Data Analysis for Alzheimer's Disease

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Summer 2023

Overview of Topics

Background on Alzheimer's disease (AD)

Goals of the Course

Description of the Data

- NACC data set
- What my work focuses on

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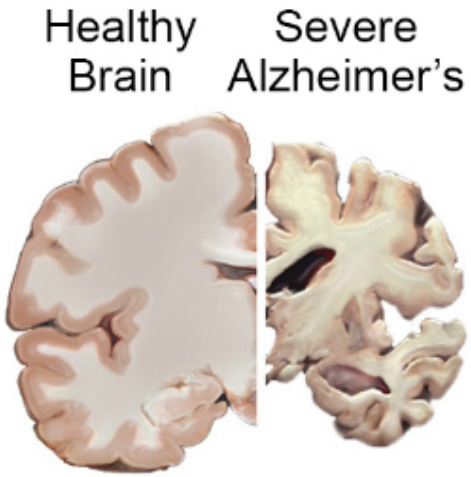
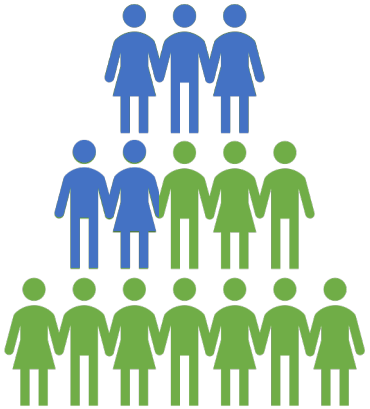
What is late-onset Alzheimer's Disease (LOAD)?



LOAD is the dominant form of AD, affecting people ≥ 65 years old

NIH National Institute on Aging



1/3 American seniors pass away with AD or dementia

Alzheimer's Association Facts & Figures, 2021

No cure for AD exist, but treatment is possible

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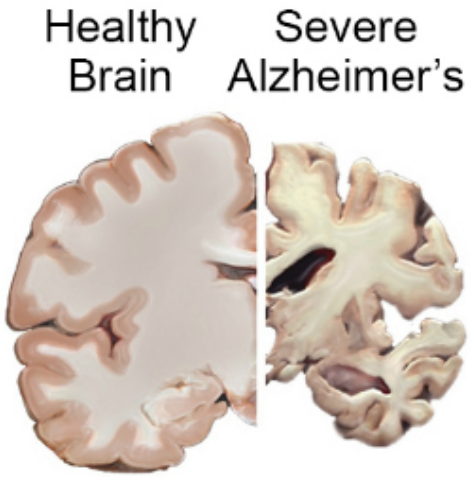

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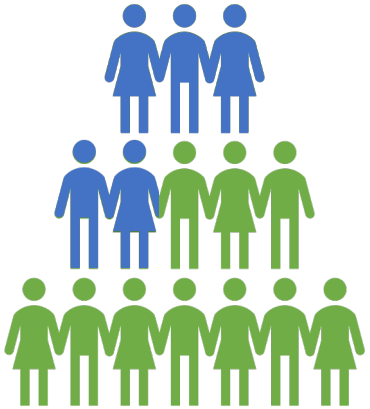


1/3 American seniors pass away with AD or dementia

Alzheimer's Association Facts & Figures, 2021

Earlier detection

No cure for AD exist, but treatment is possible

Improved therapeutic time window

Alzheimer's in Everyday Life

- What do you know about AD?

Alzheimer's in Everyday Life

- What do you know about AD?
- What *symptoms* are associated with AD?

Alzheimer's in Everyday Life

- What do you know about AD?
- What *symptoms* are associated with AD?
  - Forgetfulness
  - Misplacing items
  - Not recognizing friends or family
  - Being wrong about the day or year
  - Severe difficulty finding the right words
  - Becoming unable to navigate or drive around
  - …

Alzheimer's in Everyday Life

- What do you know about AD?
- What *symptoms* are associated with AD?
- What are some risk factors of AD?

Alzheimer's in Everyday Life

- What do you know about AD?
- What *symptoms* are associated with AD?
- What are some risk factors of AD?
  - Age
  - Genetics
  - Sex
  - Comorbidities
  - Health disparities
  - …

How the definition of AD has evolved

-1980s

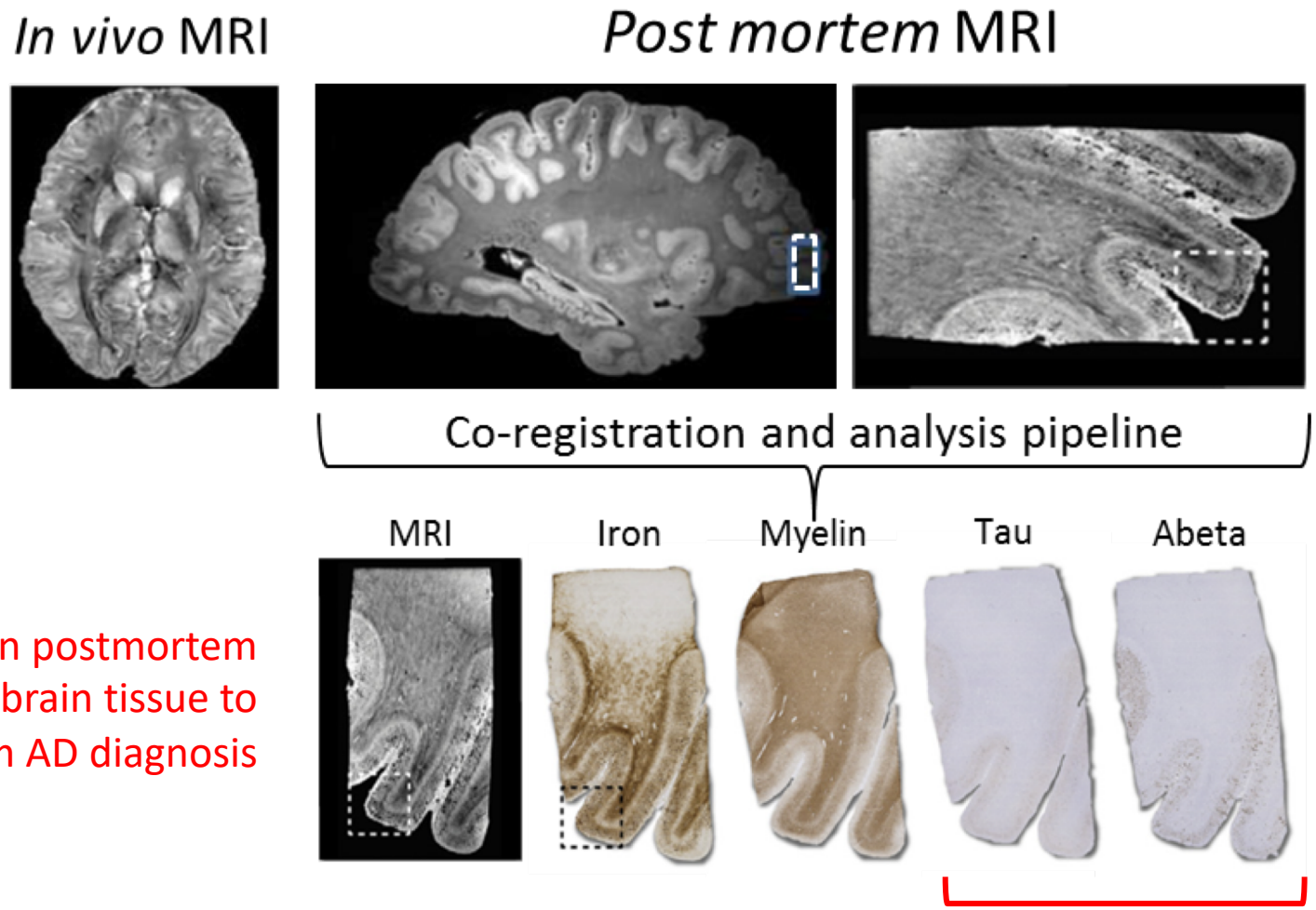
You belong to either one of the groups

Healthy Cognition

Alzheimer's Disease

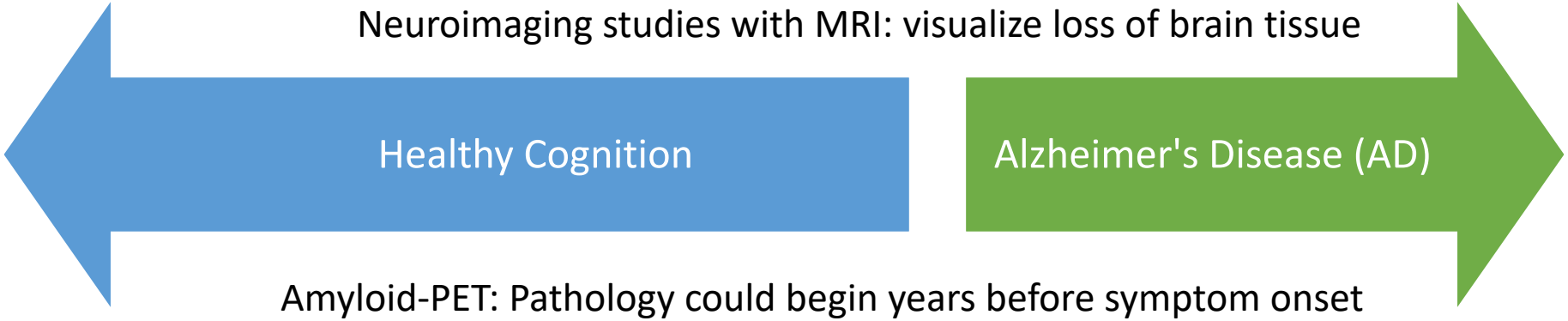
Why was the cutoff so binary?

How the definition of AD has evolved



We rely on postmortem analysis of brain tissue to confirm AD diagnosis

The Alzheimer’s continuum



The Alzheimer's continuum

CLINICAL DEMENTIA RATING (CDR™):	0	0.5	1	2	3

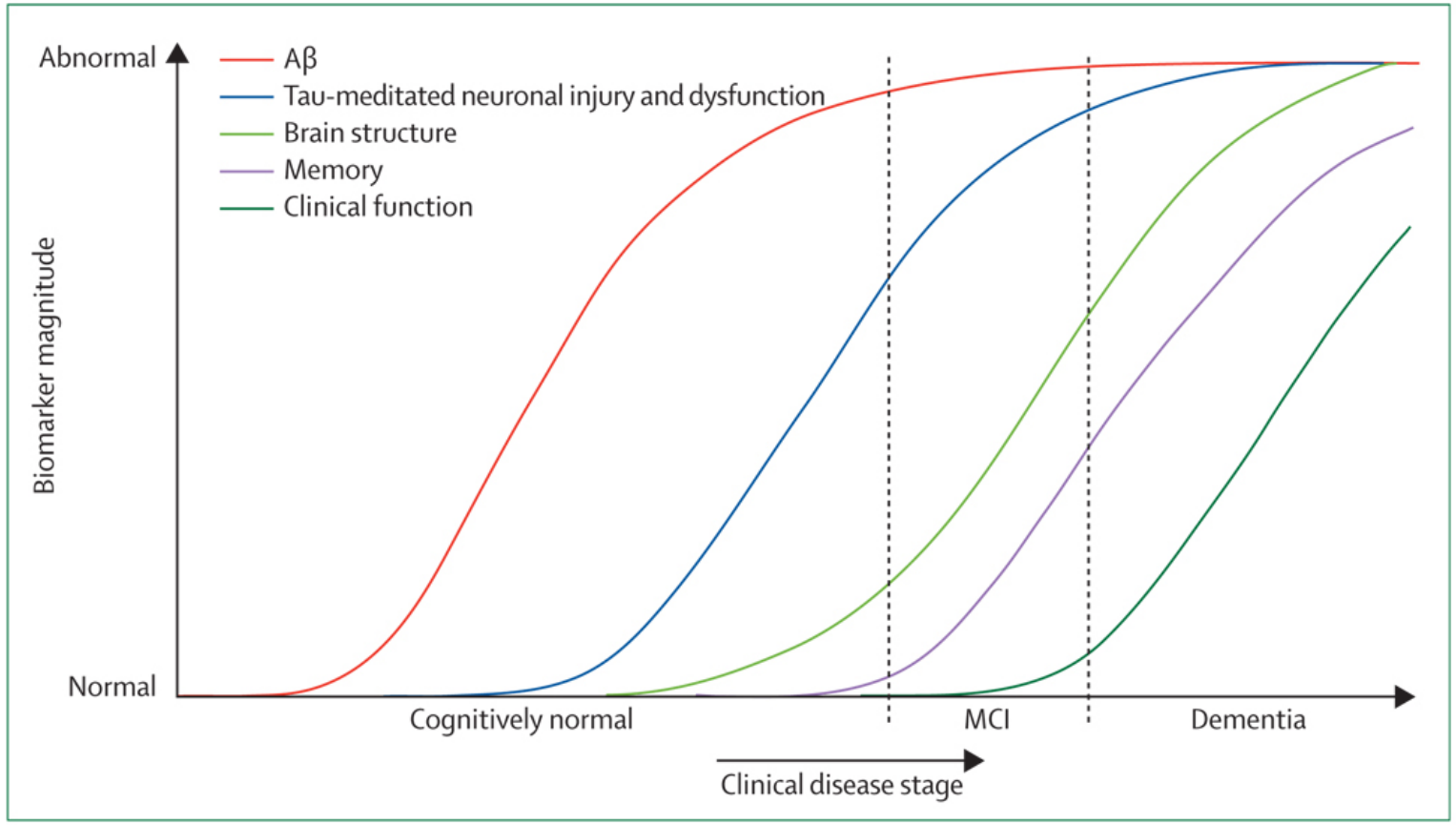
	Impairment				
	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
Judgment & Problem Solving	Solves everyday problems & handles business & financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences; social judgment usually maintained	Severely impaired in handling problems, similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems

Knight ADRC, WashU in St. Louis

The Alzheimer's continuum

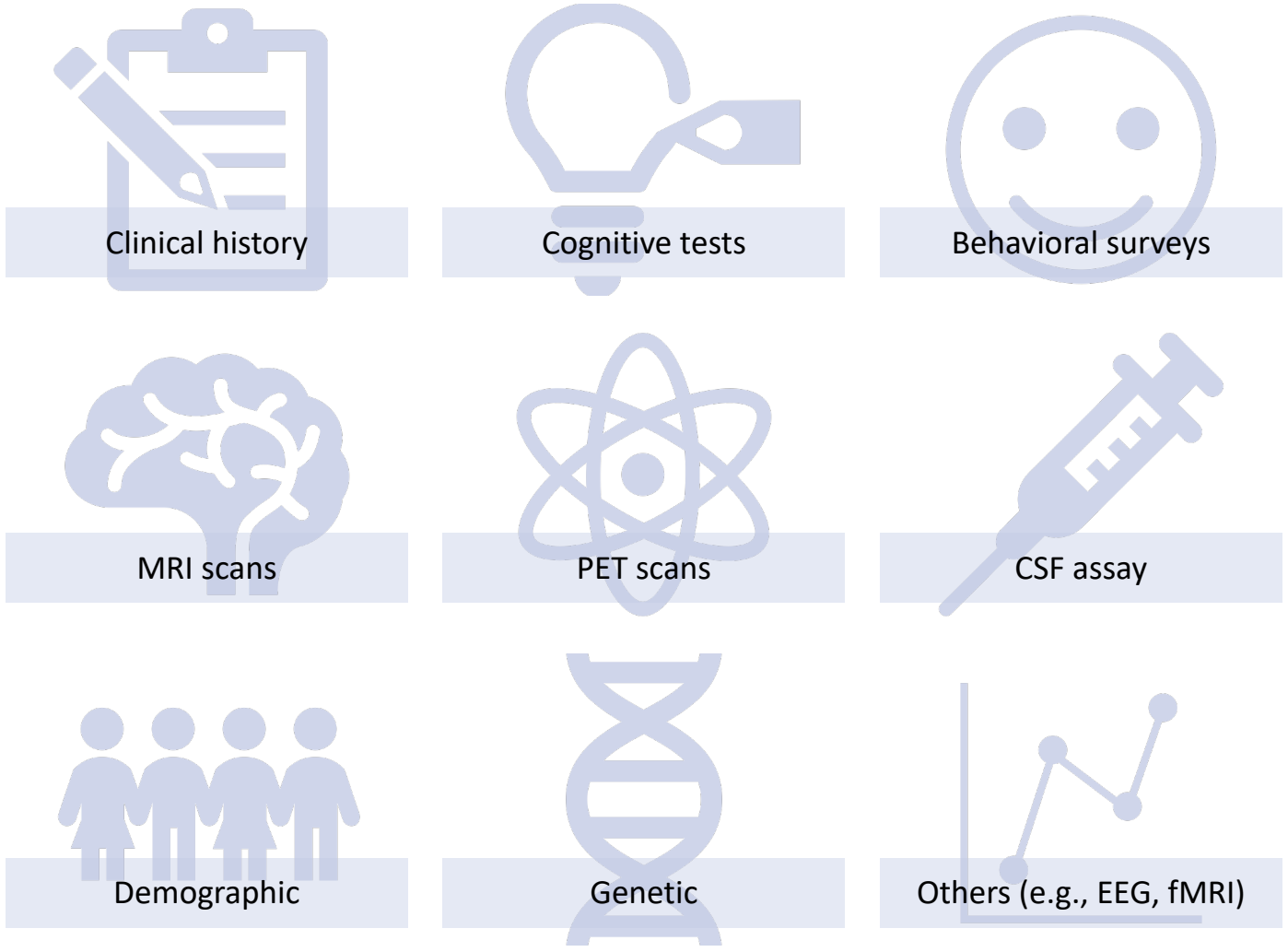
Cognitively Unimpaired → Mild Cognitive Impairment (MCI) → Alzheimer's Disease (AD)

Jack et al. 2010 *Lancet Neurol.*



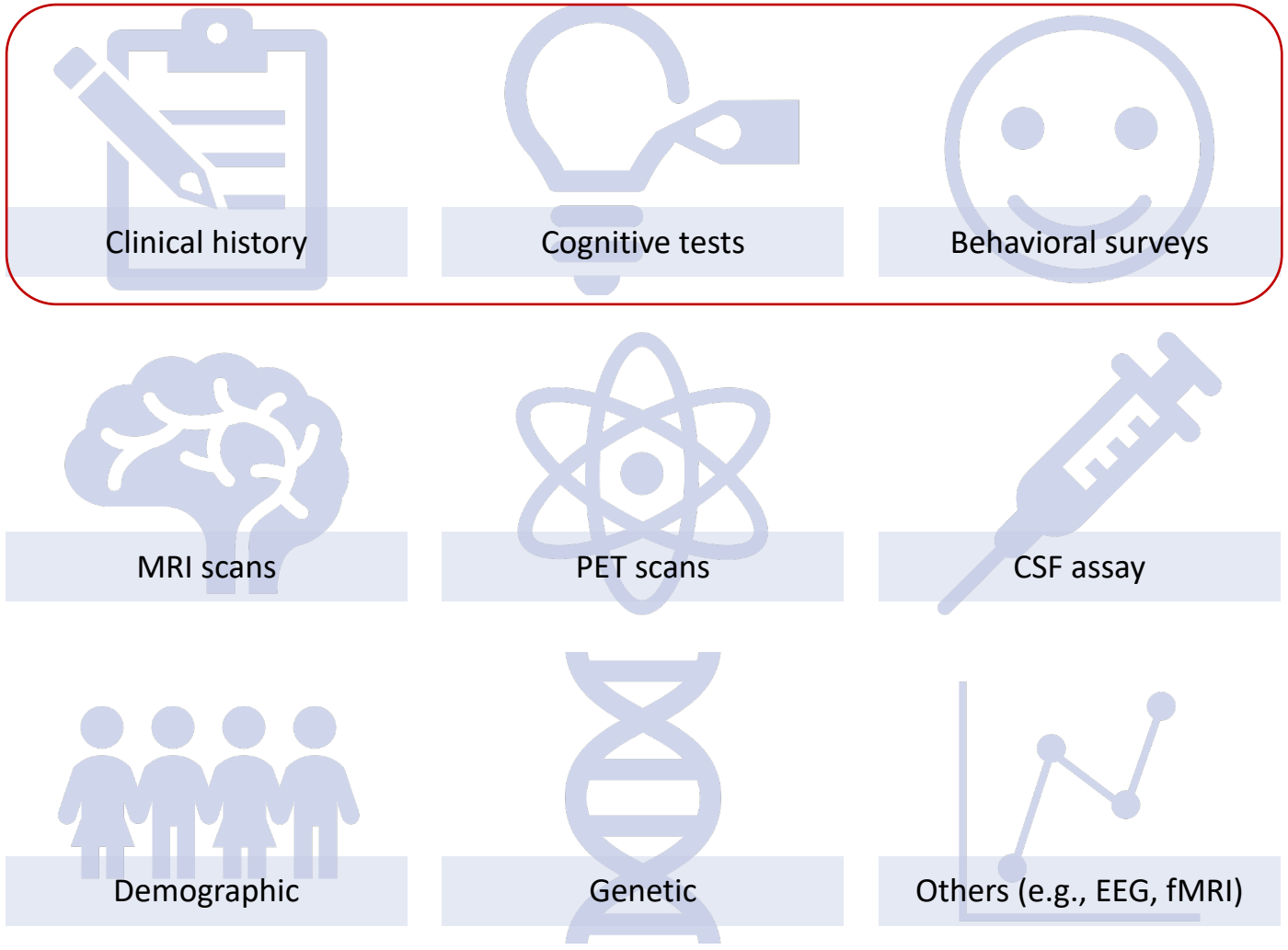
A/T(N) Framework

Types of Data for Evaluating AD



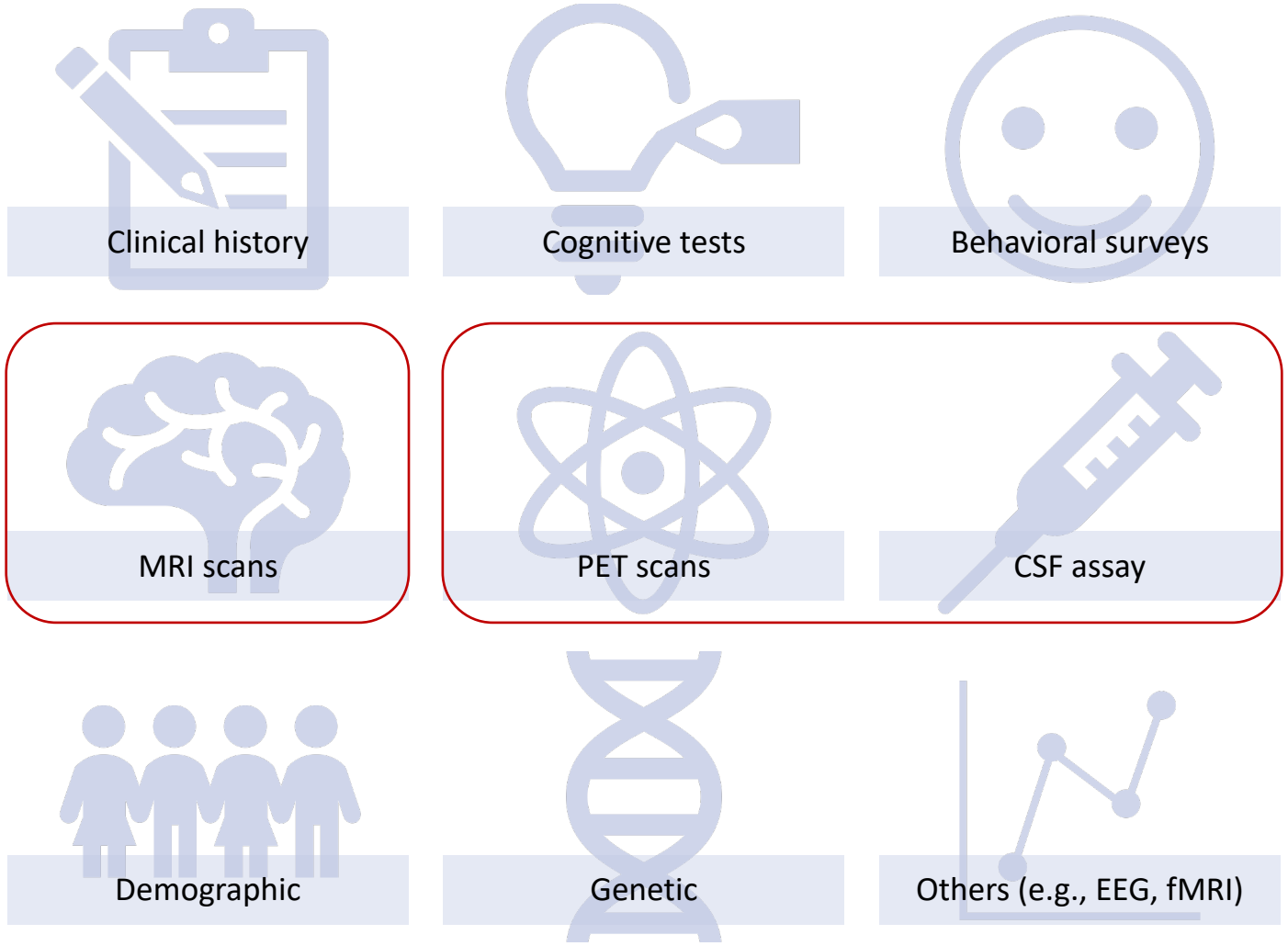
Types of Data for Evaluating AD

Obtained by the physician and/or neuropsychologist



Many tests are compared to the "normative" values found from healthy subjects

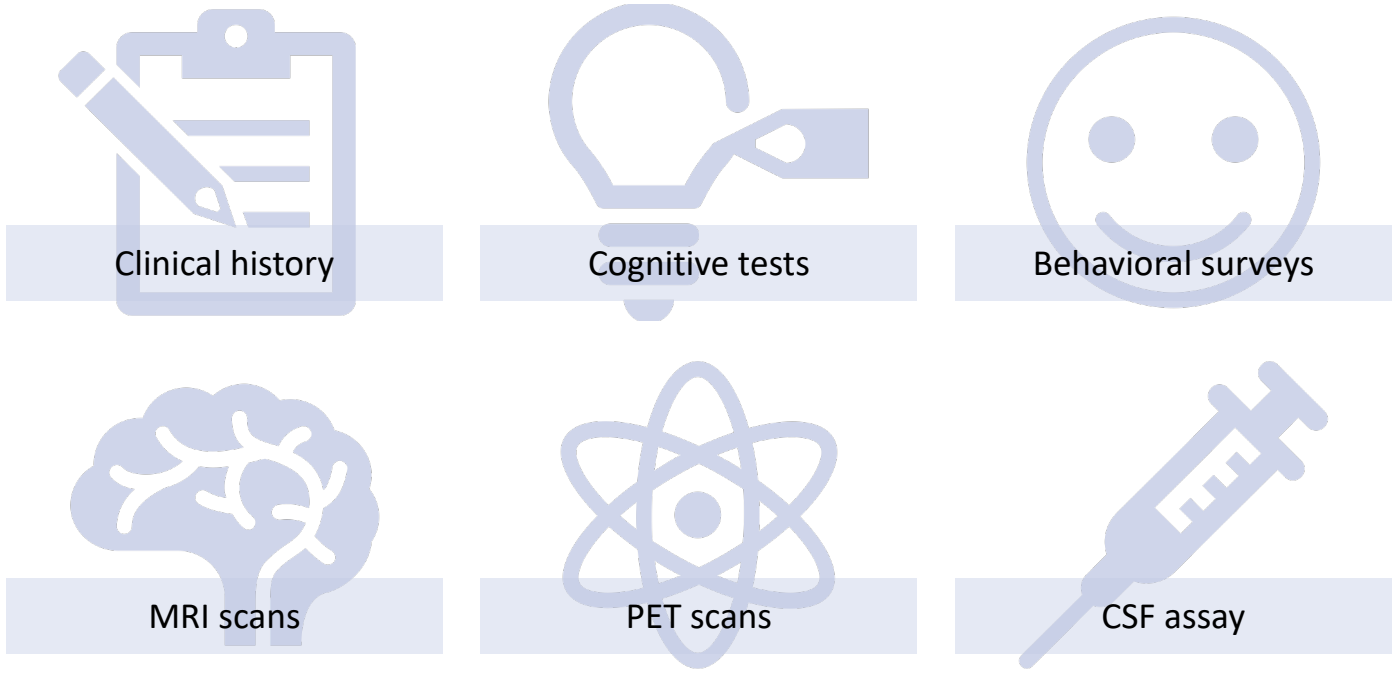
Types of Data for Evaluating AD



Useful for evaluating neurodegeneration and hemorrhages

Useful for evaluating levels of two main proteins implicated in AD

Types of Data for Evaluating AD

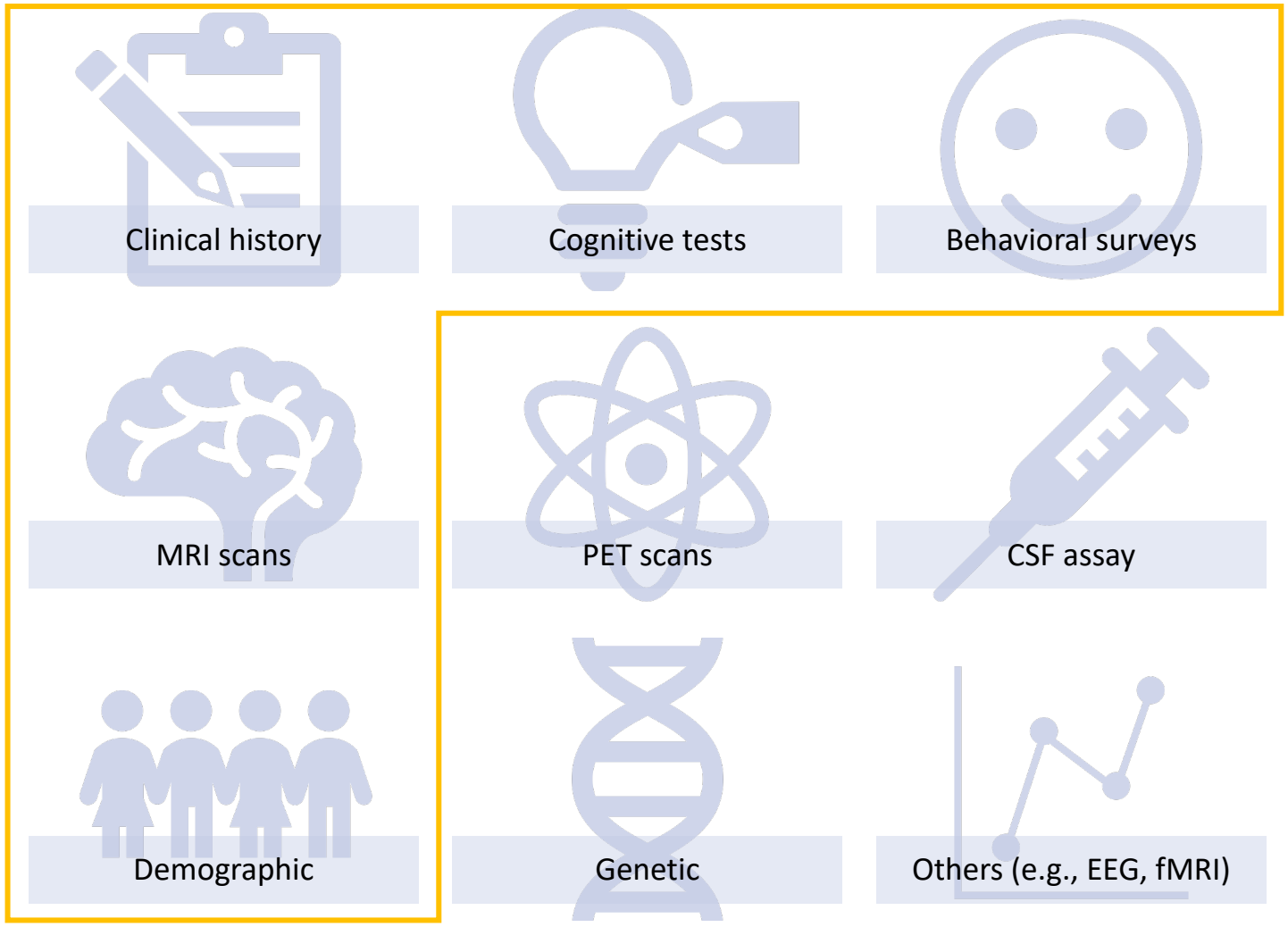


Age is strongly associated with AD; education may be protective

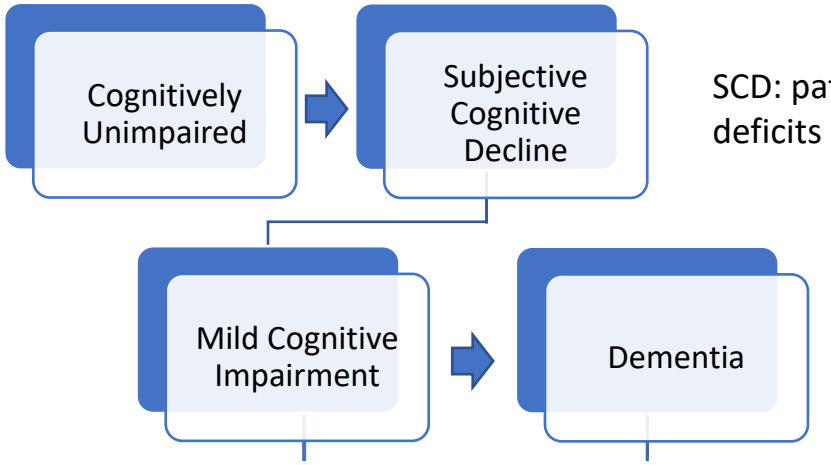
Some forms of AD are autosomal dominant (early onset); for most cases, no single gene is responsible, but **ApoE** has been shown to be strongly linked to AD

Types of Data for Evaluating AD

Our focus will be on these types of data



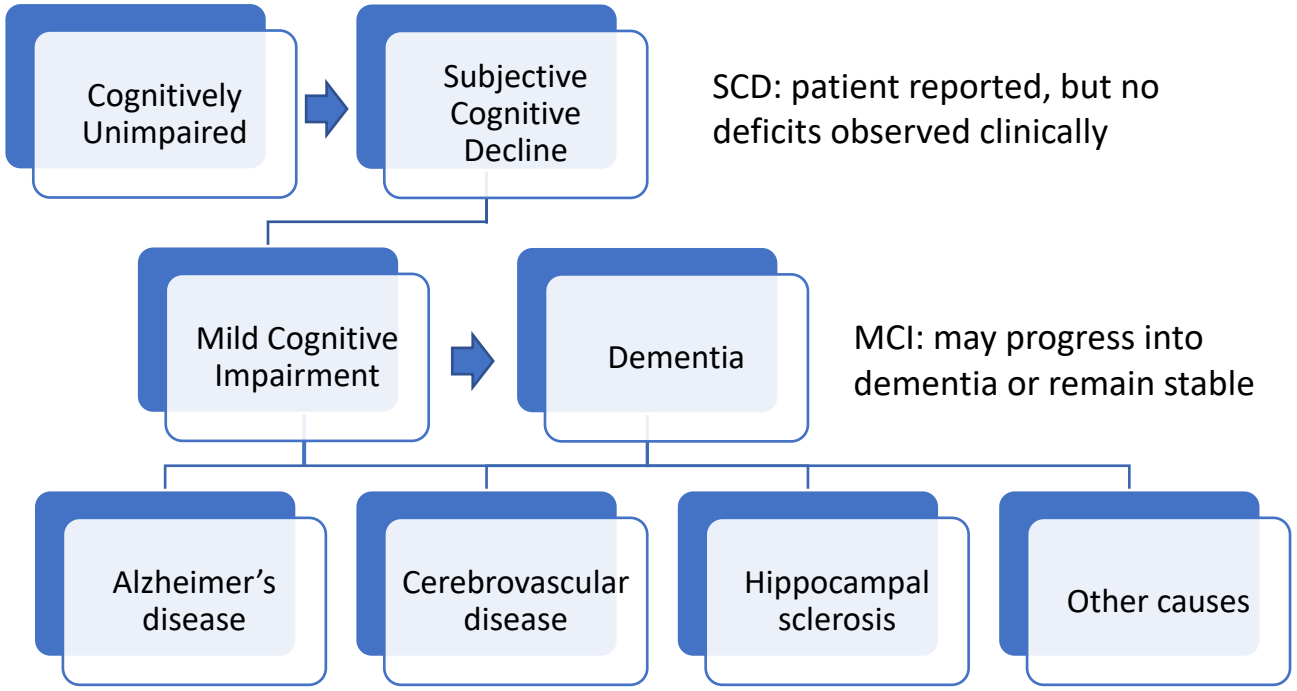
Alzheimer's Continuum: Clinical Focus



SCD: patient reported, but no deficits observed clinically

MCI: may progress into dementia or remain stable

Alzheimer's Disease and Related Dementias



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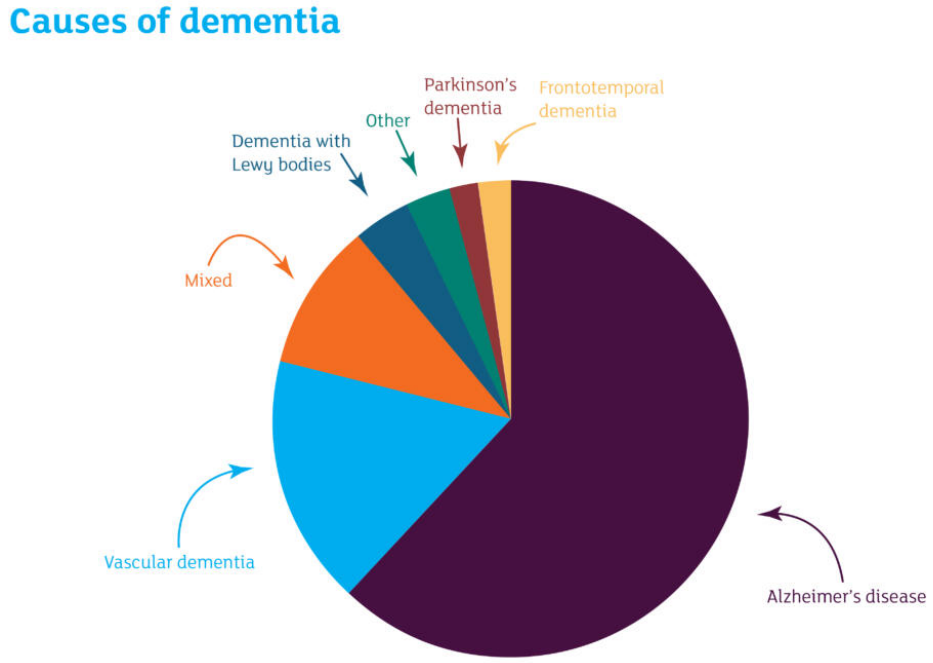

Alzheimer's Research UK

Causes of cognitive impairment are heterogeneous and not mutually exclusive

- Some patients have more than one underlying neuropathology

Summary

- ✓ Prevalence of AD
- ✓ How AD presents clinically
- ✓ Definition of AD
- ✓ Risk factors for AD
- ✓ Types of data available to clinicians and researchers
- ✓ Relationship of AD and related dementias

Any Questions?

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Important AD Topics

Improving diagnostic accuracy

- To assist physicians
- To screen more patients given limited access to experts

Understanding relationships

- Some tests are more expensive and less accessible
- What tests should be conducted more routinely?

Earlier detection of AD

- Prior to obvious symptoms
- Better clinical trials

What skills will you learn?

- One sample statistics
  - Inference for 1 sample
    - Hypothesis test and confidence intervals for the mean
- Two sample statistics
  - Inference for 2 samples
    - Hypothesis test and confidence intervals for comparing means, correlation, and simple linear regression

What else will you learn?

- Multiple regression
- Logistic regression for binary outcomes
- Resampling methods
  - Bootstrapping
- How to think like a data scientist!

Using these skills, you can answer key Qs

Improving AD diagnosis

- What variables are most informative of diagnosis?

Understanding AD pathology

- How are important clinical features related to each other?

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NACC Data Set

National Alzheimer's Coordinating Center (NACC)

- **Uniform Data Set (UDS):** demographic, behavioral, neuropsychological testing, clinical information
- **sMRI**: image-derived features from structural MRI scans

https://naccdata.org/

Clinical Data

- NACC ID: unique identifier for each subject
- DIAGNOSIS: clinician diagnosis of either
  - Normal cognition (0)
  - Mild cognitive impairment (1)
  - Dementia due to AD (2)

Clinical Data

Feature Name	Definition	Data Type	Possible Values
AGE	Subject’s age (years)	Numeric	18 - 120
EDUC	Subject’s number of years of education	Numeric	0 - 36
FEMALE	Subject’s sex	Categorical	0 = male 1 = female
BPSYS	Subject blood pressure (sitting), systolic	Numeric	70 - 230
BPDIAS	Subject blood pressure (sitting), diastolic	Numeric	30 - 140
HEIGHT	Subject's height (inches)	Numeric	36.0 - 87.9
WEIGHT	Subject's weight (lbs)	Numeric	50 - 400
HRATE	Subject resting heart rate (pulse)	Numeric	33 - 160

Behavioral Survey Data

Feature Name	Definition	Data Type	Possible Values
NACCGDS	Total Geriatric Depression Scale (GDS) Score	Numeric	0 - 15
CDRGLOB	Global Clinical Dementia Rating (CDR) Score	Numeric	0.0 = No impairment 0.5 = Questionable impairment 1.0 = Mild impairment 2.0 = Moderate impairment 3.0 = Severe impairment

Behavioral Survey Data

Feature Name	Definition	Data Type	Possible Values
TRAVEL	In the past four weeks, did the subject have any difficulty or need help with: Traveling out of the neighborhood, driving, or arranging to take public transportation	Numeric	0 = Normal 1 = Has difficulty, but does by self 2 = Requires assistance 3 = Dependent 8 = Not applicable (e.g., never did)
REMDATES	In the past four weeks, did the subject have any difficulty or need help with: Remembering appointments, family occasions, holidays, medications	Numeric	0, 1, 2, 3, 8
PAYATTN	In the past four weeks, did the subject have any difficulty or need help with: Paying attention to and understanding a TV program, book, or magazine	Numeric	0, 1, 2, 3, 8
MEALPREP	In the past four weeks, did the subject have any difficulty or need help with: Preparing a balanced meal	Numeric	0, 1, 2, 3, 8
EVENTS	In the past four weeks, did the subject have any difficulty or need help with: Keeping track of current events	Numeric	0, 1, 2, 3, 8
MEALPREP	In the past four weeks, did the subject have any difficulty or need help with: Preparing a balanced meal	Numeric	0, 1, 2, 3, 8
SHOPPING	In the past four weeks, did the subject have any difficulty or need help with: Shopping alone for clothes, household necessities, or groceries	Numeric	0, 1, 2, 3, 8
GAMES	In the past four weeks, did the subject have any difficulty or need help with: Playing a game of skill such as bridge or chess, working on a hobby	Numeric	0, 1, 2, 3, 8
STOVE	In the past four weeks, did the subject have any difficulty or need help with: Heating water, making a cup of coffee, turning off the stove	Numeric	0, 1, 2, 3, 8
SHOPPING	In the past four weeks, did the subject have any difficulty or need help with: Shopping alone for clothes, household necessities, or groceries	Numeric	0, 1, 2, 3, 8
BILLS	In the past four weeks, did the subject have any difficulty or need help with: Writing checks, paying bills, or balancing a checkbook	Numeric	0, 1, 2, 3, 8
TAXES	In the past four weeks, did the subject have any difficulty or need help with: Assembling tax records, business affairs, or other papers	Numeric	0, 1, 2, 3, 8

Behavioral Survey Data

Feature Name	Definition	Data Type	Possible Values
APPSEV	Appetite and eating severity	Numeric	1 = Mild (noticeable, but not a significant change) 2 = Moderate (significant, but not a dramatic change) 3 = Severe (very marked or prominent; a dramatic change) 8 = Not applicable, no appetite or eating problems reported
NITESEV	Nighttime behaviors severity	Numeric	1, 2, 3, 8
MOTSEV	Motor disturbance severity	Numeric	1, 2, 3, 8
IRRSEV	Irritability or lability severity	Numeric	1, 2, 3, 8
DISNSEV	Disinhibition severity	Numeric	1, 2, 3, 8
APASEV	Apathy or indifference severity	Numeric	1, 2, 3, 8
ELATSEV	Elation or euphoria severity	Numeric	1, 2, 3, 8
ANXSEV	Anxiety severity	Numeric	1, 2, 3, 8
DEPDSEV	Depression or dysphoria severity	Numeric	1, 2, 3, 8
AGITSEV	Agitation or aggression severity	Numeric	1, 2, 3, 8
HALLSEV	Hallucinations severity	Numeric	1, 2, 3, 8
DELSEV	Delusions severity	Numeric	1, 2, 3, 8

Neuropsychological Testing Data

Feature Name	Definition	Data Type	Possible Values
ANIMALS	Total number of animals named in 60 seconds	Numeric	0 - 77
TRAILA	Trail Making Test Part A - Total number of seconds to complete	Numeric	0 - 150
TRAILB	Trail Making Test Part B - Total number of seconds to complete	Numeric	0 - 300
DIGIF	Digit span forward trials correct	Numeric	0 - 12
MEMUNITS	Logical Memory IIA - Delayed - Total number of story units recalled	Numeric	0 - 25
NACCMMSE	Total Mini-Mental State Exam (MMSE) score	Numeric	0 - 30

MRI Data

Feature Name	Measurement Type	Definition	Data Type
NACCICV	Regional gray matter volumes	Total intracranial volume (cc)	Numeric
CSFVOL	Regional gray matter volumes	Total brain cerebrospinal fluid volume (cc)	Numeric
LHIPPO	Regional gray matter volumes	Segmented left hippocampus volume (cc)	Numeric
RHIPPO	Regional gray matter volumes	Segmented right hippocampus volume (cc)	Numeric
FRCORT	Regional gray matter volumes	Segmented total frontal lobe cortical gray matter volume (cc)	Numeric
LPARCORT	Regional gray matter volumes	Segmented left parietal lobe cortical gray matter volume (cc)	Numeric
RPARCORT	Regional gray matter volumes	Segmented right parietal lobe cortical gray matter volume (cc)	Numeric
LTEMPCOR	Regional gray matter volumes	Segmented left temporal lobe cortical gray matter volume (cc)	Numeric
RTEMPCOR	Regional gray matter volumes	Segmented right temporal lobe cortical gray matter volume (cc)	Numeric
LCAC	Regional gray matter volumes	Left caudal anterior cingulate gray matter volume (cc)	Numeric
RCAC	Regional gray matter volumes	Right caudal anterior cingulate gray matter volume (cc)	Numeric
LENT	Regional gray matter volumes	Left entorhinal gray matter volume (cc)	Numeric
RENT	Regional gray matter volumes	Right entorhinal gray matter volume (cc)	Numeric
LPARHIP	Regional gray matter volumes	Left parahippocampal gray matter volume (cc)	Numeric
RPARHIP	Regional gray matter volumes	Right parahippocampal gray matter volume (cc)	Numeric
LPOSCIN	Regional gray matter volumes	Left posterior cingulate gray matter volume (cc)	Numeric
RPOSCIN	Regional gray matter volumes	Right posterior cingulate gray matter volume (cc)	Numeric

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- ✓ What skills will you learn?
- ✓ What questions could you answer?
- ✓ Potential research topics

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