



# ***National Alzheimer's Coordinating Center***

**Standardized data collection and  
collaborative research**

August 24, 2007 Austin, Texas

**NACC is supported by The National Institute on Aging (U01 AG16976)**



**and is located at the University of Washington's School of Public  
Health and Community Medicine**





## Enhancing Research Collaboration Through a Common Database for NIA Alzheimer's Disease Centers



ABOUT NACC REQUEST PASSWORD CONTACT INFO SEARCH

- GENERAL PUBLIC
- ADC ADMINISTRATION
- INVESTIGATORS / RESEARCHERS
- DATA CORES / DATA MANAGERS
- INTERVIEWERS / CLINICIANS

TEXT SIZE   

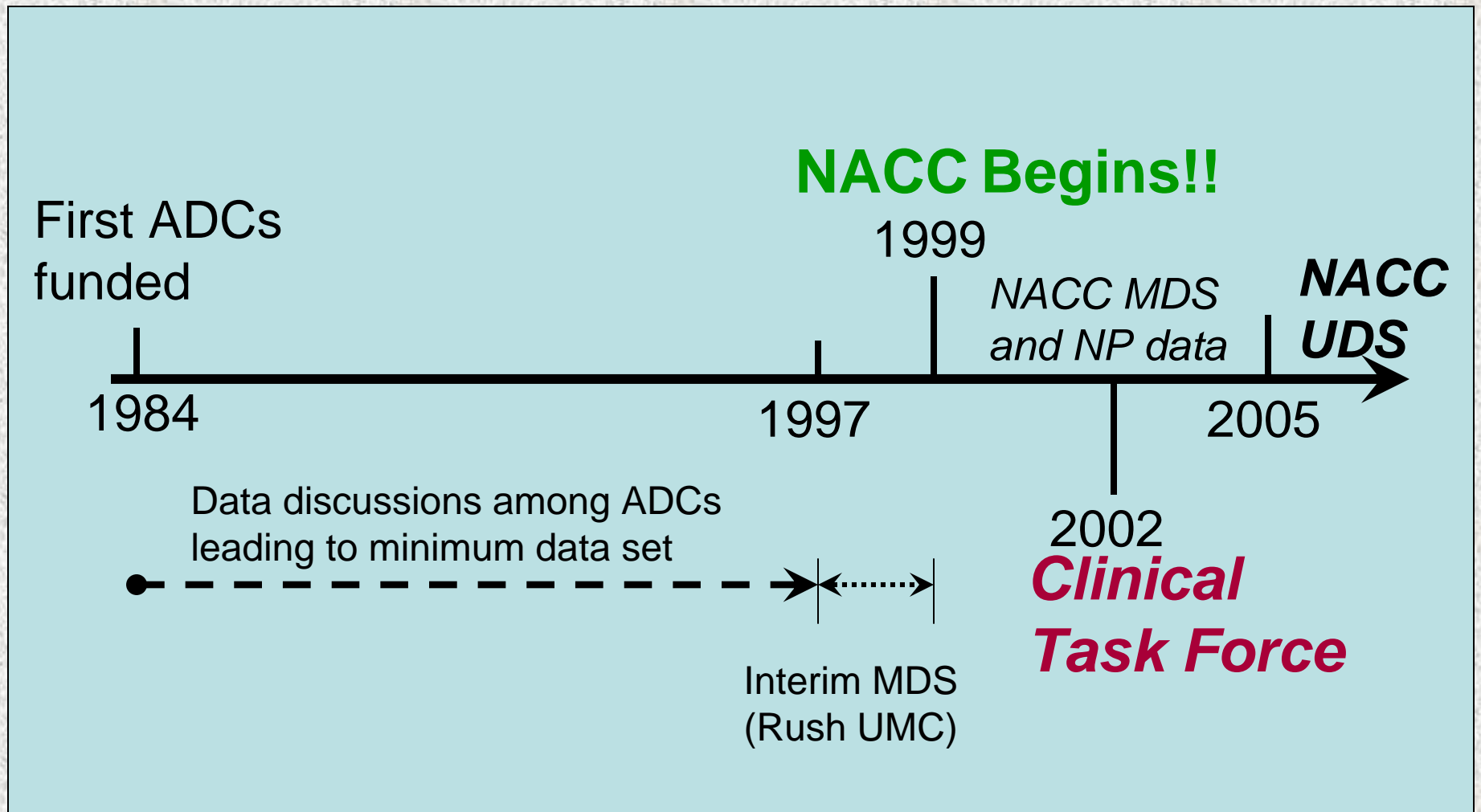
The National Alzheimer's Coordinating Center (NACC) was established by the National Institute on Aging (U01 AG016976) in 1999 to facilitate collaborative research among the 29 NIA-funded Alzheimer's Disease Centers (ADCs) nationwide. NACC developed and maintains a large relational database of standardized clinical and neuropathological research data collected from each ADC, and this database provides a valuable resource for both exploratory and explanatory Alzheimer's disease research.

### What's New

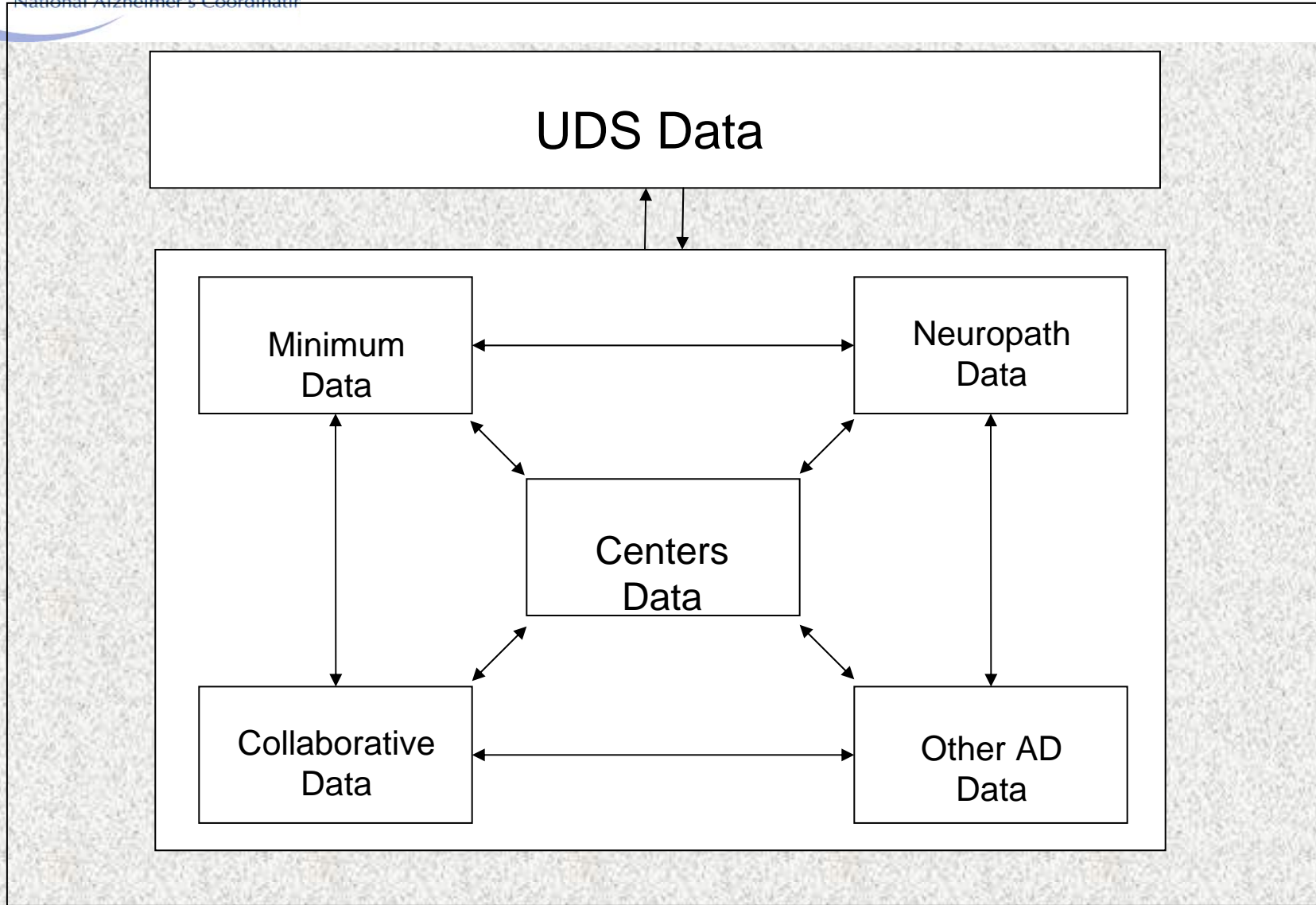
- NIA Sponsored Research Opportunity [Click here](#)
- Instructions for preparing annual ADC Progress Reports for NIA [Click here](#)
- NIH Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research



# Milestones in the NIA ADC data collection program



# The NACC Database Structure





## Database features

- Seamless integration of data sets
- Website design improvements
- Data Input/Output enhancements
- Working with the ADC personnel to provide numbers, projects and productivity





# Minimum Data Set Evolution >>Revolution

- ~ 60 data elements to characterize subjects enrolled at ADCs
  - Cross-sectional not longitudinal
- Gateway for research:
  - Additional detailed data available only at specific request and negotiation with ADC
- Standardized data reporting, not collection
  - Data mapping by data managers
- Clinical leaders and Directors improve data quality



## Neuropathology data expansion 2001

- Neuropathologists determine and define data elements—Key to success
- NACC implements database
  - Linked to MDS
- Routine and continuous data collection
  - Retrospective data completed and submitted by neuropathologists
- Neuropathological – clinical studies



# Uniform Data Set (UDS)

- Clinical Task Force formed by NIA 2002 (John Morris, chair)
  - Described clinical evaluation
  - “Informant” participation required
  - Standardized data collection (not just standard reporting per MDS);
- Longitudinal data collection
- NACC relational database and web interface input and output
- Potential future expansion for specific disease subtypes





# ADC Clinical Task Force

## Mission

To develop an expanded, standardized dataset on ADC subjects to improve clinical assessment and diagnosis, provide data in support of current projects, and stimulate research.

## Uniform Data Set collection will:

- serve as a unique research resource for:
  - natural history studies (MCI transition; rare disorders)
  - comorbidities
  - variability across ethnic groups, geographic region
- provide phenotypic descriptions to identify multiplex families (Genetics Initiative) and resource for GWAS



# ADC Clinical Task Force

## Members

**Helena Chui (USC)**

**Jeffrey Cummings (UCLA)**

**Charles DeCarli (UCD)**

**Steven Ferris (NYU)**

**Norman Foster (U Michigan)**

**Douglas Galasko (UCSD)**

**Neill Graff-Radford (Mayo Clinic)**

**John Morris (Wash U) - Chair**

**Elaine Peskind (U of Washington)**

**Sandra Weintraub (Northwestern)**

**\*Dan Mungas (UCDavis)**

**\*Joe Hesse (UCSF)**

## Affiliates

### NACC

**Walter Kukull**

### ADC Genetics Initiative

**Richard Mayeux**

### NIA

**Creighton Phelps**

**Neil Buckholtz**

**Nina Silverberg**

**Marcelle Morrison-Bogorad**

# UDS Forms: types of data

- **Forms for Initial Visit Packet**
  - “A” forms: Demographics and history
  - “B” forms: Clinical evaluation
  - “C” form: Neuropsychological battery
  - “D” form: Clinical Diagnoses
  - “E” form: Lab specimen and imaging taken
- **The Guidebook**
  - Operational definitions and Criteria
  - References to original articles
  - Appendix: Cognitive test procedures; other diagnostic criteria

- **Paper and electronic forms**
  - Available through website
- **Data Submission System**
  - Individual subject or “file” entry system direct through the web; encrypted
  - Includes multi-level error checks



- **Standardized data collection**
  - Uniform clinical assessments
  - Longitudinal follow-up
- **“The Task Force recommends that the UDS be administered as a standard protocol...”**
- **Linked to MDS and NP data**
  - MDS collection phased out





# Data Submission System



- [Previous Menu](#)
- [NACC Home](#)
- [NACC Member Home](#)
- [The NACC Database](#)
- [Personnel Directory](#)
- [Collaborative Projects](#)
- [Neuropath Data Call](#)
- [Training](#)

## UDS DATA SUBMISSION SYSTEM

- [Upload Files](#)
- [Web Data Entry](#)
- [Error Check](#)
- [Finish & Notify](#)
- [Reports](#)
- [Documentation](#)

[Edit ID](#)   [Add ID](#)   [Delete ID](#)   [Help](#)

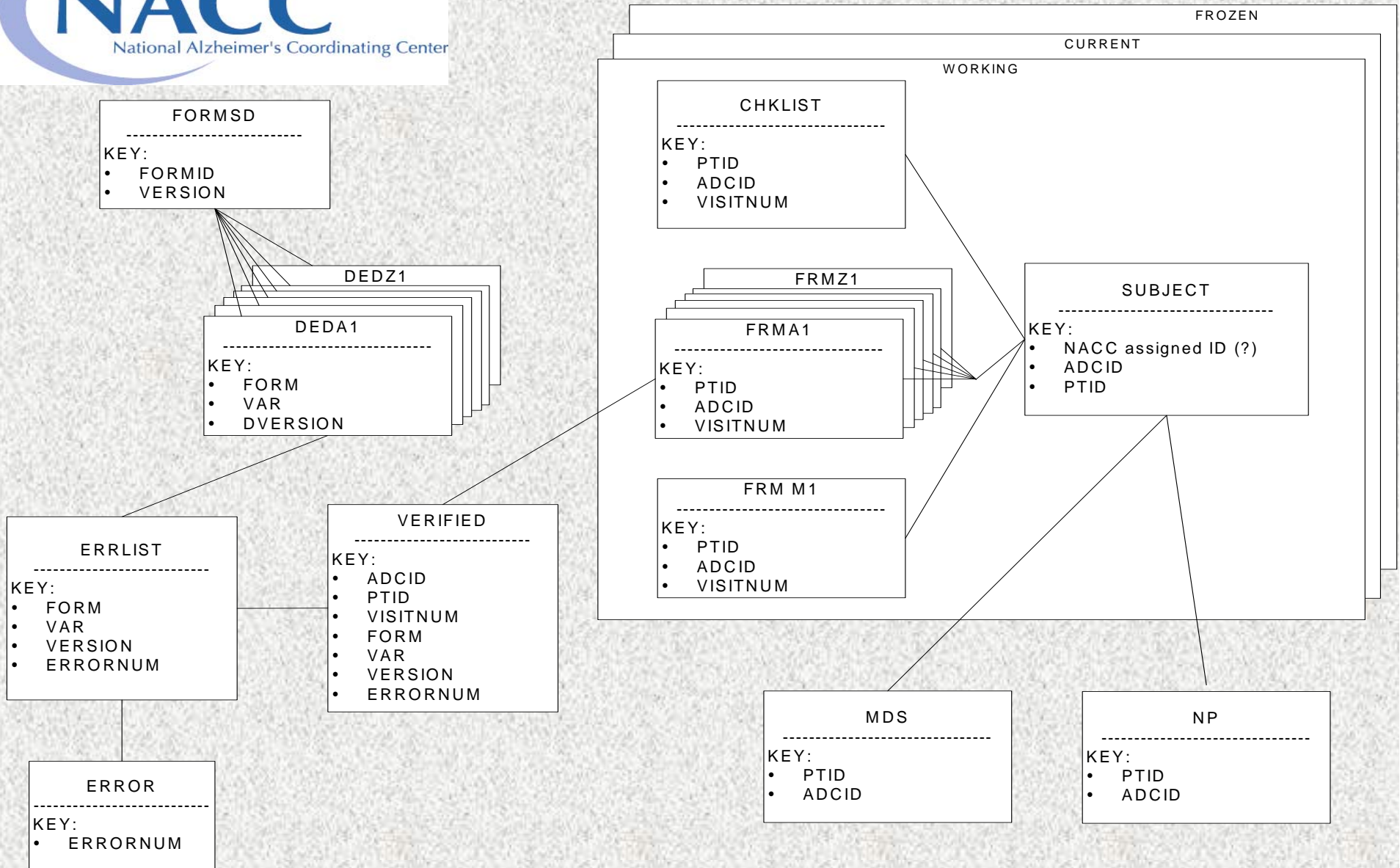
Sample Center

Select the UDS ID to Edit:

JLH001	▲
JLH002	■
JLH003	■
1	■
2	▼



# The UDS Database Design

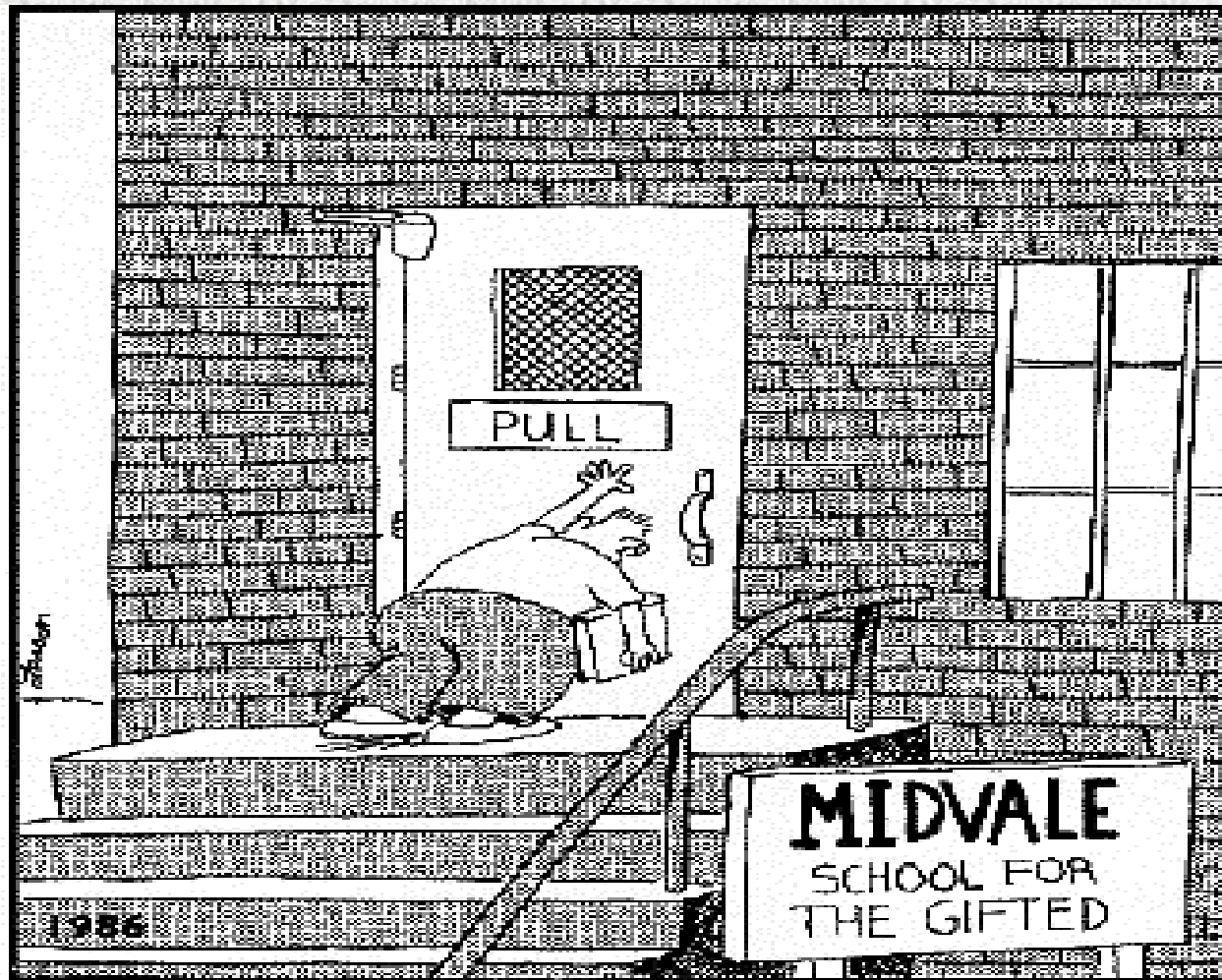




# Database Design Features

- **Oracle back end**
- **SAS front end**
- **Automated data element dictionary**
- **Form version control**
- **Automated error checks**
- **And lots of other cool and clever things**

**Everything's easy,  
once you understand  
the mechanism...**





# The NACC Database

04/2007 "Data Freeze"

<b>UDS</b> - Initial - Follow - Up	<b>8,899</b> <b>821</b>
<b>MDS</b>	<b>75,545</b>
<b>NP</b> - MDS Subjects Only - UDS / MDS Subjects - UDS Subjects Only	<b>9,626</b> <b>46</b> <b>17</b>





# Demographics

	<b>UDS</b>	<b>MDS</b>	<b>NP</b>
<b>Gender</b>			
- Male	<b>3,794</b>	<b>30,374</b>	<b>4,711</b>
- Female	<b>5,105</b>	<b>45,171</b>	<b>4,978</b>
<b>Race</b>			
- Caucasian	<b>7,413</b>	<b>62,231</b>	<b>9,140</b>
- African American	<b>1,113</b>	<b>7,805</b>	<b>284</b>
- Asian/Pacific Islander	<b>115</b>	<b>1,138</b>	<b>42</b>
- Other/Missing	<b>258</b>	<b>4,371</b>	<b>223</b>
<b>Ethnicity</b>			
- Hispanic	<b>613</b>	<b>4,331</b>	<b>145</b>



# Cognitive Status

<b><i>Clinical Dx group</i></b>	<b>UDS</b>	<b>MDS</b>	<b>NP</b>
<b>Normal</b>	<b>3,437</b>	<b>12,614</b>	<b>895</b>
<b>MCI</b>	<b>1,779</b>	<b>8,379*</b>	<b>485</b>
<b>Demented</b>	<b>3,388</b>	<b>47,631</b>	<b>7,851</b>
<b>Other</b>	<b>295</b>	<b>6,921</b>	<b>458</b>

\* "Questionable Dementia" which includes MCI and other categories.



# Clinical Diagnosis

<b><i>Clinical Diagnosis</i></b>	<b>UDS</b>	<b>MDS</b>	<b>NP</b>
<b>Alzheimer's Disease</b>			
- Probable	<b>2,420</b>	<b>30,268</b>	<b>5,134</b>
- Possible	<b>432</b>	<b>8,298</b>	<b>1,330</b>
<b>DLB</b>	<b>272</b>	<b>1,869</b>	<b>586</b>
<b>Vascular Dementia</b>	<b>168</b>	<b>2,230</b>	<b>197</b>
<b>FTLD (FTD or PPA)</b>	<b>337</b>	<b>1,879</b>	<b>412</b>



# MCI Categories

(after Petersen et al)

Subgroup	UDS
<b>Amnestic</b> - Single Domain	<b>783</b>
<b>Amnestic</b> - Multiple Domain	<b>596</b>
<b>Non-Amnestic</b> - Single Domain	<b>252</b>
<b>Non-Amnestic</b> - Multiple Domain	<b>148</b>
<b>Impaired</b> - Not MCI	<b>295</b>



## Research readiness

- Data Quality assurance and control
  - Expansion and improvement of capabilities
  - Constant scrutiny by control freaks
- Research
  - The Topic System
  - NACC-funded and other Projects
    - Large and small NACC projects
  - Statistical support
  - Methodological development





Click on “Investigators/researchers”  
Then on “UDS research ideas”



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TEXT SIZE | | |

## Staking a Claim to a UDS Research Idea

Research with UDS data is encouraged. The process described below is intended to:

- Promote high-quality research with UDS data
- Avoid wasted effort if a potential project's data needs cannot be met adequately with UDS data
- Coordinate the efforts of multiple users, so that two or more investigators do not unknowingly pursue projects with substantially overlapping aims



## The process...

- **View** the topic list or think of a topic on your own
- **Talk to NACC** about data/feasibility;
- **Submit** a ~2 pp. description for the Publications Committee to officially “claim” topic;
- After Pubs “claiming” approval, a NACC liason will be named to help with analytic issues;
- **NACC will create a data file for you;**
- **Do** analysis; write paper [NACC helps, prn];
- **Submit** final draft paper to Pubs Comm.



WORKING TITLE	STATUS	
<i>THEME 1: Description of UDS clinical population and subgroups of interest</i>		
<a href="#">101</a>	Establish Norms and Identify new Groups	Available
<a href="#">102</a>	Neuropsychological Test Scores	Claimed
<a href="#">103</a>	Description of UDS MCI, pre-MCI, and Control Subjects	Available
<a href="#">104</a>	Establish Norms and Compare with Other Published Norms	Available
<a href="#">105</a>	Age of onset	Available
<a href="#">106</a>	Hachinski Scale scores	Available
<a href="#">121</a>	Variations across Centers	Available
<a href="#">131</a>	Compare UDS to other AD Data Sets	Available
<a href="#">141</a>	Rapidly Progressive AD (Part 1)	Available
<a href="#">151</a>	Factors associated with early and late evaluation for dementia	Available
<a href="#">152</a>	Sex differences in early symptoms of dementia	Available

***THEME 3: Diagnosis***

<a href="#"><u>301</u></a>	Diagnostic Accuracy	Available
<a href="#"><u>302</u></a>	Correlation between clinical and neuropath diagnosis	Available
<a href="#"><u>311</u></a>	Improving neuropath diagnosis	Available
<a href="#"><u>312</u></a>	Detecting dementia: CDR vs Neuropsych Test Battery	Available
<a href="#"><u>321</u></a>	Consensus versus Single clinician diagnosis	Available
<a href="#"><u>322</u></a>	Self-reported History versus Informant Report	Available
<a href="#"><u>331</u></a>	Reliability of Diagnosis	Available
<a href="#"><u>341</u></a>	Stability of dementia diagnosis	Available
<a href="#"><u>342</u></a>	Stability of MCI diagnosis	Available
<a href="#"><u>351</u></a>	Initial presentation of cognitive dysfunction	Available
<a href="#"><u>361</u></a>	Analysis of FAQ data	Available





## Facilitating GWAS: Emergent Scientific Efforts

- Neuropathology specimens
- Case and Control specimens
- Inclusion of prospective studies
  
- Large sets for gene discovery and replication (>20,000 subjects?!)
- Rapidly changing technology increases the likelihood of finding new genes



Neuron

Report

Neuron 54, 713-720, June 7, 2007

Cell  
PRESS

# GAB2 Alleles Modify Alzheimer's Risk in APOE $\epsilon$ 4 Carriers

Eric M. Reiman,<sup>1,2,3,17,18,\*</sup> Jennifer A. Webster,<sup>1,17,18</sup> Amanda J. Myers,<sup>4,5,18</sup> John Hardy,<sup>5,6</sup> Travis Dunckley,<sup>1,17</sup> Victoria L. Zismann,<sup>1,17</sup> Keta D. Joshipura,<sup>1,17</sup> John V. Pearson,<sup>1,17</sup> Diane Hu-Lince,<sup>1,17</sup> Matthew J. Huentelman,<sup>1,17</sup> David W. Craig,<sup>1,17</sup> Keith D. Coon,<sup>1,7,17</sup> Winnie S. Liang,<sup>1,17</sup> RiLee H. Herbert,<sup>1,17</sup> Thomas Beach,<sup>8,17</sup> Kristen C. Rohrer,<sup>5</sup> Alice S. Zhao,<sup>5</sup> Doris Leung,<sup>5</sup> Leslie Bryden,<sup>5</sup> Lauren Marlowe,<sup>5</sup> Mona Kaleem,<sup>5</sup> Diego Mastroeni,<sup>8</sup> Andrew Grover,<sup>8,17</sup> Christopher B. Heward,<sup>9</sup> Rivka Ravid,<sup>10</sup> Joseph Rogers,<sup>8,17</sup> Michael L. Hutton,<sup>11</sup> Stacey Melquist,<sup>11</sup> Ron C. Petersen,<sup>12</sup> Gene E. Alexander,<sup>13,17</sup> Richard J. Caselli,<sup>14,17</sup> Walter Kukull,<sup>16</sup> Andreas Papassotiropoulos,<sup>1,15</sup> and Dietrich A. Stephan<sup>1,2,17,\*</sup>





# Faculty and staff

- **Administration**
  - Bud Kukull
  - Mary Lovely
  - Maggie Connor
- **Methods Group**
  - Tom Koepsell (Chair)
  - Andrew Zhou
  - Nate Mercaldo
  - Bill Lee
  - Yueh-Yun Chi
  - Erin Ramos (emeritus)
- **Data Group**
  - Duane Beekly (chair)
  - Mary Jacka
  - Joylee Wu
  - Janene Hubbard
  - Woody Dietrich
  - Bill Lee
  - Erin Ramos
- **Q/A-Q/C Comm**
  - Tom Koepsell (Chair)
  - And the usual suspects