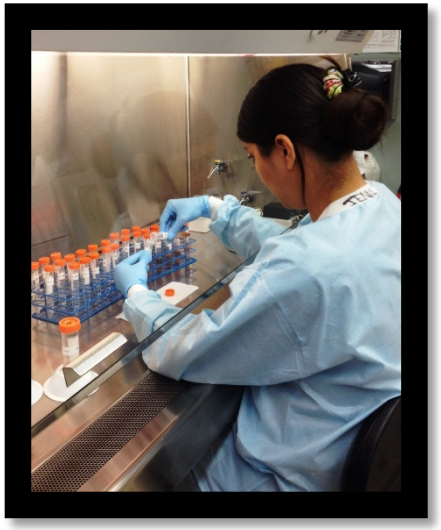
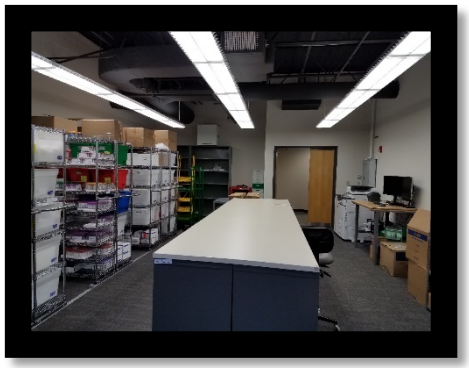
NCRAD update: How can I find NCRAD samples linked to NACC data?

Tatiana Foroud, Ph.D., Principal Investigator
Indiana University School of Medicine
U24AG21886





NCRAD

Focus of this Presentation

- What does NCRAD have and how do I find it?
- Describe how to search for ADC participants meeting particular criteria with DNA samples
  - NCRAD or NACC query
- Summarize other samples at NCRAD
  - From the ADCs
  - From other studies
- New initiatives to broaden available samples from ADC participants
- Open discussion

Navigating to the NCRAD Catalogs

Accessing Biospecimens and Data

In order to ensure that researchers have the most accurate information, the National Cell Repository for Alzheimer's Disease (NCRAD) is continually updated with new information. At the time data is requested, NCRAD will provide the researcher with the most current information. Therefore, NCRAD encourages all researchers to request an updated set of variables prior to publication and implementation of analyses involving samples acquired from the Repository. While every effort is made to verify all data and information, NCRAD cannot be responsible for any errors or omissions in the distributed data.

Cohort	Population	Genomic DNA	Cell Line DNA	RNA	Plasma	Serum	LCLs	PBMCs	CSF
ADNI	AD Cases, Controls, MCI	✓	✓	✓			✓		
AA Genetics	AD Cases, Controls		✓				✓		
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GEMS	Dementia prevention	✓			✓	✓			
GIFT	AD, FTD, Controls	✓	✓				✓		
Indianapolis-Ibadan	Elderly African Americans from Indianapolis, Yoruba living in Ibadan	✓	✓				✓		
NCRAD Family	AD and other dementia families	✓	✓				✓	✓	
NIA-LOAD	Late Onset AD Families, Controls	✓	✓				✓		
ARTFL	FTLD syndrome cases and healthy family members	✓		✓	✓	✓		✓	✓
LEFFTDS	FTLD family study with known genetic mutations (symtomatic and asymtomatic family members)	✓		✓	✓	✓		✓	✓

ADNI

AA Genetics

ADCs

4RTNI-2

ADNI

AA Genetics

ADCs

The Alzheimer's Disease Centers (ADCs) are funded at major medical institutions across the United States. Researchers at these Centers are working to translate research advances into improved diagnosis and care for people with Alzheimer's disease while focusing on the program's long-term goal—finding a way to cure and possibly prevent Alzheimer's.

Study Subjects

Although each center has its own area of emphasis, a common goal of the ADCs is to enhance research on Alzheimer's disease by creating a network that shares new ideas and research results. The clinic-based population includes subjects with Alzheimer's disease and related disorders, as well as cognitively normal subjects and those with MCI.

Available Data

The National Alzheimer's Coordinating Center (NACC) maintains a cumulative database including clinical evaluations, neuropathology data when available, and MRI Imaging. The NACC database comprises several standardized clinical and neuropathology data sets, all of which are freely available to the research community.

Available Biospecimens

Genomic DNA from blood or brain tissue, Cell Line DNA from LCLs, PBMCs from select subjects

Price Structure | Catalog | Request Access to Biospecimens

DIAN

GEMS

GIFT

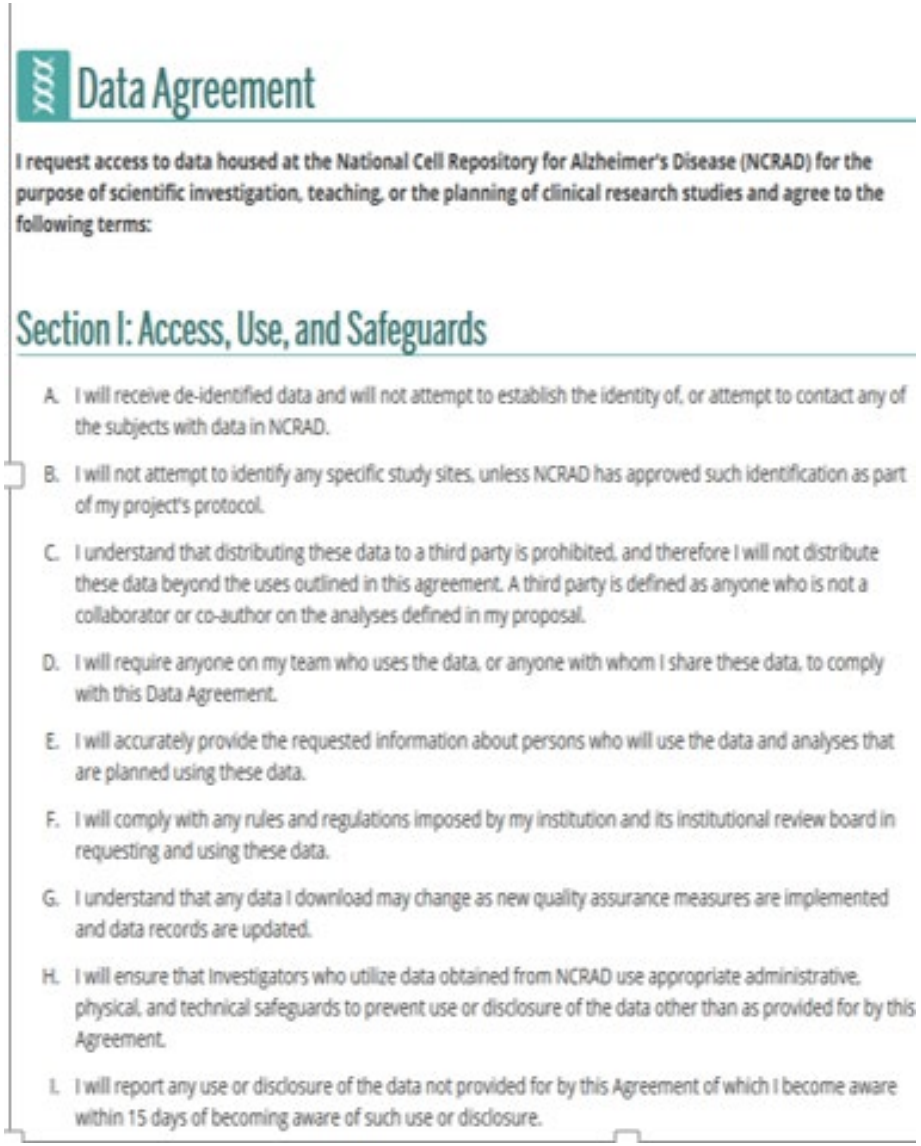
Indianapolis-Ibadan

NCRAD Family

Within the NCRAD website, in the Accessing Biospecimens and Data section, catalogs can be accessed at https://www.ncrad.org/accessing_data.html

Accessing NCRAD Catalogs

- Researchers must complete a web-based Data Agreement to obtain a username and password to the restricted catalogs.



Data Agreement

I request access to data housed at the National Cell Repository for Alzheimer's Disease (NCRAD) for the purpose of scientific investigation, teaching, or the planning of clinical research studies and agree to the following terms:

Section I: Access, Use, and Safeguards

A. I will receive de-identified data and will not attempt to establish the identity of, or attempt to contact any of the subjects with data in NCRAD.

B. I will not attempt to identify any specific study sites, unless NCRAD has approved such identification as part of my project's protocol.

C. I understand that distributing these data to a third party is prohibited, and therefore I will not distribute these data beyond the uses outlined in this agreement. A third party is defined as anyone who is not a collaborator or co-author on the analyses defined in my proposal.

D. I will require anyone on my team who uses the data, or anyone with whom I share these data, to comply with this Data Agreement.

E. I will accurately provide the requested information about persons who will use the data and analyses that are planned using these data.

F. I will comply with any rules and regulations imposed by my institution and its institutional review board in requesting and using these data.

G. I understand that any data I download may change as new quality assurance measures are implemented and data records are updated.

H. I will ensure that Investigators who utilize data obtained from NCRAD use appropriate administrative, physical, and technical safeguards to prevent use or disclosure of the data other than as provided for by this Agreement.

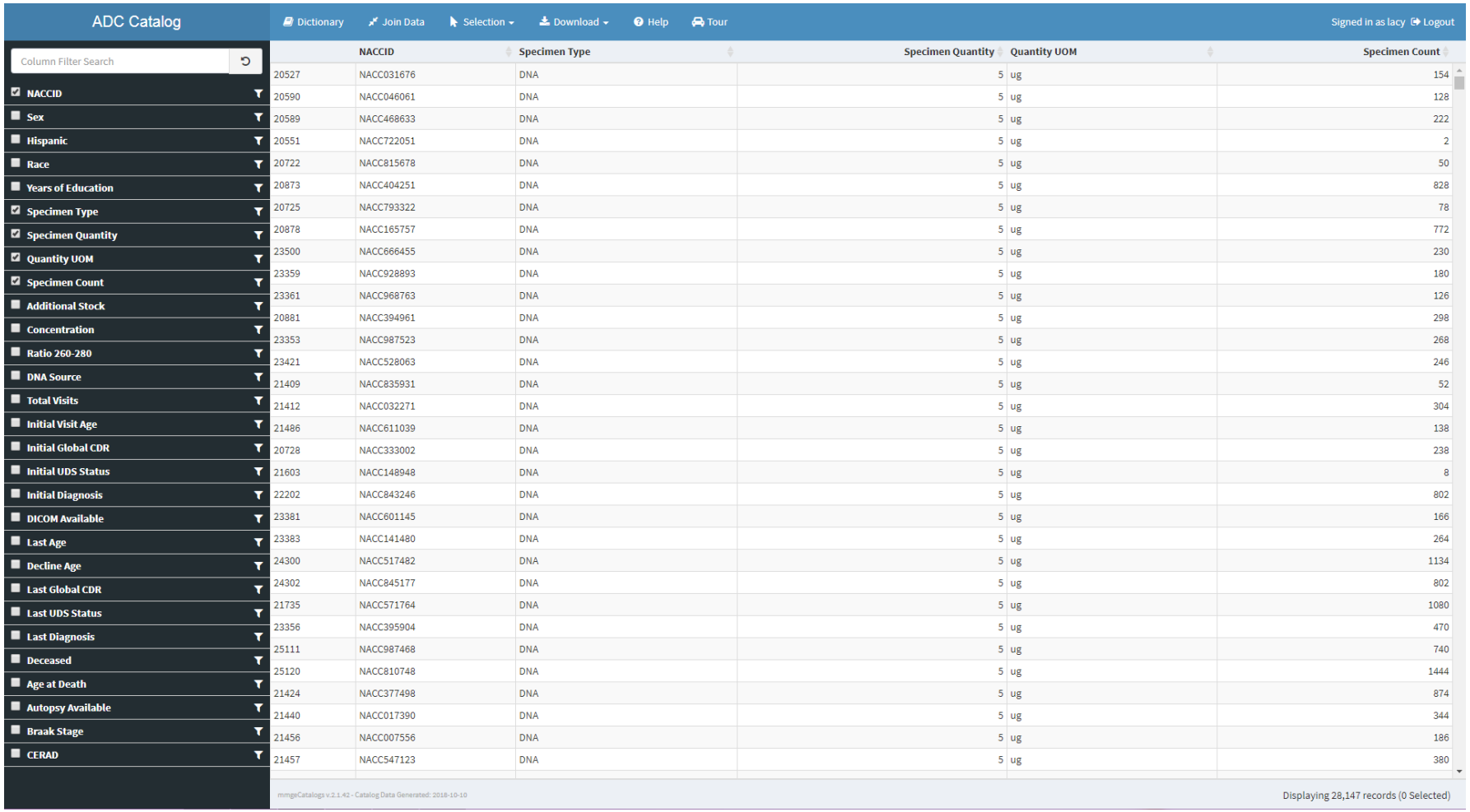
I. I will report any use or disclosure of the data not provided for by this Agreement of which I become aware within 15 days of becoming aware of such use or disclosure.

NCRAD Catalogs

After obtaining a username and password from the NCRAD staff, researchers will be able to log directly into the specimen catalog to review a subset of data.

NCRAD Catalogs

The catalog system is designed to allow researchers to determine which sample collections best fit their research needs and perform feasibility checks before applying for or requesting the samples. The researcher will have the option to download their selected sample set and include that with their application.



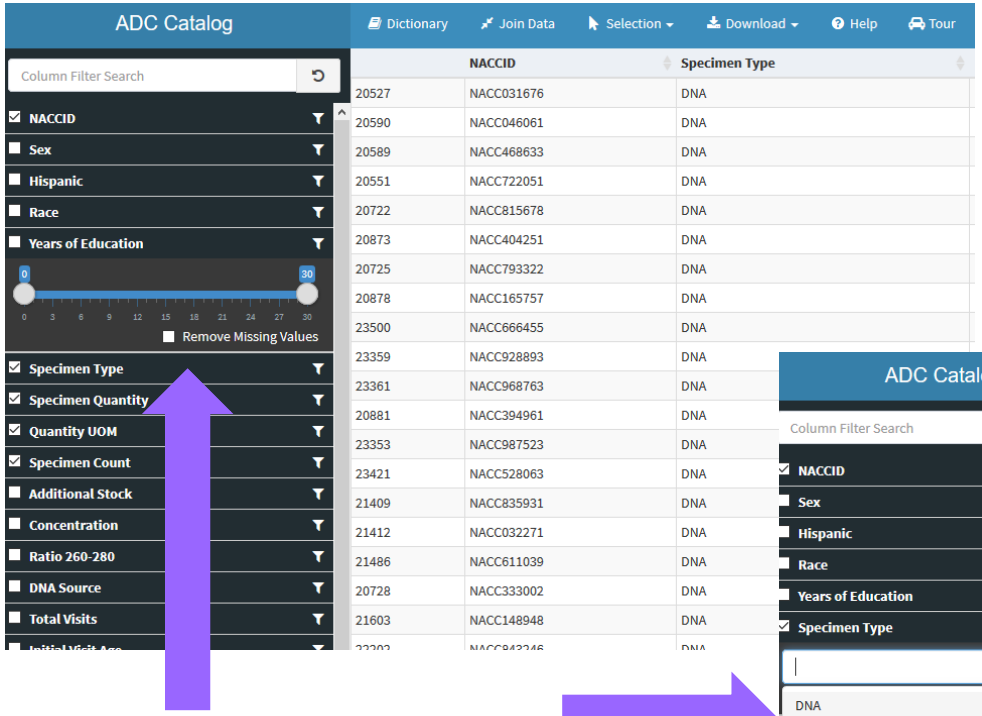
What is in the NCRAD ADC Catalog?

NACC Fields in NCRAD Limited Data Set	
• NACCID	• DICOM image file available?
• Sex	• Global CDR at Last Visit
• Ethnicity	• Cognitive Status at Last Visit
• Race	• Diagnosis at Last Visit
• Years of Education	• Deceased?
• Total Visits	• Age at Death
• Initial Visit Age	• Autopsy Available
• Global CDR at Initial Visit	• Braak Stage
• Cognitive Status at Initial Visit	• CERAD Score
• Diagnosis at Initial Visit	

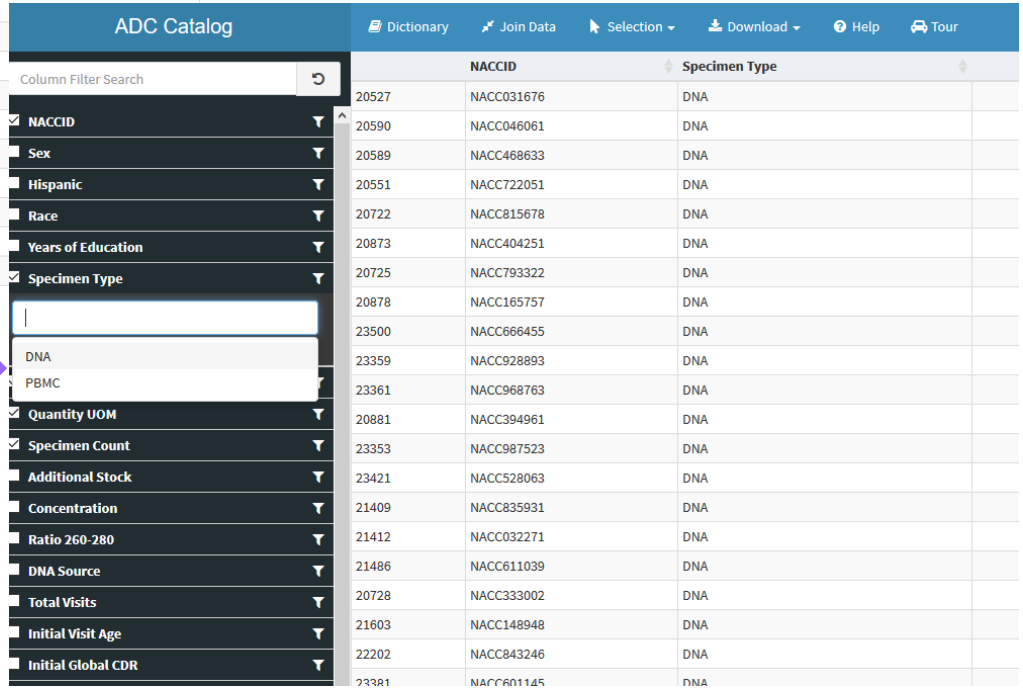
NCRAD Biospecimen Fields
• Specimen Type
• Specimen Quantity
• Quantity UOM
• Specimen Count
• Additional Stock
• Concentration
• 260/280 Ratio
• DNA Source
• Specimen Type
• Specimen Quantity

Filter by Specimen Criteria

Researchers can use the sidebar to filter for the specific samples that meet their request criteria. When the categories on the left are selected, they will appear in the dataset to the right. Variables can be chosen by range of numbers, such as age, or text options, such as baseline diagnosis.



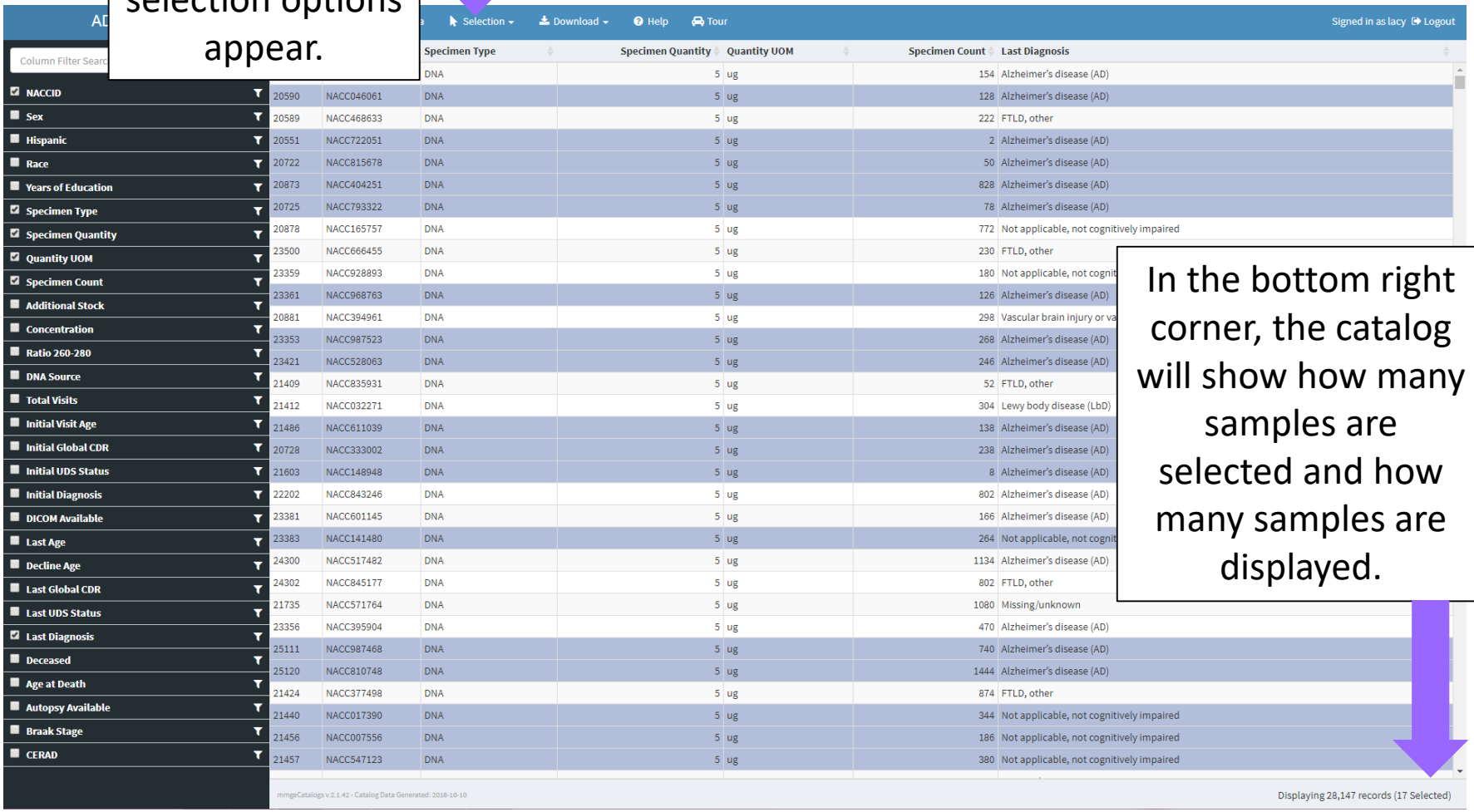
Filters are available as sliders or drop down lists



Sample Selection

Researchers can individually select the samples they want, which highlights the selection in blue. They can also use the selection tool at the top to select all, none, or invert their selection.

By clicking here, selection options appear.



In the bottom right corner, the catalog will show how many samples are selected and how many samples are displayed.

Download Selection

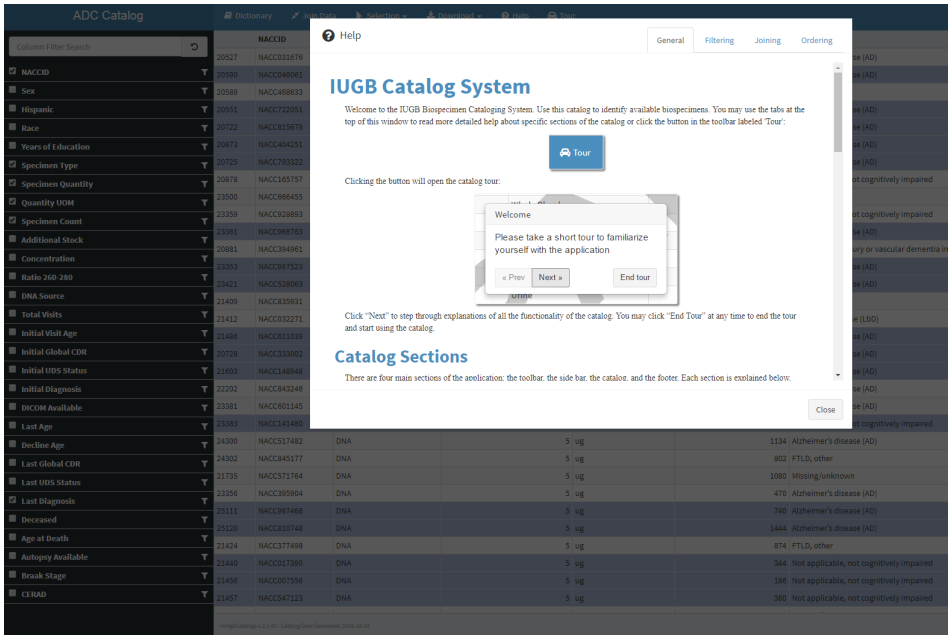
Researchers will have the option to download the entire dataset, just the filtered specimens, or their selected specimens. An excel file will download to the desktop.

By clicking here, download options appear.

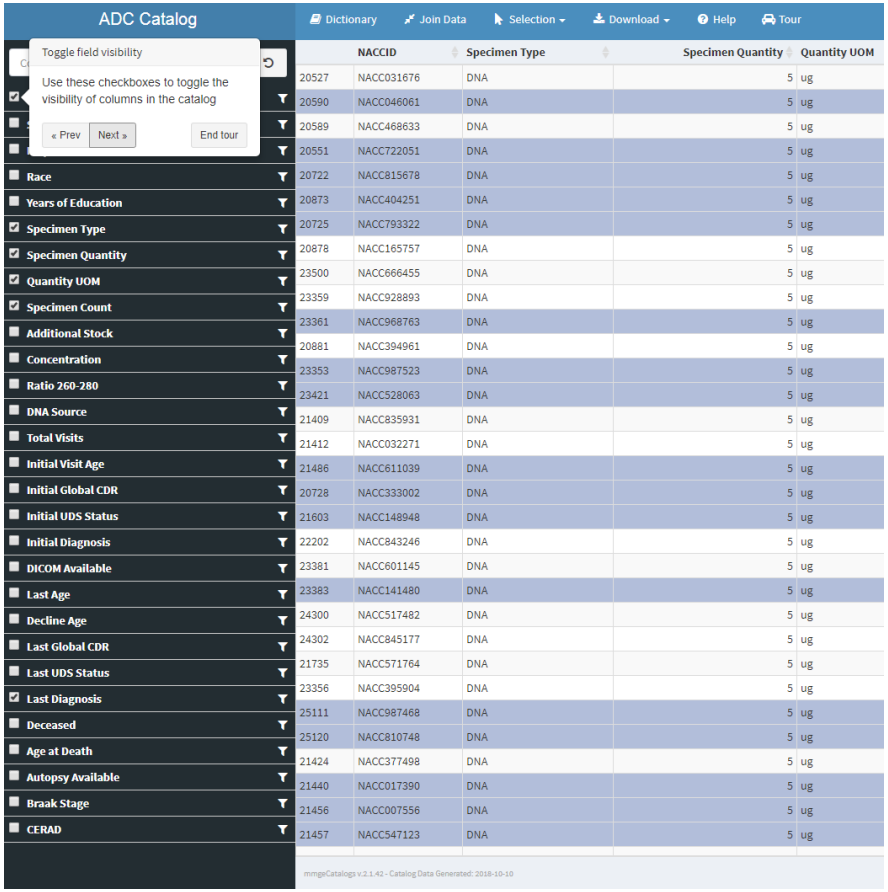
	NACCID	Specimen Type	Specimen Quantity	Quantity UOM	Specimen Count	Last Diagnosis
20527	NACC031676	DNA	5	ug	154	Alzheimer's disease (AD)
20590	NACC046061	DNA	5	ug	128	Alzheimer's disease (AD)
20589	NACC468633	DNA	5	ug	222	FTLD, other
20551	NACC722051	DNA	5	ug	2	Alzheimer's disease (AD)
20722	NACC815678	DNA	5	ug	50	Alzheimer's disease (AD)
20873	NACC404251	DNA	5	ug	828	Alzheimer's disease (AD)
20725	NACC793322	DNA	5	ug	78	Alzheimer's disease (AD)
20878	NACC165757	DNA	5	ug	772	Not applicable, not cognitively impaired
23500	NACC666455	DNA	5	ug	230	FTLD, other
23359	NACC928893	DNA	5	ug	180	Not applicable, not cognitively impaired
23361	NACC968763	DNA	5	ug	126	Alzheimer's disease (AD)
20881	NACC394961	DNA	5	ug	298	Vascular brain injury or vascular dementia including stroke
23353	NACC987523	DNA	5	ug	268	Alzheimer's disease (AD)
23421	NACC528063	DNA	5	ug	246	Alzheimer's disease (AD)
21409	NACC835931	DNA	5	ug	52	FTLD, other
21412	NACC032271	DNA	5	ug	304	Lewy body disease (LbD)
21486	NACC611039	DNA	5	ug	138	Alzheimer's disease (AD)
20728	NACC333002	DNA	5	ug	238	Alzheimer's disease (AD)
21603	NACC148948	DNA	5	ug	8	Alzheimer's disease (AD)
22202	NACC843246	DNA	5	ug	802	Alzheimer's disease (AD)
23381	NACC601145	DNA	5	ug	166	Alzheimer's disease (AD)
23383	NACC141480	DNA	5	ug	264	Not applicable, not cognitively impaired
24300	NACC517482	DNA	5	ug	1134	Alzheimer's disease (AD)
24302	NACC845177	DNA	5	ug	802	FTLD, other
21735	NACC571764	DNA	5	ug	1080	Missing/unknown
23356	NACC395904	DNA	5	ug	470	Alzheimer's disease (AD)
25111	NACC987468	DNA	5	ug	740	Alzheimer's disease (AD)
25120	NACC810748	DNA	5	ug	1444	Alzheimer's disease (AD)
21424	NACC377498	DNA	5	ug	874	FTLD, other
21440	NACC017390	DNA	5	ug	344	Not applicable, not cognitively impaired
21456	NACC007556	DNA	5	ug	186	Not applicable, not cognitively impaired
21457	NACC547123	DNA	5	ug	380	Not applicable, not cognitively impaired

Help and Tour

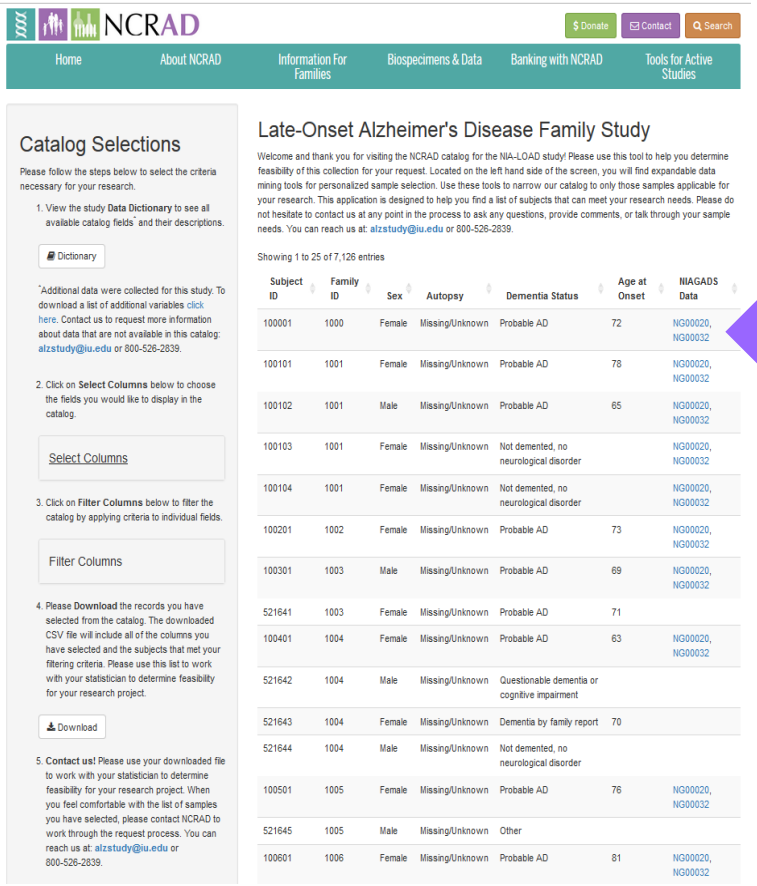
The “Help” tab walks researchers through the catalog sections such as the toolbar and sidebar. It explains in detail how to filter, join data, and download files.



The “Tour” tab walks researchers through the dataset step by step, such as explaining how to filter for specimen criteria or how to join data.

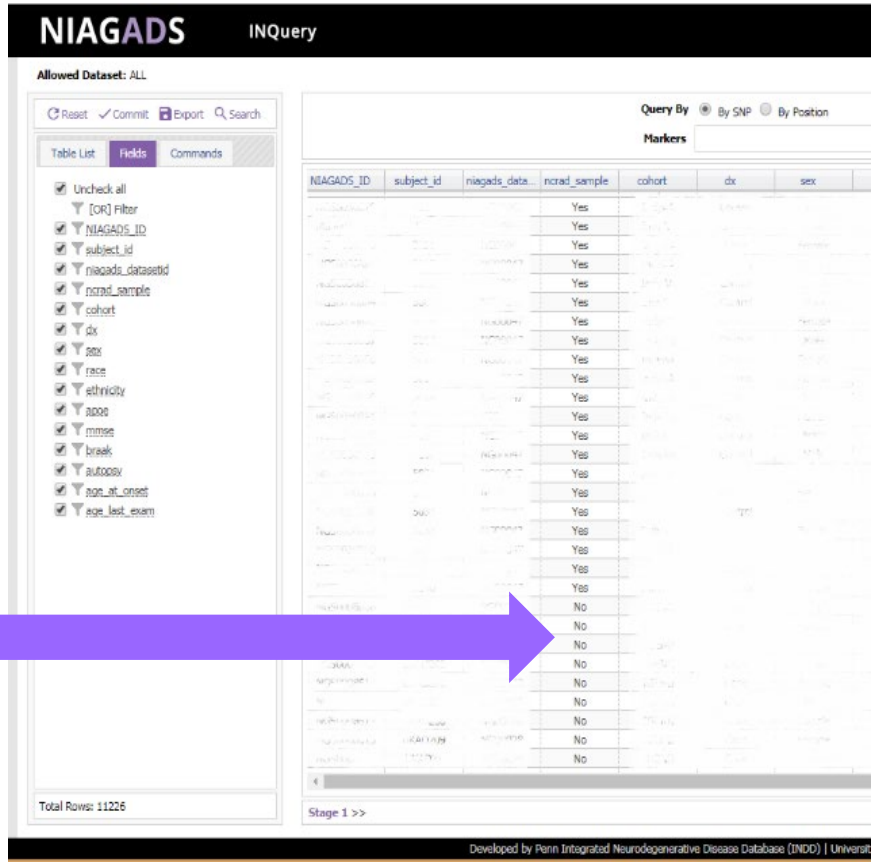


Links with NIAGADS



Samples with genetic data at NIAGADS are hyperlinked directly to the information page for the dataset.

Indication of NCRAD sample available in NIAGADS dataset.



Link at NACC to NCRAD

FTLD type, most recent FTLD module visit	○	○	

+ Genetics

Available as:	ROW	COLUMN	PAGE
APOE genotype available at NACC	○	○	○
APOE genotype	○	○	
Number of APOE e4 alleles	○	○	○
Subject/family has known AD Mutation (APP, PS1, PS2)	○	○	
Subject/family has known FTLD mutation (MAPT, PGRN, C9ORF72, FUS)	○	○	
Genomic data/DNA samples available outside of NACC (ADGC, NIAGADS, NCRAD)	◉		

NACC Query System: UDS Subjects
NOTE: This query used versions 1-3 of UDS data

These data should be used only as rough, preliminary numbers.
For publication purposes, please submit a custom data request

Genomic data/DNA samples available outside of NACC (ADGC, NIAGADS, NCRAD)

Genomic data/DNA samples available outside of NACC (ADGC, NIAGADS, NCRAD)	Frequency (n)
Genotype data available at ADGC	13187
Genotype data available at NIAGADS	3285
Exome sequencing data available from dbGaP / ADSP	3285
DNA sample available at NCRAD	24593
Total UDS subjects	38836

Data from Additional genetic data
Created on October 11, 2018
Data as of September 1, 2018
www.alz.washington.edu

What About Samples Beyond DNA

- NCRAD is often considered only a DNA repository
- NCRAD banks a broader range of samples

- Challenge: NCRAD does not have enough:
  - Plasma, serum, CSF, RNA
  - from AD, cognitively normal controls, MCI

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ADCs	AD and other dementia cases, Controls, MCI	✓	✓					✓	
DIAN	Early Onset AD Families with known mutations		✓				✓		
GEMS	Dementia prevention	✓			✓	✓			
GIFT	AD, FTD, Controls	✓	✓				✓		
Indianapolis-Ibadan	Elderly African Americans from Indianapolis, Yoruba living in Ibadan	✓	✓				✓		
NCRAD Family	AD and other dementia families	✓	✓				✓	✓	
NIA-LOAD	Late Onset AD Families, Controls	✓	✓				✓		
ARTFL	FTLD syndrome cases and healthy family members	✓		✓	✓	✓		✓	✓
LEFFTDS	FTLD family study with known genetic mutations (symtomatic and asymtomatic family members)	✓		✓	✓	✓		✓	✓

ADC Samples Coming to NCRAD

Study/PI/Grant	Subject Description	Samples to be Transferred
Study: Case Western ADC **PI:** Alan Lerner **Grant:** P50AG008012	The Case Western ADC was previously funded by the NIA and assessed and followed a large number of subjects. NCRAD will receive aliquots from subjects with MDS/UDS data at NACC.	• DNA and buffy coats • Brain tissue • Plasma aliquots • CSF aliquots
Study: Banner/Mayo **PIs:** Eric Reiman and Richard Caselli **Grant:** P30AG031581	The Arizona ADC was funded in 1998, but subjects were enrolled at the Banner and Mayo Clinic Arizona sites beginning in 1994. Samples from these subjects will be transferred to NCRAD. Clinical data for these subjects was already transferred to NACC.	• Plasma aliquots • Serum aliquots • CSF aliquots

Samples (above) collected under rapid processing protocol, but may be variable to final ADC Biomarker Initiative approved protocol

Accelerating Biomarker Development: Planning For the First Year

ADC — **Propose blood collection from 3,000 subjects**

Volume	Product
2x10 ml	Buffy coat (DNA) + Plasma aliquots
2x10 ml	PBMCs
1x10 ml	Serum aliquots
1x2.5 ml	RNA

Uniformly collected & processed blood samples

NCRAD — **Buffy coat, plasma, serum aliquots; Blood for RNA, PBMCs**

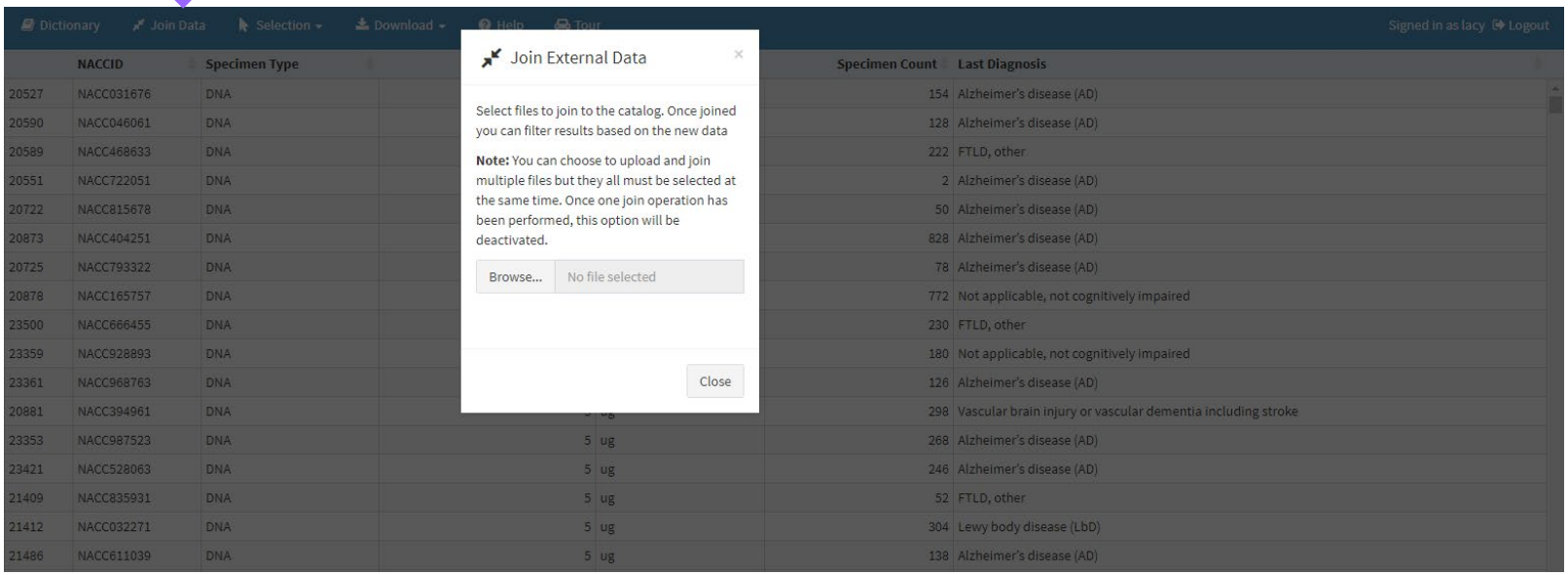
Plan to link specimens and data

- NCRAD will extend our catalogs to also display all available samples
  - Link through visit and NACC ID to NACC dataset
- How much NACC data
  - Link to NACC provided minimal dataset hosted at NCRAD
  - Link to subset of NACC variables joined to NCRAD catalog
- Suppose you want to query based on the more extensive UDS data at NACC?

Join Data

For many studies, more extensive data can be obtained from the study's data coordinating center. The catalog system supports joining this external data with the NCRAD biospecimen catalog data. This allows researchers to easily filter and select specimens based on criteria outside of those available in the catalog.

By clicking here, the join external data box appears.



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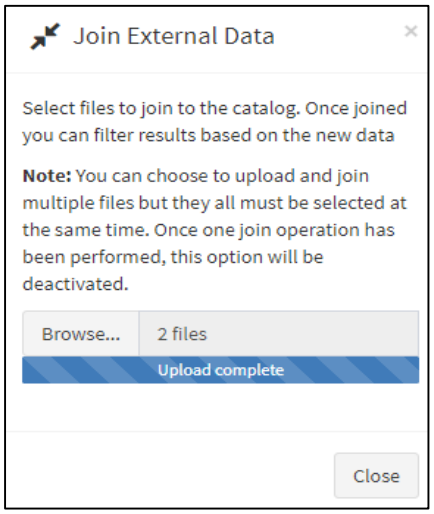
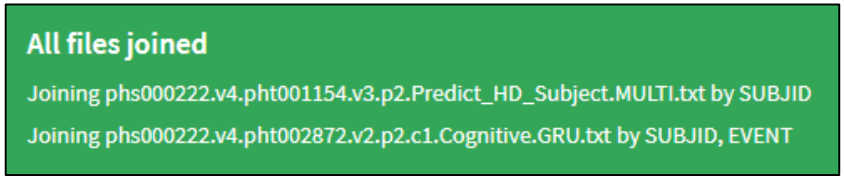
21486	NACC611039	DNA	5	ug	138	Alzheimer's disease (AD)

Join Data

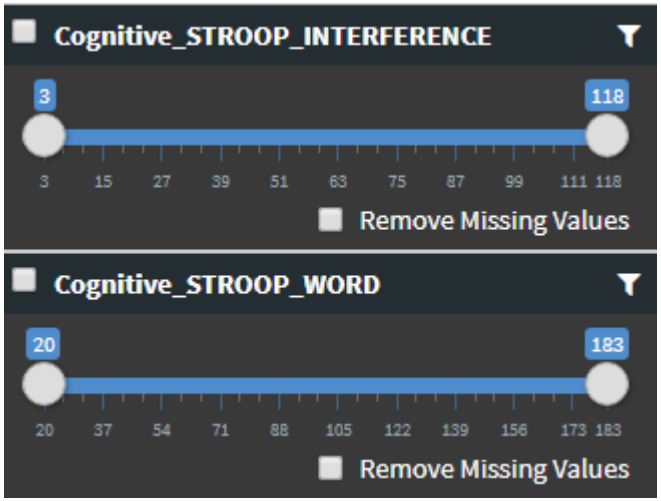
- Once data is uploaded, data is joined by the Subject Identifier and Visit Code for that study. If successful, the Join External Data window will note “Upload Complete”.



- The “All files joined” banner will be green indicating which fields were joined from the external data and catalog data. In this example, the Subject data was joined by SUBJID while the longitudinal Cognitive data was joined by SUBJID and EVENT.



- Joined data is analyzed during the upload process to determine data type along with min/max for numeric values or choices for drop-downs. Uploaded data is prefixed by the filename and is appended to the field list. other fields on the left field panel.



Questions…

- What kind of questions do you want to be able to ask with specimens?
- What kinds of specimens do you need?
- What are the criteria you want to use to select subjects?

Acknowledgement

- NCRAD Executive Committee
- NCRAD Biospecimen Review Committee
- NIA
- Alzheimer Disease Centers
- NACC
- NIAGADS
- ADGC
- Studies contributing samples to NCRAD

Questions/Contact:
kelfaber@iu.edu or
alzstudy@iu.edu

NCRAD Staff