve and insert into the airtight canister.



- d. This canister can then be placed directly on a layer of dry ice in the shipping box.

NOTE: Multiple containers may be transported in a single shipping box (i.e. RNA samples and cryobox), but they must be placed in a single layer between two layers of dry ice to maintain temperature control.

7. Next, apply a second layer of dry ice over the specimen containers. Dry ice shippers must have inner shipping containers, typically Styrofoam, and a rigid outer container such as a cardboard box. **Be sure the containers are completely covered in dry ice.**
8. Replace the lid on the inner Styrofoam shipper and place any paperwork shipping with the samples, such as blood collection forms or case report forms, on top of the Styrofoam box.

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9. Tape the box closed securely. Be sure the tape is firmly affixed to the cardboard. The shipper must be labeled with a UN code 3373 and biological substance category B which are provided for each box.



10. Use arrow stickers provided to indicate which way is the top of box to ensure it stays upright during shipment.

NOTE: Because dry ice is considered a dangerous substance, when shipping on dry ice the department of transportation has specific labeling requirements. UN1845 dry ice labels must be correctly completed prior to shipping

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11. Record the amount of dry ice used in the box in kilograms on the dry ice labels. The shipper and recipient addresses must also be written on the label. If your dry ice is in small packages indicate the number and weight of the packages on the dry ice label.



12. Dry ice must be declared on the dangerous goods section of the carrier's waybill. Be sure the weight of dry ice written on the waybill matches the weight recorded on the dry ice label. The carrier can refuse a shipment if either of the forms are completed incorrectly or do not match.
13. Clearly write the phone number and contact information for the person to be contacted if something happens to the shipment.
14. Firmly affix the label to the shipper and call the carrier for pickup. Retain a copy of the waybill or tracking number for your records and notify the recipient of the shipment.



Biofluids Glossary

ADNI-D	Alzheimer's Disease Neuroimaging Initiative Depression Project
BLD	Blood (Whole)
PL	Plasma
ACD	Acid Citrate Dextrose
EDT	EDTA (Ethylenediaminetetraacetic acid)
SER	Serum
BLD EDT	Whole blood collected in a lavender-top tube
BLD ACD	Whole blood collected in a yellow-top tube (ACD-A)
BLD SER	Whole blood collected in a plain red-top tube
CELL-I	Cell Immortalization Sample
GWAS	Genome Wide Association Study
NCRAD	National Cell Repository for Alzheimer's Disease
TBD	To Be Determined

Cognitive Assessments

General Guidelines

The goal of ADNI-D neuropsychological testing is to use standardized procedures to objectively and reliably assess a participant's cognitive abilities. However, neuropsychological testing is not a mechanical process. The examiner encounters a wide range of emotional and physical problems that can interfere with testing. The skill and judgment of the examiner can also affect the participant's willingness to be tested and the effort he/she invests. Thus, during an actual test session the examiner must simultaneously administer tests, observe and assess participant behavior, and then make necessary adjustments. The following guidelines are provided to maintain inter-rater reliability and ensure standard administration of cognitive tests for the ADNI-D protocol. Following these guidelines at your site will help generate valid and accurate measurements with a minimum of stress and discomfort for participants.

Scheduling Testing

When possible, do not schedule cognitive testing after blood draws, as this might affect results. Every effort should be made to conduct testing at the same time of day in order to reduce variability due to circadian (i.e., time of day) effects. If cognitive testing cannot be done prior to any other assessment that day, ensure the participant is given an adequate break including food or drink. Please refer to the Sample Visit Schedule (Start-up and General Information section) for more information.

Creating a Productive Testing Environment

Because the examiner can influence testing to some degree even when standardized procedures are used, it is desirable to have the same examiner conduct all assessments during the course of this protocol. As with any neuropsychological testing, it is important that the testing takes place at a desk or table, in a quiet room that is free of distractions. Before testing, question both the participant and the study partner about the participant's ability to see and hear. Also make sure the participant is wearing corrective eyeglasses or hearing aids if needed.

Introducing the Testing

The study partner should be included in the general orientation to the day's activities. Explain the purpose of the testing, what the test(s) will be like, how long testing will take, and what the day's schedule will be, including when the participant may take breaks. After answering any questions, instruct the study partner to wait outside the testing room in the designated waiting area (most participants test better if they are not observed by people they know). If the participant will comply only with a study partner present, the study partner should be instructed not to provide answers, and to sit in an area of the room where the participant will not easily turn to him/her for feedback.

COGNITIVE ASSESSMENT

Managing Testing Time

Administer the battery in the order indicated in the source doc worksheet packets with adherence to time limits and standardized instructions. This may be challenging with participants who interrupt testing or digress into excessive conversation. In these cases, the examiner must regain control and “reorient” the participant back to the task at hand.

Keeping Participants Focused

If the participant is exhibiting signs of frustration or requests to terminate the test, the examiner should acknowledge the participant’s concerns, and take note of any reported or expressed physical symptoms (e.g., pain, fatigue) that could be interfering with test performance. It may become necessary to differentiate the participant who refuses to continue a task from the participant who cannot continue a task due to physical or severe cognitive impairment (this is made more difficult by the fact that a participant may refuse testing due to frustration over their inability to perform a task). A participant may become fatigued, frustrated or merely distracted, but know there is no one approach that will work with all participants. The examiner should have a flexible style that acknowledges the participant’s concerns, while gently diverting their attention back to the task.

Assessing Participant Comprehension

It is the examiner’s responsibility to see that the participant understands the instructions before each test is started and that this understanding is maintained throughout the test. Instructions may be repeated or simplified according to the instructions for each task during the test session, taking care not to provide any new information, hints or answers.

Feedback and Prompting

Provide only neutral feedback to the participant, without indicating if their answers are right or wrong, (e.g., “okay” or “you are doing fine.”). Reward all good effort, not just good performance. Often a participant will give more than one answer. If that should occur, encourage the participant to choose one of them, without cueing for a specific response. “Which one is it?” or “Choose one” can be useful prompts to get a participant to choose a single answer.

Scoring and Recording

Since it is better to score an incorrect response than no response, participants should be encouraged to give an answer even if they are unsure. “What’s your best answer?” or “try” can be helpful prompts. An incorrect response can give some evidence that the Participant did not understand the question.

Record the participant’s responses in full and verbatim. More notes are better than too few notes. Many examiners prefer to tape record their participant’s response, and then

COGNITIVE ASSESSMENT

transcribe any words they may have missed after the session. This is acceptable if appropriate consent has been obtained.

Please remember that the participant's name should NOT be written on the worksheet.

COGNITIVE ASSESSMENT

Order of Neuropsychological Assessments

Please note that this order of assessments was designed to preserve delay intervals for the Brief Visuospatial Memory Test, Logical Memory, or the Rey Auditory Verbal Learning Test, and to separate list-learning tasks from each other. If testing goes too quickly or takes more time than anticipated, you may need to administer delayed testing in a different order. Document any deviations on the Protocol Deviations Form.

Depression Assessment Visit:

- Hamilton Depression Rating Scale
- Structured Clinical Interview of the DSM-IV (SCID-IV)
- Depression History
- Mini Mental State Exam

If by this point in the screening the participant does not meet criteria for Major Depressive Disorder and is deemed ineligible, the Depression Assessment visit will be stopped.

- Brief Visuospatial Memory Test [Please conduct other assessments that would take AT LEAST 20 AND NO MORE THAN 30 MINUTES before you proceed with the Brief Visuospatial Memory Test Delayed Recall trial. Do not administer the MMSE, the Motor-Free Visual Perception Test-3 or the Benton Judgment of Line Orientation during this time]
- Hopkins Verbal Learning Test
- Controlled Oral Word Association Test
- Penn State Worry Questionnaire
- Perceived Stress Scale
- Generalized Anxiety Disorder-7
- Patient Health Questionnaire-9
- Duke Social Support Index
- Pittsburgh Sleep Quality Index
- Geriatric Suicide Ideation Scale
- Stroop Color Word
- WAIS Digit Span
- BVMT Delayed Recall Trial (20-30 minute delay)
- WAIS Digit Symbol
- Benton Judgment of Line Orientation
- Motor-Free Visual Perception Test-3
- Grip Strength Test
- Grooved Pegboard Test

Baseline ADNI Clinical Visit:

- Geriatric Depression Scale
- ADAS-Cog 13 (with Delayed Word Recall and Number Cancellation)

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- Montreal Cognitive Assessment (MoCA)
- Logical Memory I - [Please conduct other assessments that would take AT LEAST 30 AND NO MORE THAN 40 MINUTES before you proceed with the Logical Memory II assessment (delayed recall). Do not administer the MMSE or CDR during the period of delay; other activities including the depression questionnaire (GDS) and participant demographics are permissible]
- Rey Auditory Verbal Learning Test (Trials 1-6)
- Clock Drawing
- Category Fluency (animals)
- Trails A & B
- Boston Naming Test (30 items)
- Logical Memory II (30-40 minute delay)
- Rey Auditory Verbal Learning Test (30 minute Delay)
- American National Adult Reading Test (ANART)
- Everyday Cognition - Participant Self-Report
- Everyday Cognition - Study Partner Report
- Clinical Dementia Rating Scale (CDR)
- Neuropsychiatric Inventory
- Activities of Daily Living Scale (FAQ)
- Cognitive Change Index (CCI) – Participant
- Cognitive Change Index (CCI) – Study Partner
- Modified Hachinski

Month 30 Depression Follow Up Assessment Visit:

The Month 30 Depression Follow Up Assessment cognitive battery is the same as the initial Depression Assessment with the exception of the Depression History form which has been replaced with the Follow Up Treatment Form. All previous depressive episodes should be recorded at the initial Depression Assessment visit.

- Hamilton Depression Rating Scale
- Structured Clinical Interview of the DSM-IV (SCID-IV)
- Follow Up Treatment Form
- Mini Mental State Exam
- Controlled Oral Word Association Test
- Brief Visuospatial Memory Test [Please conduct other assessments that would take AT LEAST 20 AND NO MORE THAN 30 MINUTES before you proceed with the Brief Visuospatial Memory Test Delayed Recall trial. Do not administer the MMSE, the Motor-Free Visual Perception Test-3 or the Benton Judgment of Line Orientation during this time]
- Hopkins Verbal Learning Test
- Generalized Anxiety Disorder-7
- Patient Health Questionnaire-9

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- Penn State Worry Questionnaire
- Perceived Stress Scale
- Duke Social Support Index
- Pittsburgh Sleep Quality Index
- Geriatric Suicide Ideation Scale
- Stroop Color Word
- WAIS Digit Span
- BVMC Delayed Recall Trial (20-30 minute delay)
- WAIS Digit Symbol
- Benton Judgment of Line Orientation
- Motor-Free Visual Perception Test-3
- Grip Strength Test
- Grooved Pegboard Test

Month 30 Follow Up ADNI Clinic Visit:

The Month 30 Follow Up ADNI Clinic cognitive battery is the same as the initial Baseline Assessment with the exception of ANART which has been excluded.

- Geriatric Depression Scale
- ADAS-Cog 13 (with Delayed Word Recall and Number Cancellation)
- Montreal Cognitive Assessment (MoCA)
- Logical Memory I - [Please conduct other assessments that would take AT LEAST 30 AND NO MORE THAN 40 MINUTES before you proceed with the Logical Memory II assessment (delayed recall). Do not administer the MMSE or CDR during the period of delay; other activities including the depression questionnaire (GDS) and patient demographics are permissible]
- Rey Auditory Verbal Learning Test (Trials 1-6)
- Clock Drawing
- Category Fluency (animals)
- Trails A & B
- Boston Naming Test (30 items)
- Logical Memory II (30-40 minute delay)
- Rey Auditory Verbal Learning Test (30 minute Delay)
- Everyday Cognition - Participant Self-Report
- Everyday Cognition - Study Partner Report
- Clinical Dementia Rating Scale (CDR)
- Neuropsychiatric Inventory
- Activities of Daily Living Scale (FAQ)
- Cognitive Change Index (CCI) – Participant
- Cognitive Change Index (CCI) – Study Partner

Hamilton Depression Rating Scale (HDRS)

Hamilton M. 1960. A rating scale for depression. J Neurol Neurosurg Psychiatry 23: 56–62.

Description

The 17 item Hamilton Depression Rating Scale assesses severity of depressive symptoms over the past week (7 days), with high scores indicating greater severity of depression. The HDRS will be used to assess participant's depression severity at the Depression Assessment visit, 12 month and 24 month interim telephone checks, and the Month 30 Depression Follow Up Assessment. Site staff should administer the HDRS as a direct interview with the participant only, **NOT** the study partner.

Administration

The first question from each item should be asked exactly as written. Often this question will elicit enough information about the severity and frequency of a symptom for you to rate the item with confidence. Follow-up questions are provided, however, for use when further exploration or additional clarification of symptoms is necessary. The specified questions should be asked until you have enough information to rate the item confidently. In some cases you may also have to add your own follow-up questions to obtain necessary information.

Overview: "Now I'm going to ask you some questions about your mood. Some of them may be difficult, but just try your best. When you answer the questions, just think about how you've felt over the past week. If I want you to think outside of the past week, I'll ask you to do so."

Start with Standard Questions

- **Insures uniformity & comprehensiveness**
- **Reiterate and confirm if patient has already discussed**
- **Try to avoid leading questions**

First, start by asking all questions written in bold. Asking bolded questions **increases reliability** between raters and **insures raters ask required questions**. More information is frequently needed in order to rate an item. In this case, **use provided follow up probes, or your own questions** as necessary to elicit further information. If answer to question is known because patient has given information in response to previous question, **reiterate patient's response, ask for confirmation**, and continue. The interview guide starts with open-ended questions which allows for spontaneous answers and then moves to more direct questions. This procedure **avoids leading patients towards specific answers**. For example, do not ask participants if symptom is mild, moderate, or severe without asking follow-up questions to elaborate.

COGNITIVE ASSESSMENT

Use Your Best Judgment

- If unsure, ask more questions
- Don't "rate up" or "rate down"
- If still unsure, make best rating

The general rule is, if unsure, to **ask more questions**. Knowing type of symptoms for each item and anchors for rating points should help guide questioning. Some conventions instruct raters to rate up or rate down when unsure of how to rate an item, for instance, when a symptom falls between two ratings. **Rating up or rating down is not good practice**. The best method is to ask sufficient questions then **use clinical judgment to make best rating**.

Consider Both Frequency and Severity

- **Frequency:** How often in the past week has the participant has the symptom? (For example: 1-3 days a week, 3-5 days a week, 5-7 days a week)
- **Intensity:** What has been the relative intensity of the symptom in the past week? To rate intensity it can be useful for the participant to use a 0-10 scale. Say, "**How severe was (symptom) in the past week? If you were to place this feeling on a scale of 1-10 with 1 being the best you've ever felt and 10 being the worst you've ever felt, where would you place (symptom)?**" Although this may be difficult for some participants, it allows for a reliable intensity rating throughout the HDRS. If the participant expresses difficulty with this say, "**I know it can be hard to give a number to these feelings about (symptom), but please try your best.**" If the participant still cannot place the item on a scale, ask whether the symptom would be considered mild, medium or severe.
- **Duration:** How long during the day do these symptoms last? (For example: some of the day, a good part of the day, or all day.)

For every question be sure to rate frequency, intensity and duration of the item. It is important to consider, on average, **how often** and **how long** a symptom lasts and the intensity of symptoms when they occur. **If the symptom has fluctuated** in intensity during past week, **base rating on average** intensity for past seven days.

Rate Change from Usual Self

- Rate each item based on a change in [symptom] from this week compared to the usual self
- Usual self = before depressed
- If chronically depressed: usual= last period of 2 weeks OK
- Don't consider the "usual self" as low, even when not depressed

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Ask the participant to **compare** how he/she is feeling the **past week with** how they were feeling before their depression began (i.e., **usual self**). It is important to base all ratings on change from usual self. Thus, determine time of onset of depressive symptoms and **use time prior to depression for reference to usual self**. Some participants may have underlying, low-grade **chronic depression** (i.e. dysthymia) that may occur alone or underlie a current major depressive episode. For these participants, **“usual self” is last time they remember not feeling depressed for at least two weeks**. For some participants, **“usual self” may differ from what is typical for the average person**. For example, do not rate an individual who has always had a low sex drive (even when not depressed) as symptomatic unless sex drive became lower with onset of depression.

Rate the Past 7 Days

- **Keep participants focused on past week**
- **Don't compare past week with previous week**
- **Do compare past week with usual self**
- **Don't refer to prior ratings**

Keep the participant focused on past 7 days when answering questions. This is especially important during the initial interview when participants who may have been depressed for some time may talk about symptoms they once had but no longer have. Make sure the participant is **comparing the past 7 days to their usual self, not to the previous week**. For example, a participant may say his/her energy has been better in the past week but when queried further will indicate their energy is still lower than normal. **Do not refer to past HDRS ratings** when scoring the HDRS.

Don't Count Symptoms Clearly Due to Other Causes

- **Don't rate if clearly due to cause other than depression**
- **Use temporal relationship as a clue**
- **When in doubt: default = due to depression**

Count symptom as present if temporal relationship suggests it is likely due to depression. For example, score as positive a person who has trouble sleeping due to external noise (e.g., baby crying) if noise did not disturb sleep before depression. **If in doubt** as to whether symptom is due to depression or some other cause, **rate the symptom as due to depression**. This rule also applies to study medications.

Avoid the "Halo Effect"

- **Rate each item independently**
- **Avoid rating high because other items are high**
- **Avoid rating low because other items are low**

COGNITIVE ASSESSMENT

Rate each item independently. Because patient was rated high on one item (e.g., suicide) does not necessarily mean he/she should be rated high on another item (e.g., depressed mood).

The tendency to rate one item high because another item is high is referred to as “**halo effect**” and should be avoided. Also avoid the tendency to rate one item low **because other items on scale have been rated low.**

Scoring Guide

The total score for the HDRS is calculated by adding up the score for each item. A rating of 19 or above is required for a participant to be considered eligible for the study.

ITEM 1 - Depressed Mood

Evaluates:

- **Sadness**
- **Hopelessness**
- **Helplessness**
- **Crying**
- **Other non-verbal expressions (e.g. facial expression or posture)**

Item 1 evaluates depressed mood. This item measures feelings of **sadness**, as well as feelings of **hopelessness** and **helplessness**. Any of these can indicate depressed mood. Think of these constructs on a continuum, for example, feelings of hopelessness can range from a mild feeling of discouragement to an intractable feeling that nothing will ever get better. Consider both intensity and frequency of feelings when rating this item. The HDRS also describes **crying** as one of several possible non-verbal indicators that can be used to measure depressed mood. Some participants at the more extreme end may feel so depressed they are unable to cry at all. **Other non-verbal** signs such as frowning and slumped posture can also indicate depressed mood.

Note: some participants may not use the word “sad” to describe their mood, but may say they feel “blue”, “down”, “blah” or “numb”. It is not necessary for the participants to use the word “depressed” to describe his mood to be rated positive on this item. Use your clinical judgment. Also note that mood is rated even if it is linked to a real life problem. In other words, it is not necessary for the depressed mood to occur for no apparent reason in order for you to count it as symptomatic.

SCORING FOR ITEM 1: Depressed Mood

Score 0 if the participant does not report depressed mood or only reports normal fluctuations of no clinical significance.

COGNITIVE ASSESSMENT

Score 1 if the participant reports occasional mild symptoms. Sometimes participant will indicate depressed mood only upon questioning, but this is not a necessary condition for a 1. Participants can spontaneously express depressed mood and still score a 1 if the mood is occasional and mild.

Score 2 for clear symptoms that are persistent and mild to moderate in intensity. Non-verbal symptoms may or may not be evident. Persistent, mild depressed mood would rate a 2, unless it is very mild, which would rate a 1, absent other symptoms.

Score 3 for persistent symptoms that are moderate to severe in intensity, for example, intense sadness or pervasive feelings of hopelessness or helplessness. Some non-verbal signs of depression are also necessary (but not sufficient) for a 3.

Score 4 for very severe and intractable symptoms, such as extreme sadness that does not remit or intractable feelings of complete hopelessness or helplessness. A 4 involves very severe symptoms that do not lift at all, even if something good happens. In general, a 4 is reserved for symptoms that would alarm the average, non-professional friend.

ITEM 2 - Work and Activities

Evaluates:

- **Work in and outside the home**
- **Leisure activities**
- **Family and social relationships**
- **Loss of interest**
- **Loss of pleasure**
- **Impairment in functioning**

Item 2 measures three domains: work in and outside of the home, family and social relationships, and leisure activities. Each of these domains is evaluated along three dimensions: loss of interest, loss of pleasure, and impairment in functioning.

SCORING FOR ITEM 2: Work and Activities

Score 0 if the participant has normal interest, pleasure, and functioning.

Score 1 for some reduction in interest or pleasure, but no clear impairment in functioning.

Score 2 for clear reduction in interest or pleasure, or some impairment in functioning.

Score 3 for a *profound* reduction in interest, pleasure or functioning.

COGNITIVE ASSESSMENT

Score 4 when the participant is unable to work at all due to depression, or is unable to function or perform self-care activities without assistance.

Note the following additional conventions for rating item 2 (work and activities):

- When rating a homemaker, consider the ability to do typical routines and home activities, such as caring for children and housekeeping.
- Fatigue or loss of physical energy, while related to impairment in functioning, is not rated in this item (but will be rated in item 13, general somatic symptoms).
- Score 3 for impairment in functioning, only if there is impairment in the participant's primary role functioning. For example, you would not rate a 3 for a person whose ability to concentrate on his golf swing is profoundly impaired, but who is still functioning well at work.
- Note that each of the three domains - interest, pleasure and functioning - may be affected differently. It isn't necessary to have the same level of severity on all three domains in order to obtain the rating.

Important Note: There are three types of insomnia rated on the HDRS separated into three different questions.

1. **Trouble falling asleep (initial insomnia)**
2. **Trouble staying asleep (middle insomnia)**
3. **Waking up earlier than usual (terminal insomnia)**

ITEM 3 - Initial Insomnia

Evaluates:

- **Trouble falling asleep**
- **First determine usual (pre-depression) falling asleep time for comparison.**

Item 3 evaluates the first type of insomnia, trouble falling asleep. As with all items, both frequency and severity determine the rating. Taking **more than half an hour** (30 minutes) to fall asleep is considered the threshold for counting a night as symptomatic. For all three sleep items, **occasional** means two or three nights in the past seven days, while four or more nights in the past seven days means **often** or **"nightly"**.

Guidelines:

- ½ hour is threshold to be symptomatic
- Occasional = 2-3 nights/week
- Often or "nightly" = 4 or more nights/week

NOTE: Before evaluating this item, first determine the usual sleep pattern of the participant prior to becoming depressed. This serves as a reference point for change.

SCORING FOR ITEM 3: Initial/Early Insomnia

Score 0 if the participant has no trouble falling asleep due to depression.

Score 1 for occasional (2-3 nights/week) trouble falling asleep due to depression (more than ½ hour to fall asleep).

Score 2 if often or nightly (4 or nights/week) the participant has trouble falling asleep due to depression (more than ½ hour to fall asleep).

Note: Do not count trouble falling asleep that is clearly due to an external cause unrelated to depression, for example, a neighbor's party or a baby crying. The exception is when patients report that such noise did not bother them before they became depressed. In this case, count the trouble falling asleep as symptomatic.

Other conventions for rating item 3 (initial insomnia) are:

1. Rate initial insomnia even if the participant says he is no longer sleepy at his usual bedtime because he has started napping during the day.
2. Rate initial insomnia even if the participant has pushed back his bedtime after being unable to fall asleep
3. Do not consider sleeping pills when making your rating. In other words, if the patient falls asleep with no difficulty - even with the aid of sleeping pills - rate initial insomnia as absent.

ITEM 4 - Middle Insomnia

This item evaluates

- **Waking up during the night**
- **Trouble staying asleep**

Item 4 evaluates the second type of insomnia, waking up during the night or having trouble staying asleep. The same guidelines are used for all three sleep items:

- ½ hour is threshold to be symptomatic
- Occasional = 2-3 nights/week
- Often or "nightly" = 4 or more nights/week

SCORING FOR ITEM 4: Middle Insomnia

Score 0 if the participant reports no sleep disturbance during the night.

COGNITIVE ASSESSMENT

Score 1 if the participant reports occasional (2-3 nights/week) difficulty with restless and disturbed sleep (more than half hour).

Score 2 if the participant is often or nightly (4-more nights/week) awake during the night (more than half hour) or gets out of bed, except to go to the bathroom.

Note the following additional scoring conventions:

- If a participant wakes up after having been asleep only a few minutes at the beginning of the night, rate this as initial insomnia, not middle insomnia.
- Restlessness, without being awake more than a total of 30 minutes, would not rate higher than a 1 – even if it occurs every night.
- If a participant is awake on and off several times during the night, add up the total time awake during the middle of the night to determine if the half hour threshold is met. For example, if the participant woke up 4 times and for 10 minutes each time (4X10=40), he would have met the half hour threshold for that night.
- Waking up only to use the bathroom is not scored, unless the participant cannot fall back asleep again.
- If a participant wakes up during the middle of the night and doesn't fall back to sleep for the entire night, this would count as both middle insomnia and late insomnia.

ITEM 5 - Terminal (Late) Insomnia

This item evaluates

- **Waking earlier than usual, premature awakening**
- **Frame of reference: last 2 hours before usual wake time**

This item evaluates the third type of insomnia, waking up earlier than usual or premature awakening. Consider only awakening that occurs during the last 2 hours of the night to rate terminal insomnia. All other awakening during the night is rated under middle insomnia. Use the usual waking time (when the participant is not depressed) to determine the appropriate 2-hour interval. For example, if the participant normally wakes up at 8 am, waking between 6 am and 8 am would be rated under terminal insomnia, whereas waking before 6 am would be considered middle insomnia.

SCORING FOR ITEM 5: Terminal (Late) Insomnia

The same conventions are used here as used in all three sleep items:

- ½ hour is threshold to be symptomatic
- Occasional = 2-3 nights/week

COGNITIVE ASSESSMENT

- Often or “nightly” = 4 or more nights/week

NOTE: time awake is cumulative, so if the participant wakes up 4 times in the last two hours of the night for 10 minutes each time, that night would count as symptomatic.

ITEM 6 - Sexual Interest**This item evaluates**

- **Loss of Interest (or pleasure) in sex**

This item does *not* rate amount of sexual activity or performance. Item 6 measures loss of interest in or pleasure from sex, either with a partner or alone. What is rated here is decreased interest in having sex or decreased thoughts about sex - not amount of sexual activity. Also not rated here are problems with sexual performance, as long as interest remains unchanged. For someone who has no available partner, rating may be based on decreased sexual feelings or fantasies. A skilled rater will assess this with hypothetical questions.

SCORING FOR ITEM 6: Sexual Interest

Score 0 if the participant has about as much interest in or pleasure from sex as usual.

Score 1 if there is somewhat less interest or pleasure from sex.

Score 2 if the participant reports a definite or marked loss of interest or pleasure from sex. Note that for some, their baseline level may be less than the average person. Thus, a participant whose pre-morbid level of interest was low would not be counted as symptomatic if there is no further lowering of interest with the onset of the depression.

Note: some participants may avoid their partners for another reason, such as interpersonal conflict, and would not be rated as symptomatic, as long as interest in sex is unchanged from usual. Conversely, a participant who has sex regularly despite reduced interest, for example, to accommodate a partner, would still be rated as symptomatic.

ITEM 7 - Somatic Symptoms, Gastrointestinal (appetite)**Evaluates:**

- **Appetite**
- **Hunger**
- **Desire for food/ Enjoyment of food**

COGNITIVE ASSESSMENT

Item 7 assesses appetite, that is, hunger for, desire for, and enjoyment of food. Other gastrointestinal symptoms, such as indigestion, are not rated here, but should be considered under item 13, somatic anxiety. This item evaluates appetite only, not the amount of food actually eaten. For example, a participant who has no appetite but is still eating as much as usual because he pushes himself to eat would still be rated as symptomatic. Similarly, a participant who is intentionally eating less due to dieting would NOT be counted as symptomatic.

SCORING FOR ITEM 7: Somatic Symptoms, Gastrointestinal (appetite)

Score 0 if the participant's appetite has not changed from usual.

Score 1 if there is some (mild) loss of appetite, or a mild loss of interest in or enjoyment of food.

Score 2 if there is a definite or marked loss of appetite or very little interest or pleasure in eating. A 2 is given if the participant has to force himself to eat; however, a severe loss of appetite should still rate a 2 even if the participant doesn't report having to force himself to eat.

Note: increasing severity on this item is defined by the degree to which the desire to eat is diminished and the degree to which a participant much push himself to eat. Do count as symptomatic if appetite is reduced and the participant then rationalizes reduced appetite as OK because he wanted to lose weight. Do not count as symptomatic a participant whose current depression was associated with increased appetite and who is improving, and thus appetite is decreasing towards their normal, pre-morbid level.

ITEM 8 - Weight Loss

Evaluates:

- **Loss of weight due to depression**

Refer to premorbid (pre-depression) weight for comparison. Don't rate if due solely to non-depression related circumstances. Don't count weight loss following depression related weight gain. Item 8 measures weight loss due to depression. Don't rate as symptomatic weight loss due *solely* to non-depression related causes, such as dieting, the flu or exercise. Occasionally, a patient may be dieting prior to the onset of the depressive episode. Rate only that weight loss that exceeds what could be attributed to dieting. Sometimes patients find they are losing weight and rationalize it, that is, they feel pleased and say they needed to diet anyway because they were overweight. You should still count the weight loss as symptomatic, regardless of the patient's attitude or rationalization. Occasionally, participants will have gained weight with the onset of a depressive episode, and then lose weight when they begin to feel better. Do not count

COGNITIVE ASSESSMENT

this loss as symptomatic, unless it falls below their baseline, premorbid (pre-depressed) weight.

SCORING FOR ITEM 8: Weight Loss

Score 0 if there has been no weight loss or for weight loss due solely to a non-depression related cause.

Score 1 if the participant has *probably* lost weight.

Score 2 if the participant has *definitely* lost weight.

To gauge possible weight loss, you can ask the participant if their clothes are fitting looser.

At the **initial assessment**, rate weight loss since the onset of the illness. Count the participant as symptomatic if his current weight is either probably or definitely less than his premorbid weight. **At follow-up visits**, participants who remain under their premorbid weight would still be rated as symptomatic, even if they have not lost additional weight (assuming they have not begun to gain back weight). If participants were rated positive for weight loss at screening and have begun to gain weight but are still under their premorbid weight, decrease the score in the following manner: a *probable* weight gain in past week would lower the score by one point, for example, a 2 would be lowered to a 1 or a 1 would be lowered to a 0; a *definite* weight gain in the past week would reduce either a 2 or a 1 to a 0. If participants were rated for weight loss at screening with a score of 1 (probable weight loss) and at a follow-up visit definitely weigh less (compared to their usual, premorbid weight), increase the score from 1 to 2. If participants were rated 0 at screening and begin to lose weight during the study, rate as follows: score 1 for probable weight loss in the past week and score 2 for definite weight loss. If follow-up rating is done using actual weight, standardize assessment without shoes.

ITEM 9 - Somatic Symptoms, General

Evaluates:

- **Fatigue**
- **Loss of energy**
- **Tiredness,**
- **Muscular aches and pains**
- **Heaviness in arms or legs**

COGNITIVE ASSESSMENT

Item 9 measures general somatic symptoms. These fall into two groups: the first is feelings of fatigue or loss of energy. Participants may complain of feeling tired or lacking energy. Note that this item rates loss of physical energy as opposed to lack of interest, which is rated in item 2 (work and activities). The second group of symptoms consists of muscular aches and pains, which may be diffuse and difficult to locate. Participants may also complain that their arms or legs feel heavy or weighed down.

SCORING FOR ITEM 9: Somatic Symptoms, General

Score 0 if the participant is not more tired than usual, or does not have muscle aches or heaviness.

Score 1 if the participant reports having somewhat less energy than usual, or mild, occasional muscle aches or heaviness.

Score 2 if the participant reports clear loss of energy, fatigue, tiredness, OR muscle aches or heaviness in limbs. Do not count fatigue or muscle aches due to extra exertion or other identifiable causes unrelated to depression, such as the flu.

ITEM 10 – Guilt

Evaluates:

- **Low self-esteem, self-criticism, self-reproach (mild rating)**
- **Belief one has done something bad or wrong**
- **Accompanied by feelings of regret or shame**

Item 10 measures guilt, the belief that one has done something bad or wrong that is accompanied by feelings of regret or shame. Also counted here, but rated lower, are feelings of low self-esteem, self-criticism and self-reproach.

SCORING FOR ITEM 10: Guilt

Score 0 if the participant has not felt guilty or if feelings of guilt are transient and appropriate to the situation.

Score 1 if the participant reports lowered self-esteem or is more self-critical than usual. Participants who are depressed often are critical of themselves because they are not functioning as well as usual due to their depression. Self-reproach limited to feeling one has let other people down because of their depression would rate a 1.

Score 2 if the participant clearly reports thoughts of irrational or excessive guilt, that is, they believe they have done something bad or wrong. These thoughts are typically associated with feelings of remorse or shame.

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Score 3 if thoughts of guilt are pervasive, persistent or very intense. Frequent or persistent rumination over past misdeeds would rate a 3. Thoughts that one was a bad or evil person, or that the depression is a punishment for bad things they have done would also receive a 3. Note, however, that this is not the same thing as believing their depression is a result of mistakes they have made in their lives, which would not rate a 3.

Score 4 if the participant has hallucinations of guilt. For example he may hear voices telling him that he is a bad person and deserves to be punished.

Note: realistic self-reproach or guilt would not be counted.

ITEM 11 – Suicide

Evaluates:

- **Suicidal ideation (thoughts of suicide)**
- **Suicidal behavior**

SCORING FOR ITEM 11: Suicide

Score 0 if the symptom is not present.

Score 1 if the participant has thoughts that life isn't worth living, but expresses no wish to die. Feeling like life is a burden and they'd like to escape and go away somewhere - without thoughts of suicide or death - would not rate higher than a 1.

Score 2 if the participant wishes he were dead, or says he would not care if he were dead, but has no suicidal thoughts, plans or intent. For example, participants may say it wouldn't bother them if they were in a fatal accident or didn't wake up tomorrow. Frequent thoughts about death or thoughts about their own death in particular are also counted here.

Score 3 if the participant has actual thoughts of suicide or makes a gesture. This score covers thoughts of killing oneself with a wide range of intent, from no clear intention of doing it, to having a specific plan. An example of a gesture is someone who cuts himself superficially at a spot that poses little risk of serious injury and does not expect to die.

Score 4 for an actual attempt at suicide. Note that any attempt *with the expectation of death* is considered a suicide attempt, regardless of whether it is actually lethal.

COGNITIVE ASSESSMENT

ITEM 12 - Psychic Anxiety**Evaluates:**

- **Apprehension**
- **Fear**
- **Worry**
- **Panic**
- **Irritability**
- **Anticipatory anxiety**
- **Non-verbal signs**

Item 12 assesses feelings of apprehension, fear, worry, and panic, as well as irritability. Physical symptoms of anxiety are not rated here, but are rated in item 13, somatic anxiety. Each of these symptoms should be evaluated in terms of frequency, severity, and impact on functioning. For participants with panic attacks, the anticipatory anxiety over having a panic attack is also rated here, as well as worrying about the meaning of the attacks (e.g., going crazy or going to die). Non-verbal signs are also taken into consideration.

SCORING FOR ITEM 12: Psychic Anxiety

Score 0 when there are no symptoms or only clinically insignificant symptoms.

Score 1 for some mild feelings of tension or irritability, or difficulty being able to relax.

Score 2 for moderate feelings of excessive worry. Note that a 2 is given not only for worrying about minor matters, but also for excessive worrying about real problems. Use your clinical judgment to determine if the worry is excessive.

Score 3 for severe or pervasive feelings of worry, or for feelings of dread or panic. For a score of 3, the anxiety needs to be apparent in the participant's demeanor or behavior (although this feature alone is not enough to warrant a 3), and there must be impairment in functioning due to the anxiety.

Score 4 for very severe anxiety, in which the participant is incapacitated and unable to function due to the anxiety.

ITEM 13 - Somatic Anxiety**Evaluates:**

- **Autonomic hyperactivity due to anxiety**

COGNITIVE ASSESSMENT

- **Gastrointestinal symptoms:** gas, indigestion, diarrhea, constipation, stomach cramps, belching
- **Cardiovascular symptoms:** heart pounding or racing
- **Respiratory symptoms:** sighing, hyperventilation, shortness of breath
- **Other symptoms:** headaches, urinary frequency, sweating, light headedness, dry mouth

Item 13 measures somatic (physical) symptoms of anxiety resulting from autonomic arousal. Symptoms fall under one of the following body systems: gastrointestinal, cardiovascular, respiratory, and other.

SCORING FOR ITEM 13: Somatic Anxiety

Note: to rate this item, consider the overall impact of all the symptoms, based on the following factors: how many symptoms are present, how often the symptom or symptoms occur, how bad it is on average, how much distress it causes, and, the degree of impairment the symptoms cause. For example, give the same rating of 2 for a severe symptom that occurs only occasionally as well as for several symptoms that are only present to a moderate degree but occur frequently.

Score 0 if symptoms are absent, insignificant, or clearly due to a cause other than anxiety, such as a concurrent medical condition or medication. Remember, there must be clear and convincing evidence the symptom is due to another cause in order to discount it.

Score 1 for mild symptoms associated with mild distress but no impairment in functioning.

Score 2 when there is moderate distress associated with the symptom. There may or may not be some impairment in functioning due to the symptom.

Score 3 for severe distress. For a 3 there must be significant impairment in functioning due to the somatic symptoms.

Score 4 for very severe symptoms that incapacitate the individual.

ITEM 14 – Hypochondriasis

This item evaluates

- **Preoccupation with having a general medical illness that is not present**
- **Exaggerated or unrealistic concerns about one's body or physical health**

COGNITIVE ASSESSMENT

Item 14 measures unjustified preoccupation with having a general medical illness. It may also include exaggerated or unrealistic concerns about one's body or physical health. The degree to which a participant is concerned about and believes he has a medical illness *that is not present*, forms the basis for rating this item. If a somatic symptom has been rated as present in somatic anxiety (item 13), only rate here the participant's worry about the meaning of the symptom or his preoccupation with it.

SCORING FOR ITEM 14: Hypochondriasis

Score 0 if no symptoms are present.

Score 1 if the participant is preoccupied with his bodily functions or physical sensations, but has no firm belief he has a specific illness.

Score 2 if the participant has excessive or unrealistic worries about having a specific illness. For example, he may worry that indigestion means he has stomach cancer.

Score 3 if the participant has a strong conviction that he actually has an illness and continues to believe this despite medical reassurance. For example, the person who continues to strongly believe he has stomach cancer in spite of numerous medical tests to the contrary.

Score 4 for somatic delusions or hallucinations, for example, the person feels insects eating away at his cancer ridden and rotting stomach.

Note: do not rate culturally normative concerns, such as the desire to look thin or to lose weight, unless tied to thoughts of having an illness. Concerns about depressive symptoms, such as being tired or not sleeping, are rated only if the patient worries that these suggest a medical disease is present.

ITEM 15 – Insight

Evaluates:

- **Severe pathological denial of illness when clearly symptomatic**
- **Rating is based on observation**
- **Do not rate if due to cultural norms**
- **Only active denial is symptomatic**

Item 15 measures the presence of severe denial of being depressed in participants who are clearly ill. As such, it can only be rated as positive in participants who are clearly symptomatic. Always rate a 0 for participants who are not clearly depressed. This item is scored based on information gathered in the course of prior questioning. This symptom

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is not often positive in outpatients and should be rated conservatively. Ordinarily, rate a 0 in outpatients who consent to participate in depression trials because of the insight that consent suggests. Do not rate loss of insight in participants who acknowledge improvement as symptoms decrease.

SCORING FOR ITEM 15: Insight

Score 0 if the participant acknowledges being depressed and ill OR if the patient is not symptomatic.

Score 1 if the participant acknowledges their symptoms, but attributes them to a cause other than depression.

Score 2 if the participant is in complete denial of having any illness. A rating of 2 is unusual in outpatients.

Note: often participants know something is wrong, but they are coming for help for the first time and thus may not know for sure what depression is. In such cases they may be unsure if their symptoms are a result of being depressed or due to something else. Score 0 if participants allow for the possibility that they may be depressed

ITEM 16 - Psychomotor Agitation

Evaluates:

- **Agitation in motor behavior**
- **Agitation in speech**

Item 16 assesses agitation in motor behavior and speech. The rating is based on observation during the interview.

SCORING FOR ITEM 16: Psychomotor Agitation

Score 0 if movements are within the normal range of behavior. Don't automatically score a 1 for a participant who is only somewhat fidgety, like the average, non-depressed person would be when discussing personal information with a relative stranger.

Score 1 if there is slight agitation or mild restlessness, seen in frequent change of position in seat, foot tapping, or playing with hair, hands, or clothes.

Score 2 if there is moderate to marked restlessness or agitation, manifested, for example, by hand wringing, more persistent restlessness, excessive scratching or picking.

Score 3 if the participant cannot sit still at all for even a short period of time, or cannot remain seated. This rating is unusual in outpatients.

A Score of 4 is rare, and given when the interview cannot be conducted because of extreme agitation, manifested by pulling off clothes, tearing out hair, or extreme and constant pacing.

Note: the Hamilton states that occasionally it is possible for a participant to be rated on both agitation and retardation when both scores are a 1. Scoring symptomatic on both agitation and retardation is rare for scores higher than a 1.

ITEM 17 - Psychomotor Retardation

Evaluates:

- **Slowed movements**
- **Slowed speech**

Item 17 assesses retardation in movement and speech. The rating is based on observation during the interview.

SCORING FOR ITEM 17: Psychomotor Retardation

Score 0 if the participant speaks and moves without clear slowness.

Score 1 when movement or rate of speech is slightly reduced.

Score 2 when rate of speech is clearly reduced and there are obvious pauses.

Score 3 when the pauses are so long or speech so slowed that the interview is very difficult to conduct (it is unusual to have this level of severity in outpatient trials).

Score 4 when the interview cannot be completed because the participant is unresponsive. Obviously, this rating could not be obtained in an outpatient trial.

Structured Clinical Interview of the DSM-IV

First M, Spitzer RL, Gibbon M, et al. 1997. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Clinician Version. American Psychiatric Publishing: Arlington, VA.

Description

The Structured Clinical Interview for DSM-IV Axis 1 Disorders (SCID 1) is a semi-structured interview diagnostic tool. The SCID is commonly used among clinicians, researchers, and health care professionals working in the psychiatric field in an attempt to diagnose major DSM-IV Axis 1 disorders. Because the SCID is able to be used in numerous settings, there are several different versions, each with their own slight modifications tailored to the needs of the interviewer. Particular to the ADNI Depression Project, this refers to the research version (SCID-R). The SCID is an especially unique diagnostic tool because it includes an overview section which allows the interviewer to get a general sense of the presence or absence of particular DSM-IV disorders. This allows the interviewer to easily navigate through each module, skip through irrelevant sections, and collect appropriate information during the interview.

Administration

When administering the SCID, the interviewer begins at the overview section. Here, the interviewer is able to get a sense of the underlying problem that the subject is experiencing as well as any past episodes of psychopathology. By the end of the overview section, the interviewer should have gathered enough information to formulate a tentative differential diagnosis. After, the interviewer then moves on to relevant modules highlighted from the overview. These modules include: mood episodes, psychotic symptoms, psychotic disorders, mood disorders, substance use disorders, anxiety disorders, somatoform disorders, eating disorders, adjustment disorder, and an optional module. Typically, the average time to administer the SCID takes 60-90 minutes depending on the complexity of the subject's psychiatric history.

Throughout each module, the Interviewer must ask the questions verbatim (excluding questions that state to use one's own words), record and code the subject's responses accordingly. The interviewer must code the response as either 1 (absent or false), 2 (subthreshold), 3 (threshold), or "?" (inadequate information). When coding a response as 1, the interviewer has determined that the symptom described in the criterion is clearly absent or false. When coding a response as 2, the interviewer has determined that the threshold for the criterion is almost, but not quite, met. When coding a response as 3, the interviewer has determined that the threshold for the criterion is met and is true. Lastly, when coding a response as "?", the interviewer has determined that there is insufficient information for a definitive diagnosis. The interviewer is encouraged to ask the subject to provide specific details of thoughts, feelings and behaviors in order to increase the validity of the criterion rating. This information should be recorded on the SCID in order to document the evidence used to justify the interviewer's rating.

COGNITIVE ASSESSMENT

Major Depressive Disorder

Classified as a mood disorder in the DSM-IV, Major Depressive Disorder (MDD) is characterized by a period of at least two weeks in which an individual experiences symptoms such as depressed mood, loss of interest/pleasure in activities, significant weight loss/gain, insomnia or hypersomnia, psychomotor agitation or retardation that is observable by others, fatigue or loss of energy, feelings of worthlessness or excessive/inappropriate guilt, diminished ability to think or concentrate, and recurrent thoughts of death or suicidal ideation. To meet criteria for MDD, an individual must have at least 5 of the symptoms listed above, all of which have been present during the same 2-week period and represent atypical behavior or functioning. Of the 5 symptoms, the individual must primarily experience depressed mood and/or significant loss of interest/pleasure in activities to qualify for MDD. Furthermore, the symptoms must cause clinically significant distress or impairment in functioning and cannot be due to the direct physiological effects of a substance or general medical condition. Lastly, the symptoms must remain separate of Bereavement (the loss of a loved one). When assessing the severity of MDD, it is imperative to account for the frequency and intensity of each symptom.

If the participant meets criteria for a Major Depressive Disorder, fill out the provided treatment form attached to the SCID to gather more detailed information on the current episode.

Scoring

Once the Interviewer has administered the SCID, he/she then records the diagnoses on a summary score sheet. The score sheet includes: ratings of lifetime and current prevalence, certain subtypes and specifiers, an indication of the principal diagnosis, as well as ratings of psychosocial/environmental problems and an assessment of the subject's functionality. After everything has been administered, completed, scored, and assessed, the interviewer should have a clear idea regarding the subject's underlying diagnosis.

The SCID User's Manual including more detailed instructions on how to reliably administer the SCID will be provided in the document repository.

Brief Visuospatial Memory Test

Benedict RH. 1997. *Brief Visuospatial Memory Test-Revised*. Psychological Assessment Resources, Inc.: Lutz.

Description

The Brief Visuospatial Memory Test (BVMT) is an assessment of visuospatial processing and visual memory (right hippocampus and frontal lobe) and measures the two streams of information (what and where) involved in visual processing. Form 1 of the BVMT will be administered at the Depression Assessment visit and Form 2 will be used for the Month 30 Depression Follow Up Visit.

After the timer has been set for the delayed recall trial engage the participant with predominately verbal tasks.

Administration

Learning Trial 1

First say, **“I will show you a sheet that has six figures on it. I want you to study the figures so that you can remember as many of them as possible. You will have just 10 seconds to study the entire display. I will present the figures here** (place T-1 sheet and pencil in front of the examinee). **After I take the display away, try to draw each figure exactly as it appeared and in its correct location on the page.”**

Open the stimulus binder to the appropriate form and place it face down in front of the participant. When the participant is ready, turn over the stimulus form and expose for a full 10 seconds. Do not begin timing until sure that the participant has begun scanning the stimulus.

At the end of the 10-second period, remove stimulus and say, **“Now draw as many of the figures as you can in the correct location on this page.”**

The participant is permitted as much time as necessary for the task. When the participant has indicated they have finished, remove response sheet T-1. Place response form for trial 2 (T-2) in front of the participant.

Learning Trial 2

With the T-2 response sheet in front of the participant, say **“Now I would like to see whether you can remember more of the figures if you have another chance. I will present the display again for 10 seconds. Try to remember as many of the figures as you can this time, including the ones you remembered on your last attempt. Try to draw each figure precisely and in its correct location.”**

When the participant has indicated they have finished, remove response sheet T-2 and place the response form for trial 3 (T-3) in front of the participant.

COGNITIVE ASSESSMENT

Learning Trial 3

With the T-3 response sheet in front of the participant, say **“Now I would like to see whether you could remember more of the figures if you have another chance. I will present the display again for 10 seconds. Try to remember as many of the figures as you can this time, including the ones you remembered on your last attempt. Try to draw each figure precisely and in its correct location.”**

The participant is permitted as much time as necessary for the task. When the participant has indicated they have finished, remove response sheet T-3 and say, **“Try not to forget the display because I may ask you to remember the figures later.”**

Prompts for Trials 1-3: Use the following prompts if the participant seems to be struggling to complete the task:

- If the participant is unsure, you should advise them, **“Just give it your best guess.”**
- If the subject is drawing the figures too quickly/sloppily or trying to rush through their drawings, remind them, **“Remember, try to draw the figures as accurately as possible.”**

Set timer for 25 minutes and administer delayed recall trial 20-25 minutes after trial 3.

Delayed Recall Trial

“Earlier I showed you some figures. I want to see how many of the figures you can remember now. Remember, try to draw them accurately and do the best you can.”

Place the delayed recall response sheet (DR) in front of the participant. The participant is permitted as much time as necessary for the task. When the participant has indicated they have finished, remove response sheet DR.

Prompts:

- If the participant has been struggling during the assessment, say **“I know it sounds difficult, but try to draw as many of the figures as you can in their correct location on the page.”**

COGNITIVE ASSESSMENT

Scoring**General Guidelines:**

- **Award 2 points** for each figure that is both accurately drawn and correctly located on the response sheet.
- **Award 1 point** for each figure that is either correctly located but not accurately drawn (but still recognizable as a target figure) OR that is accurately drawn but not correctly located.
- **Award 0 points** when drawings are missed or when drawing doesn't resemble any of the target figures.
- If a figure is drawn twice in the same trial, only one of the two drawings should be selected as representative of target figure
- Slight inaccuracies (crooked lines and minor distortions) should be ignored
- Award full credit for drawings that are borderline between full and partial credit

Scoring the accuracy of the drawing:

1. **Award 1 point** if the drawing includes all essential details of the target
2. **Award 1 point** if drawing has only minor distortions such as:
 - a. Lines that aren't completely straight
 - b. Small gaps between intersecting lines
 - c. Drawings that are rotated 10 degrees or less
 - d. Minor distortions in the overall size of the figure
 - e. Double lines due to sketching
3. **Award 0 Points** if drawings have intrusions (extraneous lines)



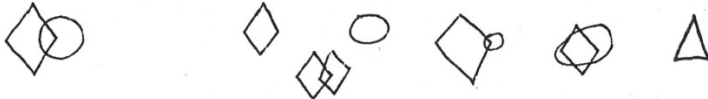
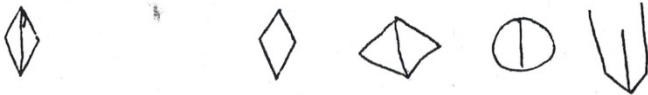


Mild distortions that reflect poor motor coordination should be graded leniently

Scoring the placement of the drawing:

1. **Award 1 point** for drawings that are inaccurate but recognizable as a target figure (share at least one common element with the target feature)
2. **Award 1 point** for correct location if most or all of the reproduction fits into the proper space
3. **Award 0 points** if most or all of the drawing does not fall inside the proper space
4. Score the locations of all recognizable drawings for placement, regardless of whether the drawings are accurate.
5. Consider not only the absolute placement of the drawing to the response page, but also the relative position of the drawings to the other figures
 - a. Sometimes it's beneficial to determine the perimeter of the entire response and then divide it into 6 equal sections.




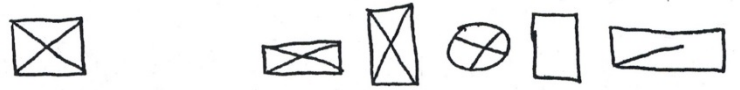

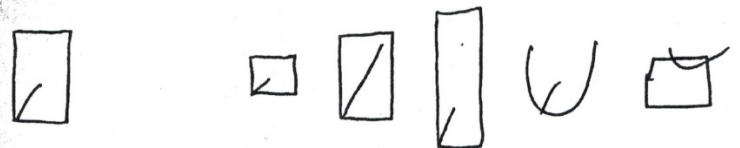
Scoring Guide:

Form 1, Figures A-F

<p>Form 1, Figure A</p> <p>Full Credit Criteria: The vertical lines should be longer than the angled lines. The base horizontal line and the vertical lines should be approximately the same length.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 1, Figure B</p> <p>Full Credit Criteria: The upper left angle should be approximately 90°. The length of the vertical line should be greater than or equal to the length of the horizontal line.</p> <p>Full Credit Example Partial Credit Examples</p> 
<p>Form 1, Figure C</p> <p>Full Credit Criteria: The diamond and circle should overlap. The two figures should be approximately the same size, with neither figure greater than twice the size of the other. The height and width of the circle should be approximately equal.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 1, Figure D</p> <p>Full Credit Criteria: The vertical line should bisect the diamond. The height of the figure should be greater than the width. The left and right angles of the diamond should be approximately positioned at the midpoint of the height of the figure.</p> <p>Full Credit Example Partial Credit Examples</p> 
<p>Form 1, Figure E</p> <p>Full Credit Criteria: The height of the figure should be greater than the width. The small rectangle in the lower left corner of the figure should cover less than 1/4 the area of the larger rectangle.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 1, Figure F</p> <p>Full Credit Criteria: The length of the vertical lines should be greater than or equal to the length of the angled lines. The interior line that projects from the lower left corner of the figure should span between 1/4 and 3/4 of the width of the figure.</p> <p>Full Credit Example Partial Credit Examples</p> 

Scoring Guide:

Form 2, Figures A-F

<p>Form 2, Figure A</p> <p>Full Credit Criteria: All sides of the triangle should be of equal length. The horizontal line (base of the triangle) is at the top of the figure, whereas the apex of the triangle is at the bottom.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 2, Figure B</p> <p>Full Credit Criteria: The length of the right vertical line should be greater than $\frac{1}{2}$ the length of the left vertical line. The length of the left vertical line should be greater than the length of the base of the figure. The length of the top horizontal line should be between $\frac{1}{3}$ and $\frac{2}{3}$ the length of the base.</p> <p>Full Credit Example Partial Credit Examples</p> 
<p>Form 2, Figure C</p> <p>Full Credit Criteria: The triangles should overlap at the bottom right and top left corners. The triangles should be approximately equal in size, length of line segments, and magnitude of angles. Neither figure should be greater than twice the size of the other.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 2, Figure D</p> <p>Full Credit Criteria: The interior lines of the square should connect to the four corners of the square and should bisect each other to form a 90° angle. The height of the figure should be within $\frac{2}{3}$ and $1\frac{1}{3}$ of the width.</p> <p>Full Credit Example Partial Credit Examples</p> 
<p>Form 2, Figure E</p> <p>Full Credit Criteria: The height of the circle should be approximately equal to the width. The interior lines that project from top and right points on the perimeter of the circle should intersect and form a 90° angle.</p> <p>Full Credit Example Partial Credit Examples</p> 	<p>Form 2, Figure F</p> <p>Full Credit Criteria: The height of the figure should be greater than the width. The interior line that projects from the lower left corner of the rectangle should span between $\frac{1}{4}$ and $\frac{3}{4}$ of the width of the figure.</p> <p>Full Credit Example Partial Credit Examples</p> 

COGNITIVE ASSESSMENT

Generalized Anxiety Disorder-7 (GAD-7)

Spitzer RL, Kroenke K, Williams JBW, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006; 166:1092-97.

Description

The GAD-7 is a brief self-reported questionnaire assessing the participant's severity of anxiety. The 7 items included in the GAD-7 measure severity of various signs of Generalized Anxiety Disorder on a 4 point scale. Assessment is indicated by the total score, which is made up by adding together the scores of all 7 items.

When a participant is unwilling or unable to come to the psychiatry site for their Month 30 Follow Up Assessment, the **GAD-7** should be mailed to the participant prior to the scheduled telephone visit. The participant should then mail their completed questionnaires back to the site for data entry.

- Check all mailed forms before their telephone visit to ensure they are completed fully and if necessary, ask the participant to complete the form over the phone.
- If the reading level of the participant is low, you may read them the items out loud and record their ratings.

Instructions

Ask the participant to rate their feelings of anxiety on the response form provided based on their past two weeks.

Ratings are reflected on a four-point scale:

0 = Not at all

1 = Several Days

2 = More than half the days

3 = Nearly every day

Scoring

The GAD-7 score is calculated by assigning scores of 0, 1, 2, and 3 to the responses categorized above and adding together the scores for all 7 questions. Scores of 5, 10, and 15 are taken as the cut off points for mild, moderate, and severe anxiety.

You will not need to calculate a total score, as the eCRF will auto calculate the total score for this assessment.

COGNITIVE ASSESSMENT

Patient Health Questionnaire-9

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an education grant from Pfizer. No permission required to reproduce, translate, display, or distribute.

Description

The PHQ-9 is a nine symptom checklist which rates issues such as mood, worth, concentration, and suicide ideation based on the frequency of which they occur. The PHQ-9 is a specific tool to rate depression.

When a participant is unwilling or unable to come to the psychiatry site for their Month 30 Follow Up Assessment, the **PHQ-9** should be mailed to the participant prior to the scheduled telephone visit. The participant should then mail their completed questionnaires back to the site for data entry.

- Check all mailed forms before their telephone visit to ensure they are completed fully and if necessary, ask the participant to complete the form over the phone.
- If the reading level of the participant is low, you may read them the items out loud and record their ratings.

Instructions

Ask the participant to rate their feelings of depression on the response form provided based on their past two weeks.

Ratings are reflected on a four-point scale:

0 = Not at all

1 = Several Days

2 = More than half the days

3 = Nearly every day

Scoring

The PHQ-9 score is calculated by assigning scores of 0, 1, 2, and 3 to the responses categorized above and adding together the scores for the first questions with the score for the second question.

Major Depressive Syndrome is suggested if:

- Of the 9 items, 5 or more are circled as at least “More than half the days”
- Either item 1a or 1b is positive, that is, at least “More than half the days”

Minor Depressive Syndrome is suggested if:

- Of the 9 items, b, c, or d are circled as at least “More than half the days”
- Either item 1a or 1b is positive, that is, at least “More than half the days”

You will not need to calculate a total score, as the eCRF will auto calculate the total score for this assessment.

COGNITIVE ASSESSMENT

Duke Social Support Index (DSSI)

George, L. K., Blazer, D. G., Hughes, D. C., & Fowler, N. (1989). Social support and the outcome of major depression. *Br J Psychiatry*, 154, 478-485.

Description

The Duke Social Support Index is used to measure multiple dimensions of social support in the elderly. Both size of social network and subjective social support have shown to be significant predictors of depression symptoms with subjective social support being most strongly associated with major depression. The Duke Social Support Index is a self-report, consisting of 25 questions for the participant to answer.

When a participant is unwilling or unable to come to the psychiatry site for their Month 30 Follow Up Assessment, the **DSSI** should be mailed to the participant prior to the scheduled telephone visit. The participant should then mail their completed questionnaires back to the site for data entry.

- Check all mailed forms before their telephone visit to ensure they are completed fully and if necessary, ask the participant to complete the form over the phone.
- If the reading level of the participant is low, you may read them the items out loud and record their ratings.

Scoring

No scoring is necessary for this form.

COGNITIVE ASSESSMENT

Stroop Color Word

Golden C, Freshwater SM. 2002. Stroop Color and Word Test. Stoelting: Wood Dale.

Description

The oral version of the Stroop Color Word is a motor free measure of executive function, information processing speed, set-shifting/perseveration, and impulsivity.

Word Stimulus Trial

First show the participant the stimulus page with the names of colors written in black in. Say, **“This is a test of how fast you can read the words on this page. When I tell you to start, you are to read down each of the columns starting here** (point to the top first column) **continuing down the page** (demonstrate), **and then beginning with the next column** (point), **and so on. If you get to the end of the page before I say stop, begin again here** (point to the top first column) **and continue down.**

“If you make a mistake, I will say ‘No’. Correct yourself, and continue without stopping. Read out loud as quickly as you can, but as accurately as you can. Do not stop reading until I say ‘Stop’.”

Paraphrase: **“So the object is to do it as quickly as you can, but with as few errors as possible.”**

Do not allow the participant to lift the paper off the table and do not let the participant cover part of the word with their hand/pen. **Time for 45 seconds.**

Colored XXXX Stimulus

Show the participant the second stimulus page with XXXX written in different colors of ink. Say, **“This one is a test of how fast you can name the colors on the page. When I tell you to start, begin here** (point to beginning of first row), **and go down the column, and so on** (demonstrate). **Read out loud as quickly as you can, but as accurately as you can.”**

Before starting the trial go through an example of each color on the bottom of the page to ensure they can distinguish the colors correctly. Say, **“So if this was the first item** (point to the last item in the first column) **what would you say?”** (Repeat for all three colors)

Paraphrase: **“So the object is to name the colors on the page as quickly as you can, but with as few errors as possible.”**

Do not allow the participant to lift the paper off the table and do not let the participant cover part of the word with their hand/pen. **Time for 45 seconds.**

COGNITIVE ASSESSMENT

Color Word Trial

Show the participant the last stimulus page with the names of colors in different colors of ink. Say, **“This page is like the page you just finished. I want you to name the color of the ink the words are printed in, ignoring the actual word that is printed. For example, if this was the first item (point to the last item on the list), what would you say?”**

If correct, point to the second to last item, **“What about this item?”** (wait for response) **Good.”**

If incorrect, say **“No, that’s the word spelled there. I want you to say the color of the ink the word is printed in. Try not to read the word.”** If correct, proceed; if incorrect, repeat as many times as necessary until the subject understands or it becomes clear that it is impossible to continue.

Do not allow the participant to lift the paper off the table and do not let the participant cover part of the word with their hand/pen. **Time for 45 seconds.**

Scoring

Record the participant’s responses, both correct and incorrect. If the participant initially answers incorrectly and then corrects themselves, mark as SC (self-correct) and give them the point.

Record the total correct and the total errors at the bottom of each response sheet. Scaled Scores for the Stoop Color Word test will be available in the scoring manual located in the document repository.

COGNITIVE ASSESSMENT

WAIS-III Digit Span

Wechsler D. 1997. Wechsler Memory Scale- Third Edition, Administration and Scoring Manual. The Psychological Corporation: San Antonio.

Description

Performance on the Digit Span task requires the participant to access working memory, attention and concentration to successfully encode, recall and sequence information. Although both tasks may be relatively difficult for the participant, the Digit Backward trial will require greater mental effort.

Digit Forward

First say, **“Now we’re going to try something a little different. I want you to listen carefully and when I finish, I would like you to repeat the numbers back to me exactly in the order they were said. Let’s try one as an example.”**

Example	Response
2-4	(2-4)

Wait for the participant to respond. If correct say, **“Good, we are going to start the testing trial now. Before we start do you have any questions?”** If incorrect, explain the instructions once more before beginning the trial.

For **BOTH** Digit Forward and Digit Backward trials read each digit at the rate of one per second and record the participant’s response. Try not to use any inflection in your voice.

Digit Backward

After the Digit Forward trial is completed, continue on to the Digit Backward trial. Say, **“Now I’m going to say a series of numbers. Again I want you to listen carefully except this time I’d like you to repeat the numbers to me backwards. Let’s try one as an example.”**

Example	Response
8-6	(6-8)

Wait for the participant to respond. If correct, say **“Good, we are going to start the testing trial now. Before we start do you have any questions?”** If incorrect, explain the instructions once more before beginning the trial.

Discontinue Rule: Stop administration when examinee obtains a score of 0 on BOTH trials of any item. Administer Digit Backwards even if examinee scores 0 on Digit Forward.

COGNITIVE ASSESSMENT

Prompts

Prompting may be necessary for the participant to continue with both trials. If the participant seems to be struggling use the following prompts:

- If the participant refuses to do an item or discontinues an item, say **“Just try once more. See if you can do it.”**, **“Try it just a little longer.”**, or **“Just give it your best guess.”**
- If the participant asks for help, say **“I want to see how well you can do it by yourself.”**

Scoring

The maximum score is found by adding the sum of correct Digit Forward items and correct Digit Backward items. To find the scaled score and z-score for the WAIS-III Digit Span test use the scoring manual located in the document repository.

COGNITIVE ASSESSMENT

WAIS Digit Symbol

Wechsler D. 1997. Wechsler Memory Scale- Third Edition, Administration and Scoring Manual. The Psychological Corporation: San Antonio.

Description

For the WAIS Digit Symbol subtest, the participant copies symbols that are paired with numbers. Using a key, the participant draws each symbol under the corresponding number. The participants score is determined by the number of symbols correctly drawn within the 120 second time limit.

Before administering this test, make sure a smooth drawing surface has been provided. If the table has a rough surface, the record form should be placed on a clipboard, a piece of cardboard, or another flat surface.

Administration

To introduce the subtest, say **“In this section, I’m going to ask you to copy some symbols.”**

Turn to the Digit Symbol stimulus sheet in the record form. Make sure only Digit Symbol is showing and place it in front of the participant. Hand him/her a pencil without an eraser, point to the key above the test items, and say **“Look at these boxes. Notice that each has a number in the upper part and a special mark in the lower part. Each number has its own mark.”**

Next point to 1 and its mark in the key and point to the 2 and its corresponding mark. Then point to the seven squares located to the left of the heavy black line and say **“Now look down here where the squares have numbers in the top part but the squares at the bottom are empty. In each of the empty squares, put the mark that should go there. Like this”** (point to the first Sample Item, then point back to the key to show its corresponding mark) **“Here is a 2; the 2 has a mark. So I put it in this empty square, like this”** (write in the symbol).

Point to the second Sample Item and say, **“Here is a 1; the 1 has a mark** (point to the second Sample Item, then to the mark below the 1 in the key), **so I put it in this square”** (write in the symbol).

Point to the third Sample Item and say, **“This number is a 3; the 3 has this mark** (point to the third square and to the mark below the 3 key). **So I put it in the square “**(write in the symbol).

After marking the first three Sample Items, say **“Now you fill in the squares up to this heavy line.”**

COGNITIVE ASSESSMENT

If the participant makes an error on any of the Sample Items, correct the error immediately and review the use of the key. Continue to provide help if needed. Do not proceed with the subtest until the participant clearly understands the task.

When the participant completes a Sample Item correctly, offer encouragement by saying **“Yes”** or **“Right”**. When all the Sample Items have been completed, say **“Now you know how to do them. When I tell you to start, you do the rest of them.”**

Point to the first square to the right of the heavy line and say **“Begin here and fill in as many squares as you can one after the other without skipping any. Keep working until I tell you to stop. Work as quickly as you can without making any mistakes.”**

Sweep across the first row with your finger and say **“When you finish this line, go on to this one.”** Point to the first square in the second row. Then point to the heavy black line and say **“Go ahead.”**

Provide no further assistance except to remind the participant to continue until instructed to stop.

Begin timing for 120 seconds. At the end of the 120 seconds say **“Stop.”**

Prompts

- If a participant asks what they should do if they make a mistake, encourage them to continue to work as fast as they can. However, do not discourage participants from making spontaneous corrections unless they do so repeatedly and it impedes their performance.
- If, after completing a row, a participant tries to complete the next row in reverse order, remind them to start at the beginning of the row and not to skip any.
- If the participant omits an item or starts to do only one type (e.g., only the 1's), say **“Do them in order. Don't skip any.”**
- Point to the first item omitted and say **“Do this one next.”**

Scoring

Record 1 point for each correctly drawn symbol completed within the 120-second time limit. **Responses to the seven Sample Items are NOT included in the participant's score.** Do not give credit for items completed out of sequence.

A response is scored as correct if it is clearly identifiable as the keyed symbol, even if it is drawn imperfectly or if it is a spontaneous correction of an incorrect symbol.

Motor-Free Visual Perception Test-3

Colarusso RP, Hammill DD. 2005. Motor-Free Visual Perception Test. Academic Therapy Publications: Novato.

Administration

This task is designed to assess overall visual perceptual abilities including; spatial relationships, visual discrimination, figure-ground, visual closure, and visual memory. The participant is asked to identify the correct answer from among four alternatives for each item.

Administer the example items when you come to them, which are designed to introduce the instructions for that section of the test. Be sure to tell the examinee that a specific item is an “example” item. Age 11 and older start from item 14; administer items 14-65.

Instructions for each individual item will be available on the stimulus palate.

Test Items 14-21

Example: Each item is presented on two pages. Show the first page “a” (the stimulus item) and say:	“I’m going to show you a shape and then you’ll find it on the next page. Look at this one...”
Present this page for 5 seconds. Now turn the page to “b” showing the four answer choices. Say:	“Now find it here”

If the participant does not answer the example item correctly explain what the error was by pointing to the part of the plate that was incorrectly interpreted. Then go on to the second example if one is provided for that section. Be sure the participant understands the task being asked of them before proceeding with the rest of the test. If more practice is needed go back to the first example for that set of items and proceed with the items only when the examinee fully understands the task.

For items 14-21 continue with instruction, Present the item for 5 seconds and say:	“Look at this one”
Turn the page to “b” showing the four answer choices. Then, say:	“Now find it here”

If the participant says that he/she doesn’t know the answer, encourage the participant to respond by making his/her best guess. If the participant refuses to respond, mark the item incorrect and move on.

Do not give feedback during the test as to the correctness of each answer. Mark all item responses. Do not comment on the correctness of items either during or after test administration. If the participant inquired about their performance, respond with either **“good”** or **“OK”** but do not give any indication as to whether the answer is right or wrong.

COGNITIVE ASSESSMENT

Test Items 22-34

<i>Example:</i> Point to the figures on the bottom and say: (then point to the top figure)	“If we finished drawing these figures and didn’t move any of the lines, which one would look <i>just like</i> the one on top?”
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Repeat For items 22-34, presenting each item to the participant.

Test items 35-45

<i>Example:</i> Point to the figures and say:	“Which one of these is different from the others? It could be turned around or a part of it could be different.”
For items 35-45, present item and say:	“Which one of these is different from the others?”

Repeat For items 35-45, presenting each item to the participant.

Test items 46-50

<i>Example (1):</i> Point to the bottom row of figures and say:	“All of these are the same figure; three have just been turned so that their heads are in different places but one has been flipped over – like a pancake – so that it faces the opposite direction from the others.
You may want to use your hands to mimic lifting something up off the page, flipping it over and then back onto the page, say:	“Which one has been flipped over and can’t be turned to face the same direction as the others?”
If the participant can’t see a difference between the figures, say:	“Three of the ducks were turned so that their heads are in different positions; and if all were turned more to put them back on their feet, three (B, C, and D) would face toward <i>the right</i>. Only this duck (choice A), if it’s put back on its feet, faces <i>left</i>. It can’t just be turned to face the right...it has to be flipped over like a pancake to face the same direction as the others. Now let’s try another...”

<i>Example (2):</i> Point to the bottom row of figures and say:	“All of these are the same figure with a pointy “tail” at one end; three have been turned so that the pointy “tails” are in different places, but one has also been flipped over – like a pancake – so that the “tail” points in the opposite direction from the others.”
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COGNITIVE ASSESSMENT

You may want to use your hands to mimic lifting something up off the page, flipping it over and then back onto the page, say:	“Which one has been flipped over and can’t be turned to face the same direction as the others?”
If the participant can’t see a difference between the figures, say:	“Figures A, B, and D can be turned more so that the pointy “tails” could all point in the same direction. Figure C can’t just be <i>turned</i> to point in the same direction as the others, it has been flipped over like a pancake and so the “tail” end always points in the direction opposite to the others.”

Be sure the participant understands the task before proceeding with test items 46-50

For items 46-50, point to the figures and say:	“Which one of these has been flipped over?”
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No further explanations are permitted at this time.

Test items 51-55

<i>Example (1):</i> Point to the single circle just below the top (bordered) figure and say:	“How many circles do you find here?”
Point to the top bordered figure, say:	“It could be a different size, but it has to be the <i>exact</i> same shape.”

<i>Example (2):</i> Point to the single shape just below the top (bordered) figure and say:	“How many of this shape do you find here?”
Point to the top bordered figure, say:	“It could be a different size, but it has to be the <i>exact</i> same shape.”

Repeat For items 51-55, presenting each item to the participant.

Test items 56-60

<i>Example (1):</i> Point to the bottom figures and say:	“If the holes were filled in, which shape would look <i>just like</i> the top one? None have been turned around.”
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<i>Example (2):</i> Point to the bottom figures and say:	“If the holes were filled in, which shape would look <i>just like</i> the top one? None have been turned around.”
--	--

Repeat For items 56-60, presenting each item to the participant.

COGNITIVE ASSESSMENT

Test items 61-65

<i>Example (1):</i> Each item is shown on two pages. Say:	"I'm going to show you a figure, then I'll take it away and you will find the <i>exact</i> same figure on the next page. Ready?"
Show the first page "a" and say:	"Look at this."
Present the figure "a" for 5 seconds. Then turn the page to "b". Say:	"Now find it here."

<i>Example (2):</i> Show the first page "a" and say:	"Look at this"
Present the figure for 5 seconds. Turn the page to "b" showing the four answer choices. Then, say:	"Now find it here"

Repeat For items 61-65, presenting each item to the participant.

Scoring

The total score is calculated by subtracting the number of errors made from the number of the last item administered: item number 40 for ages 4-10 or item number 65 for ages 11 or older (this gives credit for the unadministered items 1-13). Examples are NOT scored or included in the total score.

Benton Judgment of Line Orientation (JLO)

Benton AL. 1994. Judgement of Line Orientation. In Psychological Assessment Resources, Inc.: Lutz.

Description

The Benton JLO is an assessment of visuospatial ability. Participants are presented with a stimulus book of 30 items. Each item shows two lines which correspond to a specific angle and direction, and participants are asked to identify the corresponding angle and direction for each item.

Administration

Turn to practice item 1 in the stimulus booklet- Form H, and say **“Notice here that there are two lines on this page (refer to the lines clockwise). These two lines correspond in angle and direction to 2 of these 11 lines below. Your task is to tell me which two numbered lines below, exactly match the angle of the 2 lines above here. Do you have any questions? Are you having any trouble seeing the lines? Let’s try the rest of the practice items.”**

If the participant gives the incorrect response for a practice item, correct the participant before moving on to the next item. Demonstrate (by pointing) how each line above corresponds to the correct line below. If the subject refers to the lines counterclockwise, write them in the correct way on the record form.

Scoring

The total score for the JLO ranges from 0 to 30. Record the participant’s response for each item and mark whether the participant got the item Correct or Incorrect. Find a scaled score based on the participant’s total correct score by using the scoring manual provided in the document repository.

COGNITIVE ASSESSMENT

Penn State Worry Questionnaire

Meyer TJ, Miller ML, Metzger RL, Borkovec TD (1990). Development and validation of the Penn State Worry Questionnaire. Beh Research and Therapy, 28, 487-495

Description

The Penn State Worry Questionnaire is a brief self-reported questionnaire assessing the participant's severity of anxiety. The 16 items included in the questionnaire measure severity of various signs of anxiety/worry on a 5 point scale.

When a participant is unwilling or unable to come to the psychiatry site for their Month 30 Follow Up Assessment, the **Penn State Worry Questionnaire** should be mailed to the participant prior to the scheduled telephone visit. The participant should then mail their completed questionnaires back to the site for data entry.

- Check all mailed forms before their telephone visit to ensure they are completed fully and if necessary, ask the participant to complete the form over the phone.
- If the reading level of the participant is low, you may read them the items out loud and record their ratings.

Instructions

Ask the participant to rate their feelings of anxiety/worry on the response form provided.

Ratings are reflected on a five-point scale:

0 = Not at all like me

1 = Not very like me

2 = Like me to some extent

3 = Moderately like me

4 = Very like me

Scoring

The Penn State Worry Questionnaire score is calculated by assigning scores of 0, 1, 2, 3 and 4 to the responses categorized above. Items 1, 3, 8, 10, and 11 are reverse scored. Total score is the sum of all 16 items.

You will not need to calculate a total score, as the eCRF will auto calculate the total score for this assessment.

COGNITIVE ASSESSMENT

Perceived Stress Scale (PSS)

Cohen, S., & Williamson, G. (1988). Perceived stress in a probability sample of the United States. In S. Spacapan & S. Oskamp (Eds.), The social psychology of health: Claremont Symposium on applied social psychology. Newbury Park, CA: Sage.

Description

The Perceived Stress Scale is a brief self-reported questionnaire assessing the participant's perception of stress. The PSS is adept at measuring the degree to which situations in one's life are viewed as stressful.

When a participant is unwilling or unable to come to the psychiatry site for their Month 30 Follow Up Assessment, the **Perceived Stress Scale** should be mailed to the participant prior to the scheduled telephone visit. The participant should then mail their completed questionnaires back to the site for data entry.

- Check all mailed forms before their telephone visit to ensure they are completed fully and if necessary, ask the participant to complete the form over the phone.
- If the reading level of the participant is low, you may read them the items out loud and record their ratings.

Instructions

Ask the participant to rate their perceived feelings of stress on the response form provided.

Ratings are reflected on a five-point scale:

- 0 = Never
- 1 = Almost never
- 2 = Sometimes
- 3 = Fairly often
- 4 = Very often

Scoring

The Perceived Stress Scale score is calculated by assigning scores of 0, 1, 2, 3 and 4 to the responses categorized above. Items 4, 5, 7 and 8 are reverse scored. Total score is the sum of all 10 items.

You will not need to calculate a total score, as the eCRF will auto calculate the total score for this assessment.

Alzheimer's Disease Assessment Scale - Cognitive (ADAS-COG)

Introduction to the ADAS-COG

The ADAS is a brief cognitive test battery that assesses learning and memory, language production, language comprehension, constructional praxis, ideational praxis, and orientation.

The test items on the cognitive part of the ADAS should be given in the order indicated.

The *word recall* test is given first and the *word recognition* task is given last with the other cognitive tests given in between.

Separating the two word memory tasks in this way minimizes the chance that a participant will confuse the words from the two tasks. Following the objective testing, subjective clinical ratings of language ability and the ability to remember test instructions are performed by the examiner.

The ADAS is not a timed test and the participant's score does not depend upon how rapidly the test is completed. The cognitive items should be given so that the session moves smoothly and quickly, but also so that the participant does not feel pressured to respond rapidly.

Feedback to the participant should be neutral and, usually, should not indicate whether or not the response was correct. Comments such as **"That's fine"** or **"You're doing well"** are appropriate as long as the Participant is trying. If the participant specifically asks whether or not they were correct, feedback can be given.

Beginning the Testing Session

At the start of the test session, before giving the **Word Recall** test, engage the participant in a short conversation about neutral topics (i.e., weather, hobbies). This conversation will help to put the participant at ease before the testing begins and will give the tester an opportunity to observe how well the participant can use and understand language. It is recommended not to use conversation topics that rely heavily on memory as that could start the testing session with anxiety.

The rating of the participant's language ability (i.e., spoken language, word finding difficulty and comprehension) will be based on this introductory conversation as well as the participant's speech throughout the ADAS testing session.

Administer the test using the ADNI-D worksheets and stimuli, provided on the document repository. You are not required to calculate the scoring of the ADAS.

**Adapted from the Administration and Scoring Manual for the
Alzheimer's Disease Assessment Scale,
1994 Revised Edition, Richard C. Mohs, Ph.D. Copyright © 1994 by
The Mount Sinai School of Medicine**

ADAS-Cog: Word Recall Task

On this task, the participant is given three trials to learn a list of 10 high-frequency, high-imagery nouns. The 10 words are printed in block letters on white cards.

At the start of the first trial, the tester gives the following instructions:	"I am going to show you some words printed on these white cards. Please read each word out loud and try to remember it, because later I will ask you to try to remember all of the words I have shown you. Ready? Read the word and try to remember it."
The examiner can prompt, as necessary, with:	"Read it out loud and try to remember it"

If the participant cannot read the word or is slow, the examiner can say the word out loud and have the participant repeat it. In some cases (*e.g.*, anopsia), the examiner may have to say all of the words and have the participant repeat them. Regardless, make sure the participant looks at each word while repeating it.

- The presentation of each word is not timed.

After presentation of the 10 words, the tester asks the participant to try to recall as many of the words as possible by saying:	"Good, now tell me all the words you remember that were on the list."
Once the participant appears to have recalled as many words as possible, prompt with:	"Any others?"

- Encouragement can also be given if the participant is nervous or giving up.

For trials 2 and 3, say to the participant:	"Now I'm going to show you that same list of words again. Read each word out loud and try to remember it."
Again, say:	"Good, now tell me all the words you remember that were on the list."

Encouragement can be given if the participant is nervous or giving up.

Scoring

Check each word recalled correctly and record total number of words recalled for each trial.

ADAS-Cog: Commands/Instructions

This task is designed to assess receptive speech. The participant is asked to carry out five separate commands with 1 to 5 steps per command.

Each command should be read once. Speak in a clear voice with adequate volume. If the participant does not respond, looks confused or asks for a repetition; the examiner should give the **ENTIRE** command one more time. After, proceed to the next command.

To begin testing, say:	“Now I am going to ask you to do a few things. First...”
------------------------	---

- All commands should be given to every participant. Each command should be read once; however, if the subject does not respond or looks confused or asks for a repetition; the examiner can give the command one (and only one) additional time.

If the participant demonstrates hearing or attentional difficulties, orient them by saying:	“Ready?” or “Now, I want you to...” prior to giving the command.
---	--

Do **not** give the command more than twice.

Commands three and four require the use of stimulus materials (a pencil, a watch, and a card) that are placed on the table directly in front of the subject

- There should be no other materials near the pencil, watch and card (pens, paper, etc.).
- Each underlined element represents a single step.
- Remove all materials before giving last command (“tap each shoulder...”).

Scoring

- Each command is scored as a whole (no partial credit). All components must be correct for the response to be scored as correct.
- Check each command performed correctly.

COGNITIVE ASSESSMENT

ADAS-Cog: Constructional Praxis

This test assesses the participant's ability to copy 4 geometric forms ranging from a very simple one (circle) to a fairly difficult one (cube).

- The forms should be presented one at a time.
- The tester should give the participant a lead pencil with an eraser along with the figure.

The instructions to the participant should be similar to the following:	"On this piece of paper is a shape. Try to draw another one that looks just like this, somewhere on the page." (Examiner may point to shape)
If the participant's response is quick or sloppy, prompt with:	"Take your time and try to draw it just like this one."

The participant may be allowed **two attempts** for each shape (make sure that attempts are clearly numbered). Allow a second attempt if the participant asks or indicates a problem with his/ her drawing. **The participant may erase if he/she needs to.** If the participant draws on top of the printed design, count this as one attempt. Then indicate that he/she should try again on an empty part of the page. If the participant indicates the reproduction is poor, query if the participant wants another attempt. When two attempts are made, ask the participant to indicate which one is best and then score that attempt.

- If the participant cannot reproduce the figure in two attempts, the tester should go on to the next item.

NOTE: We permit the tester to write brief explanations or comments on the stimuli regarding the participant's efforts on the drawings.

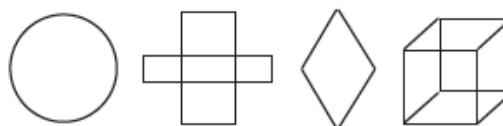
The stimuli should be presented in the following order:

Circle

Two overlapping rectangles

Diamond

Cube



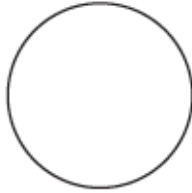
Scoring

A drawing should be scored correct if the participant has reproduced all of the essential geometric features of the original.

- Changes in size do not count as errors.
- Small gaps between lines do not indicate an error, as long as the shape has been reproduced.
- A "recognizable attempt", is an attempt that shows at least one line that might represent a side or portion of the shape.

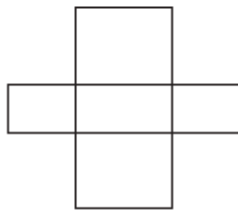
ADAS-Cog: Constructional Praxis

CIRCLE: A closed curved shape



TWO OVERLAPPING RECTANGLES:

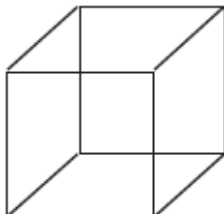
Each shape must be four-sided and overlap must be similar to presented diagram.



DIAMOND: Shape must be four-sided, oriented so that the points are at the top and bottom, and the sides approximately equal length (e.g., longest side is not >1.5 times the length of the shortest side).



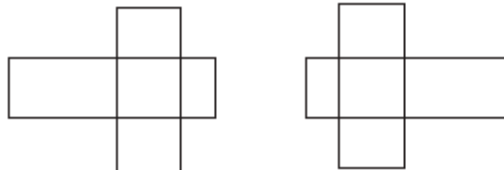
CUBE: The shape is 3-dimensional, with front face in the correct orientation, internal lines drawn correctly between corners. Opposite sides of faces should be approximately parallel.



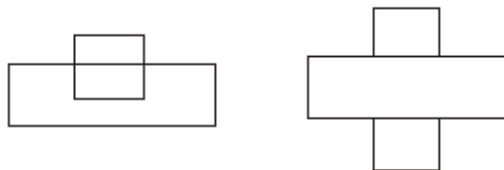
Examples of Correct and Incorrect Drawings:

OVERLAPPING RECTANGLES

Correct



Incorrect



DIAMOND

Correct

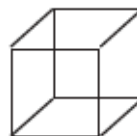


Incorrect

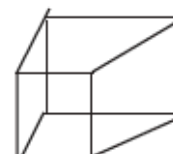
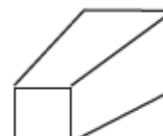


CUBE

Correct



Incorrect



- On the online CRF, indicate if each shape was drawn correctly, shape drawn incorrectly or no recognizable attempt at drawing any side/section of shape.

COGNITIVE ASSESSMENT

ADAS-Cog: Delayed Word Recall

Delayed free recall of the word list should be attempted approximately 5 minutes after trial 3 of the Word Recall Task. The interval should be filled with the ADAS Commands and Constructional Praxis items. If these tasks are completed in less than 5 minutes, fill the rest of the delayed interval with the continuation of the interview to assess language, concentration, etc. before beginning delayed word recall.

To begin the Delayed Word Recall task say:	"A few minutes ago I had you read some words printed on these cards (point to wordlist). Tell me all of the words you can remember that were on the cards."
Prompt with:	"Any others?" as necessary.

- Discontinue when there is no further respond or if the participant indicates that he/she cannot recall any more words after prompting.

Scoring

On the online CRF, click the checkbox for every word recalled **correctly**.

COGNITIVE ASSESSMENT

ADAS-Cog: Naming Task

For this task, the participant is asked to name the 12 randomly presented real objects, with:

- **High** (Flower, Bed, Whistle, Pencil),
- **Medium** (Rattle, Mask, Scissors, Comb), and
- **Low** (Wallet, Harmonica, Stethoscope, Tongs) **frequency values.**

The participant is also asked to name the fingers on his/her dominant hand.

- Objects should be presented in random order. Do not allow the participant to touch the objects.

Give the participant instructions similar to the following:	“Now I am going to show you some objects. I want you to tell me what their names are. What is this called?” (present object)
Continue to present objects in random order. The first question about each object should be:	“What is this called?” or “What is the name of this thing?”
If the participant responds with the object’s function say:	“Yes, that’s what it does, but what is its name?”

- If the participant does not respond, the examiner should give the clue for that item provided below. If the participant still does not respond or makes an error, go on to the next object.

ITEM	CLUES
Flower	grows in a garden
Wallet	a baby’s toy
Rattle	holds your money
Bed	used for sleeping in
Mask	hides your face
Harmonica	a musical instrument
Whistle	makes a sound when you blow on it
Scissors	cuts paper
Stethoscope	doctor uses it to listen to your heart
Pencil	used for writing
Comb	used on hair
Tongs	picks up food

COGNITIVE ASSESSMENT

ADAS-Cog: Naming Task

- The participant is also asked to name the fingers of his/her dominant hand (e.g., thumb, index finger [pointer/forefinger], middle finger, ring finger, and pinky/little finger).

Give the participant instructions similar to the following:	“Place your right (or left) hand on the table. Now I am going to point to a part of your hand and I want you to tell me what it’s called. What is this finger called?”
For the 4 fingers, if a query is necessary, say:	“What is another name for this finger?”

Scoring

ITEM
Thumb
Index/forefinger/pointer
Middle
Ring
Pinky

NOTE: **“Little”** is an acceptable response for **“pinky”** finger

The hardest part of scoring the naming task is determination of the range of correct responses based on the participant’s cultural and geographical background. A response other than the name given on the response form should be scored as correct if it is a name that would be used by a non-demented person with the same cultural background as the participant.

FOR EXAMPLE: the **Mask** might be called a **“false face”** in some parts of the U.S.; the **Wallet** might be called a **“billfold”** or the **Harmonica** might be called a **“mouth organ”**.

- Descriptions of the object, semantic or phonemic paraphasias should not be scored as correct.

EXAMPLES OF INCORRECT RESPONSES ARE:

“Listening thing” for **Stethoscope**, **“cutter”** for **Scissors**, and **“prongs”** for **Tongs**.

- On the online CRF, check each object and finger named correctly.

COGNITIVE ASSESSMENT

ADAS-Cog: Ideational Praxis

This task is designed to determine whether the participant can perform a familiar but complex sequence of actions.

- A long envelope, an 8.5" x 11" sheet of paper and a pencil are placed in front of the participant. (Do not permit the participant to handle any of the materials yet.)

Give the participant instructions similar to the following:	<p>"I want you to pretend you have written yourself a letter. Take this piece of paper, fold it so that it will fit into the envelope, and then put it into the envelope. Then, seal the envelope, address the envelope to yourself, and show me where the stamp goes."</p>
---	--

- There are 5 components to this task.
- If the participant forgets part of the task, or is having difficulty, the tester should repeat the instruction for the component of the task where the participant is having difficulty.

For example:

If the participant stops after folding the paper and putting it into the envelope, the tester should give one reminder on the next component:	"Now seal the envelope."
If the participant cannot do this part, move on and give one reminder on the next component:	"Now address the letter to yourself."

After the first complete instruction only one additional reminder should be given for each component.

- Have the participant place an "X" on the envelope to indicate where the stamp goes. If the Participant merely points to where the stamp goes, the rater should write the "X" on the envelope.
- Any address which would enable a postal worker to deliver the envelope is counted as correct, even though it might not contain the participant's current address.

The address should contain: **Name**
Street
City
State
Zip code is *not* required

Scoring: Check each component of the task correctly completed.

NOTE: To maintain participant anonymity, do NOT upload the envelope to the Source Doc Upload eCRF.

COGNITIVE ASSESSMENT

ADAS-Cog: Orientation

This task is designed to determine how well-oriented the participant is with regard to time and place.

- The components of orientation are: -Person - Month - Year - Time of Day
- Day of Week - Date - Season - Place
- Ask the participant for each of these pieces of information **one at a time**.
- One restatement of each question is allowed (e.g., if participant confuses day and date).
- Make sure no watches, clocks, calendars, etc. are visible to the participant.

Preface the clock/time question with:	"Without looking at your watch, tell me approximately what time it is."
Prompt the place question with:	"Where are we now?" or "What is the name of this place?"

DO NOT give any clues about your location with questions such as:

"What's the name of this hospital?"

Scoring: Check each item answered correctly. Guidelines regarding the range of appropriate correct responses and information about the seasons are provided here:

SCORING	
Full Name:	Must be exact
Month:	Must be exact
Date:	± 1 day.
Year:	Must be exact
Day of week:	Must be exact
Season:	Within 1 week of upcoming season or within 2 weeks of previous season.
Time:	± 1 hour.
Place:	Partial names are acceptable (e.g., the name of hospital, the clinic, or the professional building), but generic terms are not acceptable (e.g., "hospital", or "doctor's office").

SEASONS		
2	Winter =	12/22/10 – 3/19/11
0	Spring =	3/20 – 6/20
1	Summer =	6/21 – 9/22
1	Fall =	9/23 – 12/21
2	Winter =	12/22/11 – 3/19/12
0	Spring =	3/20 – 6/19
1	Summer =	6/20 – 9/21
2	Fall =	9/22 – 12/21
2	Winter =	12/22/12 – 3/19/13
0	Spring =	3/20 – 6/20
1	Summer =	6/21 – 9/22
3	Fall =	9/23 – 12/20
2	Winter =	12/21/13 – 3/19/14
0	Spring =	3/20 – 6/20
1	Summer =	6/21 – 9/22
4	Fall =	9/23 – 12/20
2	Winter =	12/21/14 – 3/19/14
0	Spring =	3/20 – 6/20
1	Summer =	6/21 – 9/22
5	Fall =	9/23 – 12/20
2	Winter =	12/21/15 – 3/19/16
0	Spring =	3/20 – 6/19
1	Summer =	6/20 – 9/22
6	Fall =	9/23 – 12/20

COGNITIVE ASSESSMENT

ADAS-Cog: Word Recognition

On this task the participant is given one trial to learn a list of 12 words, presented one at a time, that are printed in block letters on white cards.

The examiner can prompt, as necessary, with: **“Read it out loud and try to remember it”.**

- If the participant cannot read a word or is slow, the examiner can say the word out loud and have the participant repeat it. In some cases, (e.g., anopsia), the examiner may have to say all of the words and have the participant repeat them. Regardless, make sure the participant looks at each word while repeating it.

NOTE: The presentation of each word is not timed.

Recognition Trial

Immediately after the last word is read aloud, the examiner says:	“Now I’m going to show you another set of words. Some of the words were on the list I just showed you and others are new. For each word I want you to tell me whether it is one of the words I just showed you.”
The tester shows the first word and says either:	“Is this one of the words I showed you before, yes or no?”, or “Did I show you this word before?”

The same instruction is given before the second test word.

For the remaining test words the tester should say:	“How about this one?”
The participant may be encouraged with:	“Just take your best guess”.

If the participant does not remember the task (e.g., reads the word rather than responding yes or no) then the tester should repeat or rephrase the entire question and make a check in the “Reminder” column that the participant had to be reminded of the task instructions. The participant’s ability to stay on task will be reflected in Question 9 of the ADAS (Remembering Test Instructions), which is automatically calculated on the eCRF.

Please note that the participant is prompted for the first two words as part of standard instructions. The rating reflected in Question 9 (Remembering Test Instructions) will not include the prompts given for the first two words.

Word Recognition Task Scoring:

Check the **“yes”** or **“no”** response made by the participant for each of the target and distractor items.

ADAS-Cog: Remembering Test Instructions & Comprehension

Remembering Test Instructions

This item is based **ONLY** on observations during the Word Recognition task (Question 8) and evaluates the participant's ability to remember the requirements of the **Word Recognition** task. This is automatically calculated in the EDC for ADNI-D. If the participant fails to respond (e.g., yes/ no) in the recognition trials, this signifies that the instructions have been forgotten and the instructions should be repeated. Each instance of memory failure for the test instructions **after the first two items** are noted. The eCRF will automatically score this item. Ensure the paper source document matches the eCRF.

Check level of impairment:

None - Participant never needs extra reminders of instructions
Very mild - forgets once
Mild - must be reminded 2 times
Moderate - must be reminded 3 or 4 times
Moderately severe - must be reminded 5 or 6 times
Severe - must be reminded 7 or more times

Comprehension

This item evaluates the participant's ability to understand speech. To rate this item the tester should consider how well the participant was able to understand the tester's speech during the opening discussion and during the test session. **Do not include responses to commands.**

Check level of impairment:

None - no evidence of poor comprehension
Very mild - one or two instances of misunderstanding
Mild - 3-5 instances of misunderstanding
Moderate - requires several repetitions and rephrasing
Moderately severe - Participant only occasionally responds correctly; i.e., yes/no questions
Severe - Participant rarely responds to questions appropriately, not due to poverty of speech

ADAS-Cog: Word-Finding Difficulty & Spoken Language Ability

Word Finding Difficulty

This item rates impairment in expressive speech. The examiner rates the level of difficulty the participant had in finding the desired word in spontaneous speech during the interview and test session.

NOTE: The participant may attempt to mask word finding difficulty by circumlocution (i.e., giving explanatory phrases or nearly satisfactory synonyms). **DO NOT** include the participant's responses on the formal object and finger naming tasks in this rating.

Check the best response:

None - no evidence of word-finding difficulty in spontaneous speech
Very mild - 1 or 2 instances, not clinically significant
Mild - noticeable circumlocution or synonym substitution
Moderate - loss of words without compensation on occasion
Moderately severe - frequent loss of words without compensation
Severe - nearly total loss of content of words; speech sounds empty; 1-2 word utterances

Spoken Language Ability

This item is a global rating of the quality of speech, i.e., clarity, difficulty in making oneself understood. In rating this item the tester should consider all of the speech produced by the participant. Quantity of speech and word-finding difficulty, i.e., circumlocutions, are not rated on this item. It should be noted that moderately severe and severe rating for this item are reserved for participants whose expressive language abilities are impaired to such an extent that they seldom communicate without difficulty.

Check level of impairment:

None - no instances where it is difficult to understand the Participant
Very mild - one instance of lack of understandability
Mild - Participant has difficulty less than 25% of the time
Moderate - Participant has difficulty 25-50% of the time
Moderately severe - Participant has difficulty 50% of the time
Severe - one or two word utterance; fluent, but empty speech; mute

COGNITIVE ASSESSMENT

ADAS-Cog: Number Cancellation

Example Instructions

Place the practice form in front of the participant and say:	<p>“On the top of this page are two numbers. Throughout this page you will find these numbers mixed in with other numbers. I’d like you to begin here...”</p> <p>(point to the beginning of the first line),</p> <p>“...and going across (line by line), cross off each number that matches either of the two numbers at the top of the page. Please work as quickly as you can.”</p>
--	---

Discontinue the example after 30 seconds.

Task Instructions

Place the form in front of the participant and say:	<p>“On the top of this page are two numbers. Throughout this page you will find these numbers mixed in with other numbers. I’d like you to begin here...”</p> <p>(point to the beginning of the first line),</p> <p>“...and going across (line by line), cross off each number that matches either of the two numbers at the top of the page. Please work as quickly as you can.”</p>
If the first cancellation done by the participant is incorrect, say:	<p>“These are the correct numbers to cross out,” and point to the numbers at the top of the page in the heading.</p>

If the participant becomes confused or stops while doing the test, repeat the standard instructions as needed. **Discontinue the test after 45 seconds.**

Scoring

Enter the following:

- 1) The number of correct targets crossed out.
- 2) The number of total errors of commission (i.e., crossing out a non-target number).
- 3) The number of times the participant needed to be reminded of the task or re-directed back to the task.

ADAS Certification Instructions

ADAS raters must meet ADCS certification requirements prior to administering the ADAS in this trial.

Certification may only be accomplished by completion of the ADAS Standardization/Certification Questionnaire. Raters who have previously completed the Questionnaire and received a letter of certification from the ADCS in the last five (5) years are certified and do not need to repeat the certification process.

Raters who have not been certified for previous ADCS studies or if it has been over 5 years since you have been certified as an ADAS rater, must complete the Standardization/Certification Questionnaire.

To request an ADAS Certification Package:

Email the ADCS Helpdesk:
adcs-clinops@ucsd.edu

**Completed questionnaires should be faxed to
Clinical Operations:
(858) 246-1415**

COGNITIVE ASSESSMENT

American National Adult Reading Test (ANART)

Grober, E. & Sliwinski, M. (1991). Development and validation of a model for estimating premorbid verbal intelligence in the elderly. *Journal of Clinical and Experimental Neuropsychology*, 13, 933-949.

Administration Instructions

Present the participant with the word list and say, **“I’m going to ask you to read a list of words aloud. Some of the words may be unfamiliar and difficult to pronounce, but do the best you can to pronounce them.”**

- The participant may self-correct; however, do not prompt him/her to repeat a word unless it was difficult to hear what was said and necessary to determine whether the pronunciation was correct or incorrect.
- If the participant reads a word with two different pronunciations, one correct and the other incorrect, ask which one he/she thinks is best.
- Administer all words, even when the participant begins having difficulty pronouncing them.

Scoring

- Total score = # of **errors** made.
- Manually enter the total number of errors made on the online case report form.

NOTE: Some words have multiple correct pronunciations. Be familiar with these, so as to score accurately!

COGNITIVE ASSESSMENT

Boston Naming Test

Kaplan, E., Goodglass, H., Weintraub, S. *The Boston Naming Test*. Philadelphia: Lea and Febiger, 1983.

Description

This reduced version of the Boston Naming Test is a measure of the ability to orally label (name) 30 line drawings of objects. The objects are presented in order of frequency, from most frequent (i.e., bed) to least frequent (i.e., protractor). This test is sensitive to aphasia and also to object recognition deficits. Boston Naming Test cards used at the in-person visits contain a short form and standard form. Use the standard form where card 1 is bed, 3 is pencil and 5 is whistle. For the purposes of this study, only the odd-numbered items from the full test will be administered.

Administration Instructions

Begin at item 1 and present all 30 items (i.e., odd #s 1 – 59) in order.

Place the test booklet in front of the participant and say:	“I am going to show you some pictures in this book, one at a time. I would like you to tell me the name of the object that you see.”
Expose the first item and say:	“Tell me what this is called.”

Allow 20 seconds for each response, unless the participant says he/she does not know the word before the 20 seconds has elapsed. If the answer is correct; check the first column on the Worksheet for Boston Naming Test –30 (Odd-numbered items). Record any response other than the correct one.

If the participant has given a response that indicates misperception of the picture, he/she is supplied with the semantic cue. This is printed in brackets under the response line for each item.

The participant is allowed up to 20 seconds to name the picture after the stimulus cue is given. If the item is named correctly within that time, check the column “correct with semantic cue”. Otherwise check “incorrect with semantic cue” and again record the response verbatim.

The semantic cue is presented only when the participant’s response reflects misperception. If the response following the stimulus cue is incorrect, move on to the phonemic cue. The phonemic cue is also given after every failure to respond or after any incorrect response. Provide the first sound in the name of the item (indicated on the test form in bold). If the participant succeeds with a phonemic cue, place a check mark in the column “correct with phonemic cue”. If the participant fails, place a check mark in the column “incorrect with phonemic cue.” **The number correct following phonemic cues is of clinical interest but is not included in the total score.**

COGNITIVE ASSESSMENT

Discontinue testing after 6 consecutive failures (i.e., failure to name correctly either without assistance or with a stimulus cue).

Scoring

There are 6 scores:

1. Total correct without a cue
2. Total semantic cues given
3. Total correct with a semantic cue
4. Total phonemic cues given
5. Total correct with phonemic cues
6. Total correct = sum of 1 + 3 above

The total score (i.e., #6) is the number of items that are named correctly without assistance **PLUS** the number of items named correctly following a stimulus cue if one had to be given (maximum total score = 30).

Calculate and enter the total score on the online form. After submitting the form, an error will be generated if the total score entered doesn't equal the summation of items 1 and 3.

- Record the participant's responses verbatim if incorrect or circumlocutory, and write in 'DK' only if the participant actually says she or he doesn't know.
- Mispronunciations are treated as incorrect unless they clearly reflect a regional or dialect specific pronunciation (e.g. someone from the Boston area may omit the 'r' sound in 'dart').
- If a mispronunciation does not reflect such a regionalism (e.g. 'escalator'), the answer is incorrect and cueing proceeds as appropriate.
- If the participant gives a more general or circumlocutory response (e.g. 'boat' or 'it floats on water' for the word 'canoe'), say "Can you think of a more specific name for it?"
- If the participant gives a more specific response (e.g. 'daisy' for 'flower'), say "Can you think of a more general name for it?"
- If the participant gives the correct name, but says it is not that object (e.g. "Well it's not a canoe"), the response is considered incorrect and cueing proceeds if appropriate.

COGNITIVE ASSESSMENT

Category Fluency Test

Adapted from the CERAD administration and scoring procedures for Verbal Fluency (Morris et al., 1989).

Description

This is a widely used measure of semantic memory (verbal fluency, language). The participant is asked to name different exemplars from a given semantic category. The number of correct unique exemplars named is scored.

Administration

Read the initial instruction:

"I am going to give you a category and I want you to name, as fast as you can, all of the things that belong in that category. For example, if I say 'articles of clothing,' you could say 'shirt,' 'tie,' or 'hat.' Can you think of other articles of clothing?"

Allow up to 20 seconds for the subject to produce two responses. Circle the number corresponding to the participant's responses, and read the associated instruction.

RESPONSE CODE	INSTRUCTION
0 (No response)	"You could have said 'shoes' or 'coat' since they are articles of clothing."
1 (One or more incorrect responses, no correct response)	"No, ____ is (are) not an article(s) of clothing. You could have said 'shoes' or 'coat' since they are articles of clothing."
2 (One or more correct responses, no incorrect responses)	"That's right. You also could have said 'shoes' or 'coat.' "
3 (One or more correct responses, one or more incorrect responses)	"____ is (are) correct, but ____ is (are) not an article of clothing. You also could have said 'shoes' or coat.' "
4. (Two or more correct responses)	"That's right."

Next, read the instructions for the Animal category:

"Now I want you to name things that belong to another category: Animals. You will have one minute. I want you to tell me all the animals you can think of in one minute. Ready? Begin."

Start timer as you say **"Begin"**. Write actual responses as legibly as possible on the Worksheet for Category Fluency–Animals. Stop the procedure at 60 seconds. One prompt (**"Tell me all the animals you can think of."**) is permitted if the participant makes no response for 15 seconds or expresses incapacity (e.g., **"I can't think of any more"**). It is also permissible to repeat the instruction or category if the participant specifically requests it.

Defer scoring until after test administration is finished.

COGNITIVE ASSESSMENT

Scoring

The total score on the Worksheet for Category Fluency–Animals is the number of correct unique animal names produced within the one-minute time limit. Intrusions are defined as any word that does not fit the category of animals spoken by the participant during the one-minute fluency test. Any word repeated, even if an intrusion, is counted as a perseveration. The non-categorical word is counted as an intrusion the first time, then a perseveration the second time, not as a second intrusion.

Example: Carrot, cat, carrot would be scored as one correct response (cat), one intrusion (carrot), and one perseveration (carrot #2).

CREDIT: breeds (e.g., terriers); male, female, and infant names of a species (e.g., bull, cow, calf); both superordinate and subordinate examples of a species (e.g., both dog and terrier are credited); birds; fish; reptiles, insects.

DO NOT CREDIT: Repetitions, mythical animals.

COGNITIVE ASSESSMENT

Clock Drawing Test

Goodglass, H., & Kaplan, E. (1983). *The assessment of aphasia and related disorders*. Philadelphia: Lea & Febiger.

Description

This is a test of constructional ability that has two components: a command condition in which the participant draws a clock to verbal instructions, and a copy condition in which the participant copies a model clock drawn at the top of response form.

Clock Drawing Administration

Before beginning the task, make sure there are no clocks visible to the participant.

- To begin, present the participant with a felt-tipped pen (or a pencil without an eraser) and an 8 1/2" x 11" blank sheet of white paper and say, **"Draw the face of a clock showing the numbers and two hands set to ten after eleven."**

Allow the participant to work without feedback; interrupt only if the participant starts to scratch out or destroy any of their drawing.

- If the participant tries to erase or scratch out an error, immediately intervene and gently instruct them to try again by saying, **"Don't take the time to make corrections."** While pointing to a clean area of the paper, say, **"You may start over here and draw the clock again. Remember you are to draw the face of a clock showing the numbers and two hands set to ten after eleven."**

Allow only two attempts on the clock drawing task. If a participant needs an additional reminder about the specific time that is to be indicated on the clock, the examiner may repeat the time again, e.g., **"set the clock to ten after eleven."** Although this task is not timed, keep the participant actively engaged in the task; the examiner may use their clinical judgment as to when the task should be abandoned in order to spare the participant undue anxiety or frustration when they are unable to perform the clock drawing task.

Clock Copying Administration

Immediately after the Clock drawing is completed, present the participant with the response form with the model clock drawn at the top and say, **"Copy this clock** (point to the model) **in the space provided below."**

Allow the participant to work without feedback; interrupt only if the participant starts to scratch out or destroy any of their drawing.

- If the participant tries to erase or scratch out an error, immediately intervene and gently instruct them to try again. Allow only two attempts on the clock copying task. Although this task is not timed, keep the participant actively engaged in the task; the examiner may use their clinical judgment as to when the task should be abandoned in order to spare the participant undue anxiety or frustration when they are unable to perform the clock copying task.

COGNITIVE ASSESSMENT

Scoring

Clock drawings from both the command and copy conditions are scored in the same manner. Determine if each of the criteria listed below has been met:

1. Approximately circular face. The clock face may be slightly oval, especially if the subject hastily begins to draw. The examiner may always determine that the subject was “too” impulsive and/or careless in their attempt, and re-administer the instructions and have them start over, “taking time to give their best effort.” Do not penalize the subject for tremor. In some cases, participants will draw an “old fashioned” mantle clock or grandfather clock (i.e., with a square clock face). If this occurs, ask the subject to draw a “regular clock.”
2. Symmetry of number placement. One method to assist the examiner in determining if the numbers are symmetrical is to visually “line up” the opposing numbers, e.g., 3-9, 12-6, 4-10. If there are any obvious gaps or misalignments, then the numbers may be considered asymmetrical.
3. Correctness of numbers. All numbers must be present and in the correct order, and inside the face of the clock. If a subject draws the numbers outside the circle, this item would be **INCORRECT**.
4. Presence of two hands. Two hands (and only two hands) must be present on the clock face to receive credit for this item.
5. Presence of two hands set to ten after eleven. To receive credit for this item, the two hands must be set to the numbers eleven and two and of the appropriate relative lengths (i.e., shorter hand to eleven, longer hand to two).

See the examples of scored clock drawings on the next page.

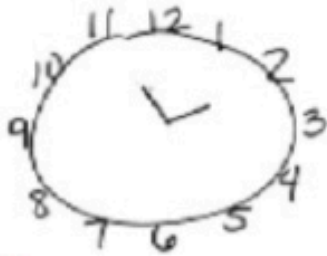


5 points



3 points

- approximately circular face
- presence of 2 hands
- presence of 2 hands, set to 10 after eleven



3 points

- circular face
- symmetry of number placement
- presence of 2 hands



3 points

- approximately circular face
- correct numbers
- presence of 2 hands



0 points

COGNITIVE ASSESSMENT

Logical Memory Test I – Immediate Recall (Story “A” Anna Thompson)

Modified from Wechsler D. Wechsler Memory Scale-Revised. San Antonio, Texas: Psychological Corporation; 1987.

Description

This test assesses the ability to recall a short passage or story. The examiner reads the story to the participant in a clear voice. Immediately after hearing the story, the participant is asked to retell the story from memory. The story should be read with adequate volume and clarity for the participant to understand during the presentation. No repetitions are permitted.

It is important for the examiner to get a sense of the participant’s hearing acuity and modulate their voice accordingly. Of note, for the hard of hearing, it is not necessarily helpful to merely increase the volume, but rather change the pitch; a lower pitched voice sometimes is more audible than a loud, high-pitched voice. As with all neuropsychological testing, it is best if the examiner projects his/her voice at the participant, rather down “into” their clipboard.

Use of the alternate story (Greg Fortune) is permitted if a participant had been testing on the Anna Thompson story within 3 months of the Baseline Assessment visit or any subsequent visit where the Logical Memory task is administered under ADNI-D. **Prior approval from the protocol PI is required in any instance where the alternative story will be administered.**

Administration

The following standard instructions are printed on each worksheet and are to be read verbatim.

Say:	<p>“I am going to read to you a little story of just a few lines. Listen carefully and try to remember it just the way I say it, as close to the same words as you can remember. When I am through I want you to tell me everything I read to you. You should tell me all you can remember even if you are not sure. Are you ready?”</p>
When the examiner has finished reading the story, say to the participant:	<p>“Now what did I read to you? Tell me everything and begin at the beginning.”</p>

Always permit the participant to include additional information by prompting with **“Anything else?”** Record any additional “bits of information” and score appropriately.

After the participant appears to be able to recall no more of the story, say:	<p>“Later on I will ask you to tell me this story again, so try not to forget it.”</p>
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COGNITIVE ASSESSMENT

Recording

Record the participant's responses directly on the case report form between the lines of the text. To simplify the process of recording, underline each unit or word that is reported verbatim and write in above the text units that are reported, but not verbatim. Many examiners prefer to tape record their participant's response, and then transcribe any words they may have missed after the session. This is acceptable if appropriate consent has been obtained.

Scoring

The phrases and words separated by diagonal lines in the passages are treated as items (or units), and each item correctly repeated is worth one point, for a total of 25 points.

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Non-verbatim responses that are acceptable and receive full credit are listed in the Wechsler Memory Scale-Revised manual, as follows:

TEXT FOR STORY A	GENERAL RULE	EXAMPLES OF ALTERNATIVE 1-POINT RESPONSES	EXAMPLES OF 0-POINT RESPONSES
Anna	"Anna" or variant of the name	Ann; Annie; Annette	Angela; Allison
Thompson	"Thompson" is required	NONE	Thompkins; Thomas
of South	"South" (in any context)	from South; who lived in South; who came from the South	NONE
Boston,	"Boston" (in any context)	who worked in Boston; on a trip to Boston	NONE
employed ¹	An indication that she held a job	worked; had a job as; who was; who earned a living as	who wanted to be; employed a cook
as a cook ¹	"Cook" or some form of the word is required	who cooked	as a waitress; in the kitchen
in a school	"School" is required	at a high school; by a school	in a hospital; at a company
cafeteria,	"Cafeteria" is required	NONE	lunchroom; dining hall; diner; restaurant; kitchen
reported	Indication that a formal statement was made to someone in authority (in any context)	filed a complaint; said to the police; made a statement; notified the police; called the police; told the police	said; told how
at the City Hall	"City Hall" (in any context)	went to City Hall; called City Hall	NONE
Station	"Station" in any context, or a word or phrase denoting a police station	police station; train station; stationhouse; police headquarters; precinct house; police department	office; building
that she had been held up	An indication that she had been held up (i.e., gun point or knife)	that someone held her up; that she was in a stick-up	that she was beaten; she was attacked; that she was robbed; she got mugged
on State Street	"State Street" (in any context)	she lived on State Street; on her way to State Street	on some street; State Avenue
the night before	Indication that the hold-up occurred the previous night	last night; the previous night	at night; one night; yesterday; the day before
and robbed	Indication that a robbery took place	was robbed; her money was stolen; they took her money; someone took her purse	lost her money somebody took her things

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TEXT FOR STORY A	GENERAL RULE	EXAMPLES OF ALTERNATIVE 1-POINT RESPONSES	EXAMPLES OF 0-POINT RESPONSES
of fifty-six dollars	Indication that an amount of money greater than \$49 but less than \$60 was taken from her	fifty-some dollars; fifty-five dollars; about fifty dollars	sixty-five dollars; a lot of money; the police collected fifty-six dollars for her
She had four	"Four" is required together with an indication that the children were hers	she was the mother of four	she had two; she had some; there were some
small children,	"Children" or a synonym is required	little children; kids; small kids; young children	babies; girls; sons; small boys
the rent was due,	A phrase indicating that the rent was due	she had not paid the rent; she owed for the rent; the landlord had to be paid; she needed money for the rent	she owed money; she needed money; there was no money
and they had not eaten	Indication that her children, or the family, were without food	they had gone without food; they were hungry; there was no food; her kids had nothing to eat; she couldn't feed her family	there wasn't much food; they had only a little food; she had not eaten; didn't have money to buy food
for two days.	"Two days" is required, or a phrase meaning about two days	for a couple of days; for one or two days; for two or three days	for days; for several days; for a day; for three days
The police,	A word or phrase signifying one or more members of the police department (in any context)	the cops; the policeman; the detectives; the police officer; they (where police is clearly meant)	they (unspecified); some people; her neighbors; somebody
touched by the woman's story,	An indication that her story evoked sympathy	were touched; felt sorry for the woman; wanted to help her; were sympathetic; were impressed by her story (implying emotional reaction)	listened to her story; helped her; believed her
took up a collection	A phrase indicating that money was collected	chipped in; collected money; donated; collected some food	gave her some money; found some money
for her.	An indication that the money collected was for her or her children	and gave it to her; for her children; for her family; for them; to help her out	as a gift; to make things better; for food

1 "Anna Thompson, a cook in a..." gets credit for "employed" and "as a cook".

Logical Memory Test II – Delayed Recall (Story “A” only)

Administration

Administer this test at least 30 minutes and no more than 40 minutes after Logical Memory I

- Immediate Recall. Complete other cognitive testing during the interval between Immediate and Delayed Recall.

NOTE: If the 30 – 40 minute delay period has elapsed and another test is being administered, interrupt the additional test and administer the Logical Memory II. Once the Logical Memory II has been fully completed, resume the interrupted test.

The following standard instructions are printed on each worksheet and are to be read verbatim.

Say,	“Do you remember the little story I read to you a few minutes ago? Now I want you to tell me the story again. Tell me everything; begin at the beginning.”
------	---

If the participant does not recall the story, it is permissible to offer the following reminder which is also printed on the testing worksheets.

Say,	“The story was about a woman who was robbed.”
------	--

Do not give any further help other than general encouragement. Note if the reminder was given and do not then give a point for that item (i.e., “robbed”) when scoring. After the participant has recalled the story, prompt with **“Anything else?”** Record any additional information recalled and score appropriately.

Recording

As specified in the directions for Logical Memory I – Immediate Recall, record the participant’s responses directly on the case report form between the lines of the text. To simplify the process of recording, underline each unit or word that is reported verbatim and write in above the text units that are reported, but not verbatim. Many examiners prefer to tape record the participant’s response and then transcribe any words they may have missed after the session. This is acceptable if appropriate consent has been obtained.

Scoring

Use the same scoring procedure as for Logical Memory I - Immediate Recall. Non-verbatim responses that are acceptable and receive full credit are posted in the document repository.

The Logical Memory II – Delayed Recall score is used to demonstrate abnormal memory function in potential participants. Please see the section on Inclusion/Exclusion Criteria for education-adjusted scores.

If the Greg Fortune story was used, please see the worksheet posted on the document repository under supplemental worksheets for directions on how to administer and score.

COGNITIVE ASSESSMENT

Mini Mental State Exam

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Description

The Mini-Mental State Examination (MMSE) is a widely used, well validated and reliable screening tool for evaluation of cognitive impairment, as well as course of cognitive change over time and an individual's response to treatment. The brief assessment measures orientation to time and place, immediate recall, short-term verbal memory, calculation, language and construct ability.

- It is strongly recommended that the same person administer the MMSE at all appropriate visits.
- If the participant is unable to perform any item, the item should be scored as "incorrect."
- **MMSE total score will be calculated on the electronic case report form based on the item level data entered.**

Administration Instructions

Following a polite and friendly introduction to the participant, begin the MMSE by asking, **"Do you have any trouble with memory?"** Regardless of his or her answer, say, **"May I ask you some questions about your memory?"** These two questions are not scored; however, they serve to orient the participant to the nature of the examination. This conversation also can assess the person's hearing, alertness, attention, and responsiveness.

- Prior to administration, ensure that eyeglasses (if needed) are being worn and hearing aids (if needed) are adjusted appropriately.
- If the participant is anxious, it may be helpful to periodically say, "You're doing fine."

Orientation Instructions

Items 1-10: Each scoreable item should be queried separately as indicated on the online CRF.

- For each item, record the participant's response in the space provided on the worksheet. Indicate on the worksheet if each response was correct or incorrect.
- If a participant gives the date when prompted for day, he/she should be given credit for date if the response is correct. If a participant gives a partial response for year (e.g. "11", prompt with, "what is the full year?") **Give credit only if the full year is given.**

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Orientation Scoring

Each item is worth one point. No partial credits are given.

- For hospital, any correct name is acceptable except for generic names such as “medical center” or “hospital”.
- For county, only the county, in which they are currently in, is considered correct. The participant’s home county (if different from their current location) is considered incorrect.
- If it is near the transition between 2 seasons, that is one week before and two weeks after the onset of a new season, either season is acceptable and considered correct.
- All other items require EXACT answers to be considered correct.

Immediate Recall Instructions

Say, **“Listen carefully. I am going to say three words. You say them back after I stop. Ready? Here they are....”**

Pause 1 second after each of the three words.

“Now repeat those words back to me.”

Immediate Recall Scoring

Score one point for each correct response in the FIRST trial (the order of the answers does not matter). Continue to repeat the three words until he/she is able to say all three words back to you, with a maximum of five additional trials to repeat all three words. If the participant does not repeat all three words correctly by the sixth trial, stop the task and enter “6” for 13a.

Attention Instructions

The examiner should give the instructions as follows:

“The word WORLD is spelled W-O-R-L-D. Spell WORLD backwards.”

Repeat the instructions if the participant asks for a repetition or appears confused. As clarification, the examiner may say, **“Start from the end and go to the beginning.”**
Allow additional trials if the subject requests them

Attention Scoring

Record the actual letters of the participant’s final response. Score one point for each correct letter as indicated on the score sheet. For example, “D-L-O-W” would receive two points for the correct placement of the “D” and the “L”.

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Delayed Recall Instructions

After a 3 minute delay from Immediate Recall, ask the participant, **“Now what were those three objects I asked you to remember?”** If needed, explain the source of these three objects with: **“I asked you to repeat three words earlier and to remember them. Can you recall them now?”**

Delayed Recall Scoring

One point for each correct response for a total of three points. The order of answers does not matter. If the participant is unable to recall an item, the item should be scored as “Incorrect.”

If the attention task is completed in less than 3 minutes, perform remaining non-verbal parts of the MMSE until 3 minutes have elapsed. Go directly to questions 25, 26, 27, and 30. Once 3 minutes have elapsed, return to the Delayed Recall task.

Language Naming Instructions

Show the participant a wristwatch and say, **“What is this?”** If participant gives a function say **“Yes, but what is this called?”** or **“What’s its name?”** Repeat for pencil. No other clues should be provided.

Language Naming Scoring

Score one point for each correct response.

Command Instructions

Present a piece of paper at the mid-line of the participant. Say, **“Take the paper in your right hand, fold it in half and put it on the floor.”** One repetition is permitted at the participant’s request, but the entire command must be repeated. The participant is allowed to fold the paper using both hands.

Command Scoring

One point for each of the three segments:

1. Takes paper in right hand
2. Folds in half
3. Places on the floor

Reading Instructions

Present card with command. Say, **“Please read this and do what it says.”** Then show the participant the words CLOSE YOUR EYES that appear on the stimulus card. Participant can be reminded not just to read the sentence, but to obey it. If the participant is unable to read, read the sentence out loud to him/her.

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Reading Scoring

Instructions must be followed completely to give one point.

Writing Instructions

The next task tests the participant's ability to write a sentence. Give the participant a pencil (or pen) and a blank sheet of paper and say, **"Write a sentence."** If needed, prompt the participant with **"Write a sentence about the weather."**

Writing Scoring

One point for any complete sentence even if not about weather. Grammar, spelling, and punctuation are not scored, but the participant must write a sensible sentence that contains a subject and a verb. A sentence with an implied subject (e.g., close the door) is acceptable. If the sentence is illegible, ask the participant to read it aloud for scoring.

Construction Instructions

The drawing task assesses the participant's visuospatial ability. Turn over the paper on which the individual previously wrote a sentence, and place it in front of him/her so that the blank side is up. Then place the stimulus card showing the interlocking pentagons design next to the blank paper, and say, **"Please copy this design."**

Do not allow erasures. If the participant appears dissatisfied with his/her drawing or requests a second attempt, allow the participant to redraw the figure. Clearly label the first and second attempt. The best drawing should be scored.

Construction Scoring

The design should be two intersecting pentagons (i.e., five-sided designs). The intersection should result in a four-sided figure. All ten angles must be present and two must intersect.

Reminder: MMSE Total score will automatically be calculated on the electronic case report form based on the item level data entered.

Montreal Cognitive Assessment (MoCA)

Adapted from the official MoCA Instruction Guide, Version November 12, 2004 © Z Nasreddine

Description

The Montreal Cognitive Assessment (MoCA) was designed as a rapid screening instrument for mild cognitive dysfunction. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation. Time to administer the MoCA is approximately 10 minutes.

- Use a check mark on the worksheet to indicate correct items. The EDC will ask for each item to be entered as correct or incorrect.
- Record verbatim responses so that scoring can be confirmed.

IMPORTANT
<p>Use the ADNI-adapted worksheet and ADNI administration and scoring procedures provided here rather than instructions provided by the instrument author. ADNI scoring and test administration differs slightly from the published instrument. Rather than calculating a total score, please enter the item level data as specified on the worksheet and eCRF.</p>

1. Alternating Trail Making:

Administration: Instruct the participant, **“Please draw a line, going from a number to a letter in ascending order. Begin here [point to (1)] and draw a line from 1 then to A then to 2 and so on. End here [point to (E)].”**

Scoring: Mark as correct if the participant successfully draws the following pattern:

1 - A - 2 - B - 3 - C - 4 - D - 5 - E, without drawing any lines that cross. Any error that is not immediately self-corrected would result in this task being scored as incorrect.

NOTE: If a participant starts at 2 rather than 1 they should be instructed to start at 1. Task should be scored as correct if the participant successfully draws the pattern even when starting at 2.

2. Visuoconstructional Skills (Cube):

For Cube and Clock, the participant may be allowed to use an area other than those provided on the MoCA test sheet to reproduce the items (*e.g.*, an additional blank page, with participant ID and visit date.)

Administration: Pointing to the cube, say: **“Copy this drawing as accurately as you can, in the space below.”**

Scoring: A correctly executed drawing must meet each criteria:

- Drawing must be three-dimensional
- All lines are drawn
- No line is added

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- Lines are relatively parallel and their length is similar (rectangular prisms are accepted)

Place a checkmark on the worksheet next to the cube drawing task if all criteria are met.

3. Visuoconstructional Skills (clock):

Administration: A separate blank piece of paper may be used for the MoCA Clock drawing. Indicate the right third of the space and give the following instructions: **“Draw a clock. Put in all the numbers and set the time to 10 after 11.”**

- Please note that Clock Draw and Copy is repeated again separately in the ADNI battery on a separate piece of paper.
- Do not use the MoCA administration to replace this separate trial of clock draw and copy.

Scoring: Each of the three items must be scored as correct/incorrect based on the following criteria:

- **Contour:** The clock face must be a circle with only minor distortion acceptable (*e.g.*, slight imperfection on closing the circle).
- **Numbers:** All clock numbers must be present with no additional numbers; numbers must be in the correct order and placed in the approximate quadrants on the clock face; Roman numerals are acceptable; numbers can be placed outside the circle contour.
- **Hands:** There must be two hands jointly indicating the correct time; the hour hand must be clearly shorter than the minute hand; hands must be centered within the clock face with their junction close to the clock center.

4. Naming:

Administration: Beginning on the left, point to each figure and say: **“Tell me the name of this animal”**

Scoring: Indicate each item is correct with a checkmark:
(1) camel or dromedary, (2) lion, (3) rhinoceros or rhino.

5. Memory:

Administration: Read a list of 5 words at a rate of one per second, after giving the following instructions: **“This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn’t matter in what order you say them”.**

- Mark a check in the allocated space for each word the participant **CORRECTLY** produces on this first trial.

When the participant indicates that he/she has finished (has recalled all words), or can recall no more words, read the list a second time with the following instructions: **“I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time.”**

- Put a check in the allocated space for each word the participant recalls correctly after

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the second trial.

At the end of the second trial, inform the participant that he/she will be asked to recall these words again by saying, **“I will ask you to recall those words again at the end of the test.”**

Scoring: For the standard MoCA, Trials One and Two are not scored, but for ADNI-D, these items are entered on the eCRF.

6. Attention:

Digit Span Forward

Administration: Give the following instruction: **“I am going to say some numbers and when I am through, repeat them to me exactly as I said them”**. Read the five number sequence at a rate of one digit per second.

Digit Span Backward

Administration: Give the following instruction: **“Now I am going to say some more numbers, but when I am through you must repeat them to me in the backwards order.”**

Read the three number sequence at a rate of one digit per second.

Scoring: Place a checkmark on the worksheet for each sequence correctly repeated (the correct response for the backwards trial is 2-4-7).

Vigilance - Letters and Tapping:

Administration: Read the list of letters at a rate of one per second, after giving the following instruction: **“I am going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand”**.

- Circle any incorrect responses on the worksheet.

Scoring: Record the **NUMBER OF ERRORS** made (*i.e.*, either a tap on a wrong letter, or failure to tap on an A).

Vigilance - Serial 7s

Administration: Give the following instruction: **“Now, I will ask you to count by subtracting seven from 100, and then, keep subtracting seven from your answer until I tell you to stop.”**

- Give this instruction twice if necessary.

Scoring: Record participant’s verbatim response. If a participant makes an error on the first subtraction, but then correctly subtracts 7 from that number, the second subtraction would be considered a correct response. Place a checkmark next to each correct subtraction.

7. Sentence Repetition:

Administration: The examiner gives the following instructions: **“I am going to read you a sentence. Repeat it after me, exactly as I say it [pause]: I only know that John is the one to help today.”**

Following the response, say: **“Now I am going to read you another sentence. Repeat it after**

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me, exactly as I say it [pause]: The cat always hid under the couch when dogs were in the room.”

Scoring: A checkmark is given for each sentence correctly repeated. **REPETITION MUST BE EXACT.**

- Be alert for errors that are omissions (e.g., omitting “only”, “always”) and substitutions/ additions (e.g., “John is the one who helped today;” substituting “hides” for “hid”, altering plurals, are all not correct).

8. Verbal Fluency:

Use the separate page provided in the worksheet packet to record the verbatim responses for this test.

Administration: Give the following instruction: “Tell me as many words as you can think of that begin with a certain letter of the alphabet that I will tell you in a moment. You can say any kind of word you want, except for proper nouns (like Bob or Boston), numbers, or words that begin with the same sound but have a different suffix, for example, love, lover, loving. I will tell you to stop after one minute. Are you ready? [Pause] Now, tell me as many words as you can think of that begin with the letter F [time for 60 sec]. Stop.”

- Any duplication of words (perseverations) should not be counted as correct words.
- If a participant begins to say proper nouns or numbers you should quickly inform the participant that proper nouns or numbers cannot be used during the task.

Scoring: The score is the number of words correctly recalled (*i.e.*, total number of words recalled minus any repetitions, perseverations, intrusions, or variations).

9. Abstraction:

Administration: Ask the participant to explain what each pair of words has in common, starting with the example: “Tell me how an orange and a banana are alike”.

- If the participant answers in a concrete manner, then say only one additional time: “Tell me another way in which those items are alike”.
- If the participant does not give the appropriate response (fruit), say, “Yes, and they are also both fruit.” Do not give any additional instructions or clarification.

After the practice trial, say: “Now, tell me how a train and a bicycle are alike”. Following the response, administer the second trial, saying: “Now tell me how a ruler and a watch are alike”.

- Do not give any additional instructions or prompts. **Record the participant’s verbatim response.**

Scoring:

The following responses are considered correct:

Train-bicycle = means of transportation, means of travelling, you take trips in both.

Ruler-watch = measuring instruments, used to measure.

Examples of incorrect responses:

Train-bicycle = they have wheels.

Ruler-watch = they have numbers.

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10. Delayed Recall:

Administration: Give the following instruction: **“I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember.”**

- Give a checkmark for each of the words correctly recalled spontaneously without any cues.

For any word not free recalled, prompt the subject with the semantic category cue provided below.

- If the participant does not recall the word after the category cue, give him/her a multiple choice trial, using the following example instruction, **“Which of the following words do you think it was NOSE, FACE, or HAND?”**
- Make a check mark (✓) in the allocated space if the participant remembered the word with the help of a category or multiple-choice cue.

Use the following category and/or multiple-choice cues for each word, when appropriate:

FACE:	category cue: <i>part of the body</i>	multiple choice: <i>nose, face, hand</i>
VELVET:	category cue: <i>type of fabric</i>	multiple choice: <i>denim, cotton, velvet</i>
CHURCH:	category cue: <i>type of building</i>	multiple choice: <i>church, school, hospital</i>
DAISY:	category cue: <i>type of flower</i>	multiple choice: <i>rose, daisy, tulip</i>
RED:	category cue: <i>a colour</i>	multiple choice: <i>red, blue, green</i>

Scoring: place a check mark in the allocated space on the worksheet indicating if recall with no cue, recall with category cue, recall with multiple choice cue or incorrect.

11. Orientation:

Administration: Give the following instructions: **“Tell me the date today.”**

- If the participant does not give a complete answer, then prompt accordingly by saying: **“Tell me the [year, month, exact date, and day of the week].”**
- Then say: **“Now, tell me the name of this place, and which city it is in.”**

Scoring: Place a check mark in the allocated space on the worksheet next to each item correctly answered. The participant must tell the exact date and the exact place (name of hospital, clinic office) to be considered correct.

The MOCA total score is not calculated for ADNI-D.

Rey Auditory Verbal Learning Test (AVLT)

Rey, A. (1964). *L'examen clinique en psychologie*. Paris: Presses Universitaires de France.

Description

This is a test of episodic memory that assesses the ability to acquire 15 words across five immediate learning trials, to recall the words immediately after an intervening interference list, and to recall and recognize the words after a 30-minute delay interval.

Trial I Administration

After engaging the participant's attention, the examiner should say, **"I am going to read a list of words. Listen carefully, for when I stop you are to repeat back as many words as you can remember. It doesn't matter in what order you repeat them, just try to remember as many as you can."** The examiner then reads the words aloud.

Immediately after the words are read, the participant recalls as many as possible and these are recorded by the examiner.

Trial II – V Administration

Immediately after each preceding trial, the examiner says, **"Now I am going to read the same words again, and once again when I stop I want you to tell me as many words as you can remember, including words you said the first time. It doesn't matter in what order you say them, just say as many words as you can remember, whether or not you said them before."** Immediately after the words are read on each trial, the participant recalls as many as possible and these are recorded by the examiner.

List B Administration

Immediately after the fifth learning trial, the examiner says, **"Now I'm going to read a second list of words. Listen carefully, for when I stop you are to repeat back as many words as you can remember. It doesn't matter in what order you repeat them, just try to remember as many as you can."** Immediately after the words are read on each trial, the participant recalls as many as possible and these are recorded by the examiner.

Trial VI Administration

Immediately after the list B trial, the examiner says, **"Now tell me all the words you can remember from the first list."** The participant recalls as many as possible and these are recorded by the examiner. **Note:** the words from the original list are **NOT** read again before recall is elicited on this trial.

30 Minute Delay Administration

After 30-minutes of interpolated testing (timed from the completion of List B recall), the examiner says, **"A while ago I read a list of words to you several times, and you had to**

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repeat back the words. Tell me the words from that list.” The participant recalls as many as possible and these are recorded by the examiner. **Note:** the words from the original list are **NOT** read again before recall is elicited on this trial.

Scoring

For each trial, record verbatim all responses. Correct responses are defined as stimulus words recalled correctly by the participant.

Please note: pluralization and singularization of an actual stimulus word are counted as correct.

Intrusions are defined as any non-stimulus word (i.e. a word that is not on the list) recalled by the participant. Preservations are defined as repetition of a word (either an intrusion or correct stimulus word) in the same trial. The first time a subject recalls a stimulus word it is counted as correct. If later, in the same trial, the same stimulus word is recalled, the second recall is a perseveration. With non-stimulus words, it is considered an intrusion the first time the subject recalls the word and if the same non-stimulus word is recalled again (in the same trial), it is counted as a perseveration.

Total correct and total intrusions are recorded on the eCRF. Total perseverations are not captures.

Recognition Administration

Present the participant with a pencil and the word recognition sheet and say,
“Sometimes people can remember more of the words if they see them. Read all these words and circle the ones that you think were on that first list I read...the list I read 5 times to you.”

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Trail Making Test

Partington JE, Leiter RG. Partington's Pathway Test. *The Psychological Service Center Bulletin*. 1949;1:9-20. Reitan RM. Validity of the Trail-Making Test as an indication of organic brain damage. *Perceptual Motor Skills*. 1958;8:271-276. ; Reitan R, Wolfson D. *The Halstead- Reitan Neuropsychological Test Battery*. Tucson: Neuropsychology Press; 1985.; Spreen O, Strauss E. *A compendium of neuropsychological tests*. New York: Oxford University Press; 1998.

Description

This is a test of processing speed and executive function. Although both Parts A and B depend on visuomotor and perceptual-scanning skills, Part B also requires considerable cognitive flexibility in shifting from number to letter sets under time pressure.

- PART A** consists of 25 circles numbered 1 through 25 distributed over a white sheet of 8 1/2" x 11" paper. The participant is instructed to connect the circles with a drawn line as quickly as possible in ascending numerical order.
- PART B** also consists of 25 circles, but these circles contain either numbers (1 through 13) or letters (A through L). The participant must connect the circles while alternating between numbers and letters in ascending order (e.g., A to 1; 1 to B; B to 2; 2 to C).

The participant's performance is judged in terms of the time, in seconds, required to complete each Trail. The time to complete Part A (150-second maximum) and Part B (300-second maximum) will be the primary measure of interest (testing is stopped if the maximum time is reached). Both parts of the Trail Making Test are available in multiple forms of equal difficulty for purposes of repeated evaluation.

Administration:

PART A:

Place the form for Part A sample in front of the participant. Read aloud the instructions:

"There are numbers in circles on this page. Please take the pencil and draw a line from one number to the next, in order. Start at 1 (point to the number), then go to two (point to the number), then go to three (point to the number) and so on. Please try not to lift the pencil as you move from one number to the next. Work as quickly as you can."

If the participant makes an error, mark through the line and go back to the point at which the error was made and say, for example:

"You were at number two. What is the next number?"

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Wait for the participant's response and say:

"Please start here and continue."

If the participant completes the sample correctly, go to Test A. Repeat the instructions given for the sample. Start timing as soon as the instruction is given to begin. Stop timing when Trail is completed, or stop participant when maximum time is reached. Allow a maximum of 150 seconds for the test.

PART B:

Place the form for Part B sample practice in front of the participant. Read aloud the instructions:

"There are numbers and letters in circles on this page. Please take the pencil and draw a line, alternating in order between the numbers and letters. Start at number 1 (point to the number), then go to the first letter, A (point to the letter), then go to the next number, 2 (point to the number) and then the next letter, B (point to the letter) and so on. Please try not to lift the pencil as you move from one number or letter to the next. Work as quickly as you can."

If the participant makes an error, mark through the line and go back to the point at which the error was made and say, for example:

"You were at number two. What is the next letter?"

Wait for the participant's response and say:

"Please start here and continue."

If the participant completes the sample correctly, go to Test B. Repeat the instructions given for the sample. Start timing as soon as the instruction is given to begin. Stop timing when trail is completed or stop participant when maximum time is reached. Allow a maximum of 300 seconds for the test.

Scoring

Record the total number of seconds to complete Part A, up to a maximum of 150 seconds. If the participant is not finished by 150 seconds, the score is 150.

Record the total number of seconds to complete Part B, up to a maximum of 300 seconds. If the participant is not finished by 300 seconds, the score is 300.

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For both Part A and Part B, record errors of commission and omission as described below:

‘Errors of commission’ are defined as errors occurring when the participant connects two circles in the incorrect sequence. Each time this occurs, one error of commission is scored.

‘Errors of omission’ are defined as errors occurring because the participant failed to draw a connecting line to a given circle in the correct sequence. This only occurs when the participant is very slow and does not complete the task in the time allotted.

One incorrectly sequenced number/letter may, in rare instances, be counted as both an error of commission and an error of omission (e.g., if the participant incorrectly draws a line to the letter ‘K’, but then never makes it back to that letter in the correct sequence).

If it is clear that the participant intended to touch a circle but barely missed it, do not count it as an omission. However, caution the participant to touch circles when you first observe this.

If the participant passes through another circle while clearly on the way to the next circle in the sequence, caution to avoid touching circles other than the ones intended, and make a note of what occurred on the raw data form, but do not count as an error of commission.

The participant may be unable to complete this test due to physical problems (e.g., tremor, dystonia). In that event, indicate the reason for incomplete data (i.e., physical problem, other problem, cognitive/behavioral problem, refusal) by completing an additional comment form online, referencing the test not administered and reason.

Global, Functional, and Behavioral Assessments

Telephone Visit in Replace of In-Clinic Visit Option

Please note that there is a telephone visit in replace of in-clinic visit option that should be presented to participants who are unwilling or unable to come into the clinic for their in-clinic visit. This telephone visit would replace the in-clinic visit and is separate from the interim phone checks.

The following participants are eligible for telephone visits:

1. ADNI-D enrollees who have completed all baseline assessments under ADNI-D but then after this visit are only available by phone.

The Global, Functional, and Behavioral Assessments that can be done over the phone include:

- **Clinical Dementia Rating (CDR)**
- **Geriatric Depression Scale (GDS)**
- **Neuropsychiatric Inventory (NPI)**
- **Activities of Daily Living (FAQ)**

The Everyday Cognition is also part of the telephone visit; however, it must be mailed to the participant and study partner **PRIOR** to the scheduled visit. The participant and study partner then have to mail the assessment back to the site for data entry.

If either the participant or study partner are unable to return the assessment by mail, the interview may be done over the phone as long as the participant and/or study partner are looking at the worksheet.

Clinical Dementia Rating (CDR) Versions

CDR Version 1- Full interview with informant and participant

- Should be used at every in clinic visit where a CDR interview is conducted with both the participant and informant.

CDR Version 2- Full interview with only informant

- Used in cases where a telephone visit is being conducted in replace of the in person clinic visit, as CDR version 1 should NOT be used for telephone visits.
- Or in cases when a standard in clinic study visit is being conducted but the participant is unable to participate in the interview.

CDR Version 3- Abbreviated interview with only informant

- Limited interview that should only be used when the study participant is unable to participate in the interview and the informant is not willing to complete CDR version 2 interview. This version is a very brief questionnaire and can be used when the informant has limited time available.

CDR Version 4- Full interview with only participant

- If the study participant doesn't have a study partner/informant this version should be used when conducting the CDR interview.

All four versions of the CDR interview are able to determine a global CDR score.

Clinical Dementia Rating (CDR)

Morris, JC "Clinical Dementia Rating" 1993 *Neurology* 43: 2412-2414

CDR Rater

CDR certification is required prior to administering the CDR for ADNI-D. It would be preferable for the CDR rater to conduct only the CDR on a given visit. If this is not possible due to staffing, the CDR should be conducted prior to other assessments. If possible, the same person should administer the CDR at each participant's visit throughout the study.

Anyone administering the CDR must be certified. Certification is required every five years and can be done online through the Washington University website:

<http://alzheimer.wustl.edu/cdr/Application/Step1.htm>.

A certificate is sent to the rater upon completion. Please ensure to email a copy of the certificate to adcs-clinops@ucsd.edu or fax to (858) 246-1415.

Instructions

Worksheets have been created with a semi-structured interview for the informant and participant. A certified CDR Rater must conduct the interviews and complete the provided worksheets. Supplementary information may be added to the existing questions on the worksheet to support the assigned box scores.

- Use all information and make the best judgment. Score each category (M, O, JPS, CA, HH, PC) as independently as possible.
- Mark in only one box, rating impairment as decline from the person's usual level due to cognitive loss alone, not impairment due to other factors, such as physical handicap, depression, or personality change.
- Occasionally the evidence is ambiguous and the clinician's best judgment is that a category could be rated in either one of the two adjacent boxes, such as mild (1) or moderate (2) impairment. In that situation, the standardized procedure is to check the box of greater impairment.

Determining Global CDR Score

The global CDR is derived from the scores in each of the six categories ("box scores"):

- | | |
|---------------------------------|----------------------|
| 1. Memory | 4. Community Affairs |
| 2. Orientation | 5. Home and Hobbies |
| 3. Judgment and Problem Solving | 6. Personal Care |

Memory (M) is considered the primary category and all others are secondary.

CDR = Global Box Score

M = Memory Box Score

CDR = M if at least three secondary categories are given the same score as memory.

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- When $M = 0.5$, $CDR = 1$ if at least three of the other categories are scored 1 or greater.
- If $M = 0.5$, CDR cannot be 0; it can only be 0.5 or 1.
- If $M = 0$, $CDR = 0$ unless there is impairment (0.5 or greater) in two or more secondary categories, in which case $CDR = 0.5$.

Whenever three or more secondary categories are given a score greater or less than the memory score, $CDR =$ score of majority of secondary categories on whichever side of M has the greater number of secondary categories. In the unusual circumstance in which three secondary categories are scored on one side of M and two secondary categories are scored on the other side of M , $CDR = M$.

The above rules do not cover all possible scoring combinations. Unusual circumstances are scored as follows:

1. With ties in the secondary categories on one side of M , choose the tied scores closest to M for CDR (e.g. M and another secondary category = 3, two secondary categories = 2, and two secondary categories = 1; $CDR = 2$).
2. When only one or two secondary categories are given the same score as M , $CDR = M$ as long as no more than two secondary categories are on either side of M .
3. When $M = 1$ or greater, CDR cannot be 0; in this circumstance, $CDR = 0.5$ when the majority of secondary categories are 0.

Aphasia is taken into account by assessing both language and non-language function in each cognitive category. If aphasia is present to a greater degree than the general dementia, the participant is rated according to the general dementia. Supply evidence of non-language cognitive function.

To verify the global CDR, you may also access the Washington University CDR web page:

<http://www.biostat.wustl.edu/adrc/>

Sum of Boxes CDR Score

The eCRF will automatically calculate the CDR Sum of Boxes (SOB) score based on the assigned box scores, upon submission of the eCRF.

Cognitive Change Index

Adapted from Saykin et al 2006

Description

The Cognitive Change Index is a subset of items that are focused on memory concerns adapted from a longer panel of self- and informant-report measures originally used to calculate a cognitive complaint index. The Cognitive Change Index is a self-report scale, consisting of 20 items that the subject rates on a scale from 1 to 5 as to whether there has been no change or some degree of change in each of these functions compared to 5 years ago.

Scoring

The total score for the entire self-report can range from 20 (no change) to 100 (severe change). Only the first 12 questions that specifically address memory concerns are used to calculate the CCI-Memory Total Score in ADNI-D, which has a range from 12 (no change) to 60 (severe change).

Everyday Cognition (ECOG)

Farias ST, Mungas D, Reed BR, Cahn-Weiner D, Jagust W, Baynes K, Decarli C. The measurement of everyday cognition (ECog): scale development and psychometric properties. Neuropsychology. 2008 Jul;22(4):531-44.

Description

The ECog is a brief questionnaire assessing the participant's capability to perform normal everyday tasks, in comparison to activity levels 10 years prior, on a 5 point scale. Three domains are assessed: Memory, Language and Executive Functioning. The ECog is conducted at baseline and the Month 30 Follow Up visit by both the participant and the study partner (if applicable)

When a participant is unwilling or unable to come into the clinic their follow up visit, the ECog should be mailed to the participant and study partner **PRIOR** to the scheduled visit. The participant and study partner should then mail their completed questionnaires back to the site for data entry.

- Participants and their study partners will independently complete a separate questionnaire, within the clinic, at the time of their ADNI-D in-clinic visits.
- Check all ECog forms before the end of the visit to ensure they are completed fully and, if necessary, direct the participant or study partner to complete the form.
- If the reading level of either the participant or the study partner is low, you may read the items out loud and record their ratings.

Instructions

Ask the participant/caregiver/study partner to rate the participant's ability to perform certain everyday tasks now as compared to his/her ability to do these same tasks 10 years ago. In other words, the response should reflect how he/she was doing 10 years ago and indicate any change in the participant's capacity at present.

Ratings should reflect the amount of change on a five-point scale:

1. No change or actually performs better than 10 years ago
2. Occasionally performs the task worse but not all of the time
3. Consistently performs the task a little worse than 10 years ago
4. Performs the task much worse than 10 years ago
5. Participant/caregiver doesn't know.

ECog Scoring

You do not need to calculate a total score, as the eCRF will not capture total score for this assessment.

Geriatric Depression Scale (GDS)

Sheikh JL, Yesavage JA, Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. Clinical Gerontology: a Guide to Assessment and Intervention 165-173, NY: The Haworth Press, 1986.

The Geriatric Depression Scale is a brief questionnaire that consists of 15 questions and is designed to identify symptoms of depression in the elderly. The GDS is conducted at Baseline and Month 30 Follow Up visits, and is not used as an inclusion criterion for ADNI-D. Site staff should administer the GDS as a direct interview with the participant only, **NOT** the study partner.

Instructions

Say, **“In the next part of this interview, I will ask you questions about your feelings. Some of the questions I will ask you may not apply, and some may make you feel uncomfortable. For each question, please answer ‘yes’ or ‘no’, depending on how you have been feeling in the past week, including today.”**

- Answers in **BOLD CAPS** suggest depression. Although differing sensitivities and specificities have been obtained across studies, for clinical purposes a score >5 points is suggestive of depression and should warrant a follow-up interview. Scores >10 are almost always depression.
- If the participant becomes aphasic, use a point board or a board with the scale and yes/no next to the items and have the participant point out the correct answer.
- If the participant does not comprehend the first 5 questions adequately enough to give answers, then check the box that states “Participant is unable to complete the GDS based on the clinician’s best judgment.”

Choose the best answer for how you have felt over the past week:

- | | |
|------------------|---|
| yes or NO | 1. Are you basically satisfied with your life? |
| YES or no | 2. Have you dropped many of your activities and interests? |
| YES or no | 3. Do you feel that your life is empty? |
| YES or no | 4. Do you often get bored? |
| yes or NO | 5. Are you in good spirits most of the time? |
| YES or no | 6. Are you afraid that something bad is going to happen to you? |
| yes or NO | 7. Do you feel happy most of the time? |
| YES or no | 8. Do you often feel helpless? |
| YES or no | 9. Do you prefer to stay at home, rather than going out and doing new things? |
| YES or no | 10. Do you feel you have more problems with memory than most? |
| yes or NO | 11. Do you think it is wonderful to be alive now? |
| YES or no | 12. Do you feel pretty worthless the way you are now? |
| yes or NO | 13. Do you feel full of energy? |
| YES or no | 14. Do you feel that your situation is hopeless? |
| YES or no | 15. Do you think that most people are better off than you are? |

NOTE: If the participant says he/she cannot choose an answer, ask him/her to select the best response.

Functional Assessment Questionnaire (FAQ)

Pfeffer, RI, Kurosaki TT, Harrah CH, et al. Measurement of functional activities of older adults in the community. J Gerontol 37:323-9, 1982.

Description

Based on an interview with a study partner or qualified informant, the FAQ measures the participant's ability to carry out ten complex activities of daily living. The interview is conducted at Baseline and the Month 30 Follow Up visit.

Instructions

The study partner should be queried based on the participant's level of difficulty on each item in the past four weeks.

FAQ Score

Individual responses are only captured on the eCRF. You do not need to calculate the total score for the FAQ. The total score is calculated automatically in the data system and will not be displayed on the eCRF.

Modified Hachinski

Rosen, *Modification of Hachinski Ischemic Score* (*Ann Neurol* 7: 486-488, 1980)

The form should be completed by a clinician familiar with the participant.

Instructions

Complete the Modified Hachinski using information obtained from the medical history, physical and neurological exams and/or medical records. Indicate if a characteristic is present by checking 'present' or 'absent'.

CLARIFICATION OF TEST ITEMS

- 1. Abrupt Onset of Cognitive Impairment**
Reported rapid onset with acknowledgement that gradual changes may have also occurred.
- 2. Stepwise Deterioration of Cognitive Impairment**
Cognitive decline, aside from onset, noted to occur over days and followed by plateaus.
- 3. Somatic Complaints**
e.g., headache; tinnitus; chest pain; malaise.
- 4. Emotional Incontinence**
Occasional displays of intense emotional expression such as crying, beyond that which would be considered appropriate to a given situation.
- 5. History of Hypertension**
History of blood pressure of >150/95 for 6 months.
- 6. History of Strokes**
Hemiparesis, aphasia.
- 7. Focal Neurological Symptoms**
Transient dizziness; diplopia lasting hours; seizures.
- 8. Focal Neurological Signs**
Unequal deep tendon reflexes, extensor plantar response, nystagmus.

Scoring

The eCRF will automatically calculate the modified hachinski total score as data is entered.

Neuropsychiatric Inventory (NPI)

© J. L. Cummings, 1994

The purpose of the Neuropsychiatric Inventory (NPI) is to obtain information on the presence of psychopathology in participants with brain disorders. The NPI was developed for application to participants with Alzheimer’s disease and other dementias, but it may be useful in the assessment of behavioral changes in other conditions. The NPI is to be administered by a site clinician. Certification is not required.

Twelve behavioral areas are included in the NPI:

Delusions	Agitation / Aggression	Anxiety
Apathy	Irritability	Night-time behavior
Hallucinations	Depression	Euphoria
Disinhibition	Aberrant motor behavior	Appetite and eating changes

The NPI is based on responses from a study partner, preferably one living with the participant. The interview is best conducted with the study partner in the absence of the participant to facilitate an open discussion of behaviors that may be difficult to describe with the participant present.

If there is no study partner available, the interview should not be conducted and the first question on the eCRF and worksheet ‘was the assessment completed by the study partner’ should be documented as ‘not applicable – no study partner’

Several points should be made when you introduce the NPI interview to the study partner:

- Purpose of the interview
- Ratings – frequency, severity, distress (described below)
- Answers apply to behaviors that are new since the onset of the disease and have been present for the past four weeks or other defined period
- Questions usually can be answered with “yes” or “no” and responses should be brief

Questions should be asked exactly as written.

- Clarification should be provided if the study partner does not understand the question.
- Acceptable clarifications are restatements of the questions in alternate terms.

The questions pertain to changes in the participant’s behavior that have appeared since the onset of the illness:

- Behaviors that have been present throughout the participant’s life and have not changed in the course of the illness are not scored even if they are abnormal (e.g., anxiety, depression).
- Behaviors that have been present throughout life but have changed since the illness are scored (e.g., the participant has always been apathetic but there has been a notable increase in apathy during the period of inquiry).

GLOBAL, FUNCTIONAL, AND BEHAVIORAL ASSESSMENTS

The NPI is typically used to assess changes in the participant's behavior that have appeared in a defined period of time (e.g., in the past four weeks). Emphasize to the study partner that the questions pertain to behaviors that have appeared or changed since the onset of illness. For example: The questions might be phrased, "Since he/she began treatment with the new medications..." or "Since the dosage of _____ was increased..."

For all visits, ask the study partner to indicate whether the participant behaviors occurred during the previous 4 weeks. If so, use the following scales to rate the frequency, severity, and amount of distress that behaviors caused the caregiver.

The SCREENING QUESTION is asked to determine if the behavioral change is present or absent. If the answer to the screening question is negative, mark NO and proceed to the next screening question without asking the subquestions.

- If the answer to the screening question is positive or if there are any uncertainties in the study partner's response or inconsistencies between the response and other information known by the clinician (e.g., the study partner responds negatively to the euphoria screening question but the participant appears euphoric to the clinician), the category is marked YES and is explored in more depth with the subquestions.
- If the subquestions confirm the screening question, the severity and frequency of the behavior are determined according to the criteria provided with each behavior. When determining frequency and severity, use the behaviors identified by the subquestions as most aberrant.

For Example: If the study partner indicates that resistive behavior is particularly problematic when you are asking the subquestions of the agitation section, then use resistive behavior to prompt judgments regarding the frequency and severity of agitation.

- If two behaviors are very problematic, use the frequency and severity of both behaviors to score the item.

For Example: If the participant has two or more types of delusions, then use the severity and frequency of all delusional behaviors (all types) to phrase the questions regarding severity and frequency. In some cases, the study partner will provide a positive response to the screening question and a negative reply to all subsections. If this happens, ask the study partner to expand on why they responded affirmatively to the screen.

- If they provided information relevant to the behavioral domain but in different terms, the behavior should be scored for severity and frequency as usual.
- If the original affirmative response was erroneous, leading to a failure to endorse any subquestions, then the behavior is changed to "NO" on the screen.

GLOBAL, FUNCTIONAL, AND BEHAVIORAL ASSESSMENTS

Some sections, such as the questions pertaining to appetite, are framed so as to capture whether there is an increase or decrease in the behavior (increased or decreased appetite or weight).

- If the study partner answered “yes” to the first member of the paired question (such as has the participant’s weight decreased?), do not ask the second question (has the participant’s weight increased?) since the answer to the second question is contained in the answer to the first.
- If the study partner answers “no” to the first member of the pair of questions, then the second question must be asked.

When determining FREQUENCY , say to the study partner:	<p>“Now I want to find out how often these things [define using the description of the behaviors they noted as most problematic on the subquestions] occur.”</p> <p>“Would you say that they occur less than once per week, about once per week, several times per week but not every day, or every day?”</p>
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Some behaviors, such as apathy, eventually become continuously present, and then “are constantly present” can be substituted for “every day.”

When determining SEVERITY , tell the study partner:	<p>“Now I would like to find out how severe these behaviors are. By severity, I mean how disturbing or disabling they are for the participant.” “Would you say that [the behaviors] are mild, moderate, or severe?”</p>
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Additional descriptors are provided in each section that may be used to help the interviewer clarify each grade of severity.

- In each case, be sure that the study partner provides you with a definite answer as to the frequency and severity of the behaviors.
- Do not guess what you think the study partner would say based on your discussion.

We have found it helpful to provide the study partner with a cue card on which is written the frequency and severity descriptions to allow them to visually see the response alternatives.

Frequency Descriptions:

- Less than once per week
- About once per week
- Several times per week
- Daily or continuous

Severity Descriptions:

- Mild
- Moderate
- Severe

This also saves the examiner from reiterating the alternatives with each question.

GLOBAL, FUNCTIONAL, AND BEHAVIORAL ASSESSMENTS

In very impaired participants or in participants with special medical circumstances, a set of questions may not be applicable.

For Example: Bed-bound participants may exhibit hallucinations or agitation but could not exhibit aberrant motor behavior.

If the clinician or study partner believes that the questions are inappropriate, then the section should be marked NA (upper right corner of each section), and no further data are recorded for that section. Likewise, if the clinician feels that the responses are invalid (e.g., the study partner did not seem to understand the particular set of questions asked), NA should also be marked.

When each domain is completed and the study partner has completed the frequency and severity rating, you may want to ask the associated **STUDY PARTNER DISTRESS** question if your protocol includes the distress assessment.

- To do this, ask the study partner how much, if any, “emotional or psychological” distress the behavior he/she just discussed causes him or her (the study partner).

The study partner must rate their own distress on a five point scale:

0	no distress
1	minimal
2	mild
3	moderate
4	severe
5	very severe or extreme

The distress scale of this instrument was developed by Daniel Kaufer, M.D.

Scoring the NPI

FREQUENCY is rated as:

1.	Occasionally	less than once per week
2.	Often	about once per week
3.	Frequently	several times per week but less than every day
4.	Very frequently	daily or essentially continuously present

GLOBAL, FUNCTIONAL, AND BEHAVIORAL ASSESSMENTS

SEVERITY is rated as:

1.	Mild	produces little distress in the participant
2.	Moderate	more disturbing to the participant but can be redirected by the study partner
3.	Severe	very disturbing to the participant and difficult to redirect

DISTRESS is scored as:

0	no distress
1	minimal
2	mild
3	moderate
4	severe
5	very severe or extreme

THUS, FOR EACH BEHAVIORAL DOMAIN THERE ARE FOUR SCORES:

1.	Frequency
2.	Severity
3.	Total (frequency x severity)
4.	Caregiver distress

THE SCORE FOR EACH DOMAIN IS:

DOMAIN SCORE = FREQUENCY X SEVERITY

- A **TOTAL NPI SCORE** can be calculated by adding all domain scores together
- The distress score is not included in the total NPI score.
- Individual and total distress scores can be generated from the NPI.

NPI REFERENCES

Instructional Videotape

An instructional videotape demonstrating the use of the NPI is available through:

**UCLA Alzheimer's Disease Center
Neuropsychiatric Institute
710 Westwood Plaza
Los Angeles, California 90095-1769**

The cost of the videotape is \$25.00 (subject to change).

GLOBAL, FUNCTIONAL, AND BEHAVIORAL ASSESSMENTS

References

Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44: 2308-2314.

Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. *Neurology* 1996; 46: 130-135.

Acknowledgments

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Psychiatric Emergency/Suicidal Ideation Action Plan

Suicidal Risk Assessment and Suicidal Ideation

Asking questions about suicide ideation, intent, plan, and attempts is never easy. Sometimes the participant will provide the opening to ask about suicide, but usually the topic does not readily flow from the presenting topic. Nevertheless it is important to ask questions about suicidal ideation and/or behavior whenever it is thought that the participant is endorsing aspects of suicidal ideation or when it is deemed that a suicidal risk assessment is warranted. It's worth keeping in mind that suicidality can be understood as an attempt by the individual to solve a problem, one that they find overwhelming.

Asking about suicidal ideation and intent does NOT increase the likelihood of someone thinking about suicide for the first time or engaging in such behaviors.

Warning Signs for Suicidal Behavior:

- Threatening to hurt or kill self
- Looking for ways to kill self; seeking access to pills, weapons or other means
- Talking or writing about death, dying or suicide

The remaining list of warning signs should alert you that a mental health evaluation needs to be conducted in the **VERY** near future and that precautions need to be put into place **IMMEDIATELY** to ensure the safety, stability and security of the individual.

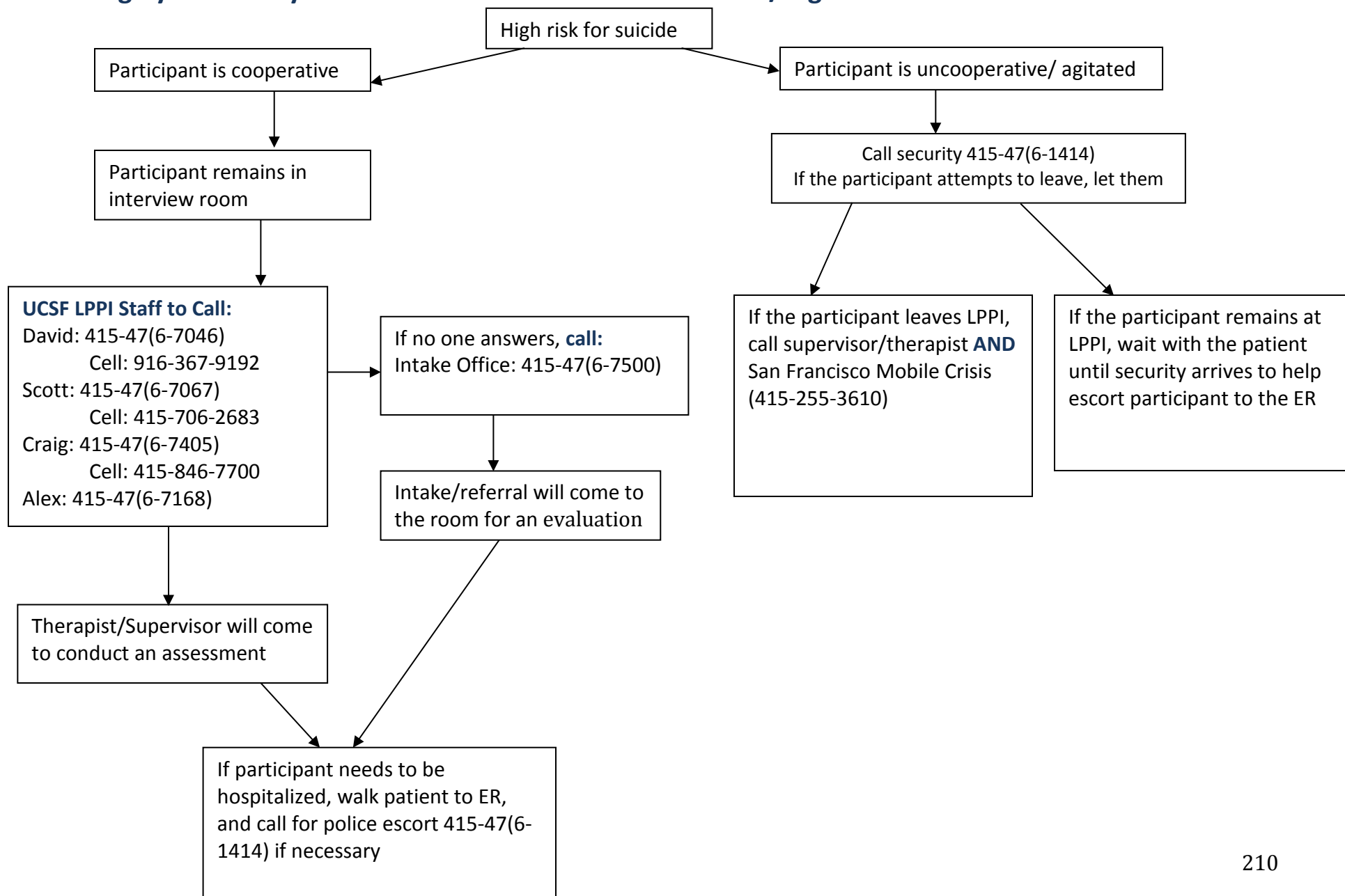
- Hopelessness
- Rage, anger, seeking revenge
- Acting reckless or engaging in risky activities, seemingly without thinking
- Feeling trapped – like there's no way out
- Increasing alcohol or drug abuse
- Withdrawing from friends, family or society
- Anxiety, agitation, unable to sleep or sleeping all the time
- Dramatic changes in mood
- No reason for living, no sense of purpose in life

Other behaviors that may be associated with increased short-term risk for suicide are when the participant makes arrangements to divest responsibility for dependent others, or making other preparations such as updating wills, making financial arrangements for paying bills, saying good bye to loved ones, etc.

If the participant is deemed to be at immediate risk for engaging in self-destructive behaviors, follow the Emergency Suicide Action Plan below. Any endorsement of suicidal ideation warrants a suicide risk assessment to be performed.

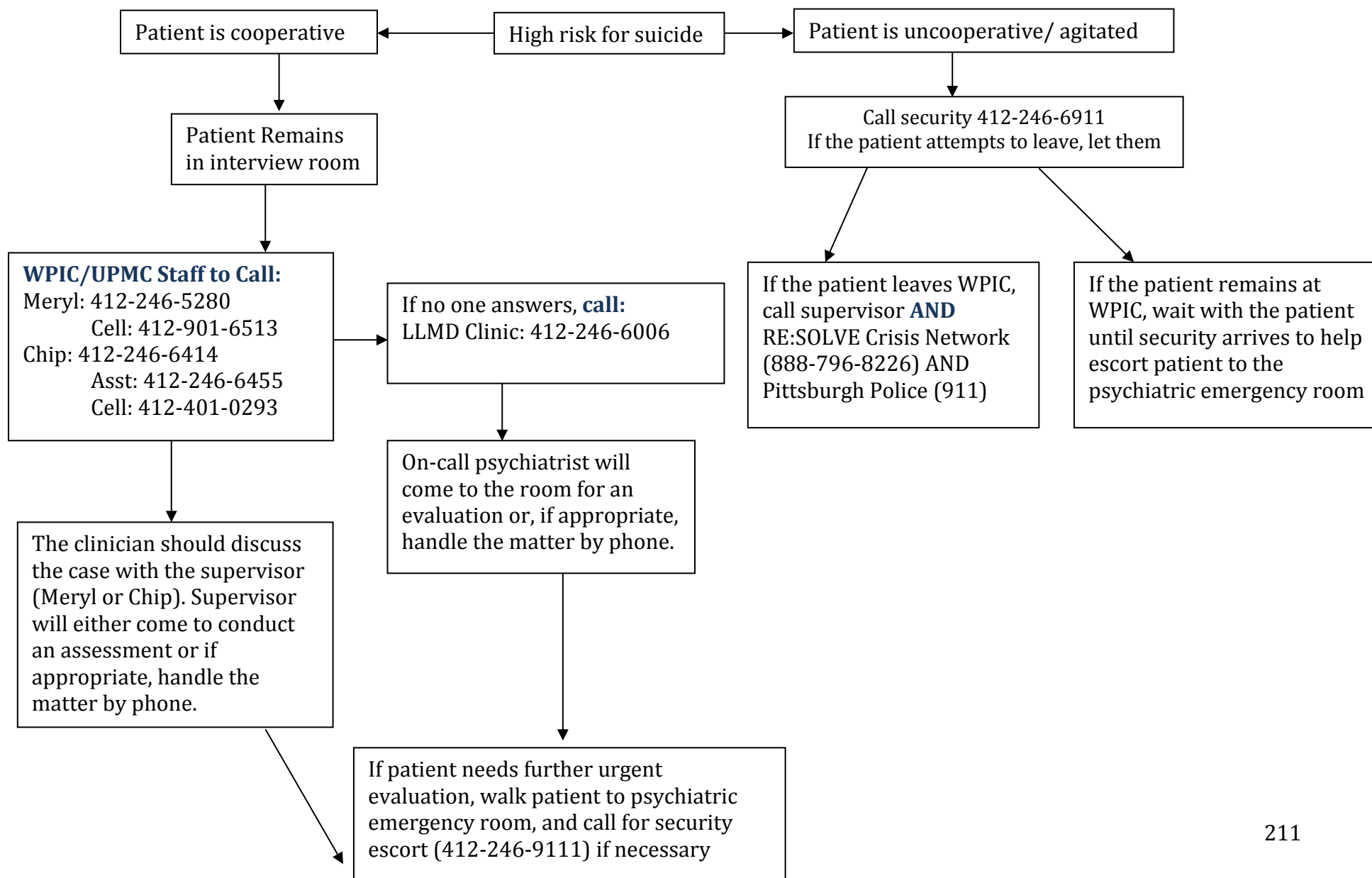
PSYCHIATRIC EMERGENCY ACTION PLAN

Langley Porter Psychiatric Institute Protocol for Medium/High Suicide Risk Assessment



PSYCHIATRIC EMERGENCY ACTION PLAN

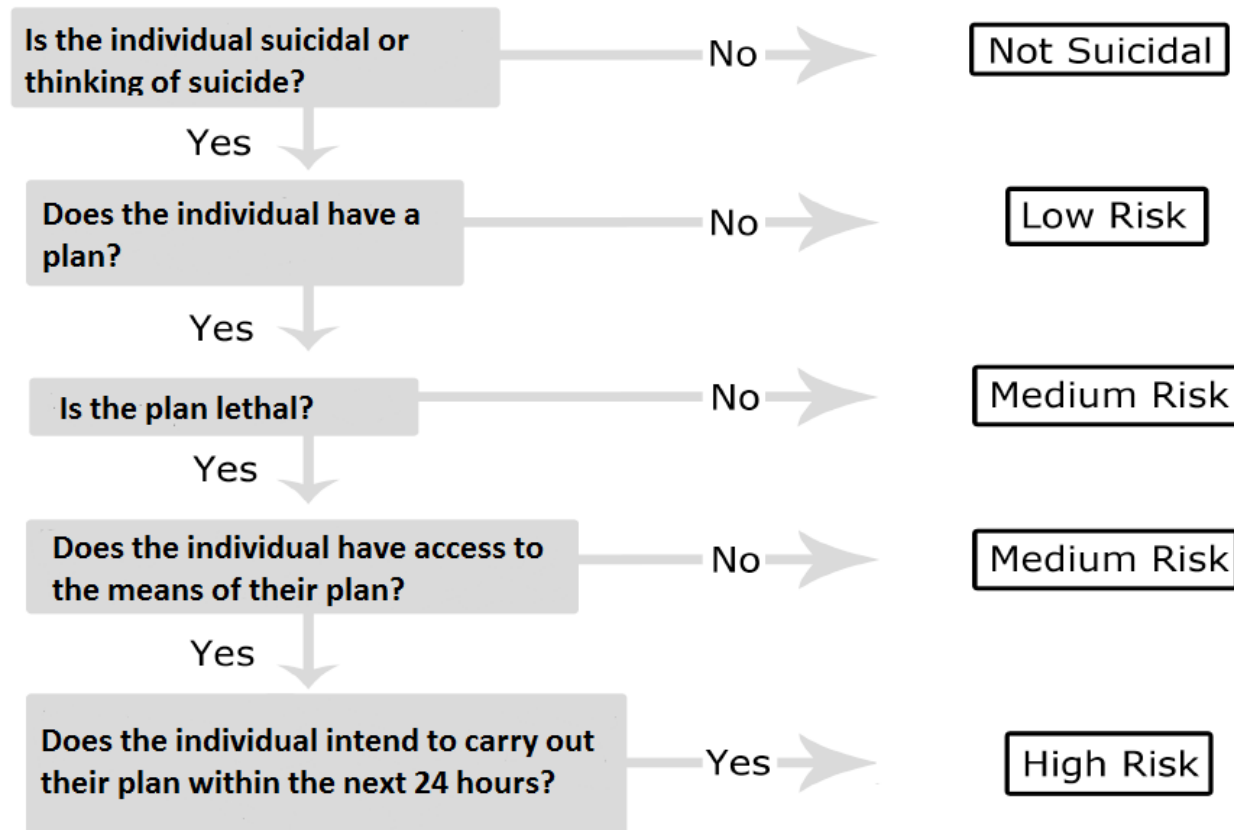
University of Pittsburgh Medical Center's Western Psychiatric Institute & Clinic Protocol for Medium/High Suicide Risk Assessment



	<u>WHAT IT MEANS</u>	<u>WHAT TO ASK</u>
DESIRE	The first critical element of suicide assessment is to investigate if the person at risk has any desire to end their own life. In order to investigate desire, all a person has to do is clearly and directly ask about suicide.	<i>Are you feeling suicidal?</i>
		<i>With everything that you're saying today, it makes me wonder, are you thinking of taking your own life?</i>
		<i>Often people who are having these feelings are thinking about suicide. Are you considering killing yourself?</i>
CAPABILITY	Physical capability is about the development of a plan to attempt, availability and access to the means of that plan, and lethality of the plan. If an individual doesn't have the means, it is important to check to see if they have a realistic plan about how to procure the means.	<i>I'd really like to know, do you have a plan?</i>
		<i>Have you thought about a method you'd use to attempt?</i>
		<i>Do you have access to your plan? How will you get the means?</i>
		<i>Are you alone right now?</i>
	Emotional capability is a demonstrated set of attitudes on suicide by the person at risk, and their willingness to attempt. Prior exposure to suicide is an important risk factor. Lack of basic self-care may also make someone more impulsive. Similarly, substance abuse, or severe mental illness can cause a person at risk to have a diminished connection with reality, and thus be more likely to take severe measures.	<i>Have you attempted suicide before? What happened then?</i>
		<i>Have you been feeling hopeless/guilty/worthless?</i>
		<i>Have you had a chance to eat lunch today? What about drinking water?</i>
		<i>Are you on any substances today? Have you been drinking?</i>
INTENT	While individuals may have thoughts of suicide, and even have developed a plan, that doesn't necessarily mean they have a high level of intent. It's important to ask about a timeline for attempting. The timeline of an expected attempt highly affects the acuity of the crisis, and the way a caregiver will intervene.	<i>When do you plan on carrying out your plan?</i>

Determining Risk Level and Intervention

While all suicidal ideation is serious and needs to be addressed, some is more likely to result in an attempt.



Levels of Risk and Interventions

LEVEL OF RISK	LEVEL OF INTERVENTION
Low Risk To be at low risk of a suicide attempt is to have thoughts of suicide, but no plan or scheduled attempt. The person at risk may have desire, but will have no capability or intent.	Assess the individual's outside resources and sources of social support, and offer relevant referrals for long-term care. Make a safety plan: help the individual come up with a set of steps that he or she promises to follow in order to stay safe. Have them contract to call the lab, their doctor, a friend or family member, or even the suicide prevention hotline (1-800-273-8255) if they start to feel worse. Encourage self-care and plans for the immediate future.
Medium Risk An individual at medium risk of a suicide attempt has suicidal ideation and some sort of inoperative plan. While they have thought about a method, they have no access to the means of their attempt, their plan isn't lethal, or they don't have the intent to attempt in the near future.	In addition to assessing the individual's outside resources and sources of social support, have the individual contract a safety plan, including who to contact during a suicidal crisis, and how to separate themselves from the means of their plan. For example, if they plan on overdosing, come up with a plan that they'll talk to their doctor to temporarily give back the pills, and work with doctors to monitor their prescriptions more carefully. Often times the individual might have emotional capability, but no intent. If necessary, call the local mobile crisis (San Francisco Mobile Crisis: 415-970-4000) or emergency services (911) to do a wellness check. Come up with a specific self-care plan. Follow up in a few days.
HIGH RISK When someone is at high risk, it means that they're thinking about suicide, they have the capability to attempt, and they have the intention to attempt within 24 hours.	Once the individual has been determined to be at high risk for suicide, do not leave the individual alone. Call for the supervisor/therapist/staff. If the individual is cooperating, accompany them to the nearest psychiatric emergency unit or call for emergency services or Mobile Crisis. If the individual is uncooperative, call building security or 911.

Effective ways to communicate during Suicide Risk Assessment

WHAT TO DO	WHAT IT IS	WHAT TO SAY
Reflecting	Often when someone is in a state of crisis they think about the problem that put them in the emotional state of a crisis, but not about that emotional state. Redirect the conversation to their actual feelings as opposed to fixating on the problem that triggered the feelings. Simply naming what someone is feeling, and giving it importance, helps people at risk grow more confident in giving priority to their needs.	<p><i>Person at risk: I never have anyone to talk to. It's like no one cares.</i></p> <p><i>You: It sounds like you are feeling lonely because you have no one to talk to.</i></p>
Open-ended Questions	Open-ended questions are the opposite of closed-ended questions. A closed-ended question is a question with a limited set of possible answers. Open-ended questions are a great way to move the conversation along. If no content is being voiced, you will have to come up with questions to ask.	<p><i>You: How are you doing today?</i></p> <p><i>You: What has been on your mind to make you feel this way?</i></p>
Attending	Attending is the set of behaviors attached to being attentive. In person, these cues include establishing eye contact, sitting forward, and nodding. Each of these things communicates, nonverbally, that the listener cares about what is being said.	<p><i>You: Mmmhm</i></p> <p><i>You: I hear you</i></p>
Clarifying	Clarifying is an effective way to reestablish rapport. It's better to ask what the individual is feeling, rather than to assume and potentially cause conflict. Asking clarifying questions lets the individual know that you are listening closely enough to recognize when you understand or don't understand their sentiments. Additionally, it lets them know that you respect them and are truly interested in what they have to say.	<p><i>You: I'm not sure I understand what you mean by that.</i></p> <p><i>You: Can you repeat that? I'm not sure I got it.</i></p> <p><i>You: Wait, would you mind explaining again? I really want to understand what you mean.</i></p>

San Francisco Resources

Westside Crisis	Crisis Clinic is a sliding-scale community mental health clinic. It offers a voluntary, drop-in service open to any adult in need of emergency psychiatric care. Visits include suicide assessment, brief counseling, medication, and referral to longer term therapy.	Monday - Friday: 8 am–6 pm Saturday: 9 am – 4 pm Closed on Sundays	245 11 th Street San Francisco, CA 94103 415-355-0311 http://westside-health.org/
Mobile Crisis	Mobile Crisis is an emergency crisis intervention service that offers immediate treatment or triage for individuals suffering from emotional crisis or symptoms of acute psychiatric illness. When called, they will triage patients at their location, and will provide brief crisis treatment and follow-up care or resources as needed. Mobile Crisis will not come if there is a firearm present.	Monday – Friday: 8:30 am - 11 pm Saturdays: 12 pm - 8 pm Closed on Sundays	415-970-4000 City and County of San Francisco
San Francisco Suicide Prevention	San Francisco Suicide Prevention is a crisis hotline which offers emotional support and brief intervention for callers who are in crisis.	24 hours/ 7 days a week	Local: 415-781-0500 National: 1-800-273-8255
Friendship Line	The Friendship Line at Institute on Aging is the nation's only 24-hour toll-free hotline for older and disabled adults. Trained staff and volunteers make and receive calls to and from individuals who are either in crisis or just in need of a friend.	24 hours/ 7 days a week	Local: 415-752-3778 National: 1-800-971-0016
San Francisco Behavioral Health Access	Access is a mental health referral line used to match eligible individuals seeking specialty mental health services with the appropriate community mental health resources. Services are provided for residents of San Francisco on a sliding scale bases.	24 hours/ 7 days a week	1280 Howard Street San Francisco, CA 94103 415-225-3737

Pittsburgh Resources

Western Psychiatric Institute and Clinic (WPIC)	<p>The University of Pittsburgh Medical Center (UPMC) provides a full range of adult and geriatric psychiatric services. The flagship psychiatric hospital, Western Psychiatric Institute and Clinic (WPIC), is accredited by JCAHO as well as the State of Pennsylvania's Departments of Health and of Public Welfare. Over the preceding 12 months, 6,407 unique patients (adult and geriatric) were evaluated at the hospital's emergency room.</p> <p>The adult service line has 186 adult inpatient beds available at WPIC. Over the last 12 months, 3,262 unique adult patients received inpatient services at WPIC and 32,195 unique adult patients received services through various outpatient clinics. The adult service line runs the Outpatient Assessment Center whose mission is to provide rapid psychiatric intake and evaluation of adults seeking mental health services. After centralized intake and initial assessment, the Outpatient Assessment Center directs patients to the appropriate site of service; this process can include referral to research studies.</p> <p>The geriatric service line at WPIC has an inpatient unit, with a total capacity of 42 beds. Over the last 12 months, over 500 unique patients (aged 60 year or older) were admitted to the inpatient unit. The interdisciplinary staff (psychiatry, medicine, nursing, neuropsychology, and social work) has special expertise in working with the geropsychiatric population. On an outpatient basis, a similar program integrating psychiatric, medical, and social services is offered at Benedum Geriatric Center, located in Montefiore Hospital (part of UPMC main campus; located less than a quarter mile from WPIC). Over the last 12 months, over 1,100 unique geriatric patients received</p>	24 hours/ 7 days a week	3811 O'Hara Street Pittsburgh, PA 15213 1-877-624-4100
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PSYCHIATRIC EMERGENCY ACTION PLAN

	services at Benedum.		
Late-Life Depression Prevention Program	The Late-Life Depression Prevention Program (ACISR/LLDP) outpatient clinic, directed by Charles F. Reynolds III, M.D., is located on the 7 th floor of Bellefield Towers (part of the university campus; located a half mile from WPIC). All outpatient research activities can be performed for both adult and geriatric patients, including activities related to recruitment, psychiatric evaluation, medical evaluation, and research assessments. The 2,000 sq. ft clinic has a lounge for subjects and their families. Bellefield Towers is handicapped accessible and has a circular drive for vans or cars to deliver and pick up passengers safely. A bus stop is located at the corner of the building and a public parking garage is adjacent to the building.	Monday-Friday 8am-4:30pm On call service 24 hours/7 days a week	100 North Bellefield Avenue Pittsburgh, PA 15213 412-246-6006
Allegheny County Crisis Intervention Hotline	Allegheny County Department of Human Services Crisis Intervention Hotline is a crisis hotline which offers emotional support and brief intervention for callers who are in crisis.	24 hours/ 7 days a week	Local: 1-888-424-2287 National: 1-800-SUICIDE (1-800-784-2433) OR 1-800-273-TALK (1-800-273-8255)
RE:SOLVE Crisis Network	Resolve Crisis Network is an emergency crisis intervention service that offers mental health crisis intervention and stabilization services for residents of Allegheny county in Pennsylvania. When called, they will have you speak with a trained counselor. A mobile dispatch unit of trained crisis counselors can travel to the person in crisis. Resolve has a walk in clinic to receive services as well as residential services.	24 hours/ 7 days a week	333 North Braddock Ave. Pittsburgh, PA 15208 1-888-7-YOU-CAN (1-888-796-8226) www.upmc.com/resolvecrisis

Adult Protective Services

Any adult who is over 65 years in age qualifies for adult protective services. However, anyone over 18 who has a developmental disorder or some other cognitive impairment is also protected by Adult Protective Services (APS).

When making a report, never take into consideration how this report may affect your client in the future, because it may prevent you from filing the report. We are legally mandated to do so under any of the circumstances described. To file a report, determine the type of abuse and gather information. Contact the local APS hotline, available 24/7. They will confirm whether or not to file a report.

Reportable Elder Abuse:

- **Physical:** Any non-accidental abuse that results in injury.
- **Emotional:** Can be verbal or nonverbal. Verbal includes demeaning, humiliating, scapegoating, or gas lighting. Nonverbal is often associated with neglect, and it involves preventing individuals from accessing friends or family or self-care.
- **Sexual:** Any unwanted sexual contact with an elder is considered sexual abuse. This includes unwanted viewing of pornographic material.
- **Financial:** Elders often have financial assets that make them targets. You may hear cases in which an elder's 'caretaker' is regularly depleting the elder's bank accounts or cashing their social security checks, while providing substandard care.
- **Neglect:** An elder may be considered neglected if they have a caretaker but are not receiving adequate care. This includes lack of access to food, housing, clothing, and very frequently healthcare.
- **Self-Neglect:** Many elderly individuals may have difficulty taking care of themselves and are unaware that their conditions are untenable or dangerous.

To file an APS Report, determine the type of abuse, and gather information. If in doubt, APS will confirm whether a report needs to be filed. Contact the local APS hotline at 415-355-6700, available 24/7.

PSYCHIATRIC EMERGENCY ACTION PLAN

Like Child Protective Services, Adult Protective Services (APS) is interested in providing victims of abuse with social services that will improve their situation. These services include:

- Coordination with law enforcement or legal interventions
- Finding alternative living arrangements
- Arrangement of medical and mental health assessments
- Financial management services
- Assistance applying for health or basic needs benefits
- Guardianship
- Counseling for the adult and family

HOMICIDE THREATS

Homicide threats must be reported to the person-at-risk. Please inform the police, who will inform the threatened party.

A threat is reportable for a combination of **risk** and **identifiability**. The format for assessing homicidal risk is very similar to identifying suicidal risk.

- **Desire:** How clear is the person's desire to kill the victim?
- **Capability:** Does the person have a feasible plan?
- **Intent:** When does the person plan on attempting murder?

Using the same metrics, determine if someone is low, medium, or high risk for attempted murder. Report to the police immediately if someone is high risk (exhibits desire, capability, and intent).

Additionally, the person they're threatening must be "**reasonably identifiable**."

Reasonable identification may include knowing a specific relation to the person-at-risk (ex: my wife), someone with an identifiable job (ex: the MUNI station attendant at Powell St), or someone who was clearly named.

When calling 911, you are only permitted to report information **relevant** to the homicide threat. Any other participant information, especially potentially sensitive details, such as HIV status, sexuality or psychiatric diagnoses are confidential.