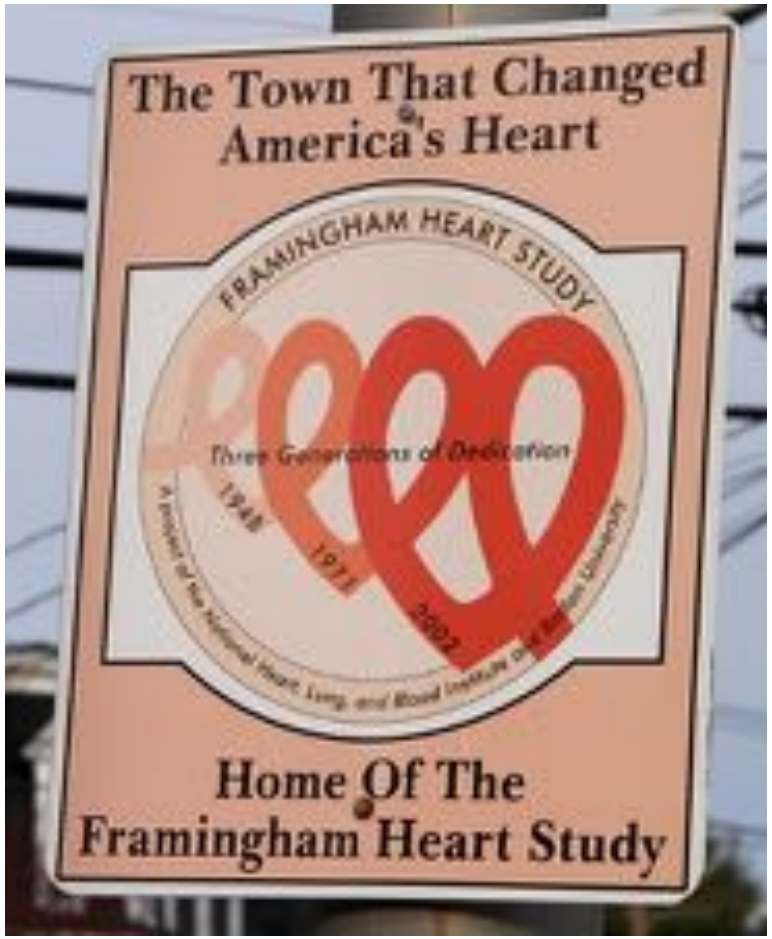
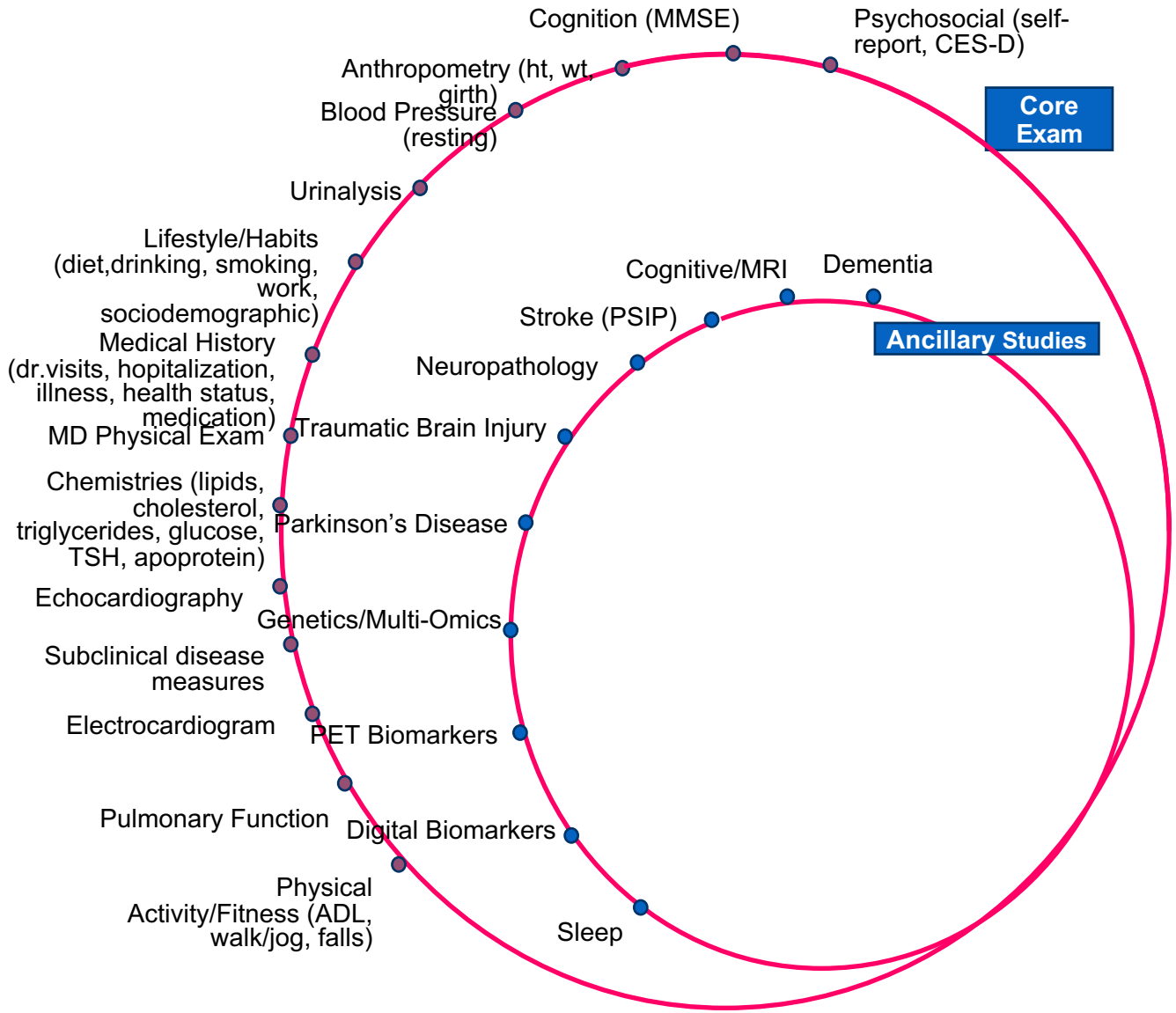
Cognitive Aging in the Framingham Heart Study (FHS)



FHS Core exams vs Ancillary exams



Phenome Wide FHS Aging Database

Cognition Neuroimaging

Dementia
Stroke
Parkison's Disease
Traumatic Brain Injury
Pulmonary
Vascular
Osteoporosis
Osteoarthritis

Cardiac
Depression
Hearing
Eye
Renal
Reproductive Health

Omic
Genomic
Epigenomic
Transcriptomic
Proteomics
Metabolomic

Alcohol Diabetes Pollution

Centers for Medicare & Medicaid Services (CMS)

FHS Cognitive Aging Timeline

1984
NINDS-ADRDA
AD Diagnostic
Criteria

1948

Gen 1

5,209 participants age 30-62
32 evaluations

1976-78
Baseline NP

1981
MMSE

FHS Cognitive Aging Timeline

1984
NINCDS-ADRDA AD Diagnostic Criteria

1948 — **2016**

Gen 1

1976-78
Baseline NP

1981
MMSE

1999
Brain MRI/NP (n= 331)

1971 — **2016**

Gen 2

1991
MMSE

1999
Brain MRI/NP (n= 2617)

5,124 of the original participants' adult children and their spouses
9 evaluations

FHS Cognitive Aging Timeline

1984
NINCDS-ADRDA AD Diagnostic Criteria

Gen 1
1948

2016

1976-78
Baseline NP

1981
MMSE

1999
Brain MRI/NP

Repeat
NP/MRI

Gen 2
1971

2016

1991
MMSE

1999
Brain MRI/NP

Repeat
NP/MRI

4,095 grandchildren
of the Original cohort
4 evaluations

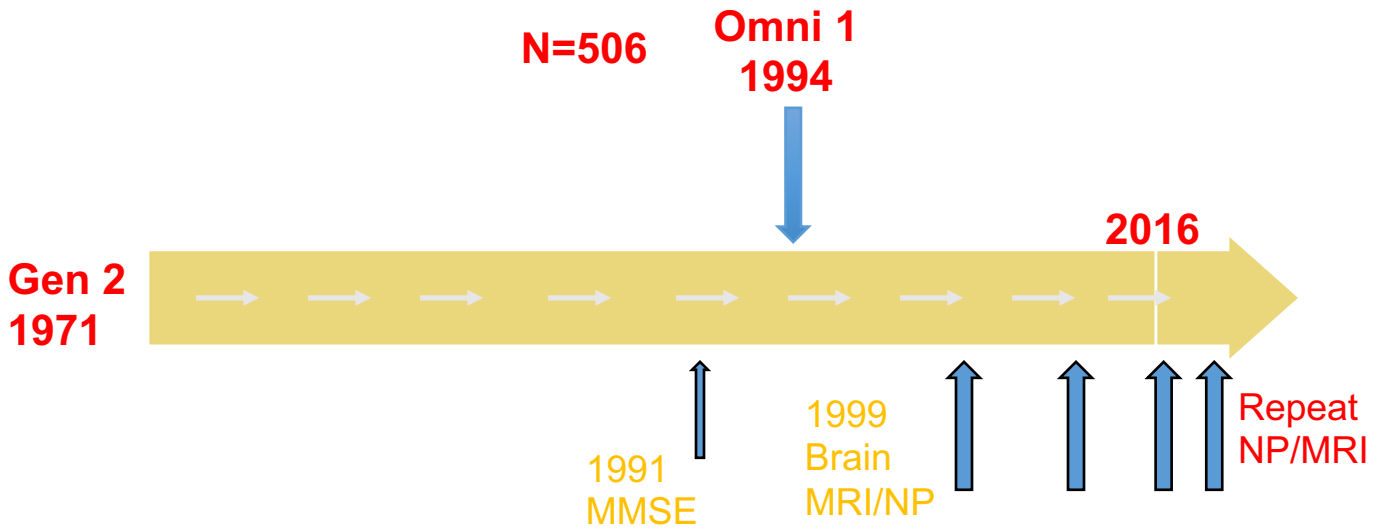
Gen 3
2002

2020

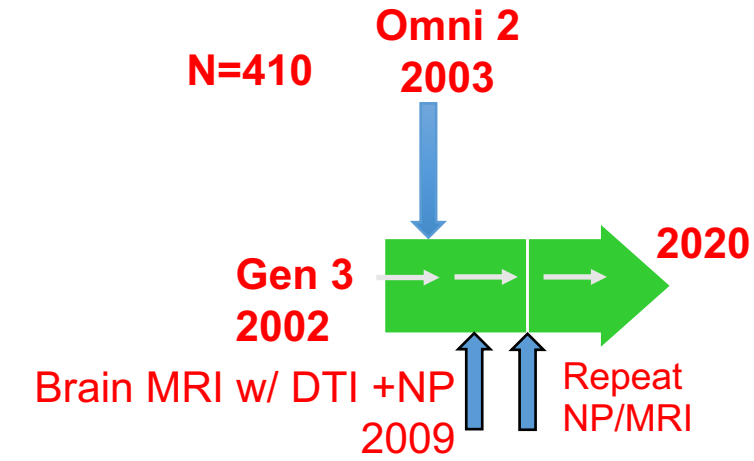
Brain MRI w/ DTI +NP
2009

Repeat
NP/MRI

FHS Cognitive Aging Timeline



Omni participants are of African-American, Hispanic, Asian, Indian, Pacific Islander and Native American origins



Timeline for Neuropsych Variables

Cognitive Domain	Neuropsychological Test Measures Defined	1976-78*	1999-05	2005-11^	2009-16
Verbal Memory	WMS - Logical Memory-Immediate Recall	X	X	X	X
	WMS – Logical Memory-Delayed Recall	X	X	X	X
	WMS Logical Memory-Delayed Recognition			X	X
Visual Memory	WMS Visual Reproductions Immediate Recall	X	X	X	X
	WMS Visual Reproductions – Delayed Recall		X	X	X
	WMS Visual Reproductions – Delayed Recognition			X	X
Verbal Learning	WMS Paired Associates – Immediate Recall	X	X	X	X
	WMS PA Delayed Recalll				
	WMS Paired Associates - Delayed Recognition		X	X	X
Attention & Executive Function	Trail-making Test A (Trails A) and Test B (Trails A)		X	X	X
	WMS – Digit Span Forward (DS-F) & Backward (DS-B)	X		X	X
Abstract Reasoning	WAIS – Similarities subtest	X	X	X	X
Language	Boston Naming Test 30 item version		X	X	X

Timeline for Neuropsych Variables

Cognitive Domain	Neuropsychological Test Measures Defined	1976-78*	1999-05	2005-11^	2009-16
Verbal Fluency	Controlled Word Association Test (FAS)	X		X	X
	Category Naming (Animals)			X	X
Visuo-perceptual Skill	Hooper Visual Organization Test		X	X	X
Visuo-construction	Clock Drawing Test*			X	X
Premorbid Intelligence, Verbal	Wide Range Achievement Test (WRAT)-3 Reading Subtest		X	X	X
Premorbid Intelligence, Non-verbal	WISC-III Math Fluency			X	X
Multi-domain	Digit Symbol			X	X

WMS: Wechsler Memory Scale WAIS: Wechsler Adult Intelligence Scale; WISC-III: Wechsler Intelligence Scale for Children, version III

^BPA scoring added; * computerized scoring added in 2011 in collaboration with Penne and Libon;

Dementia Review

- Flags for dementia review
  - Objective evidence of significant decline from a previous NP exam or MMSE
  - Greater self-reported change in cognition than same age peers
  - Clinical judgment of impairment by the NP examiner or other FHS clinical staff
  - Family report of significant cognitive or functional change.
- For participants who are flagged, dementia review usually occurs once or twice per participant
- Neurologist, neuropsychologist both present

Dementia Review

- Information reviewed:
  - Cognitive testing
  - Neurology notes
  - Other medical records, including imaging

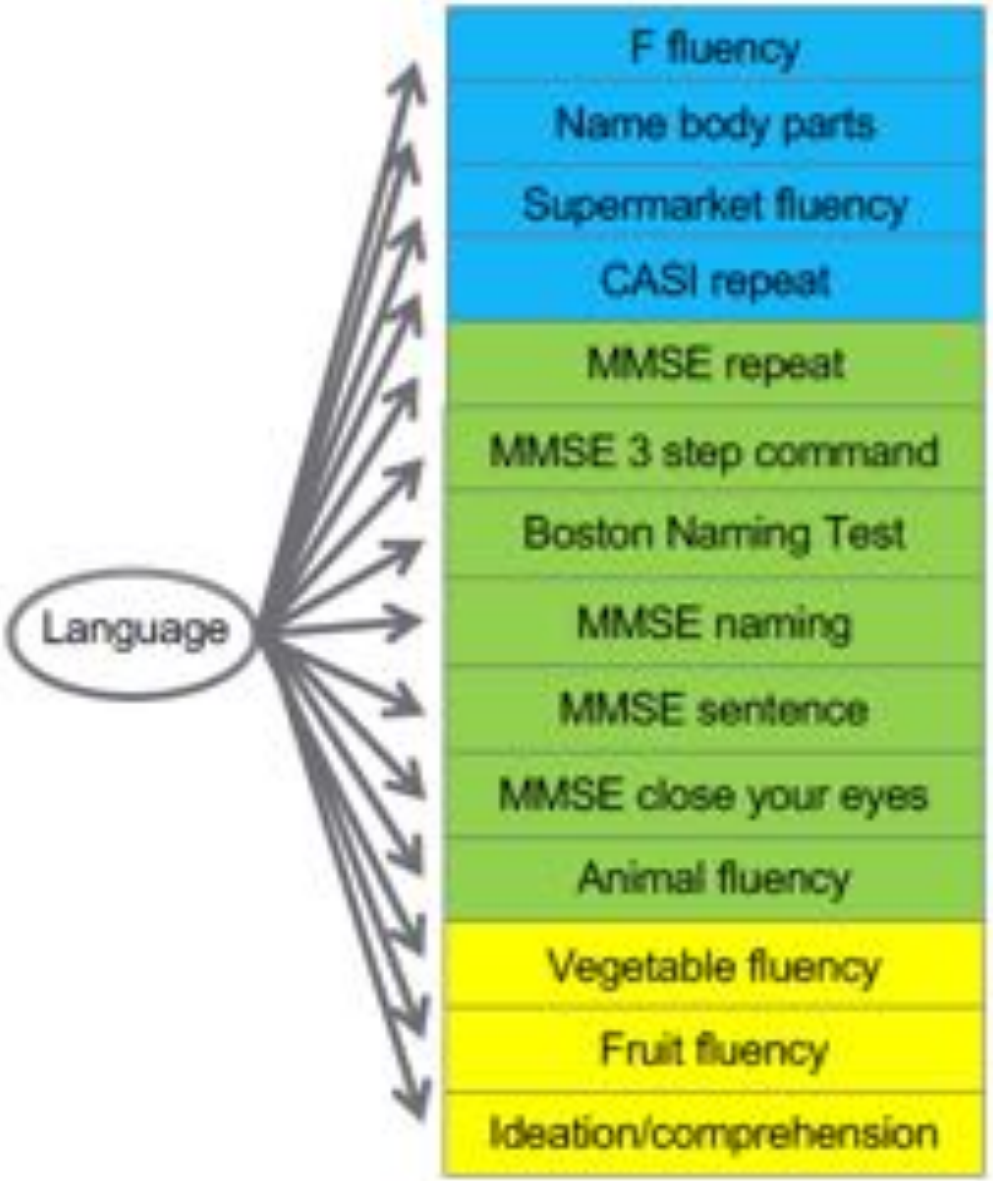
- Diagnoses
  - Cognitive impairment, mild dementia, moderate dementia, severe dementia
  - Corresponding dates
  - Etiology of dementia (usually AD or mixed dementia (AD+vascular))

Tahoe Dataset

- Generation 1
- Data included:
  - Demographics
  - Longitudinal MMSE
  - Longitudinal Neuropsych
  - Dementia review
  - *APOE* genotype
- Long format with separate row and age/time for each MMSE (core visit), neuropsych visit and dementia diagnosis
- After Tahoe, workshop data and much additional FHS data will be available for work on 2 recently funded TBI-related grants (BU, Sinai, Rush, U of Wash). Investigators at other sites should be able to access data through DMDAs and IRB approval at these sites.

Co-calibration of Neuropsych Data in ROS, MAP, MARS and ACT

- Creation of composite scores for memory, executive function, language, and visuospatial abilities.
- There is substantial item overlap across studies, which is critical because we use these common “anchor” items to co-calibrate.
- Begin with theory-driven approach to conceptualize the construct(s) being measured. Content experts (Trittschuh, Saykin, Mez) consider every item and test (“indicators”) available for each study, assigning each indicator to a primary cognitive domain.



Co-calibration of Neuropsych Data in ROS, MAP, MARS and ACT

- Using SEM/IRT, we fit various models to these indicators, allowing residual correlations or secondary factors for indicators that share methods effects
- Ultimately identify the best-fitting and theoretically informative model.
- Already completed for ROS/MAP/MARS/ACT and are part of the Tahoe dataset. FHS is planned.