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COMPLEXITY OF ADNI

ADNI is a complex and rich collection of data, imaging and biospecimens gathered longitudinally from carefully phenotyped subjects. It has massive potential for breakthrough discoveries in the field of Alzheimer's research. ADNI's development of standardized protocols allows results from both within the study and worldwide to be directly compared. Monitoring of participants provides us with longitudinal datapoints including progression from HC (Healthy Control) to MCI (Mild Cognitive Impairment) to AD (Alzheimer's Disease). This, along with data (neuropsych and clinical phenotyping), imaging (including FBP PET, MRI, and FDG PET scans) and biospecimens (including CSF and blood) taken at baseline and during follow ups, position the ADNI study as a uniquely comprehensive database and biobank. The data collected changed over time as technology advanced: ADNI1 was limited to 1.5T MRI & CSF, then Amyloid PET was developed & added in ADNI-GO & 2, then Tau PET at the end of ADNI2 & in 3. 3T MRI became the standard. Analysis of CSF Abeta & Tau was increasingly standardized until ADNI3 added the Elecsys IVD. With all of this comprehensive data, no other study in the world has anything comparable. To date, several 1000s of scientific publications have used ADNI data (complete listing of all publications available elsewhere on this site: http://adni.loni.usc.edu/news-publications/publications/). Many of these studies give insight to diagnostic and prognostic biomarkers explored thus far and potential future directions. ADNI serves as a valuable resource for replicating important new findings and validating novel biomarkers. Any scientist may apply for access to data and samples collected by ADNI. However, ADNI samples are precious and governed accordingly by policies and protocols. The final decision concerning release of ADNI samples is made by National Institutes of Aging which funds ADNI.

More information about the ADNI study design is at http://adni.loni.usc.edu/study-design/

SAMPLE BIOBANK

ADNI is a large undertaking with hundreds of subjects across multiple phases with specimens, data, and imaging collected over multiple timepoints. Thus, there is potential to accommodate requests for specific and complex covariates with rich data to accompany the samples. To fully understand the number of subjects and sample collection, refer to the ADNI Protocol and Biofluids section of the ADNI procedures manuals: http://adni.loni.usc.edu/methods/documents/

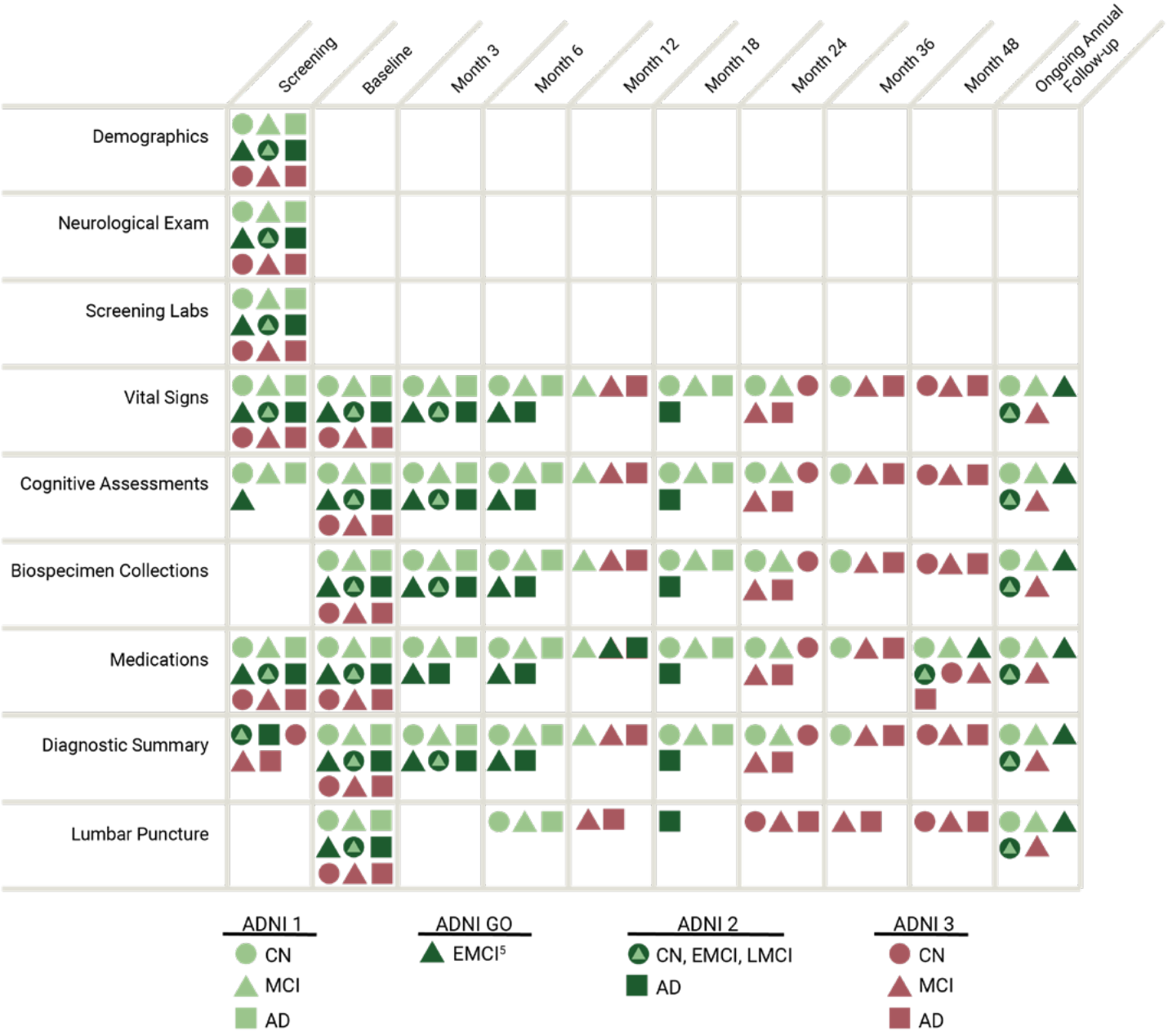
As of October 2020, there have been four ADNI participant groups/phases. ADNI1 began in 2004, and there have been 2 competitive renewals (ADNI2 in 2011, and ADNI3 in 2016). ADNI GO was funded in 2008 as part of the American Recovery and Reinvestment Act (ARRA). The ADNI4 renewal will be in Summer 2022. CSF, plasma, serum, and genetic material are collected at ADNI baseline and follow-up visits. Urine was collected in ADNI-1, but not thereafter. For subjects who consented and passed away, brain tissue was collected and evaluated. Many subjects consented to autopsy and brain donation, but relatively few brains were collected during ADNI1, GO, and 2 (relatively few deaths and logistical difficulties). The autopsy rate has improved in ADNI3 and will be a new emphasis in ADNI4.

The schedule of visits and sample collection differed between subject groups and changed somewhat in the transitions between participant groups. The exact schedule of events can be found here: http://adni.loni.usc.edu/study-design/

Details of collection and methodology can be found here: http://adni.loni.usc.edu/methods/documents/.

An accounting of the biospecimens available through ADNI can be found in the ADNI database. Several analyses of general interest (homocysteine, species of isoprostanes, tau and Aβ) have been performed by the ADNI Biomarkers Core, with results made available on the ADNI web site as soon as the laboratory analyses are complete. Non-ADNI scientists may request biosamples for additional studies. Understanding the longitudinal aspect of ADNI and richness of data can be important in formulating these requests.

The complexity and richness of data collected over the multiple phases of ADNI are captured on the following page.


Screening
Baseline
Month 3
Month 6
Month 12
Month 18
Month 24
Month 36
Month 48
Ongoing Annual Follow-up
Demographics
Neurological Exam
Screening Labs
Vital Signs
Cognitive Assessments
Biospecimen Collections
Medications
Diagnostic Summary
Lumbar Puncture
ADNI 1
CN
MCI
AD
ADNI GO
EMCI[5]
ADNI 2
CN, EMCI, LMCI
AD
ADNI 3
CN
MCI
AD

Distributable Aliquot Sizes

Sample Type	Distributable Quantity
Genomic DNA	5ug
Cell Line DNA	5ug
Lymphoblastoid Cell Lines	1 vial
PBMC	1 vial
RNA	2ug
RBC	1000 µl
Plasma	0.5 mL
Serum	0.5 mL
CSF	0.5 mL
Urine	0.5 mL
Brain tissue	Please contact the RARC/BRC for information

APPROPRIATE USES FOR SAMPLES

The ADNI Biomarkers Core have performed several analyses of general interest (homocysteine, species of isoprostanes, tau and Aβ). Non-ADNI investigators may apply for use of the samples and have contributed additional studies. These applications will be reviewed by the appropriate review committee (Resource Allocation Review Committee (RARC) for brain tissue and biofluids requests (plasma, serum, CSF, urine) and/or Biospecimen Review Committee (BRC) for genetics requests (DNA, RNA, LCLs, PBMCs, RBCs) under criteria such as potential for advancing clinically useful biomarkers of AD and potential impact on our understanding of AD and related dementias. Use of ADNI samples for technology development or comparisons among different technologies is not recommended for well-established analytes unless there is preliminary data showing clearly superior performance.

Previous ADNI studies can be found here: http://adni.loni.usc.edu/study-design/

Previous add-on studies (RARC-approved studies) can be found here: http://adni.loni.usc.edu/methods/

REVIEW COMMITTEE BACKGROUND

ADNI samples are precious and governed accordingly by policies and protocols by multiple review committees. The history behind how these policies came into place are as follows.

ADNI has always collected biosamples (CSF, blood, and in ADNI 1, urine) to measure and track biologically informative analytes. The initial focus was on β-amyloid, tau, and hyperphosphorylated tau, and the Biomarker Core measures these peptides in CSF as part of the ADNI database. NIA and the ADNI investigators realized that biosamples - collected longitudinally from carefully phenotyped subjects - would be a valuable resource for replicating important new findings, and validating novel biomarkers developed in the future. However, unlike the neuroimaging and clinical data shared by ADNI, the biosamples collected in ADNI

can only be used once: each aliquot of CSF or sample of genomic DNA is a precious, non-renewable resource.

As a condition of funding, NIA required the ADNI investigators to curate and store biosamples collected in ADNI, and to share them with non-ADNI scientists. NIA was to be the gatekeeper for these biosamples. The Resource Allocation Review Committee (RARC) , made up of non-ADNI investigators, was created to review requests for biosamples and advise NIA on final decisions concerning sample release. Biofluid (CSF, plasma and serum) samples collected in ADNI are stored at the Biomarker Core, at the University of Pennsylvania and distribution is managed by the Biofluids RARC.

After ADNI began in 2005, it soon became clear that genetic materials would be important in the future. ADNI 1 included ApoE genotyping and GWAS on subjects, and collected and immortalized lymphocytes to provide a renewable source of DNA. A limited amount of genomic DNA - remaining from the GWAS - was kept, but the quantities are such that access to ADNI 1 genomic DNA is possible only under extraordinary circumstances. ADNI 2 collected genomic DNA and RNA, along with blood cells (e.g., PBMCs) on a longitudinal basis. ADNI 3 has continued these collections and is considering creating iPSC cell lines. ADNI genetic materials are stored at the National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD) at Indiana University. The distribution of genetic materials is managed by a review committee at NCRAD called the Biospecimen Review Committee (BRC).

It has always been clear that postmortem neuropathologic evaluation of ADNI subjects would be essential. A Neuropathology Core was added to ADNI 1, and over time, as ADNI subjects passed away, having consented to brain donation, brains were collected, evaluated, and stored by the Neuropathology Core at Washington University. Neuropathology reports are available in the ADNI database. While still quite limited, there are now enough subjects to allow qualified investigators to apply for access to ADNI postmortem brain tissue. Requests for these tissues is managed by a Neuropath RARC.

Sample Type	Review Committee
Genomic DNA	Genetics RARC AKA NCRAD BRC
Cell Line DNA	
Lymphoblastoid Cell Lines	
PBMC	
RNA	
RBC	
Plasma	Biofluids RARC
Serum	
CSF	
Urine	
Brain tissue	Neuropath RARC

The RARC/BRC review process and instructions for investigators wanting access to any of the ADNI biospecimen types above are explained here: How to Apply