

# Rush Alzheimer's Disease Center

Codebook for data set 611

Generated: 04-23-2019

This codebook contains 109 variables.

## Longitudinal cycle explanation

All longitudinal data sets are organized by projid + visit or fu\_year

visit	fu_year	explanation
00	0.0	Baseline
01	1.0	1st year follow-up
02	2.0	2nd year follow-up
03	3.0	3rd year follow-up
04	4.0	4th year follow-up
XX	XX.0	XXth year follow-up

variable suffix	type	explanation
_bl	cross-sectional	baseline cycle score; for medical history questions, the score may cover the period from prior to study participation to baseline visit.
_ever	cross-sectional	reported in any cycle at least one time
_l	cross-sectional	last cycle score
_lv	cross-sectional	last valid score

_cum	longitudinal	reported in past history or in at least one follow-up cycle up to this cycle
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## ApoE and TOMM40

### ApoE and TOMM40 > ApoE

ApoE genotype :  
apoe\_genotype

Apolipoprotein E genotype

**Apolipoprotein E (APOE) genotype**

value	coding
22	E2E2
23	E2E3
24	E2E4
33	E3E3
34	E3E4
44	E4E4

DNA was extracted from PBMCs or brain. Genotyping was performed by Agencourt Bioscience Corporation utilizing high-throughput sequencing of codon 112 (position 3937) and codon 158 (position 4075) of exon 4 of the APOE gene on chromosome 19.

Data updated 6/23/2015

Participants were genotyped for APOE alleles by Polymorphic DNA Technologies.

All APOE data were generated by Polymorphic DNA Technologies as part of a collaboration with Allan Roses and Zinfandel. <http://www.polymorphicdna.com/> (<http://www.polymorphicdna.com/>)

## References

**TOMM40'523 variant and cognitive decline in older persons with APOE ?3/3 genotype.**

Yu L, Lutz MW, Wilson RS, Burns DK, Roses AD, Saunders AM, Gaiteri C, De Jager PL, Barnes LL, Bennett DA  
Journal: Neurology 2017 Feb 14; 88(7) 661-668

### ApoE and TOMM40 > TOMM40

r523\_a1

r523\_a2

TOMM40 genotype :  
tomm40\_hap

### Translocase of outer mitochondrial membrane 40 genotype

**TOMM40** (translocase of outer mitochondrial membrane, 40kD) encodes a membrane-bound mitochondrial protein that is adjacent to, and in linkage disequilibrium with, the apolipoprotein E gene. Genotyping is performed by Polymorphic DNA Technologies, Inc. (Alameda, California), blinded to all clinical and pathologic data. The TOMM40'523 genotypes are determined by rs10524523 (chr19:44,899,792-44,899,826, human genome reference assembly GRCh38/hg38), a homopolymer length polymorphism (poly-T), at intron 6 of the TOMM40 gene, as described by Roses et al., 2014. Allele lengths are then categorized based on the number of the poly-T repeats: a short allele [523-S] is defined by poly-T repeats $\leq$ 19, a long [523-L] allele by  $20 \leq$  poly-T repeats  $\leq$  29;, and a very long allele [523-VL] by poly-T repeat $\geq$ 30.

TOMM40'523 genotypes:

Value	Code
1	S/S
2	S/L
3	S/VL
4	L/L
5	L/VL
6	VL/VL

### References

**TOMM40'523 variant and cognitive decline in older persons with APOE  $\epsilon$ 3/3 genotype.**

Yu L, Lutz MW, Wilson RS, Burns DK, Roses AD, Saunders AM, Gaiteri C, De Jager PL, Barnes LL, Bennett DA  
Journal: Neurology 2017 Feb 14; 88(7) 661-668

Blood Measures

Blood Measures > Routine laboratory tests

## Fasting status : fasting

## Fasting status at time of blood draw

**Fasting status** is reported at the time of blood draw. Participants are asked to report the time of their last meal. If a participant is unable to answer the question, a nurse or caregiver's response is recorded, if available. Participants who are impaired and cannot answer questions clearly are marked as "don't know." A participant is considered fasting if the last meal was consumed at least 8 hours prior to the time of blood draw.

Value	Coding
1	Yes
2	No
3	Don't know

## Glucose level : glucose

## Glucose level in blood samples

**Blood glucose level** is measured with a basic metabolic panel performed by Quest Diagnostics. See the routine laboratory tests subcategory description for blood sample collection and analysis procedures. Results can be fasting/non-fasting (see the fasting variable).

Blood glucose level is expressed in mg/dL.

Reference range: 65 - 99 mg/dL

## Hemoglobin A1c level : hba1c

## Hemoglobin A1c in blood samples

**Hemoglobin A1c** is measured by Quest Diagnostics. See the routine laboratory tests subcategory description for blood sample collection and analysis procedures.

Hemoglobin A1c is expressed as a percentage of hemoglobin.

Reference range: <5.7% of total hemoglobin

## Hemoglobin : hemoglobin

## Hemoglobin in blood samples

**Hemoglobin** is measured with a complete blood count performed by Quest Diagnostics. See the routine laboratory tests subcategory description for blood sample collection and analysis procedures.

The variable is expressed in g/dL.

Reference range:

Male: 13.2 - 17.1 g/dL

Female: 11.7 - 15.5 g/dL

## References

### **Relation of hemoglobin to level of cognitive function in older persons.**

Shah RC, Wilson RS, Tang Y, Dong X, Murray A, Bennett DA

Journal: Neuroepidemiology 2009; 32(1) 40-6

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## Brain Proteins

### Brain Proteins > Presynaptic proteins (ELISA)

Complexin-I (inhibitory) :  
synap\_6\_complex1

Complexin-I protein density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Complexin-I protein density** is determined by immunoassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). Monoclonal antibody SP33 is used to quantify complexin-I immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater complexin-I protein concentrations.

## References

### **Presynaptic proteins complexin-I and complexin-II differentially influence cognitive function in early and late stages of Alzheimer's disease.**

Ramos-Miguel A, Sawada K, Jones AA, Thornton AE, Barr AM, Leurgans SE, Schneider JA, Bennett DA, Honer WG

Journal: Acta neuropathologica 2016 Nov 19; 133(3) 395-407

Complexin-II (excitatory) :  
synap\_6\_complex2

### Complexin-II protein density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Complexin-II protein density** is determined by immunoassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). Monoconal antibody LP27 is used to quantify complexin-II immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater complexin-II concentrations.

### References

**Presynaptic proteins complexin-I and complexin-II differentially influence cognitive function in early and late stages of Alzheimer's disease.**

Ramos-Miguel A, Sawada K, Jones AA, Thornton AE, Barr AM, Leurgans SE, Schneider JA, Bennett DA, Honer WG

Journal: Acta neuropathologica 2016 Nov 19; 133(3) 395-407

SNAP-25 :  
synap\_6\_snap25

### Synaptosomal-associated protein 25 (SNAP-25) density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Synaptosomal-associated protein 25 (SNAP-25) density** is determined by immunoassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). SP12 antibody is used to quantify SNAP-25 immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus

4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, the mean is determined for each participant across the 6 regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater SNAP-25 protein concentrations.

## References

### **Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA  
Journal: Translational psychiatry 2012; 2e114

### **A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ, Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG  
Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 2010 Apr; 35(5) 1226-38

## Synaptophysin : synap\_6\_synaptophys

### Synaptophysin protein density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Synaptophysin protein density** is determined by immunoassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). EP10 antibody is used to quantify synaptophysin immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, a mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels,

scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater synaptophysin protein concentrations.

## References

### **Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA  
Journal: Translational psychiatry 2012; 2e114

### **A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ, Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG  
Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 2010 Apr; 35(5) 1226-38

Syntaxin-1 :  
synap\_6\_syntaxin

Syntaxin-1 protein density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Syntaxin-1 protein density** is determined by immunoassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). SP6 antibody is used to quantify syntaxin-1 immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater syntaxin-1 protein concentrations.

## References

### **Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA



Journal: Translational psychiatry 2012; 2e114

**A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ, Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG

Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology  
2010 Apr; 35(5) 1226-38

VAMP : synap\_6\_vamp

Vesicle-associated membrane protein (VAMP) density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Vesicle-associated membrane protein (VAMP) density** is determined by immunassay in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). SP10 antibody is used to quantify VAMP immunodensities from frozen samples of gray matter in 6 cortical regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

Values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. Higher values indicate greater VAMP protein density.

## References

**Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA

Journal: Translational psychiatry 2012; 2e114

**A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ,

Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG

Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology

2010 Apr; 35(5) 1226-38

Mean SNARE protein-  
protein interactions :  
zcapture\_syn\_6

Mean SNARE protein-protein interactions - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Mean Soluble *N*-ethylmaleimide-sensitive factor Attachment protein Receptor (SNARE) protein-protein interactions** captures the functional capacity of the presynaptic terminals to release neurotransmitters upon stimuli. Protein-protein interactions between different antigens are quantified from frozen samples of gray matter in 6 cortical regions. The measure is determined in the Honer Lab at the University of British Columbia (Vancouver BC, Canada).

Antibodies	Synaptic protein interaction
SP7 + SP10	Syntaxin-1 - VAMP interaction
SP7 + SP12	Syntaxin-1 - SNAP-25 interaction
SP12 + SP7	SNAP-25 - Syntaxin-1 interaction
SP12 + SP10	SNAP-25 - VAMP interaction

Brain regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate
6. Posterior putamen

For each of the 4 protein-protein interactions, values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a standardized score is calculated across all participants. Since reported values are inversely proportional to protein-protein interaction levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. The mean SNARE protein-protein interactions is the average of the 4 protein-protein interactions. Higher values indicate more SNARE protein-protein interactions.

Note: This variable is not recommended to account for synaptic pathology.

**Key:**

SNAP-25 = Synaptosomal-associated protein 25

VAMP = Vesicle-associated membrane protein

**References****Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA

Journal: Translational psychiatry 2012; 2e114

**A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ,

Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG

Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology

2010 Apr; 35(5) 1226-38

**Mean complexin density :**  
**zcomplexin\_6****Mean complexin density - Average of 6 regions (MAP only)**

This variable is only available in MAP.

**Mean complexin protein density** is based on complexin-I (/radc/var/displayVariable.htm?id=1117) and complexin-II protein densities (/radc/var/displayVariable.htm?id=1116), determined by immunoassay at the Honer Lab at the University of British Columbia (Vancouver BC, Canada). Monoclonal antibodies (see below) are used to quantify complexin-I and complexin-II immunodensities from frozen samples of gray matter in 6 cortical regions.

Antibody	Target protein
SP33	Complexin-I (inhibitory)
LP27	Complexin-II (excitatory)

Brain regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate

## 6. Posterior putamen

For each protein, values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. The mean complexin density is the average of the complexin-I and complexin-II densities. Higher values indicate greater complexin density.

## References

### **Presynaptic proteins complexin-I and complexin-II differentially influence cognitive function in early and late stages of Alzheimer's disease.**

Ramos-Miguel A, Sawada K, Jones AA, Thornton AE, Barr AM, Leurgans SE, Schneider JA, Bennett DA, Honer WG

Journal: Acta neuropathologica 2016 Nov 19; 133(3) 395-407

### Mean SNARE protein density : zsnare\_6

### Mean SNARE protein density - Average of 6 regions (MAP only)

This variable is only available in MAP.

**Mean Soluble *N*-ethylmaleimide-sensitive factor Attachment protein Receptor (SNARE) protein density** is based on syntaxin-1 (/radc/var/displayVariable.htm?id=1106), vesicle-associated membrane protein (/radc/var/displayVariable.htm?id=1105) (VAMP), and synaptosomal-associated protein 25 (/radc/var/displayVariable.htm?id=1111) (SNAP-25) densities, determined in the Honer Lab at the University of British Columbia (Vancouver BC, Canada). Immunodensities for each protein are quantified from frozen samples of gray matter in 6 cortical regions.

Antibody	Target protein
SP6	Syntaxin-1
SP10	VAMP
SP12	SNAP-25

Brain regions:

1. Hippocampus
2. Middle frontal gyrus
3. Inferior temporal gyrus
4. Calcarine (visual) cortex
5. Ventromedial caudate

## 6. Posterior putamen

For each protein, values are expressed in log10 units, the mean is determined for each participant across the 6 brain regions, and a z-score is calculated across all participants. Since reported values are inversely proportional to protein levels, scores are multiplied by negative 1 to make results directly related to the amount of target antigen. The mean SNARE protein density is the average of the syntaxin-1, VAMP, and SNAP-25 densities. Higher values indicate greater SNARE protein concentrations.

## References

### **Cognitive reserve, presynaptic proteins and dementia in the elderly.**

Honer WG, Barr AM, Sawada K, Thornton AE, Morris MC, Leurgans SE, Schneider JA, Bennett DA  
Journal: Translational psychiatry 2012; 2e114

### **A novel mechanism and treatment target for presynaptic abnormalities in specific striatal regions in schizophrenia.**

Barakauskas VE, Beasley CL, Barr AM, Ypsilanti AR, Li HY, Thornton AE, Wong H, Rosokilja G, Mann JJ, Mancevski B, Jakovski Z, Davceva N, Ilievski B, Dwork AJ, Falkai P, Honer WG  
Journal: Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 2010 Apr; 35(5) 1226-38

## Clinical Diagnosis

### Clinical Diagnosis > Dementia

Age at first Alzheimer's  
dementia dx :  
age\_first\_ad\_dx

Age at cycle where first Alzheimer's dementia diagnosis was given

The **age at first Alzheimer's dementia diagnosis (dx)** variable represents the age at the first cycle where an Alzheimer's dementia diagnosis was rendered. This is calculated using the variables age at visit (/radc/var/displayVariable.htm?id=617) and clinical diagnosis summary (/radc/var/displayVariable.htm?id=349) (value = 4 or 5). This is the best approximation of "age at onset of Alzheimer's dementia" available, as most participants are seen on a yearly basis. This measure is not available for participants that were demented at baseline cycle.

Clinical cognitive  
diagnosis summary :  
dcfdx

Clinical diagnosis of cognitive status (Alzheimer's dementia, other dementia, MCI, or no impairment)

A **clinical diagnosis of cognitive status** is rendered at every assessment based on a three-stage process including computer scoring of cognitive tests, clinical judgment by a neuropsychologist, and diagnostic

classification by a clinician.

All participants undergo a uniform, structured, clinical evaluation including a battery of 19 cognitive tests. These tests were scored by computer using a decision tree designed to mimic clinical judgment and a rating of severity of impairment was given for 5 cognitive domains. A neuropsychologist, blinded to participant demographics, reviews the impairment ratings and other clinical information and renders a clinical judgment regarding the presence of impairment and dementia. A clinician (neurologist, geriatrician, or geriatric nurse practitioner) then reviews all available data and examines the participant and renders a final diagnostic classification.

Clinical diagnosis of dementia and clinical Alzheimer's dementia are based on criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA). The diagnosis of Alzheimer's dementia requires evidence of a meaningful decline in cognitive function relative to a previous level of performance with impairment in memory and at least one other area of cognition.

Diagnosis of mild cognitive impairment (MCI) is rendered for persons who are judged to have cognitive impairment by the neuropsychologist but are judged to not meet criteria for dementia by the clinician.

Persons diagnosed with MCI or Alzheimer's dementia may also be diagnosed with another condition that contributes to their cognitive impairment (CI).

Persons without dementia or mild cognitive impairment (MCI) are categorized as having no cognitive impairment (NCI).

Value	Coding
1	NCI: No cognitive impairment
2	MCI: Mild cognitive impairment, no other condition contributing to CI
3	MCI+: Mild cognitive impairment AND another condition contributing to CI
4	AD: Alzheimer's dementia, no other condition contributing to CI (NINCDS/ADRDA Probable AD)
5	AD+: Alzheimer's dementia AND other condition contributing to CI (NINCDS/ADRDA Possible AD)
6	Other dementia: Other primary cause of dementia, no clinical evidence of Alzheimer's dementia

Other Forms : \_l, \_lv, \_bl

## References

### **Natural history of mild cognitive impairment in older persons.**

Bennett DA, Wilson RS, Schneider JA, Evans DA, Beckett LA, Aggarwal NT, Barnes LL, Fox JH, Bach J  
Journal: Neurology 2002 Jul 23; 59(2) 198-205

**Decision rules guiding the clinical diagnosis of Alzheimer's disease in two community-based cohort studies compared to standard practice in a clinic-based cohort study.**

Bennett DA, Schneider JA, Aggarwal NT, Arvanitakis Z, Shah RC, Kelly JF, Fox JH, Cochran EJ, Arends D, Treinkman AD, Wilson RS

Journal: Neuroepidemiology 2006; 27(3) 169-76

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Clinical Diagnosis > Final consensus diagnosis

Final consensus cognitive  
diagnosis : cogdx

Clinical consensus diagnosis of cognitive status at time of death

Physician's overall cognitive diagnostic category

At the time of death, all available clinical data were reviewed by a neurologist with expertise in dementia, and a summary diagnostic opinion was rendered regarding the most likely clinical diagnosis at the time of death. Summary diagnoses were made blinded to all postmortem data. Case conferences including one or more neurologists and a neuropsychologist were used for consensus on selected cases.

Value	Coding
1	NCI: No cognitive impairment (No impaired domains)
2	MCI: Mild cognitive impairment (One impaired domain) and NO other cause of CI
3	MCI: Mild cognitive impairment (One impaired domain) AND another cause of CI
4	AD: Alzheimer's dementia and NO other cause of CI (NINCDS PROB AD)
5	AD: Alzheimer's dementia AND another cause of CI (NINCDS POSS AD)
6	Other dementia: Other primary cause of dementia

References

**Mixed brain pathologies account for most dementia cases in community-dwelling older persons.**

Schneider JA, Arvanitakis Z, Bang W, Bennett DA

Journal: Neurology 2007 Dec 11; 69(24) 2197-204

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Cognition

Cognition > Domains

## Episodic memory : cogn\_ep

### Episodic memory domain - Average of 7 tests

We formed a composite measure of the cognitive domain **episodic memory** by converting raw scores on each cognitive test to z scores, using the mean and standard deviation of the cohort(s) at baseline visit, and then averaging the z scores to yield the composite.

The following 7 cognitive tests are used to compute this score:

test score	z-score	cognitive test
cts_wli	z_WLI	word list
cts_wlii	z_WLII	word list recall
cts_wliii	z_WLIII	word list recognition
cts_ebmt	z_EBMT	East Boston immediate recall
cts_ebdr	z_EBDR	East Boston delayed recall
cts_story	z_Story	Logical memory I (immediate recall)
cts_delay	z_Delay	Logical memory II (delayed recall)

*Item level variables are available upon request.*

NOTE: Every time a new participant completes a study baseline, values for ALL participants change slightly. therefore it is essential that if participants are added to a dataset, ALL values must be updated.

The variable is calculated if more than half the z-scores are non-missing.

Other Forms : \_I, \_Iv, \_bl

### References

#### **Temporal course and pathologic basis of unawareness of memory loss in dementia.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA  
Journal: Neurology 2015 Aug 26; 85(11) 984-91

## Perceptual orientation : cogn\_po

### Perceptual orientation/visuospatial ability domain - Average of 2 tests

#### Perceptual Orientation Domain

We formed a composite measure of the cognitive domain **perceptual orientation**, aka visuospatial ability, by converting raw scores on each cognitive test to z scores, using the mean and standard deviation of the cohort, and then averaging the z scores to yield the composite.



The following 2 cognitive tests are used to compute this score:

test score	z-score	cognitive test
cts_lopair	z_LOpair	line orientation
cts_pmat	z_PMat	progressive matrices (16 items)

*Item level variables are available upon request.*

Note: The variable is calculated if more than half the z-scores are non-missing.

Other Forms : \_l, \_lv, \_bl

## References

### **Temporal course and pathologic basis of unawareness of memory loss in dementia.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA

Journal: Neurology 2015 Aug 26; 85(11) 984-91

Perceptual speed :  
cogn\_ps

### Perceptual speed domain - Average of 4 tests

We formed a composite measure of the cognitive domain **perceptual speed** by converting raw scores on each cognitive test to z scores, using the mean and standard deviation of the cohort, and then averaging the z scores to yield the composite.

The following 4 cognitive tests are used to compute this score:

test score	z-score	cognitive test
cts_sdmtd	z_SDMT	symbol digits modality test (oral)
cts_nccrtd	z_NCcrttd	number comparison
cts_stroop_cname	z_cname	stroop color naming
cts_stroop_wread	z_wread	stroop word reading

*Item level variables are available upon request.*

Note: The variable is calculated if more than half the z-scores are non-missing.

Other Forms : \_l, \_lv, \_bl

## References

### **Temporal course and pathologic basis of unawareness of memory loss in dementia.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA  
Journal: Neurology 2015 Aug 26; 85(11) 984-91

Semantic memory :  
cogn\_se

Semantic memory domain - Average of 3 tests

### Semantic Memory Domain

We formed a composite measure of the cognitive domain **semantic memory** by converting raw scores on each cognitive test to z scores, using the mean and standard deviation of the cohort, and then averaging the z scores to yield the composite.

The following 3 cognitive tests are used to compute this score:

test score	z-score	cognitive test
cts_bname	z_BName	Boston naming (15 items)
cts_catflu	z_CatFlu	category fluency (animals - fruits/vegetables)
cts_read_nart*	z_read_nart*	reading test - (10 items)

\*For the MARS study, the NART reading test is replaced with the 15-item WRAT reading test

*Item level variables are available upon request.*

Note: The variable is calculated if more than half the z-scores are non-missing.

Other Forms : \_l, \_lv, \_bl

### References

**Temporal course and pathologic basis of unawareness of memory loss in dementia.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA  
Journal: Neurology 2015 Aug 26; 85(11) 984-91

Working memory :  
cogn\_wo

Working memory domain - Average of 3 tests

### Working Memory Domain

We formed a composite measure of of the cognitive domain **working memory** by converting raw scores on each cognitive test to z scores, using the mean and standard deviation of the cohort, and then averaging the z scores to yield the composite.

The following 3 cognitive tests are used to compute this score:

test score	z-score	cognitive test
cts_df	z_DF	digits forward
cts_db	z_DB	digits backward
cts_doperf	z_DOperf	digit ordering

*Item level variables are available upon request.*

Note: The variable is calculated if more than half the z-scores are non-missing.

Other Forms : \_l, \_lv, \_bl

## References

### Temporal course and pathologic basis of unawareness of memory loss in dementia.

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA

Journal: Neurology 2015 Aug 26; 85(11) 984-91

## Cognition > Global cognition

Global cognitive function :  
cogn\_global

### Global cognitive function - Average of 19 tests

Cogn\_global is the main variable for overall (i.e. global) cognitive function. This variable replaces GLOBCOG.

Raw scores from a battery of cognitive tests were converted to Z scores and averaged to yield a **global cognitive function** summary. Mean and standard deviation at baseline were used to compute the z-scores. Z-score has mean 0 and standard deviation of 1. Each z-score corresponds to a point in a normal distribution. z-score describes how much a point deviates from a mean or specific point. A negative z-score simply means that someone has an overall score that is lower than the average of the entire cohort at baseline.

The following 19 tests are used to compute the global cognitive function score

test score	z-score	cognitive test	calculated domain
cts_wli	z_WLI	word list	episodic memory (cogn_ep)
cts_wlii	z_WLII	word list recall	episodic memory (cogn_ep)
cts_wliii	z_WLIII	word list recognition	episodic memory (cogn_ep)
cts_ebmt	z_EBMT	East Boston immediate recall	episodic memory (cogn_ep)

test score	z-score	cognitive test	calculated domain
cts_ebdr	z_EBDR	East Boston delayed recall	episodic memory (cogn_ep)
cts_story	z_Story	Logical memory I (immediate)	episodic memory (cogn_ep)
cts_delay	z_Delay	Logical memory II (delayed)	episodic memory (cogn_ep)
cts_bname	z_BName	Boston naming (15 items)	semantic memory (cogn_se)
cts_catflu	z_CatFlu	category fluency	semantic memory (cogn_se)
cts_read_nart	z_read_nart	reading test - (10 items)	semantic memory (cogn_se)
cts_df	z_DF	digits forward	working memory (cogn_wo)
cts_db	z_DB	digits backward	working memory (cogn_wo)
cts_doperf	z_DOperf	digit ordering	working memory (cogn_wo)
cts_lopair	z_LOpair	line orientation	perceptual orientation (cogn_po)
cts_pmat	z_PMat	progressive matrices (16 items)	perceptual orientation (cogn_po)
cts_sdmr	z_SDMT	symbol digits modality-oral	perceptual speed (cogn_ps)
cts_nccrtd	z_NCcrttd	number comparison	perceptual speed (cogn_ps)
cts_stroop_cname	z_cname	stroop color naming	perceptual speed (cogn_ps)
cts_stroop_wread	z_wread	stroop word reading	perceptual speed (cogn_ps)

*Item level variables are available upon request.*

Note: This variable is calculated if more than half of the z-scores are non-missing. Since the variable is calculated based on the number of valid test scores independent of the domain score calculations, participants may have a valid global score but be missing one or more domain scores.

The number of tests used to compute the global cognitive function score may vary based on the combination of studies used in analysis.

Other Forms : \_l, \_lv, \_bl

## References

### **Temporal course and pathologic basis of unawareness of memory loss in dementia.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Sytsma J, Buchman AS, Bennett DA, Schneider JA

Journal: Neurology 2015 Aug 26; 85(11) 984-91

## cts\_animals

## Category Fluency - Animals - 2014

**Category fluency - animals** is a modified version of the CERAD verbal fluency measure (Morris et al., 1989). Participants are asked to generate exemplars from each of 2 categories (animals, fruits and vegetables) within a 60-second time limit. This variable is the number of unique animals named.

Similar measures have been shown to be impaired in Alzheimer's disease .

Scoring: The total number of animals named is recorded. Repetitions are omitted.

**Range**

0-75 = animals named

98 = REFUSAL

99 = DON'T KNOW

## cts\_bname

## Boston Naming - 2014

## SUMMARY: BOSTON NAMING, NUMBER OF ITEMS CORRECT

This test is used in the calculation of semantic memory domain (cogn\_se).

This measure of visual confrontation naming, from the widely used Boston Naming Test, include 15 items from the CERAD version of the test. Participants are shown pictures of certain objects. Then they are requested to name the objects. The primary measure of performance is the number of pictures correctly named.

Short term temporal stability and internal consistency of the CERAD version are excellent. Longitudinal change in visual naming in Alzheimer's disease has been previously demonstrated.

The Boston Naming Test (BNT) represents a measure of object naming from line drawings. Items have been rank ordered in terms of their ability to be named, which is thought to be correlated with their frequency. This type of picture-naming vocabulary test is useful in the examination of children with learning disabilities and the evaluation of brain-injured adults.

Ref: Weintraub, S., *The Psychological Corporation*.

**Range**

00 - 15

variable	coding	question
tree	0-error/1-correct	1. Tree

variable	coding	question
bed	0-error/1-correct	2. Bed
whistle	0-error/1-correct	3. Whistle
flower	0-error/1-correct	4. Flower
house	0-error/1-correct	5. House
canoe	0-error/1-correct	6. Canoe
toothbr	0-error/1-correct	7. Toothbrush
volcano	0-error/1-correct	8. Volcano
mask	0-error/1-correct	9. Mask
camel	0-error/1-correct	10. Camel
harmon	0-error/1-correct	11. Harmonica
tongs	0-error/1-correct	12. Tongs
hammock	0-error/1-correct	13. Hammock
funnel	0-error/1-correct	14. Funnel
domino	0-error/1-correct	15. Domino

## cts\_catflu

### Category Fluency - 2014

**Category fluency** is a modified version of the CERAD verbal fluency measure (Morris et al., 1989). Participants are asked to generate exemplars from each of 2 categories (animals, fruits and vegetables) within a 60-second time limit per category. This variable is the sum of unique exemplars generated from both categories. If one of the category scores is missing, the remaining valid score is multiplied by 2.

Similar measures have been shown to be impaired in Alzheimer's disease.

This test is used in the calculation of semantic memory domain (cogn\_se).

Range: 00 - 150

## cts\_db

### Digits Backwards - 2014

**Digit span backwards** is a test in which sequences of increasing length are read to participants, one at a time. Participants are then asked to repeat each sequence backwards. Testing stops after two consecutive errors at a given sequence length. The primary measure of performance is the number of digit sequences correctly recalled.

The psychometric properties are well documented. It has been used in prior epidemiologic and longitudinal studies of Alzheimer's disease.

This test is used in the calculation of working memory domain (cogn\_wo).

Range: 00 - 12

Variable	Coding	Sequence	Answer key
digbak1a	0-error/1-correct	1a. 5-1?	15
digbak1b	0-error/1-correct	1b. 3-8?	83
digbak2a	0-error/1-correct	2a. 4-9-3?	394
digbak2b	0-error/1-correct	2b. 5-2-6?	625
digbak3a	0-error/1-correct	3a. 3-8-1-4?	4183
digbak3b	0-error/1-correct	3b. 1-7-9-5?	5971
digbak4a	0-error/1-correct	4a. 6-2-9-7-2?	27926
digbak4b	0-error/1-correct	4b. 4-8-5-2-7?	72584
digbak5a	0-error/1-correct	5a. 7-1-5-2-8-6?	682517
digbak5b	0-error/1-correct	5b. 8-3-1-9-6-4?	469138
digbak6a	0-error/1-correct	6a. 4-7-3-9-1-2-8?	8219374
digbak6b	0-error/1-correct	6b. 8-1-2-9-3-6-5?	5639218

Note: This is one of two forms of Digit Span. See digit span forwards (</radc/var/displayVariable.htm?id=1160>).

## cts\_delay

## Logical Memory IIa - 2014

**Logical memory IIa - delayed recall** is a measure from the Wechsler Memory Scale - Revised, 1987. A brief story is read to the participant, then the participant is asked to retell the story from memory immediately after it is read and again following an approximately 30 minute delay. This measure is the number of story units (out of 25) recalled after the delay.

Inter rater reliability and short term temporal stability are excellent. It has been used in epidemiological and numerous clinical studies of Alzheimer's disease.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 to 25

cts\_df

## Digits Forwards - 2014

**Digit span forward** is a test in which sequences of increasing length are read to participants, one at a time. Participants are then asked to repeat each sequence. Testing stops after two consecutive errors at a given sequence length. The primary measure of performance is the number of digit sequences correctly recalled.

This test is used in the calculation of working memory domain (cogn\_wo).

Range: 00 - 12

Variable	Coding	Sequence	Answer key
digFor1a	0-error/1-correct	1a. 6-2-9?	629
digFor1b	0-error/1-correct	1b. 3-7-5?	375
digFor2a	0-error/1-correct	2a. 5-4-1-7?	5417
digFor2b	0-error/1-correct	2b. 8-3-9-6?	8396
digFor3a	0-error/1-correct	3a. 3-6-9-2-5?	36925
digFor3b	0-error/1-correct	3b. 6-9-4-7-1?	69471
digFor4a	0-error/1-correct	4a. 9-1-8-4-2-7?	918427
digFor4b	0-error/1-correct	4b. 6-3-5-4-8-2?	635482
digFor5a	0-error/1-correct	5a. 1-2-8-5-3-4-6?	1285346
digFor5b	0-error/1-correct	5b. 2-8-1-4-9-7-5?	2814975
digFor6a	0-error/1-correct	6a. 3-8-2-9-5-1-7-4?	38295174
digFor6b	0-error/1-correct	6b. 5-9-1-8-2-6-4-7?	59182647

cts\_doperf

## Digit Ordering - 2014

The **digit ordering** test is modified from procedures used by Cooper, Sagar, Jordan, Harvey, and Sullivan (1991). A series of numbers are read aloud to the participants, one series at a time. After each series, participants are asked to order the digits in the series from smallest number to largest number. Each correct answer is scored. The test is administered from 2 to 8 digit length pairs. If both pairs of a certain length are not ordered properly, testing stops.

This test is used in the calculation of working memory domain (cogn\_wo).

**Range**



00 - 14

Variable	Coding	Sequence	Answer key
item1	0-error/1-correct	1. 4-1?	14
item2	0-error/1-correct	2. 9-8?	89
item3	0-error/1-correct	3. 1-0-4?	014
item4	0-error/1-correct	4. 2-6-3?	236
item5	0-error/1-correct	5. 2-4-1-3?	1234
item6	0-error/1-correct	6. 4-2-1-6?	1246
item7	0-error/1-correct	7. 3-7-5-7-0?	03577
item8	0-error/1-correct	8. 7-9-2-1-0?	01279
item9	0-error/1-correct	9. 9-5-6-2-7-2?	225679
item10	0-error/1-correct	10. 9-6-3-0-1-9?	013699
item11	0-error/1-correct	11. 8-9-5-7-9-1-4?	1457899
item12	0-error/1-correct	12. 8-5-4-7-5-3-6?	3455678
item13	0-error/1-correct	13. 2-8-9-1-8-6-9-5?	12568899
item14	0-error/1-correct	14. 6-3-5-3-4-0-9-6?	03345669

cts\_ebdr

### East Boston Story - delayed recall - 2014

**East Boston Memory Test - Delayed Recall** is a measure from the East Boston studies of cognitive function. A three-sentence story is read to the participant. Participants are then asked to immediately recall as much of the story as possible (see East Boston Memory Test - Immediate Recall (</radc/var/displayVariable.htm?id=1163>)) and again after a delay of approximately 3 minutes. The score is the number of story units (out of 12) correctly recalled after the delay.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 - 12

Variable	Coding	Story unit
q1ebdr	1-present/0-absent/7-defer	1. Three
q2ebdr	1-present/0-absent/7-defer	2. Children

Variable	Coding	Story unit
q3ebdr	1-present/0-absent/7-defer	3. House
q4ebdr	1-present/0-absent/7-defer	4. On fire
q5ebdr	1-present/0-absent/7-defer	5. Fireman
q6ebdr	1-present/0-absent/7-defer	6. Climbed in
q7ebdr	1-present/0-absent/7-defer	7. Children
q8ebdr	1-present/0-absent/7-defer	8. Rescued
q9ebdr	1-present/0-absent/7-defer	9. Minor
q10ebdr	1-present/0-absent/7-defer	10. Injuries
q11ebdr	1-present/0-absent/7-defer	11. Everyone
q12ebdr	1-present/0-absent/7-defer	12. Well

## cts\_ebmt

## East Boston Story - immediate - 2014

**East Boston Memory Test - Immediate Recall** is a measure from the East Boston studies of cognitive function. A three-sentence story is read to the participant. Participants are then asked to immediately recall as much of the story as possible. The score is the number of story units (out of 12) correctly recalled. See East Boston Memory Test - Delayed Recall (</radc/var/displayVariable.htm?id=1162>) for the delayed recall portion of this test.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 - 12

Variable	Coding	Story Unit
q1ebmt	1-present/0-absent/7-defer	1. Three
q2ebmt	1-present/0-absent/7-defer	2. Children
q3ebmt	1-present/0-absent/7-defer	3. House
q4ebmt	1-present/0-absent/7-defer	4. On fire
q5ebmt	1-present/0-absent/7-defer	5. Fireman
q6ebmt	1-present/0-absent/7-defer	6. Climbed in
q7ebmt	1-present/0-absent/7-defer	7. Children
q8ebmt	1-present/0-absent/7-defer	8. Rescued
q9ebmt	1-present/0-absent/7-defer	9. Minor

Variable	Coding	Story Unit
q10ebmt	1-present/0-absent/7-defer	10. Injuries
q11ebmt	1-present/0-absent/7-defer	11. Everyone
q12ebmt	1-present/0-absent/7-defer	12. Well

## cts\_fruits

## Category Fluency - Fruits - 2014

This is a measure of verbal fluency or semantic memory in which participant is asked to generate exemplars from that category fruits/vegetables in successive 1 minute trials. The primary performance measure is the number of unique exemplars generated. Similar measures have been shown to be impaired in Alzheimer's disease. The CERAD implementation of this test is used with this item which adds to the reliability.

**Range**

0-75

**Scoring**

The total number of fruits/vegetables named is recorded. Repetitions are omitted.

## cts\_idea

## Complex Ideational Material

Score, Complex Ideational Material, a tests of auditory comprehension. This is a measure of verbal comprehension from the Boston Diagnostic aphasic Examination. The first eight items are used. Each item is a simple question read aloud to the participant. The participant is requested to answer with a 'yes or 'no.

For all variables below, 1 point is added for each response that matches the coding.

**Range**

0-8

Codebook variable	Coding	Calc	Codebook Question
sink1	Yes/No	No = +1	1. Will a board sink in water?
sink2	Yes/No	Yes = +1	2. Will a stone sink in water?
hammer1	Yes/No	No = +1	3. Is a hammer good for cutting wood?
hammer2	Yes/No	Yes = +1	4. Can you use a hammer to pound nails?
flour1	Yes/No	Yes = +1	5. Do two pounds of flour weigh more than one?

Codebook variable	Coding	Calc	Codebook Question
flour2	Yes/No	No = +1	6. Is one pound of flour heavier than two?
boots1	Yes/No	No = +1	7. Will water go through a good pair of rubber boots?
boots2	Yes/No	Yes = +1	8. Will a good pair of rubber boots keep water out?

### Ref for test

Goodglass & Kaplan, 1983. *The assessment of aphasia and related disorders, 2nd edition*. Philadelphia: Lea & Febiger

As described, for example, in Wilson et al. 2002, *Psychology and Aging*, vol 17, no2, 179-193, for ROS: the distribution is very skew; this test was not included in composite scores

This variable name was created in 2014, and replaces SCIDEA. When data was available for SCIDEA, CTS\_IDEA has the same value. CTS\_IDEA contains data collected since the testing battery was unified in October, 2013.

### cts\_lopair

### Line Orientation - 2014

The **line orientation** test is a 15-item version of the Judgment of Line Orientation Test, Form V (Benton, Hamsher, Varney, & Spreen, 1983; Benton, Varney, & Hamsher, 1978; Benton, Hannay, & Barney, 1975). Participants are asked to judge the angle of orientation of pairs of lines in a match-to-sample format.

Participants are asked the following question for each pair of lines:

Which two lines in the key point in the same direction as the lines up here?

The score is based upon the number of line pairs correctly judged. The test has proven to be a sensitive measure of visual spatial perception in early Alzheimer's disease.

This test is used in the calculation of perceptual orientation domain (cogn\_po).

Range: 00 - 15

**Table 1**

Value	Code	Value	Code
1	line 1	7	line 7
2	line 2	8	line 8

Value	Code	Value	Code
3	line 3	9	line 9
5	line 4	10	line 10
5	line 5	11	line 11
6	line 6	12	line 12

**Data**

Variable pairs	Coding	Question	Answer key
line1a, line1b	table1	choose line pairs that match angle	2,6
line2a, line2b	table1	choose line pairs that match angle	8,3
line3a, line3b	table1	choose line pairs that match angle	10,1
line4a, line4b	table1	choose line pairs that match angle	11,8
line5a, line5b	table1	choose line pairs that match angle	4,1
line6a, line6b	table1	choose line pairs that match angle	9,2
line7a, line7b	table1	choose line pairs that match angle	5,2
line8a, line8b	table1	choose line pairs that match angle	10,7
line9a, line9b	table1	choose line pairs that match angle	3,1
line10a, line10b	table1	choose line pairs that match angle	10,5
line11a, line11b	table1	choose line pairs that match angle	9,1
line12a, line12b	table1	choose line pairs that match angle	11,9
line13a, line13b	table1	choose line pairs that match angle	8,5
line14a, line14b	table1	choose line pairs that match angle	11,3
line15a, line15b	table1	choose line pairs that match angle	10,6

**MMSE : cts\_mmse30****Mini-Mental State Exam, 30 item**

The **Mini Mental State Examination (MMSE)** is a widely used, 30 item, standardized screening measure of dementia severity. It has previously been used in many epidemiologic studies and is a component of the CERAD protocol. Short term temporal stability is excellent and scores are highly correlated with those on other scales of severity of dementia. This test provides a global measure of cognitive function useful for descriptive purposes. The initial ten items provide a psychometric measure of orientation.

Participants are asked a series of questions to assess orientation to time and place, recall ability, short-term memory, and arithmetic ability.

The MMSE form includes the test of spelling WORLD backwards.

Other Forms : \_I, \_IV, \_bl

## References

**"Mini-mental state". A practical method for grading the cognitive state of patients for the clinician.**

Folstein MF, Folstein SE, McHugh PR

Journal: Journal of psychiatric research 1975 Nov; 12(3) 189-98

cts\_nccrtd

## Number Comparison - 2014

The **number comparison** test is used in the calculation of perceptual speed domain (cogn\_ps).

Participants are presented with pairs of three- to ten-digit sequences. Some of the pairs are exactly the same while others do not match. Participants are asked to identify pairs as “same” or “different” with a 90-second time limit. Each correct answer is scored.

Corrected score: number of items correctly identified minus the total number of wrong answers including don’t know and refused responses.

Range: 0 - 48

**Table 1**

Value	Code
s	same
d	different
8	don’t know
9	refusal

Variable	Coding	Question	Answer key
Page3-item1	table1	420__460	different
Page3-item2	table1	13897143_13897145	different
Page3-item3	table1	4327__4327	same
Page3-item4	table1	519605__519605	same

Variable	Coding	Question	Answer key
Page3-item5	table1	3201859__3201859	same
Page3-item6	table1	13603__17603	different
Page3-item7	table1	621532992__621532992	same
Page3-item8	table1	2570665292__2570665292	same
Page4-item9	table1	4821__9821	different
Page4-item10	table1	5327010538__5327010538	same
Page4-item11	table1	236__936	different
Page4-item12	table1	5911306__5911306	same
Page4-item13	table1	49471307__47471307	different
Page4-item14	table1	341798301__341798701	different
Page4-item15	table1	347820__349820	different
Page4-item16	table1	60971__60971	same
Page5-item17	table1	925660752__925660752	same
Page5-item18	table1	5930582136__5730582136	different
Page5-item19	table1	27109__27109	same
Page5-item20	table1	4951__4951	same
Page5-item21	table1	3821043__3821043	same
Page5-item22	table1	39471307__39471507	different
Page5-item23	table1	414982__415982	different
Page5-item24	table1	618__618	same
Page6-item25	table1	5471075693__5471075683	different
Page6-item26	table1	647107569__647107569	same
Page6-item27	table1	17906__17906	same
Page6-item28	table1	705__708	different
Page6-item29	table1	24179830__24179830	same
Page6-item30	table1	619605__619505	different
Page6-item31	table1	7215__7915	different
Page6-item32	table1	4714306__4715306	different

Variable	Coding	Question	Answer key
Page7-item33	table1	65382__65382	same
Page7-item34	table1	6082649875__6082647875	different
Page7-item35	table1	289414__283414	different
Page7-item36	table1	7361408__7361708	different
Page7-item37	table1	16253948__16253948	same
Page7-item38	table1	7573__7573	same
Page7-item39	table1	639__637	different
Page7-item40	table1	370543141__370543141	same
Page8-item41	table1	705731195__705731195	same
Page8-item42	table1	5082__1082	different
Page8-item43	table1	4930582136__4930582136	same
Page8-item44	table1	43210573__43710573	different
Page8-item45	table1	710__710	same
Page8-item46	table1	4573043__4573043	same
Page8-item47	table1	923452__927452	different
Page8-item48	table1	80537__80737	different

## cts\_pmat

## Progressive Matrices - 2014

The **progressive matrices** measure is a subset of items from the Standard Progressive Matrices (Raven, Court, & Raven, 1992). Participants are shown a series of 16 visual images, one at a time, with one element missing. Participants are then asked to identify the missing element from an array of six to eight alternatives. The measure of performance is the number of items correctly completed.

This test is used in the calculation of perceptual orientation domain (cogn\_po).

Range: 0-16

**Table 1**

Value	Code
1	figure 1



Value	Code
2	figure 2
3	figure 3
4	figure 4
5	figure 5
6	figure 6

Variable	Coding	Question	Answer key
a2	table1	complete the pattern	figure 5
a4	table1	complete the pattern	figure 2
a5	table1	complete the pattern	figure 6
a6	table1	complete the pattern	figure 3
a7	table1	complete the pattern	figure 6
a8	table1	complete the pattern	figure 2
a11	table1	complete the pattern	figure 4
a12	table1	complete the pattern	figure 5
b1	table1	complete the pattern	figure 2
b2	table1	complete the pattern	figure 6
b3	table1	complete the pattern	figure 1
b4	table1	complete the pattern	figure 2
b5	table1	complete the pattern	figure 1
b6	table1	complete the pattern	figure 3
b8	table1	complete the pattern	figure 6
b10	table1	complete the pattern	figure 3

Note: This harmonized version of this test was began in 2014. The same 16 items are used in ROS, MAP, and MARS.

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 cts\_pmsub

Progressive Matrices (subset) - 2014

Progressive Matrices - subset

This test is used in the calculation of perceptual orientation domain (cogn\_po).

The participant is shown a series of visual images and asked to identify the pattern below which would complete the pattern on top. A total of sixteen patterns are shown. 'Tell me which piece below [POINT] would complete the pattern on top [POINT]'

This harmonized version of this test was started in 2014. ROS, MAP, and MARS now all use the same 16 items. This subset contains 9 of the 16 items.

### Range

0-9

Table 1

value	code
1	figure 1
2	figure 2
3	figure 3
4	figure 4
5	figure 5
6	figure 6

variable	coding	question	answer key
a2	table1	complete the pattern	figure 5
a4	table1	complete the pattern	figure 2
a8	table1	complete the pattern	figure 2
b1	table1	complete the pattern	figure 2
b2	table1	complete the pattern	figure 6
b3	table1	complete the pattern	figure 1
b4	table1	complete the pattern	figure 2
b5	table1	complete the pattern	figure 1
b6	table1	complete the pattern	figure 3

The **National Adult Reading Test** is a measure of the ability to pronounce words. Participants are asked to read aloud a series of 10 words of increasing difficulty. The score is the number of words pronounced correctly.

This test is used in the calculation of semantic memory domain (cogn\_se).

Range: 0 to 10

Variable	Coding	Question
nart_ach	0-Error/1-Correct	1. Ache
nart_ind	0-Error/1-Correct	2. Indict
nart_deb	0-Error/1-Correct	3. Debt
nart_sie	0-Error/1-Correct	4. Sieve
nart_pla	0-Error/1-Correct	5. Placebo
nart_fac	0-Error/1-Correct	6. Facade
nart_imp	0-Error/1-Correct	7. Impugn
nart_bla	0-Error/1-Correct	8. Blatant
nart_cav	0-Error/1-Correct	9. Caveat
nart_cab	0-Error/1-Correct	10. Cabal

Note: This test was included in the harmonized cognitive battery in 2014 and is a new test for the MARS study. It had previously been included in ROS and MAP.

Reference: McGurn, B; Starr, JM; Topfer, JA; Pattie, A; Whiteman, MC; Lemmon, HA; Whalley, LJ; Deary, IJ (2004). *Pronunciation of irregular words is preserved in dementia, validating premorbid IQ estimation*. Neurology 62 (7): 1184–1186. PMID 15079021

## cts\_sdmt

## Symbol Digit Modalities - 2014

The **symbol digit modalities** test, developed by Aaron Smith, PhD in 1973, is a measure of the speed of perceptual processing. Participants are presented with a series of abstract symbols and a coding key consisting of the nine abstract symbols, each paired with a number. Participants are asked to identify and call out the numbers corresponding to each symbol, as quickly as possible. The total score is the number of correctly identified symbols.

This test is used in the calculation of perceptual speed domain (cogn\_ps).

Range: 0 - 110

Variable	Coding	Question
row1	2161246125	10 symbols displayed
row2	6341269438	10 symbols displayed
row3	4578137485	10 symbols displayed
row4	2934724516	10 symbols displayed
row5	4156798364	10 symbols displayed
row6	9583674523	10 symbols displayed
row7	7928169723	10 symbols displayed
row8	6491725684	10 symbols displayed
row9	2879378519	10 symbols displayed
row10	2143652164	10 symbols displayed
row11	2169735489	10 symbols displayed

Reference: Smith A. (1982). *Symbol Digits Modalities Test manual - revised*. Los Angeles: Western Psychological Services.

## cts\_story

### Logical Memory Ia - immediate - 2014

**Logical memory - immediate recall** is a measure from the Wechsler Memory Scale - Revised, 1987. A brief story is read to the participant, then the participant is asked to retell the story from memory immediately after it is read and again following an approximately 30 minute delay. This measure is the number of story units (out of 25) recalled immediately after the story is read.

Inter rater reliability and short term temporal stability are excellent. It has been used in epidemiological and numerous clinical studies of Alzheimer's disease.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 to 25

Coding:

77 = DEFERRED

98 = REFUSAL

99 = DON'T KNOW

## cts\_stroop\_cname

## Stroop - Color Naming - 2014

The **Stroop color test** is a measure of executive functioning and capacity to direct attention. Participants are asked to name aloud the color of ink that each word in the list is printed in as quickly as they can. The score is the number of colors correctly named within a 30 second limit.

This test is used in the calculation of perceptual speed domain (cogn\_ps).

Reference: Trenerry MR, Crosson B, DeBoe J, Leber WR: *The Stroop Neuropsychological Screening Test*. Odessa, Psychological Assessment Resources, 1989.

## cts\_stroop\_wread

## Stroop - Word Reading - 2014

The **Stroop word test** is a measure of executive functioning and capacity to direct attention. Participants are asked to read aloud a list of words as quickly as they can, within a 30 second limit. The score is the number of words read correctly.

This test is used in the calculation of perceptual speed domain (cogn\_ps).

Reference: Trenerry MR, Crosson B, DeBoe J, Leber WR: *The Stroop Neuropsychological Screening Test*. Odessa, Psychological Assessment Resources, 1989.

## cts\_wli

## Word List I - immediate - 2014

The **word list memory test** (trials 1-3) is a measure from the CERAD neuropsychological performance tests. Participants are asked to read 10 words presented one at a time in a booklet and immediately asked to recall the words. Three trials are given. The primary measure of performance is the total number of words recalled in all 3 trials.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 - 30

## Trial 1

Variable	Coding	Word
wordt1_1	0-error/1-correctly recalled	1. butter
wordt1_2	0-error/1-correctly recalled	2. arm
wordt1_3	0-error/1-correctly recalled	3. shore

Variable	Coding	Word
wordt1_4	0-error/1-correctly recalled	4. letter
wordt1_5	0-error/1-correctly recalled	5. queen
wordt1_6	0-error/1-correctly recalled	6. cabin
wordt1_7	0-error/1-correctly recalled	7. pole
wordt1_8	0-error/1-correctly recalled	8. ticket
wordt1_9	0-error/1-correctly recalled	9. grass
wordt1_x	0-error/1-correctly recalled	10. engine

**Trial 2**

Variable	Coding	Word
wordt2_1	0-error/1-correctly recalled	1. ticket
wordt2_2	0-error/1-correctly recalled	2. cabin
wordt2_3	0-error/1-correctly recalled	3. butter
wordt2_4	0-error/1-correctly recalled	4. shore
wordt2_5	0-error/1-correctly recalled	5. engine
wordt2_6	0-error/1-correctly recalled	6. arm
wordt2_7	0-error/1-correctly recalled	7. queen
wordt2_8	0-error/1-correctly recalled	8. letter
wordt2_9	0-error/1-correctly recalled	9. pole
wordt2_x	0-error/1-correctly recalled	10. grass

**Trial 3**

Variable	Coding	Word
wordt3_1	0-error/1-correctly recalled	1. queen
wordt3_2	0-error/1-correctly recalled	2. grass
wordt3_3	0-error/1-correctly recalled	3. arm
wordt3_4	0-error/1-correctly recalled	4. cabin
wordt3_5	0-error/1-correctly recalled	5. pole
wordt3_6	0-error/1-correctly recalled	6. shore

Variable	Coding	Word
wordt3_7	0-error/1-correctly recalled	7. butter
wordt3_8	0-error/1-correctly recalled	8. engine
wordt3_9	0-error/1-correctly recalled	9. ticket
wordt3_x	0-error/1-correctly recalled	10. letter

cts\_wlII

Word List II - delayed - 2014

## WORD LIST RECALL, DELAYED RECALL

The participant is asked to read a list of ten words one at a time. They are presented with 3 trials with the words in different order for each trial. A few minutes later the participant is asked to identify as many words as they can recall. Each identified word is scored as correct.

This test is used in the calculation of episodic memory domain (cogn\_ep).

**Range**

00 - 10

variable	coding	question
recall_1	0-error/1-correctly recalled	1. butter
recall_2	0-error/1-correctly recalled	2. arm
recall_3	0-error/1-correctly recalled	3. shore
recall_4	0-error/1-correctly recalled	4. letter
recall_5	0-error/1-correctly recalled	5. queen
recall_6	0-error/1-correctly recalled	6. cabin
recall_7	0-error/1-correctly recalled	7. pole
recall_8	0-error/1-correctly recalled	8. ticket
recall_9	0-error/1-correctly recalled	9. grass
recall_x	0-error/1-correctly recalled	10. engine

cts\_wlIII

Word List III - recognition - 2014

The **word recognition - delayed recognition** test is a modification of the CERAD Word List Recognition measure (Morris et al. 1989). Participants are shown ten sets of four words, one set at a time, and asked to select the word from each set that they were shown previously. The primary measure of performance is the number of target words correctly identified.

This test is used in the calculation of episodic memory domain (cogn\_ep).

Range: 00 - 10

Variable	Coding	Words (correct answer is capitalized)
wordrec1	0-error/1-correctly identified	1. Palace, Dollar, LETTER, Railroad.
wordrec2	0-error/1-correctly identified	2. Book, River, Stone, POLE
wordrec3	0-error/1-correctly identified	3. Animal, Village, ENGINE, Diamond
wordrec4	0-error/1-correctly identified	4. Garden, ARM, Rock, Coffee
wordrec5	0-error/1-correctly identified	5. Church, QUEEN, Temple, Ocean
wordrec6	0-error/1-correctly identified	6. CABIN, Boy, Fire, Street
wordrec7	0-error/1-correctly identified	7. Machine, Officer, String, TICKET
wordrec8	0-error/1-correctly identified	8. Sky, BUTTER, Hotel, Party
wordrec9	0-error/1-correctly identified	9. GRASS, Mountain, Clock, Camp
wordrecx	0-error/1-correctly identified	10. Troops, Pipe, SHORE, Coin

## Demographics

Age at visit : age\_at\_visit

Age at visit (longitudinal)

**Age at visit** is calculated by subtracting the date of birth from the date of the visit and dividing the difference by days per year (365.25).

The date of the visit is defined as the first valid date in the following hierarchy:

1. cognitive date
2. clinical evaluation date (neurological exam, med hx, meds)
3. interview date
4. DCF date (diagnostic classification form)
5. neuropsychologist impression date



## References

**Purpose in life is associated with a reduced risk of incident disability among community-dwelling older persons.**

Boyle PA, Buchman AS, Bennett DA

Journal: The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2010 Jun 10; 18(12) 1093-102

### Age at baseline : age\_bl

### Age at baseline assessment

The **age at baseline assessment** is calculated from subtracting the date of birth from the date of the baseline assessment and dividing by days per year (365.25).

The date of the baseline assessment is defined as the the first valid date in the following hierarchy:

1. cognitive date
2. clinical evaluation date (neurological exam, med hx, meds)
3. interview date
4. DCF date (diagnostic classification form)
5. neuropsychologist impression date

### Age at death : age\_death

### Age at death

**Age of death** is calculated from subtracting date of birth from date of death and dividing the difference by days per year (365.25).

For participants in autopsy cohorts, the exact date of death is known for most participants as it is the day an autopsy was performed. In all cohorts, in addition to annual evaluations, participants are also contacted quarterly to determine vital status and changes in health, and death is occasionally learned of during quarterly contacts.

### Education : educ

### Years of education

The **years of education** variable is based on the number of years of regular school reported at baseline cognitive testing.

## References

**Education modifies the association of amyloid but not tangles with cognitive function.**

Bennett DA, Schneider JA, Wilson RS, Bienias JL, Arnold SE

Journal: Neurology 2005 Sep 27; 65(6) 953-5

Sex : msex

Sex

Self-reported **sex**, with “1” indicating male sex.

**Allowable codes**

1 = Male

0 = Female

Race : race

Racial group

With which group do you most closely identify yourself?

value	coding
1	White
2	Black, Negro, African-American
3	Native American, Indian
4	Eskimo
5	Aleut
6	Asian or Pacific Island
.	Missing

**References**

**Biracial population study of mortality in mild cognitive impairment and Alzheimer disease.**

Wilson RS, Aggarwal NT, Barnes LL, Bienias JL, Mendes de Leon CF, Evans DA

Journal: Archives of neurology 2009 Jun; 66(6) 767-72

**A population-based study of hemoglobin, race, and mortality in elderly persons.**

Dong X, Mendes de Leon C, Artz A, Tang Y, Shah R, Evans D

Journal: The journals of gerontology. Series A, Biological sciences and medical sciences 2008 Aug; 63(8) 873-8

Spanish ethnicity :  
spanish

Spanish/Hispanic/Latino origin

Are you of **Spanish**/Hispanic/Latino origin?

value	coding
1	Yes
2	No

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## Depression

Clinical depression :  
r\_depres

Diagnosis of major depressive disorder made by clinician based on clinical review

A **clinical diagnosis of major depressive disorder** is rendered by an examining physician at each evaluation. The diagnosis is based on criteria of the Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Revised (DSM-III-R), clinical interview with the participant, and review of responses to a series of questions adapted from the Diagnostic Interview Schedule. The clinician is first presented with an algorithmic diagnosis and has the ability to modify if necessary.

Value	Coding
1	Highly probable
2	Probable
3	Possible
4	Not present

Note: Most RADC publications have analyzed depressive symptoms using a 10-item version of the Center for Epidemiologic Studies Depression (CES-D) scale.

Other Forms : \_I, \_Iv, \_bl

## References

**Cerebral infarctions and the relationship of depression symptoms to level of cognitive functioning in older persons.**

Bennett DA, Wilson RS, Schneider JA, Bienias JL, Arnold SE

Journal: The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry 2004 Mar-Apr; 12(2) 211-9

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## Lifestyle

Lifestyle > Alcohol and tobacco use

## Alcohol use : alcohol\_g\_bl

## Grams of alcohol used per day at baseline

**Grams of alcohol per day at baseline** is a measure of how much alcohol (beer, wine, and liquor) a participant consumed in the past 12 months. Participants are first asked whether or not they consumed at least 12 drinks ever and in the last 12 months. Individuals who answer “no” to both questions were given a total alcohol consumption of 0. Those who respond “yes” to consuming at least 12 drinks in the past 12 months are then asked to estimate the quantity consumed of each of the following alcoholic beverages: beer, wine, and liquor. A value is applied to each response choice based on the table below. The number of drinks value is then multiplied by grams of alcohol per drink type and then summed across all drink types to determine total grams of alcohol consumed. Totals range from 0 to 234.6g, with higher values indicating greater alcohol consumption.

Participants are asked the following questions:

1. In your entire life, have you had at least 12 drinks of alcoholic beverage?
2. In the past 12 months, did you have at least 12 drinks of any kind of alcoholic beverage?
3. During the past 12 months, on average, how much beer did you drink?
4. During the past 12 months, on average, how much wine did you drink?
5. During the past 12 months, on average, how much liquor did you drink?

Response choices for each item:

Response	Response code	Value
6+ drinks/glasses per day	1	6.0
4-5 drinks/glasses per day	2	4.5
2-3 drinks/glasses per day	3	2.5
1 drinks/glasses per day	4	1.0
5-6 drinks/glasses per week	5	0.8
2-4 drinks/glasses per week	6	0.4
1 drink/glass per week	7	0.2
1-3 drink/glass per month	8	0.1
Less than one drink/glass per month	9	0.0

Grams of alcohol per drink/glass:

Drink type	Grams of alcohol
Beer	13.2

Drink type	Grams of alcohol
Wine	10.8
Liquor	15.1

Note: This variable is not normally distributed, with the majority of values with at 0 and some high values.

## References

### Negative affect and mortality in older persons.

Wilson RS, Bienias JL, Mendes de Leon CF, Evans DA, Bennett DA

Journal: American journal of epidemiology 2003 Nov 1; 158(9) 827-35

## Lifetime daily alcohol intake : ldai\_bl

### Self-reported lifetime daily alcohol intake - baseline

**Lifetime Daily Alcohol Intake (LDAI) at baseline** is a measure of the amount of alcoholic drinks (beer, wine, or liquor) consumed per day during the period the participants drank the most in their lifetime.

Participants are asked the following questions:

1. In your entire life, have you had at least 12 drinks of any kind of alcoholic beverage?
2. In your entire life, when you drank the most, about how often did you drink any type of alcoholic beverage, including beer, wine and liquor?

If a participant replies “no” to item 1, LDAI is categorized as less than one drink per month (response code = 9).

Response choices for item 2:

Response	Response code	Value
6+ drinks per day	1	6.0
4-5 drinks per day	2	4.5
2-3 drinks per day	3	2.5
1 drink per day	4	1.0
5-6 drinks per week	5	0.8
2-4 drinks per week	6	0.4
1 drink per week	7	0.2
1-3 drinks per month	8	0.1
Less than one drink per month	9	0.0

## References

### Negative affect and mortality in older persons.

Wilson RS, Bienias JL, Mendes de Leon CF, Evans DA, Bennett DA

Journal: American journal of epidemiology 2003 Nov 1; 158(9) 827-35

## Smoking : smoking

### Smoking status at baseline

**Smoking status at baseline** is measured with smoking-related data gathered at the baseline interview. Current and former smoking habits are assessed using the following questions:

1. Do you smoke cigarettes now?
2. Did you ever smoke cigarettes regularly?

Question 1 is used to determine current smokers, and question 2 identifies previous smokers. Participants who answer “no” to both questions are categorized as “never smoked” (see below).

Value	Response
0	Never smoked
1	Former smoker (does not currently smoke)
2	Current smoker

Note: Categories are mutually exclusive.

## References

### The relation of cigarette smoking to incident Alzheimer's disease in a biracial urban community population.

Aggarwal NT, Bienias JL, Bennett DA, Wilson RS, Morris MC, Schneider JA, Shah RC, Evans DA

Journal: Neuroepidemiology 2006; 26(3) 140-6

## Lifestyle > Cognitive activity

Cognitive activity -  
childhood :  
chd\_cogact\_freq

Frequency of participation in cognitively stimulating activity in childhood - Average of 11 items

This variable is only available in MAP, MARS, and LATC.

**Childhood cognitive activity** is an 11-item composite measure of frequency of participation in cognitively

stimulating activities, issued at baseline. Participants are asked how often they engaged in cognitively stimulating activities at age 6 (3 items) and at age 12 (8 items).

Participants are asked to rate the items on a 5-point scale. Values for questions #1-3 and 5-10 are flipped so that higher values indicate more frequent participation across all items (see table below). The composite measure ranges from 1 to 5 and is the mean of the individual item scores, with higher scores indicating greater cognitive activity.

Participants are asked the following questions:

1. When you were 6, how often did you play games like tic-tac-toe, checkers, or other board games, cards, or word games?
2. How often did someone in your home read to you when you were 6?
3. How often did someone in your home tell you stories when you were 6?
4. When you were 12, about how much time did you spend reading each day?
5. When you were 12, how often did you visit a library?
6. When you were 12, how often did you read a newspaper?
7. When you were 12, how often did you read magazines?
8. When you were 12, how often did you read books?
9. When you were 12, how often did you write letters?
10. When you were 12, how often did you play games like checkers or other board games, cards, puzzles, word games, mind teasers, or any other similar games?
11. When you were 12, how much time did you spend on homework each day?

Response choices for each question:

Value	Items 1-3, 5-10 (flipped)	Items 4, 11
1	Once a year or less	None
2	Several times a year	Less than one hour
3	Several times a month	One to less than two hours
4	Several times a week	Two to less than three hours
5	Every day/almost every day	Three or more hours

Note: The variable is calculated if at least half of the items are non-missing.

## References

### **Early and late life cognitive activity and cognitive systems in old age.**

Wilson RS, Barnes LL, Krueger KR, Hoganson G, Bienias JL, Bennett DA

Journal: Journal of the International Neuropsychological Society : JINS 2005 Jul; 11(4) 400-7

### Early life conditions and cognitive functioning in later life.

Everson-Rose SA, Mendes de Leon CF, Bienias JL, Wilson RS, Evans DA

Journal: American journal of epidemiology 2003 Dec 1; 158(11) 1083-9

Cognitive activity - late life  
: late\_life\_cogact\_freq

Frequency of participation in cognitively stimulating activity in late life - Average of 7 items

**Late life cognitive activity** is a composite measure of frequency of participation in 7 cognitively stimulating activities during the past year. Activities include reading, writing letters, visiting a library, and playing games such as chess or checkers. These items involve information processing or retention and have relatively few barriers to participation.

Participants are asked to rate each item on a 5-point scale. Values for items 2-7 are flipped so that higher values indicate more frequent participation (see table below). The variable ranges from 1 to 5 and is calculated by averaging the individual item scores.

Participants are asked the following questions:

1. About how much time do you spend reading each day?
2. In the last year, how often did you visit a library?
3. Thinking of the last year, how often do you read newspapers?
4. During the past year, how often did you read magazines?
5. During the past year, how often did you read books?
6. During the past year, how often did you write letters?
7. During the past year, how often did you play games like checkers or other board games, cards, puzzles, etc.?

Response choices for each item:

Value	Item 1	Items 2-7 (flipped)
1	None	Once a year
2	Less than one hour	Several times a year
3	One to less than two hours	Several times a month
4	Two to less than three hours	Several times a week
5	Three or more hours	Every day/almost every day



Note: At baseline interview, item #2 reads, “In the last ten years, how often did you visit a library?”

The variable is calculated if at least half of the items are non-missing.

The baseline version of this variable is available upon request.

## References

### **Influence of late-life cognitive activity on cognitive health.**

Wilson RS, Segawa E, Boyle PA, Bennett DA

Journal: Neurology 2012 Apr 10; 78(15) 1123-9

Cognitive activity - lifetime  
(total) :  
lifetime\_cogact\_freq\_bl

Frequency of participation in cognitively stimulating activity in lifetime - Average of 4 subscales

This variable is only available in MAP, MARS, and LATC.

**Lifetime cognitive activity** is a 37-item measure of frequency of participation in cognitively stimulating activities, issued at baseline. Participants are asked how often they engaged in cognitively stimulating activities during the following periods of life:

1. Childhood (/radc/var/displayVariable.htm?id=357) (11 items)
2. Young adult (/radc/var/displayVariable.htm?id=363) (10 items)
3. Middle adult (/radc/var/displayVariable.htm?id=384) (9 items)
4. Late life (/radc/var/displayVariable.htm?id=373) (7 items)

Participants are asked to rate each item on a 5-point scale. The overall score ranges from 1 to 5 and is the average of the 4 subscale scores. See subscale variables for details.

Note: The variable is calculated if at least half of the items are non-missing. Since the variable is calculated based on the number of valid items, independent of the subscale score calculations, participants may have a valid lifetime score but be missing one or more subscale scores.

## References

### **Life-span cognitive activity, neuropathologic burden, and cognitive aging.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Schneider JA, Bennett DA

Journal: Neurology 2013 Jul 3; 81(4) 314-21

Cognitive activity - middle  
age :

Frequency of participation in cognitively stimulating activity in middle (adult) age -  
Average of 9 items

## ma\_adult\_cogact\_freq

This variable is only available in MAP, MARS, and LATC.

**Middle adult age cognitive activity** is assessed using a 9-item self-report scale issued at baseline. Participants are asked how often they engaged in cognitively stimulating activities at the age of 40 or from age 30 to 40. Items include reading, visiting a museum, attending theater/concert, visiting a library, reading newspapers, reading magazines, reading books, writing letters, and playing games.

Participants are asked to rate the items on a 5-point scale. Values for items 4-9 are flipped so that higher values reflect more frequent participation (see table below). The composite measure ranges from 1 to 5 and is the mean of the individual Item scores, with higher scores indicating greater cognitive activity.

Participants are asked the following questions:

1. When you were 40, about how much time did you spend reading each day?
2. From age 30 to 40, how many times did you visit a museum?
3. From age 30 to 40, how many times did you attend a concert, play, or musical?
4. From age 30 to 40, how often did you visit a library?
5. When you were 40, how often did you read newspapers?
6. When you were 40, how often did you read magazines?
7. When you were 40, how often did you read books?
8. When you were 40, how often did you write letters?
9. When you were 40, how often did you play games like checkers or other board games, cards, puzzles, etc.?

Response choices for each item:

Value	Item 1	Items 2-3	Items 4-9 (flipped)
1	None	Never	Once a year or less
2	Less than one hour	1-2 times	Several times a year
3	One to less than two hours	3-9 times	Several times a month
4	Two to less than three hours	10-19 times	Several times a week
5	Three or more hours	More than 20 times	Every day/almost every day

Note: The variable is calculated if at least half of the items are non-missing.

## References

### **Life-span cognitive activity, neuropathologic burden, and cognitive aging.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Schneider JA, Bennett DA

Journal: Neurology 2013 Jul 3; 81(4) 314-21

Cognitive activity - young adult :  
ya\_adult\_cogact\_freq

Frequency of participation in cognitively stimulating activity as a young adult - Average of 10 items

This variable is only available in MAP, MARS, and LATC.

**Young adult age cognitive activity** is assessed using a 10-item scale collected at baseline. Participants are asked how often they engaged in cognitively stimulating activities (e.g., reading, visiting museums, playing games) at the age of 18. Participating in extracurricular activities (item 10) is comprised of 4 subquestions.

Participants are asked to rate the items on a 5-point scale, with higher values indicating more frequent participation (see table below). The composite measure ranges from 1 to 5 and is the mean of the individual item scores, with higher scores indicating greater cognitive activity.

Participants are asked the following questions:

**When you were 18...**

1. how many times had you visited a museum?
2. how many times had you attended a concert, play, or musical?
3. about how much time did you spend reading each day?
4. how often did you visit a library?
5. how often did you read newspapers?
6. how often did you read magazines?
7. how often did you read books?
8. how often did you write letters?
9. how often did you play games like checkers or other board games, etc?

The following 4 subquestions are used to measure extracurricular educational experiences:

**By the age of 18...**

- 10a. had you received any instruction in a foreign language?
- 10b. had you taken any music lessons?
- 10c. had you taken any art, dance, or theater lessons?
- 10d. had you ever kept a diary or journal?

Response choices for each item:

Value	Items 1-2	Item 3	Items 4-9 (flipped)	Item 10
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Value	Items 1-2	Item 3	Items 4-9 (flipped)	Item 10
1	Never	None	Once a year or less	All 4 questions answered as “no”
2	1-2 times	Less than one hour	Several times a year	1 question answered as “yes”
3	3-9 times	One to less than 2 hours	Several times a month	2 questions answered as “yes”
4	10-19 times	two to less than three hours	Several times a week	3 questions answered as “yes”
5	More than 20 times	Three or more hours	Every day/almost every day	All 4 questions answered as “yes”

Note: The variable is calculated if at least half of the items are non-missing.

## References

### **Life-span cognitive activity, neuropathologic burden, and cognitive aging.**

Wilson RS, Boyle PA, Yu L, Barnes LL, Schneider JA, Bennett DA

Journal: Neurology 2013 Jul 3; 81(4) 314-21

## Lifestyle > Physical activity and BMI

### BMI : bmi

### Body mass index

**Body mass index** (BMI) is calculated using weight and height measurements. Weight and height are measured and recorded at each visit by a trained technician blinded to previously collected data. BMI is calculated as weight in kilograms divided by height in meters squared.

Other Forms : \_lv, \_bl

## References

### **Change in body mass index and risk of incident Alzheimer disease.**

Buchman AS, Wilson RS, Bienias JL, Shah RC, Evans DA, Bennett DA

Journal: Neurology 2005 Sep 27; 65(6) 892-7

### Physical activity (5 items) : phys5itemsum

### Hours of physical activity in late life - Sum of 5 items

**Physical activity (5 items)** is assessed using questions adapted from the 1985 National Health Interview Survey. The variable measures the sum of hours per week that the participant engages in 5 categories of

activities:

1. Walking for exercise
2. Gardening or yard work
3. Calisthenics or general exercise
4. Bicycle riding (including stationary bikes)
5. Swimming or water exercises

Participants are asked if they have engaged in any of the 5 activities within the past 2 weeks and if so, the number of occasions and average minutes per occasion. Minutes in each activity are summed and divided by 120 to yield a composite measure of participation in physical activity expressed as hours per week.

NOTE: MARS only collects information on 3 items (walk, garden, exercise). To include MARS, see phys3itemsum (Physical activity (3 items)).

Other Forms : \_lv, \_bl

## References

### **Participation in cognitively stimulating activities and risk of incident Alzheimer disease.**

Wilson RS, Mendes De Leon CF, Barnes LL, Schneider JA, Bienias JL, Evans DA, Bennett DA  
Journal: JAMA 2002 Feb 13; 287(6) 742-8

### **Physical activity and motor decline in older persons.**

Buchman AS, Boyle PA, Wilson RS, Bienias JL, Bennett DA  
Journal: Muscle & nerve 2007 Mar; 35(3) 354-62

## Lifestyle > Social engagement

Perceived discrimination :  
discrim\_cnt

Self-reported frequency of discrimination

**Perceived discrimination** is assessed with a 9 items based on a previously established scale. The scale assesses the subjective experience of being treated unfairly in common everyday situations. Items are framed in the context of general mistreatment without reference to race, age, or gender.

Participants are asked to rate how often they experienced nine instances of discrimination on a 4-point scale (see table below). Responses are then dichotomized (often or sometimes = 1 and rarely or never = 0) and summed across all items for each participant. The total score ranges from 0 to 9, with higher scores indicating more discrimination.

Participants are presented the following items:

1. You are treated with less courtesy than other people.
2. You are treated with less respect than other people.
3. You receive poorer service than other people at restaurants or stores.
4. People act as if they think you are not smart.
5. People act as if they are afraid of you.
6. People act as if they think you are dishonest.
7. People act as if they're better than you are.
8. You or your family members are called names or insulted.
9. You are threatened or harassed.

Response choices for each item:

Response	Response code	Calculated value
Often	1	1
Sometimes	2	1
Rarely	3	0
Never	4	0

Note: In preliminary analysis, the Cronback coefficient alpha, an indicator of internal consistency reliability, was 0.8.

This variable is available in the following format for each study:

MARS - longitudinal

MAP - baseline only

ROS - not available

WB, March 12, 2019: New data added

CEDHA - longitudinal

AACORE- longitudinal

LATC- baseline only

## References

**Self-reported experiences of everyday discrimination are associated with elevated C-reactive protein levels in older African-American adults.**

Lewis TT, Aiello AE, Leurgans S, Kelly J, Barnes LL

Journal: Brain, behavior, and immunity 2010 Mar; 24(3) 438-43

Social activity - late life :  
late\_life\_soc\_act

Frequency of participation in social activity in late life

Frequency of **late-life social activity** is assessed using a 6-item scale that asks how often during the past year participants engaged in common types of activities that involve social interaction.

Participants are asked to rate the items on a 5-point scale, with higher values indicating more frequent participation (see below). Item scores are averaged to yield the composite measure, with higher scores indicating greater social activity.

Participants are asked to rate the following six items:

**During the past year, how often did you...**

1. go to restaurants, sporting events or teletract, or play bingo?
2. go on day trips or overnight trips?
3. do unpaid community/volunteer work?
4. visit at relatives or friends houses?
5. participate in groups (such as senior center, VFW, Knights of Columbus, Rosary Society or something similar)?
6. attend church or religious services?

Response choices for each item:

Value	Response
1	Once a year or less
2	Several times a year
3	Several times a month
4	Several times a week
5	Every day or almost every day

References

**Association between late-life social activity and motor decline in older adults.**

Buchman AS, Boyle PA, Wilson RS, Fleischman DA, Leurgans S, Bennett DA

Journal: Archives of internal medicine 2009 Jun 22; 169(12) 1139-46

Social network size :

Size of social network based on the number of children, family, and friends seen at

## soc\_net

## least once a month

**Social network size** is quantified using standard questions about the number of children, family, and friends each participant has and how often they interact with them. Social network size is the number of these individuals (children, family, and friends) seen at least once a month.

Participants are asked the following questions:

1. How many living children do you have?
2. How many of your children do you see at least once a month?
3. Do you see your child at least once a month?
4. How many close relatives do you have?
5. How many of these close relatives do you usually see at least once a month?
6. Do you see your close relative at least once a month?
7. How many close friends do you have?
8. How many of these close friends do you see at least once a month?
9. Do you see your close friend at least once a month?

## References

**The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study.**

Bennett DA, Schneider JA, Tang Y, Arnold SE, Wilson RS

Journal: The Lancet. Neurology 2006 May; 5(5) 406-12

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Loneliness :  
social\_isolation

## Perceived social isolation (loneliness)

This variable is only available in MAP, MARS, and LATC.

**Loneliness**, or emotional isolation, refers to perceived social isolation and feeling disconnected from others. This variable is assessed at each evaluation with 5 items from a modified version of the de Jong-Gierveld Loneliness Scale. The original version of the scale has been shown to be internally consistent and associations with loss of a spouse, institutional living, and low self-esteem support its construct validity. To assess emotional loneliness, 5 items assessing social loneliness were eliminated from the original scale.

Participants are asked to rate agreement with each item on a 5-point Likert rating scale (see table below). The total score ranges from 1 to 5 and is the average of the individual item scores. Higher values indicate more loneliness.

Participants are presented the following items:



1. I experience a general sense of emptiness.
2. I miss having people around.
3. I feel like I don't have enough friends.
4. I often feel abandoned.
5. I miss having a really close friend.

Response choices for each item:

Value	Response
1	Strongly disagree
2	Disagree
3	Neutral
4	Agree
5	Strongly agree

## References

### **Loneliness and risk of Alzheimer disease.**

Wilson RS, Krueger KR, Arnold SE, Schneider JA, Kelly JF, Barnes LL, Tang Y, Bennett DA  
Journal: Archives of general psychiatry 2007 Feb; 64(2) 234-40

### **Relation of driving status to incident life space constriction in community-dwelling older persons: a prospective cohort study.**

Shah RC, Maitra K, Barnes LL, James BD, Leurgans S, Bennett DA  
Journal: The journals of gerontology. Series A, Biological sciences and medical sciences 2012 Apr 30; 67(9) 984-9

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## Medical Conditions

### Medical Conditions > Blood pressure

bp11                      Blood pressure measurement- sitting - trial 1

Sitting blood pressure reading:

The subject should be seated for five minutes prior to obtaining the seated blood pressure readings.

systolic/diastolic

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bp2

Blood pressure measurement- sitting - trial 2

Second sitting blood pressure reading

The subject should be seated for five minutes prior to obtaining the seated blood pressure readings.

systolic/diastolic

---

bp31

Blood pressure measurement- standing

STANDING BLOOD PRESSURE READING

Subject is requested to stand. The reading is repeated after 60 seconds.

Diastolic blood pressure :  
dbp\_avg

## Diastolic blood pressure - Average of 3 readings

**Diastolic blood pressure** is the pressure in the arteries between heartbeats (resting phase). This variable is measured with a mercury sphygmomanometer by trained research assistants using the Hypertension Detection and Follow-up Program protocol. For each participant, blood pressure readings are taken as follows:

1. Seated blood pressure reading (trial 1)
2. Seated blood pressure reading (trial 2)
3. Standing blood pressure reading, 1 minute later

Diastolic blood pressure is calculated by averaging the three diastolic blood pressure readings.

## References

### **Relation of blood pressure to risk of incident Alzheimer's disease and change in global cognitive function in older persons.**

Shah RC, Wilson RS, Bienias JL, Arvanitakis Z, Evans DA, Bennett DA

Journal: Neuroepidemiology 2006; 26(1) 30-6

History of hypertension :  
hypertension\_cum

## Self-reported history of hypertension

**History of hypertension** is based on self-report. For any given cycle, this variable indicates reported hypertension in past history or in at least one follow-up cycle up to and including that cycle. Participants are asked to respond “yes”, “suspect or possible”, or “no” to the following question:

Since your interview on [date of last interview], have you been told by a doctor, nurse, or therapist that you had high blood pressure?

Value	Coding
0	No history of hypertension
1	History of hypertension - Reported prior to or in the given cycle

Notes: At baseline interview, the question reads: Have you ever been told by a doctor, nurse, or therapist that you had high blood pressure?

The provided references describe the baseline version of this variable.

## References

### **Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

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## Medical Conditions > Cancer

Cancer at baseline :  
cancer\_bl

### Self-reported history of cancer at baseline

**History of cancer at baseline** is self-reported at the baseline interview.

Participants are asked the following question:

Have you ever been told by a doctor, nurse or therapist that you had cancer, malignancy or tumor of any type?

Response choices are coded into reported as present prior to baseline = 1 or not reported as present prior to baseline (includes suspect or possible) = 0.

Response choices:

Response	Response code	Value
Yes	1	1
Suspect or possible	2	0
No	3	0

## References

### **Association of Cancer History with Alzheimer's Disease Dementia and Neuropathology.**

Yarchoan M, James BD, Shah RC, Arvanitakis Z, Wilson RS, Schneider J, Bennett DA, Arnold SE

Journal: Journal of Alzheimer's disease : JAD 2016 Dec 30; 56(2) 699-706

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## Medical Conditions > Diabetes

History of diabetes :  
dm\_cum

### Self-reported history of diabetes

**History of diabetes** is based on self-report. For any given cycle, this value indicates reported hypertension in past history or in at least one follow-up cycle up to and including that cycle. Participants are asked to respond “yes”, “suspect or possible”, or “no” to each of the following questions:

1. Have you ever been told by a doctor, nurse, or therapist that you had diabetes, or sugar in the urine, or high blood sugar?
2. Has a doctor, nurse, or therapist ever told you to take insulin or injections for your high blood sugar?

3. Has a doctor, nurse, or therapist ever told you to take medicine by mouth for your blood sugar?

Value	Coding
0	No history of diabetes - Answered “no” or “suspect or possible” to all questions, in all cycles
1	History of diabetes - Answered “yes” to one or more questions or reported taking a diabetes medicine prior to or in the given cycle

## References

### **Independent and interactive impacts of hypertension and diabetes mellitus on verbal memory: A coordinated analysis of longitudinal data from England, Sweden, and the United States.**

Kelly A, Calamia M, Koval A, Terrera GM, Piccinin AM, Clouston S, Hassing LB, Bennett DA, Johansson B, Hofer SM

Journal: Psychology and aging 2016 Feb 25; 31(3) 262-73

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## Medical Conditions > Head injury

headinjrloc\_cum

Medical History - Head injury with loss of consciousness - cumulative

## Medical History - Head injury with loss of consciousness - cumu

value coding

0 never reported in past history or in follow-up cycle  
up to this cycle (includes suspect or possible)

1 reported in past history or in at least 1 follow-up cycle up to this cycle

## Codebook questions

Baseline (visit = 00)

Q: Have you EVER had a head injury?

Allowable codes:

1 = Yes (then branch to next question)

2 = No

8 = REFUSAL

9 = DON'T KNOW

IF YES then

Q: Have you EVER lost consciousness because of a head injury?

Allowable codes:

1 = Yes

2 = Suspect or possible

3 = No

8 = REFUSAL

9 = DON'T KNOW

Follow-up (visit other than 00)

Q: Since (date of last evaluation), have you had a head injury?

Allowable codes:

1 = Yes

2 = No

8 = REFUSAL (blaise code)

9 = DON'T KNOW (blaise code)

IF YES then

Q: Have you lost consciousness because of a head  
injury that occurred since (date of last evaluation)?

## Allowable codes:

- 1 = Yes
- 2 = Suspect or possible
- 3 = No
- 8 = REFUSAL (blaise code)
- 9 = DON'T KNOW (blaise code)

## References

**Participation in cognitively stimulating activities and risk of incident Alzheimer disease.**

Wilson RS, Mendes De Leon CF, Barnes LL, Schneider JA, Bienias JL, Evans DA, Bennett DA

Journal: JAMA 2002 Feb 13; 287(6) 742-8

**Depressive symptoms, cognitive decline, and risk of AD in older persons.**

Wilson RS, Barnes LL, Mendes de Leon CF, Aggarwal NT, Schneider JS, Bach J, Pilat J, Beckett LA, Arnold SE,

Evans DA, Bennett DA

Journal: Neurology 2002 Aug 13; 59(3) 364-70

**Negative affect and mortality in older persons.**

Wilson RS, Bienias JL, Mendes de Leon CF, Evans DA, Bennett DA

Journal: American journal of epidemiology 2003 Nov 1; 158(9) 827-35

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## Medical Conditions > Summary measures

med\_con\_sum\_cum                      History of medical condition - cumulative

This variable is the number of conditions reported

1. hypertension
2. diabetes
3. heart disease
4. cancer
5. thyroid disease
6. head injury with loss of consciousness.
7. stroke

value	coding
0	No conditions present
1	1 condition present
2	2 conditions present
3	3 conditions present
4	4 conditions present
5	5 conditions present
6	6 conditions present
7	7 conditions present

Seven medical conditions were present in at least 5 percent of persons at baseline. We classified hypertension, diabetes, heart disease, cancer, thyroid disease, and head injury with loss of consciousness based on self-report that a physician previously identified the condition. A clinical diagnosis of stroke was based on the history plus the neurologic examination. We used the total number of conditions present at baseline as an index of chronic illness, as previously described.

This variables covers the time period from prior to current cycle.

## References

### **Participation in cognitively stimulating activities and risk of incident Alzheimer disease.**

Wilson RS, Mendes De Leon CF, Barnes LL, Schneider JA, Bienias JL, Evans DA, Bennett DA  
Journal: JAMA 2002 Feb 13; 287(6) 742-8



**Depressive symptoms, cognitive decline, and risk of AD in older persons.**

Wilson RS, Barnes LL, Mendes de Leon CF, Aggarwal NT, Schneider JS, Bach J, Pilat J, Beckett LA, Arnold SE, Evans DA, Bennett DA

Journal: Neurology 2002 Aug 13; 59(3) 364-70

**Negative affect and mortality in older persons.**

Wilson RS, Bienias JL, Mendes de Leon CF, Evans DA, Bennett DA

Journal: American journal of epidemiology 2003 Nov 1; 158(9) 827-35

## Medical Conditions &gt; Thyroid

thyroid\_cum

Medical Conditions - thyroid disease - cumulative

Medical History: THYROID DISEASE - cumulative

value coding

0 never reported in past history or in follow-up cycle  
up to this cycle (includes suspect or possible)

1 reported in past history or in at least 1 follow-up cycle up to this cycle

Baseline (visit = 00)

Q: Have you ever been told by a doctor, nurse or therapist that  
you had thyroid disease?

Follow-up (visit other than 00)

Q: Since your interview on (insert date of last evaluation), have you been  
told by a doctor, nurse or therapist that you had thyroid disease?

Allowable codes:

1 = Yes

2 = Suspect or possible

3 = No

8 = REFUSAL

9 = DON'T KNOW

## References

### **Participation in cognitively stimulating activities and risk of incident Alzheimer disease.**

Wilson RS, Mendes De Leon CF, Barnes LL, Schneider JA, Bienias JL, Evans DA, Bennett DA  
Journal: JAMA 2002 Feb 13; 287(6) 742-8

### **Depressive symptoms, cognitive decline, and risk of AD in older persons.**

Wilson RS, Barnes LL, Mendes de Leon CF, Aggarwal NT, Schneider JS, Bach J, Pilat J, Beckett LA, Arnold SE, Evans DA, Bennett DA  
Journal: Neurology 2002 Aug 13; 59(3) 364-70

### **Negative affect and mortality in older persons.**

Wilson RS, Bienias JL, Mendes de Leon CF, Evans DA, Bennett DA  
Journal: American journal of epidemiology 2003 Nov 1; 158(9) 827-35

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## Medical Conditions > Vascular

History of congestive  
heart failure : chf\_cum

### Self-reported history of congestive heart failure

**History of congestive heart failure (CHF)** is based on self-report. For any given cycle, this variable indicates reported CHF in past history or in at least one follow-up cycle up to and including that cycle. Participants are asked to respond “yes”, “suspect or possible”, or “no” to the following question:

Since your last interview on [date of last interview], have you been told by a doctor, nurse, or therapist that you had congestive heart failure?

Value	Coding
0	No history of CHF
1	History of CHF - Reported prior to or in the given cycle

Note: At baseline interview, the question reads: Have you ever been told by a doctor, nurse, or therapist that you had congestive heart failure?

## References

### **Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA  
Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

## History of claudication : claudication\_cum

### Self-reported history of claudication

**History of claudication** is a marker of peripheral vascular disease and is based on self-report. For any given cycle, this variable indicates reported claudication in past history or in at least one follow-up cycle up to and including that cycle. Participants are asked the following questions:

1. Do you get pain in either leg while walking? [Yes/No]
2. If yes, in what part of your leg do you feel it? [Open-ended]

Value	Coding
0	No history of claudication - Never reported pain in legs or only reported pain that did not include the calves
1	History of claudication - Reported pain in calves while walking prior to or in the given cycle

### References

#### Religious Orders Study and Rush Memory and Aging Project.

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

## History of heart conditions : heart\_cum

### Self-reported history of heart conditions

**History of heart conditions** is based on self-report. For any given cycle, this variable indicates reported heart conditions in past history or in at least one follow-up cycle up to and including that cycle. Participants are asked to respond “yes”, “suspect or possible”, or “no” to the following question:

Since your last interview on [date of last interview], have you been told by a doctor, nurse, or therapist that you had a heart attack or coronary, coronary thrombosis, coronary occlusion, or myocardial infarction?

Value	Coding
0	No history of heart conditions
1	History of heart conditions - reported prior to or in the given cycle

Notes: At baseline interview, the question reads: Have you ever been told by a doctor, nurse, or therapist that you had a heart attack or coronary, coronary thrombosis, coronary occlusion, or myocardial infarction?

The provided references describe the baseline version of this variable.

### References

**Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

History of stroke :  
stroke\_cum**History of stroke based on clinician review**

**History of stroke** is based on clinician review of self-report questions, neurological exam (when available), cognitive testing, and interview of participant. The clinician is first presented with an algorithmic diagnosis and has the ability to modify if necessary. For any given cycle, this variable indicates diagnosis of stroke in past history or in at least one follow-up cycle up to and including that cycle.

Clinician diagnosis of stroke:

Value	Coding
1	Highly probable
2	Probable
3	Possible
4	Not present

The clinician rating is then dichotomized into history of stroke = 1 or no history of stroke = 0.

Value	Coding
0	No history of stroke - Diagnosis of possible or not present in all cycles
1	History of stroke - Diagnosis of highly probable or probable in at least one cycle prior to or in the given cycle

Note: The provided references describe the baseline version of this variable.

**References****Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

Vascular disease burden -  
3 items : vasc\_3dis\_sum**Cumulative vascular disease burden - Average of 3 items****Vascular disease burden** is computed using self-report questions for the following 3 items\*:

1. Claudication (</radc/var/displayVariable.htm?id=547>)
2. Stroke (</radc/var/displayVariable.htm?id=549>)\*
3. Heart conditions (</radc/var/displayVariable.htm?id=546>)

Each item is given a value of 0 or 1 (see response options below). The cumulative score for vascular disease burden ranges from 0 to 3 and is the mean of the 3 individual scores multiplied by 3. Higher scores indicate greater vascular disease burden. The score for vascular disease burden is calculated if at least 2/3 of the questions are answered.

\*In addition to self-report, evaluation of stroke is also based on neurological exam (when available), cognitive testing, and interview of participant, with which the physician may render a diagnosis of stroke.

Response values for each item:

#### Claudication

Value	Response
0	Never reported pain in legs or any reported pain that did not include the calves, from baseline to this cycle
1	Reported pain in legs while walking which includes calves, in at least one cycle from baseline to this cycle

#### Stroke

Value	Response
0	Stroke not present (Possible stroke dx or stroke not present), in all cycles, from baseline to this cycle
1	Stroke present (Highly probable or probable stroke dx) reported in at least one cycle from baseline to this cycle

#### Heart condition

Value	Response
0	Never reported in past history or in follow-up cycle up to this cycle (includes suspect or possible)
1	Reported in past history or in at least 1 follow-up cycle up to this cycle

Note: A 4-item version (</radc/var/displayVariable.htm?id=507>) of this variable includes CHF questions and is available for MAP/MARS only.

## References

**Association of muscle strength with the risk of Alzheimer disease and the rate of cognitive decline in community-dwelling older persons.**

Boyle PA, Buchman AS, Wilson RS, Leurgans SE, Bennett DA

Journal: Archives of neurology 2009 Nov; 66(11) 1339-44

**Vascular disease burden -  
4 items : vasc\_4dis\_sum**

**Cumulative vascular disease burden - Average of 4 items**

This variable is only available in MAP, MARS, and LATC.

**Vascular disease burden** is computed using self-report questions for the following 4 items\*:

1. Claudication (/radc/var/displayVariable.htm?id=547)
2. Stroke (/radc/var/displayVariable.htm?id=549)\*
3. Heart conditions (/radc/var/displayVariable.htm?id=546)
4. Congestive heart failure (/radc/var/displayVariable.htm?id=550)

Each item is given a value of 0 or 1 (see response options below). The cumulative score for vascular disease burden ranges from 0 to 4 and is the mean of the 4 individual scores multiplied by 4. Higher scores indicate greater vascular disease burden.

\*In addition to self-report, evaluation of stroke is also based on neurological exam (when available), cognitive testing, and interview of participant, with which the physician may render a diagnosis of stroke.

Response values for each item:

**Claudication**

Value	Response
0	Never reported pain in legs or any reported pain that did not include the calves, from baseline to this cycle
1	Reported pain in legs while walking which includes calves, in at least one cycle from baseline to this cycle

**Stroke**

Value	Response
0	Stroke not present (Possible stroke dx or stroke not present), in all cycles, from baseline to this cycle
1	Stroke present (Highly probable or probable stroke dx) reported in at least one cycle from baseline to this cycle

## Heart condition

Value	Response
0	Never reported in past history or in follow-up cycle up to this cycle (includes suspect or possible)
1	Reported in past history or in at least 1 follow-up cycle up to this cycle

## Congestive Heart Failure

Value	Response
0	Never reported in past history or in follow-up cycle up to this cycle (includes suspect or possible)
1	Reported in past history or in at least 1 follow-up cycle up to this cycle

Note: This variable is available in MAP/MARS. ROS does not have CHF questions. Please use the 3-item version (</radc/var/displayVariable.htm?id=506>) of this variable for analyses involving ROS.

## References

**Association of muscle strength with the risk of Alzheimer disease and the rate of cognitive decline in community-dwelling older persons.**

Boyle PA, Buchman AS, Wilson RS, Leurgans SE, Bennett DA

Journal: Archives of neurology 2009 Nov; 66(11) 1339-44

## Vascular disease risk factors : vasc\_risks\_sum

## Cumulative vascular disease risk factors - Average of 3 items

**Vascular Disease Risk Factors** is a composite measure of vascular risk burden. The variable is computed using self-report questions on the following 3 items:

1. Hypertension (</radc/var/displayVariable.htm?id=545>)
2. Diabetes (</radc/var/displayVariable.htm?id=544>)
3. Smoking history\*

Each item is given a value of 0 or 1 (see response options below). The score covers a time frame from baseline, including any past history, to the current cycle (i.e., cumulative). The cumulative score for vascular disease risk factors ranges from 0 to 3 and is the mean of the 3 individual scores multiplied by 3. Higher scores indicate higher vascular risk burden.

Response values for each item:

Hypertension

Value	Response
0	Never reported in past history or in follow-up cycle up to this cycle (includes suspect or possible)
1	Reported in past history or in at least 1 follow-up cycle up to this cycle

#### Diabetes

Value	Response
0	Never reported in past history or in follow-up cycle up to this cycle (includes suspect or possible)
1	Reported in past history or in at least 1 follow-up cycle up to this cycle

#### History of smoking

Value	Response
0	Never smoked
1	Former or current smoker

\*Smoking history (smoke\_hx) is based off smoking (/radc/var/displayVariable.htm?id=405) (never smoked vs. former smoker vs. current smoker).

## References

### The relation of cigarette smoking to incident Alzheimer's disease in a biracial urban community population.

Aggarwal NT, Bienias JL, Bennett DA, Wilson RS, Morris MC, Schneider JA, Shah RC, Evans DA

Journal: Neuroepidemiology 2006; 26(3) 140-6

## Medications

Mental health :  
mental\_health\_rx

### Mental health medication usage in last 2 weeks

**Mental health medications** include: depression medications (/radc/var/displayVariable.htm?id=973), tricyclic antidepressant medications (/radc/var/displayVariable.htm?id=952), insomnia medications (/radc/var/displayVariable.htm?id=989), anti-anxiety medications (/radc/var/displayVariable.htm?id=946), antipsychotic medications (/radc/var/displayVariable.htm?id=961), and antimanic medications (/radc/var/displayVariable.htm?id=958).

Value	Coding
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Value	Coding
0	(no) if participant was not taking a mental health medication at this visit
1	(yes) if participant was taking a <b>mental health medication</b> at this visit

Participants supplied all medications prescribed by a doctor, vitamins, supplements, and over-the-counter remedies and medicines taken in the 2 weeks prior to the evaluation. Direct visual inspection of all containers of prescription and over-the-counter agents allowed for medication documentation. Medications were subsequently coded using the Medi-Span Drug Data Base system.

Medi-Span. Master Drug Data Base Documentation Manual. Indianapolis, IN: Medi-Span, 1995.

Other Forms : \_bl, \_ever

## Neurologic : neurologic\_rx

### Neurologic medication usage in last 2 weeks

**Neurologic medications** include: anti-convulsant medications (/radc/var/displayVariable.htm?id=951), Alzheimer's medications (/radc/var/displayVariable.htm?id=938), and Parkinson's disease medications (/radc/var/displayVariable.htm?id=591).

Value	Coding
0	(no) if participant was not taking a neurologic medication at this visit
1	(yes) if participant was taking a <b>neurologic medication</b> at this visit

Participants supplied all medications prescribed by a doctor, vitamins, supplements, and over-the-counter remedies and medicines taken in the 2 weeks prior to the evaluation. Direct visual inspection of all containers of prescription and over-the-counter agents allowed for medication documentation. Medications were subsequently coded using the Medi-Span Drug Data Base system.

Medi-Span. Master Drug Data Base Documentation Manual. Indianapolis, IN: Medi-Span, 1995.

Other Forms : \_bl, \_ever

## Pathology

### Pathology > Alzheimer's disease

#### Braak stage : braaksc

#### Semiquantitative measure of neurofibrillary tangles

**Braak Stage** is a semiquantitative measure of severity of neurofibrillary tangle (NFT) pathology. Bielschowsky silver stain was used to visualize NFTs in the frontal, temporal, parietal, entorhinal cortex, and the hippocampus. Braak stages were based upon the distribution and severity of NFT pathology:

Braak stages I and II indicate NFTs confined mainly to the entorhinal region of the brain  
Braak stages III and IV indicate involvement of limbic regions such as the hippocampus  
Braak stages V and VI indicate moderate to severe neocortical involvement.

Diagnosis includes algorithm and neuropathologist's opinion.

value	coding
0	0
1	I
2	II
3	III
4	IV
5	V
6	VI

## References

### **Neuropathology of older persons without cognitive impairment from two community-based studies.**

Bennett DA, Schneider JA, Arvanitakis Z, Kelly JF, Aggarwal NT, Shah RC, Wilson RS  
Journal: Neurology 2006 Jun 27; 66(12) 1837-44

### **Neuropathological staging of Alzheimer-related changes.**

Braak H, Braak E  
Journal: Acta neuropathologica 1991; 82(4) 239-59

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CERAD score : ceradsc

Semiquantitative measure of neuritic plaques

**CERAD score** is a semiquantitative measure of neuritic plaques. A neuropathologic diagnosis was made of no AD, possible AD, probable AD, or definite AD based on semiquantitative estimates of neuritic plaque density as recommended by the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), modified to be implemented without adjustment for age and clinical diagnosis. A CERAD neuropathologic diagnosis of AD required moderate (probable AD) or frequent neuritic plaques (definite AD) in one or more neocortical regions.

Diagnosis includes algorithm and neuropathologist's opinion, blinded to age and all clinical data.

value	coding	if using a binary variable, recommendation is
1	Definite	yes
2	Probable	yes
3	Possible	no
4	No AD	no

## References

### **The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease.**

Mirra SS, Heyman A, McKeel D, Sumi SM, Crain BJ, Brownlee LM, Vogel FS, Hughes JP, van Belle G, Berg L  
Journal: Neurology 1991 Apr; 41(4) 479-86

### **Neuropathology of older persons without cognitive impairment from two community-based studies.**

Bennett DA, Schneider JA, Arvanitakis Z, Kelly JF, Aggarwal NT, Shah RC, Wilson RS  
Journal: Neurology 2006 Jun 27; 66(12) 1837-44

## Global AD pathology burden : gpath

## Global burden of AD pathology based on 5 regions

**Global AD pathology burden** is a quantitative summary of AD pathology derived from counts of three AD pathologies: neuritic plaques (n), diffuse plaques (d), and neurofibrillary tangles (nft), as determined by microscopic examination of silver-stained slides from 5 regions: midfrontal cortex (midfrontal), midtemporal cortex (midtemp), inferior parietal cortex (infparietal), entorhinal cortex (ento), and hippocampus (ca1hip). The resulting 15 regional counts are shown in the Table. Each regional count is scaled by dividing by the corresponding standard deviation. The 5 scaled regional measures for each type of pathology are then averaged to obtain summary measures (plaq\_d, plaq\_n, and nft) . The 3 summary measures are then averaged to obtain the measure of global AD pathology.

### **Table of AD pathology counts by region**

Region	Diffuse Plaques	Neuritic Plaques	Neurofibrillary tangles
Entorhinal cortex	plaq_d_ec	plaq_n_ec	nft_ec
Hippocampus (CA1)	plaq_d_hip	plaq_n_hip	nft_hip
Midtemporal cortex	plaq_d_mt	plaq_n_mt	nft_mt

Region	Diffuse Plaques	Neuritic Plaques	Neurofibrillary tangles
Inferior parietal cortex	plaq_d_ag	plaq_n_ag	nft_ag
Midfrontal cortex	plaq_d_mf	plaq_n_mf	nft_mf
Burden across region	plaq_d	plaq_n	nft

gpath = mean of (plaq\_d (/radc/var/displayVariable.htm?id=1344), plaq\_n (/radc/var/displayVariable.htm?id=1381), nft (/radc/var/displayVariable.htm?id=631))

Notes on missing data and computation of measures: Counts may be missing for regions (e.g., due to damage from infarct). If data are present for at least 2 of 5 regions, the burden summary for a specific pathology is computed. The global AD pathology burden is only computed if all 3 of the pathology-specific summaries are valid (and nonmissing).

*Item level variables are available upon request.*

## References

### Religious Orders Study and Rush Memory and Aging Project.

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

## NIA-Reagan diagnosis of AD : niareagansc

## NIA-Reagan Diagnosis of Alzheimer's disease - 4 levels (none to high likelihood)

The modified **NIA-Reagan diagnosis of Alzheimer's disease** is based on consensus recommendations for postmortem diagnosis of Alzheimer's disease. The criteria rely on both neurofibrillary tangles (Braak) and neuritic plaques (CERAD).

Value	Likelihood of AD	DICHOTOMIZED (AD_REAGAN)
1	High	1
2	Intermediate	1
3	Low	0
4	No AD	0

The criteria is modified because the neuropathological evaluation is done without knowledge of clinical information, including a diagnosis of dementia. The neuropathologist determines the level of AD pathology. Those with intermediate or high likelihood fulfill criteria for having a pathologic diagnosis of AD.

## References

**Neuropathology of older persons without cognitive impairment from two community-based studies.**

Bennett DA, Schneider JA, Arvanitakis Z, Kelly JF, Aggarwal NT, Shah RC, Wilson RS

Journal: Neurology 2006 Jun 27; 66(12) 1837-44

**Consensus recommendations for the postmortem diagnosis of Alzheimer's disease. The National Institute on Aging, and Reagan Institute Working Group on Diagnostic Criteria for the Neuropathological Asse**

Journal: Neurobiology of aging 1997 Jul-Aug; 18(4 Suppl) S1-2

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## Pathology > Autopsy - General

Post-mortem interval : pmi      Time interval in hours from time of death to autopsy

**Post-mortem interval (PMI)** refers to the interval between death and tissue preservation in hours

### References

**Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

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## Pathology > Beta-Amyloid

Amyloid : amyloid      Overall amyloid level - Mean of 8 brain regions

**Amyloid beta** protein identified by molecularly-specific immunohistochemistry and quantified by image analysis. Value is percent area of cortex occupied by amyloid beta. Mean of amyloid beta score in 8 regions (4 or more regions are needed to calculate).

### 8 regions used

amyloid\_hip - hippocampus

amyloid\_ec - entorhinal cortex

amyloid\_mf - midfrontal cortex

amyloid\_it - inferior temporal

amyloid\_ag - angular gyrus

amyloid\_calc - calcarine cortex

amyloid\_cg - anterior cingulate cortex

amyloid\_sf - superior frontal cortex

RADC recommendation: use AMYLSQRT when using as outcome variable in models. (mean of the square-root; has better statistical properties)

*Item level variables are available upon request.*

## References

### **Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

Diffuse plaque burden :  
plaq\_d

Diffuse plaque summary based on 5 regions

**Diffuse plaque burden** is determined by microscopic examination of silver-stained slides from 5 regions: midfrontal cortex, midtemporal cortex, inferior parietal cortex, entorhinal cortex, and hippocampus. The count of each region is scaled by dividing by the corresponding standard deviation. The 5 scaled regional measures are then averaged to obtain a summary measure for diffuse plaque burden.

Diffuse plaque pathology counts by region:

Region	Variable
Entorhinal cortex	plaq_d_ec
Hippocampus (CA1)	plaq_d_hip
Midtemporal cortex	plaq_d_mt
Inferior parietal cortex	plaq_d_ag
Midfrontal cortex	plaq_d_mf
Burden across regions	plaq_d

Notes: Counts may be missing for regions (e.g., due to damage from infarct). If data are present for at least 2 of 5 regions, the summary measure for diffuse plaque burden is computed.

Item level variables are available upon request.

This variable replaces dp.

## References

### **Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

## Neuritic plaque burden : plaq\_n

### Neuritic plaque summary based on 5 regions

**Neuritic plaque burden** is determined by microscopic examination of silver-stained slides from 5 regions: midfrontal cortex, midtemporal cortex, inferior parietal cortex, entorhinal cortex, and hippocampus. The count of each region is scaled by dividing by the corresponding standard deviation. The 5 scaled regional measures are then averaged to obtain a summary measure for neuritic plaque burden.

Neuritic plaque pathology counts by region:

Region	Variable
Entorhinal cortex	plaq_n_ec
Hippocampus (CA1)	plaq_n_hip
Midtemporal cortex	plaq_n_mt
Inferior parietal cortex	plaq_n_ag
Midfrontal cortex	plaq_n_mf
Burden across regions	plaq_n

Notes: Counts may be missing for regions (e.g., due to damage from infarct). If data are present for at least 2 of 5 regions, the summary measure for neuritic plaque burden is computed.

Item level variables are available upon request.

This variable replaces np.

### References

#### **Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

## Pathology > Hippocampal sclerosis

### Hippocampal sclerosis (Typical) : hspath\_typ

### Definite presence of typical hippocampal sclerosis

**Hippocampal sclerosis (typical)** was evaluated unilaterally in a coronal section of the midhippocampus at the level of the lateral geniculate body, and graded as absent or present based on severe neuronal loss and gliosis

in CA1 and/or subiculum. Involvement of other sectors was also documented.

### Coding

0 = not present or possible or rated as present but atypical

1 = Hippocampal Sclerosis was rated as definitely present with CA1 region affected

### References

#### Hippocampal sclerosis and TDP-43 pathology in aging and Alzheimer disease.

Nag S, Yu L, Capuano AW, Wilson RS, Leurgans SE, Bennett DA, Schneider JA

Journal: Annals of neurology 2015 Feb 23; 77(6) 942-52

### Pathology > Lewy body/PD

Lewy Body disease :  
dlbdx

#### Pathologic diagnosis of Lewy body diseases - 4 stages

**Pathologic diagnosis of Lewy Body disease** describes 4 stages of distribution of  $\alpha$ -synuclein in the brain based on algorithm and neuropathologist's opinion. Sections (6  $\mu$ m) of paraffin-embedded brain tissue (from midfrontal, midtemporal, inferior parietal, anterior cingulate, entorhinal and hippocampal cortices, basal ganglia and midbrain) were stained for  $\alpha$ -synuclein immunostain (Zymed; 1:50). Immunohistochemistry was performed using the VECTASTAIN ABC method with alkaline phosphatase as the colour developer. McKeith criteria (McKeith et al., 1996) were modified to assess the following categories of Lewy body disease:

value	coding
0	not present
1	nigral-predominant
2	limbic-type
3	neocortical-type

Nigral Lewy bodies were identified as round, intracytoplasmic structures with a darker halo. In the cortex, Lewy bodies were identified as round intracytoplasmic structures, often lacking any halo and with an eccentric nucleus. Only intracytoplasmic Lewy bodies were used as an indicator of positive staining.

Note: Both limbic type and neocortical lewy body disease - are considered "cortical" Lewy body disease; however in our study (and others) only neocortical are related to dementia.

### References



**Cognitive impairment, decline and fluctuations in older community-dwelling subjects with Lewy bodies.**

Schneider JA, Arvanitakis Z, Yu L, Boyle PA, Leurgans SE, Bennett DA

Journal: Brain : a journal of neurology 2012 Oct; 135(Pt 10) 3005-14

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**Pathology > PHF tau tangles****Neurofibrillary tangle  
burden : nft****Neurofibrillary tangle summary based on 5 regions**

**Neurofibrillary tangle burden** is determined by microscopic examination of silver-stained slides from 5 regions: midfrontal cortex, midtemporal cortex, inferior parietal cortex, entorhinal cortex, and hippocampus. The count of each region is scaled by dividing by the corresponding standard deviation. The 5 scaled regional measures are then averaged to obtain a summary measure for neurofibrillary tangle burden.

Neurofibrillary tangle pathology counts by region:

Region	Variable
Entorhinal cortex	nft_ec
Hippocampus (CA1)	nft_hip
Midtemporal cortex	nft_mt
Inferior parietal cortex	nft_ag
Midfrontal cortex	nft_mf
Burden across regions	nft

Notes: Counts of tangles may be missing for regions (e.g., due to damage from infarct). If data are present for at least 2 of 5 regions, the summary measure for neurofibrillary tangle burden is computed.

Item level variables are available upon request.

**References****Religious Orders Study and Rush Memory and Aging Project.**

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

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**Tangles : tangles****Tangle density - Mean of 8 brain regions**

Neuronal neurofibrillary **tangles** are identified by molecularly specific immunohistochemistry (antibodies to

abnormally phosphorylated Tau protein, AT8). Cortical density (per mm<sup>2</sup>) is determined using systematic sampling. Mean of tangle score in 8 regions (4 or more regions are needed to calculate).

### 8 regions used

tangles\_hip - hippocampus  
tangles\_ec - entorhinal cortex  
tangles\_mf - midfrontal cortex  
tangles\_it - inferior temporal  
tangles\_ag - angular gyrus  
tangles\_calc - calcarine cortex  
tangles\_cg - anterior cingulate cortex  
tangles\_sf - superior frontal cortex

*Item level variables are available upon request.*

## References

### Religious Orders Study and Rush Memory and Aging Project.

Bennett DA, Buchman AS, Boyle PA, Barnes LL, Wilson RS, Schneider JA

Journal: Journal of Alzheimer's disease : JAD 2018 May 26; 64(s1) S161-S189

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## Pathology > TDP-43

TDP-43 stage :  
tdp\_stage4

### TDP-43 pathology - 4 stages

**TDP-43** immunohistochemistry was performed on 6 sections of the brain: amygdala, hippocampus (CA1 and dentate), and midfrontal, midtemporal, and entorhinal cortices using a rat phosphorylated monoclonal TAR5P-1D3 (pS409/410; 1:100; Ascenion, Munich, Germany) TDP-43 antibody.

Three stages of TDP-43 distribution were recognized (stage 1, localized to amygdala; stage 2, extension to hippocampus and/or entorhinal cortex; stage 3, extension to the neocortex), and the severity of the TDP-43 cytoplasmic inclusions in neurons and glia were rated on a 6-point scale

value	coding
0	None
1	stage 1 - amygdala only
2	stage 2 - Limbic (TDP-43 in hippocampus)

value	coding
3	stage 3 - neocortical

## References

### **Hippocampal sclerosis and TDP-43 pathology in aging and Alzheimer disease.**

Nag S, Yu L, Capuano AW, Wilson RS, Leurgans SE, Bennett DA, Schneider JA

Journal: Annals of neurology 2015 Feb 23; 77(6) 942-52

### **Temporal lobar predominance of TDP-43 neuronal cytoplasmic inclusions in Alzheimer disease.**

Hu WT, Josephs KA, Knopman DS, Boeve BF, Dickson DW, Petersen RC, Parisi JE

Journal: Acta neuropathologica 2008 Aug; 116(2) 215-20

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## Pathology > Vascular - General measures

Arteriolosclerosis :  
arteriol\_scler

Arteriolosclerosis - 4 stages

### Arteriolosclerosis

We used the term arteriolosclerosis to describe the histological changes commonly found in the small vessels of the brain in aging. Histological changes include intimal deterioration, smooth muscle degeneration, and fibrohyalinotic thickening of arterioles with consequent narrowing of the vascular lumen. Lipohyalinosis is sometimes used to describe this change but was originally used to describe vessels that had first undergone fibrinoid change. Because there are no standard guidelines to grade severity of arteriolosclerosis (or lipohyalinosis), we evaluated the vessels of the anterior basal ganglia with a semiquantitative grading system from 0 (none) to 7 (occluded). These levels were compressed into the 4 levels listed below.

value	coding
0	None
1	Mild
2	Moderate
3	Severe

## References

### **Cerebrovascular disease pathology and parkinsonian signs in old age.**

Buchman AS, Leurgans SE, Nag S, Bennett DA, Schneider JA

Journal: Stroke 2011 Nov; 42(11) 3183-9

## Cerebral amyloid angiopathy : caa\_4gp

### Cerebral amyloid angiopathy - 4 stages

We created a semiquantitative summary of **cerebral amyloid angiopathy** (CAA) pathology in 4 neocortical regions: midfrontal, midtemporal, parietal, and calcarine cortices. Paraffin-embedded sections were immunostained for beta-amyloid using 1 of 3 monoclonal anti-human antibodies: 4G8 (1:9000; Covance Labs, Madison, WI), 6F/3D (1:50; Dako North America Inc., Carpinteria, CA), and 10D5 (1:600; Elan Pharmaceuticals, San Francisco, CA).

CAA assessment was similar to a recently proposed protocol (Love et al., 2014): for each region, meningeal and parenchymal vessels were assessed for amyloid deposition and scored from 0 to 4, where:

0=no deposition

1=scattered segmental but no circumferential deposition

2=circumferential deposition up to 10 vessels

3=circumferential deposition up to 75% of the region

4=circumferential deposition over 75% of the total region.

CAA score for each region was the maximum of the meningeal and parenchymal CAA scores. Scores were averaged across regions and summarized as a continuous measure of CAA pathology.

For the semiquantitative summary, we classified CAA scores into a 4-level severity rating using cutoffs determined by the neuropathologist:

Value	Meaning	Definition
0	None	Average = 0
1	Mild	Average <1.5 (between 0.25 and 1.4)
2	Moderate	Average 1.5 to 2.5
3	Severe	Average > 2.5

### References

#### **Cerebral amyloid angiopathy and cognitive outcomes in community-based older persons.**

Boyle PA, Yu L, Nag S, Leurgans S, Wilson RS, Bennett DA, Schneider JA

Journal: Neurology 2015 Nov 4; 85(22) 1930-6

## Cerebral atherosclerosis : cvda\_4gp2

### Cerebral Atherosclerosis Rating - 4 levels (None - severe)

Large vessel **cerebral atherosclerosis rating** was made by visual inspection after paraformaldehyde fixation, at the Circle of Willis at the base of the brain, and included evaluation of the vertebral, basilar, posterior cerebral, middle cerebral, and anterior cerebral arteries and their proximal branches. Severity was graded by visual examination of the extent of involvement of each artery and number of arteries involved. Arteries were bisected for evaluation of luminal narrowing when there was concern by appearance or palpation for occlusion; and degree of occlusion was also considered in the final score. We did not consider tortuosity or aneurysmal dilatation, and did not perform histologic evaluation.

We used a semiquantitative scale from 0 (no atherosclerosis) to 6 (severe atherosclerosis) (variable = cvda), which was then collapsed into 4 levels for analyses:

value	coding	description
0	None or Possible	No significant atherosclerosis observed
1	Mild	Small amounts in up to several arteries (typically less than 25% vessel involvement) without significant occlusion
2	Moderate	In up to half of all visualized major arteries, with less than 50% occlusion of any single vessel
3	Severe	In more than half of all visualized arteries, and/or more than 75% occlusion of one or more vessels

## References

### The Relationship of Cerebral Vessel Pathology to Brain Microinfarcts.

Arvanitakis Z, Capuano AW, Leurgans SE, Buchman AS, Bennett DA, Schneider JA

Journal: Brain pathology (Zurich, Switzerland) 2016 Feb 4; 27(1) 77-85

## Pathology > Vascular - Infarcts (Presence of)

Presence of one or more gross chronic infarcts :  
ci\_num2\_gct

### Cerebral Infarctions - Binary - Gross-Chronic-Any Location

Presence of one or more **gross chronic cerebral infarctions**, determined by neuropathologic evaluations performed at Rush, blinded to clinical data, and reviewed by a board-certified neuropathologist.

Examination of infarcts documents age (acute/subacute/chronic), size, and location (side and region) of infarcts visible to the naked eye on fixed slabs. All grossly visualized and suspected macroscopic infarcts are dissected for histologic confirmation.

Value	Coding
0	No gross chronic Infarctions
1	One or more gross chronic infarctions (regardless of location)

Total gross infarcts (acute + subacute +chronic) are available upon request.

Counts (as opposed to presence of 1 or more) are available upon request.

## References

### **The apolipoprotein E epsilon4 allele increases the odds of chronic cerebral infarction [corrected] detected at autopsy in older persons.**

Schneider JA, Bienias JL, Wilson RS, Berry-Kravis E, Evans DA, Bennett DA

Journal: Stroke 2005 May; 36(5) 954-9

### **Microinfarct pathology, dementia, and cognitive systems.**

Arvanitakis Z, Leurgans SE, Barnes LL, Bennett DA, Schneider JA

Journal: Stroke 2011 Mar; 42(3) 722-7

Presence of one or more  
chronic microinfarcts :  
ci\_num2\_mct

## Cerebral Infarctions - Binary - Micro-Chronic-Any Location

Presence of one or more **chronic microinfarcts** (i.e., chronic microscopic infarctions) as determined by neuropathologic evaluations performed at Rush, blinded to clinical data, and reviewed by a board-certified neuropathologist.

A minimum of nine regions in one hemisphere are examined for microinfarcts on 6µm paraffin-embedded sections, stained with hematoxylin/eosin. We examine six cortical regions (midfrontal, middle temporal, entorhinal, hippocampal, inferior parietal, and anterior cingulate cortices), two subcortical regions (anterior basal ganglia, thalamus), and midbrain. Age (acute/subacute/chronic) and location (side and region) of microinfarcts are recorded.

Value	Coding
0	No chronic microinfarcts
1	One or more chronic microinfarcts (regardless of location)

Total microinfarcts (acute + subacute +chronic) are available upon request.

Counts (as opposed to presence of 1 or more) are available upon request.

## References

**Microinfarct pathology, dementia, and cognitive systems.**

Arvanitakis Z, Leurgans SE, Barnes LL, Bennett DA, Schneider JA

Journal: Stroke 2011 Mar; 42(3) 722-7

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