SNOMED CT and LOINC for computable phenotypes in Alzheimer's Disease

SNOMED CT Expo 2019

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Learning Objectives

- Understand the importance of Alzheimer's Disease in geriatric medicine
- Define the concept of "computable phenotype"
- Appreciate the requirements and challenges of conducting observational research in Alzheimers Disease
- Understand the value of electronic health record data encoded with SNOMED CT and LOINC in supporting research in Alzheimers Disease

Alzheimers Dementia(AD)

- US population is aging; geriatric medicine and supporting function of elderly increasingly important in healthcare
- Causes of progressive dementia:
  - Alzheimers disease 50-70%
  - Lewy Body disease
  - Frontotemporal disorders (age < 65)
  - Vascular disease
  - …

Alzheimers Dementia

- Historically, an autopsy diagnosis without clinical prevention or treatment
- Genomic research has demonstrated APOE, PSEN*, APP genes are contributory
- CNS degeneration relates to formation of beta amyloid deposition and subsequent neurofibrillary tangles/degeneration and ultimately cerebral atrophy
- Current nosology and research indicates that amyloid involvement and neurodegeneration is progressive with stages of CNS neuropathology increasingly understood and characterized
- Clinical (symptomatic) correlation is variable and not definitive but understood; asymptomatic → mild cognitive impairment → dementia

BD2K Extension
NIH 5U01HG009455-02

"The National Institute on Aging Alzheimer's Association (NIA-AA) Research Framework released in February 2018 clearly states the need for a common language with which researchers can communicate findings clearly and unambiguously to reliably compare research results and discovery. "

Develop, deploy and test extended standards in support of research, clinical care and epidemiology

BD2K Extension
NIH 5U01HG009455-02

- Develop, test, and deploy ONC national data standards to support EHR data repurposing and interoperability for AD and related dementias
- Support computable phenotyping of critical diagnostic, findings and treatment datasets
- Workplan:
  - Evaluate ONC data standardization for reference professional organization datasets
  - Evaluate standardization deficits: SNOMED CT, LOINC-SNOMED Observables, RXNORM-SNOMED Pharmaceuticals
  - Develop, deploy and test extended standards in support of research, clinical care and epidemiology

Computable Phenotype

- "A **computable phenotype** refers to a set of findings or conditions that can be evaluated via a computerized query to an EHR or clinical data research network"
- In the era of the Learning Healthcare System, CPs are increasingly important in semi-automated network patient recruitment and outcomes research
- Requires that the EHR maintain well-structured, coded and interoperable data

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Clinical Professional Standards

- National Institute on Aging
- Alzheimers Association
- NIAA-AA diagnostic framework and criteria (2011, 2018)
- National Alzheimers Coordinating Center
- World Health Organization: IWG-2 diagnostic criteria (2014)

Clinical Assessment Tools

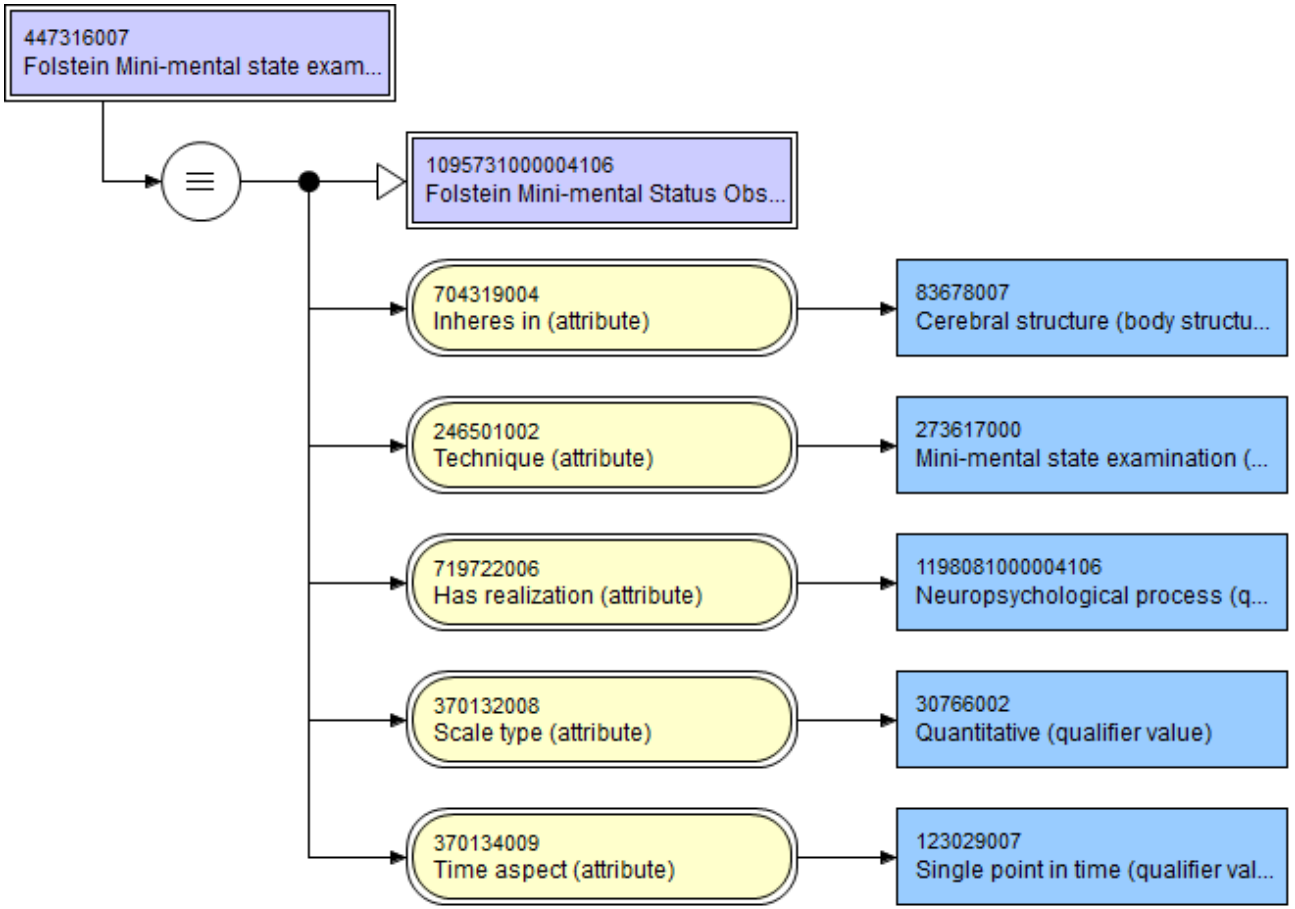
Cognitive Impairment, Mood Disorders and Functional Assessment

- Montreal Cognitive Assessment (27)
- Mini-mental Status Examination (12)
- Short Test of Mental Status (9)
- Geriatric Depression Scale (36)
- Barthel Index (ADLs) (11)
- Functional Activities Questionnaire (IADLs) (11)
- Unified Parkinsons Disease Rating Scale (42)
- Neuropsychological examination

Terminology Development Procedures

- Coordinated with IHTSDO Observables project to assure consistency in use of concept model for cognitive testing and autopsy
- Extended SNOMED CT for genomic observables and clinical findings
- From semantic analysis of instruments, developed Observables for results and Clinical findings for diagnoses as needed

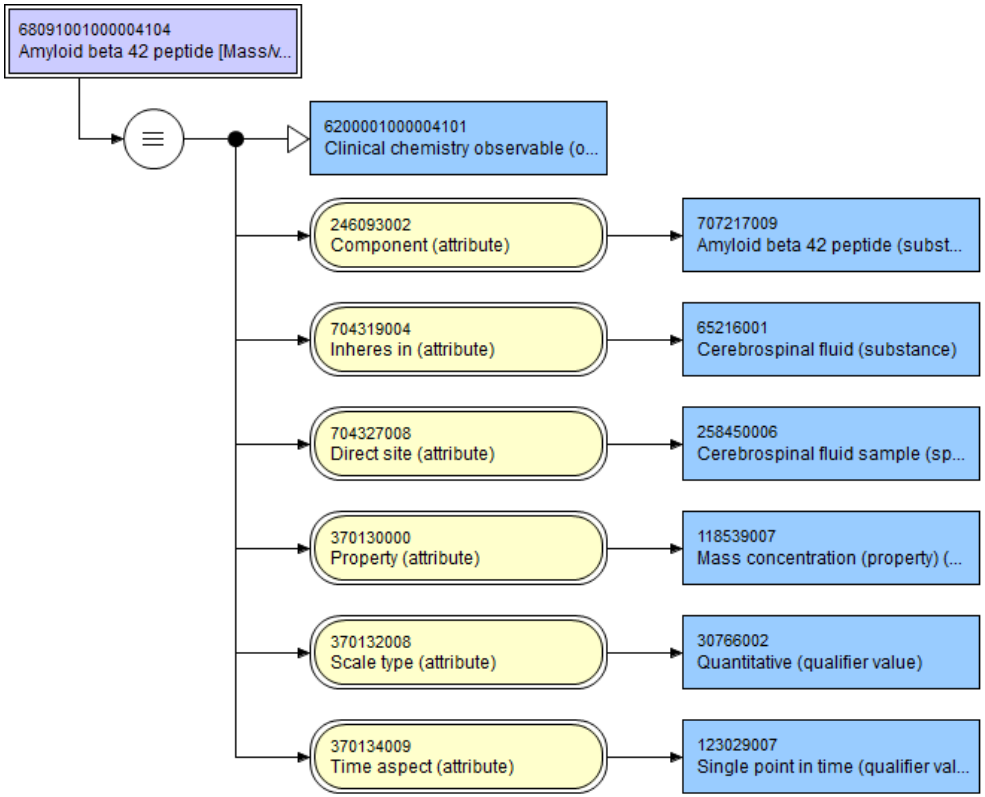
LOINC:72106-8 Folstein mini-mental state examination total score (Observable entity)



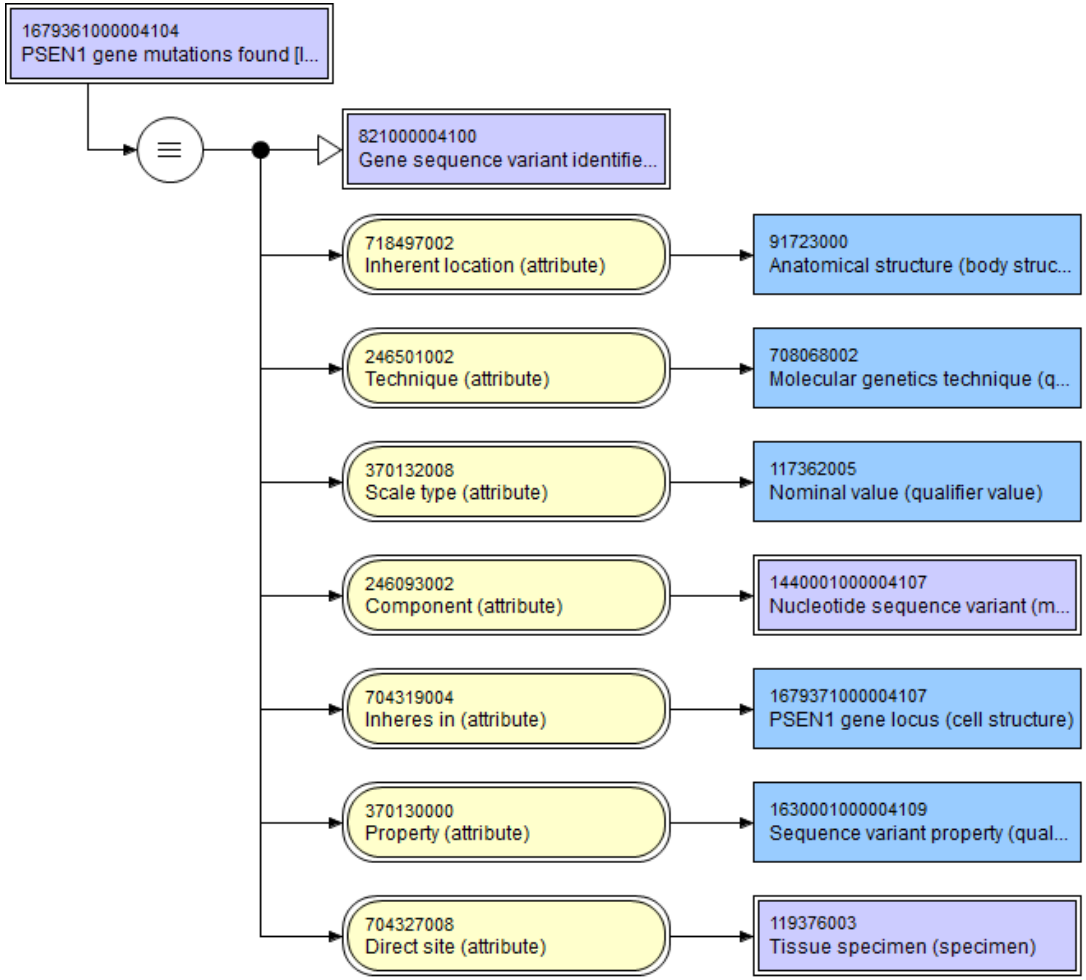
Clinical Biomarkers
Amyloid/Tau protein/Neurodegeneration

- Laboratory: LOINC coding comprehensive since v2.04
  - CSF Aβ42, phosphorylated Tau, total Tau
  - Gene sequencing PSEN*, APP, APOE; (FUS, C9ORF72, MAPT, GRN, SNC*, CHMP2B, GRN, TARDBP)
- Radiology: LOINC > v2.63
  - Head CT
  - Brain and spinal MRI, functional MRI
  - Brain PET with FDG, amyloid, tau
- No interoperation definitions for IUPAC or SNOMED community

LOINC:33203-1 Amyloid beta 42 peptide [Mass/volume] in Cerebral spinal fluid (Observable entity)



LOINC:35299-7 PSEN1 gene mutations found [Identifier] in Tissue by Molecular genetics (Observable entity)



Supportive Therapies

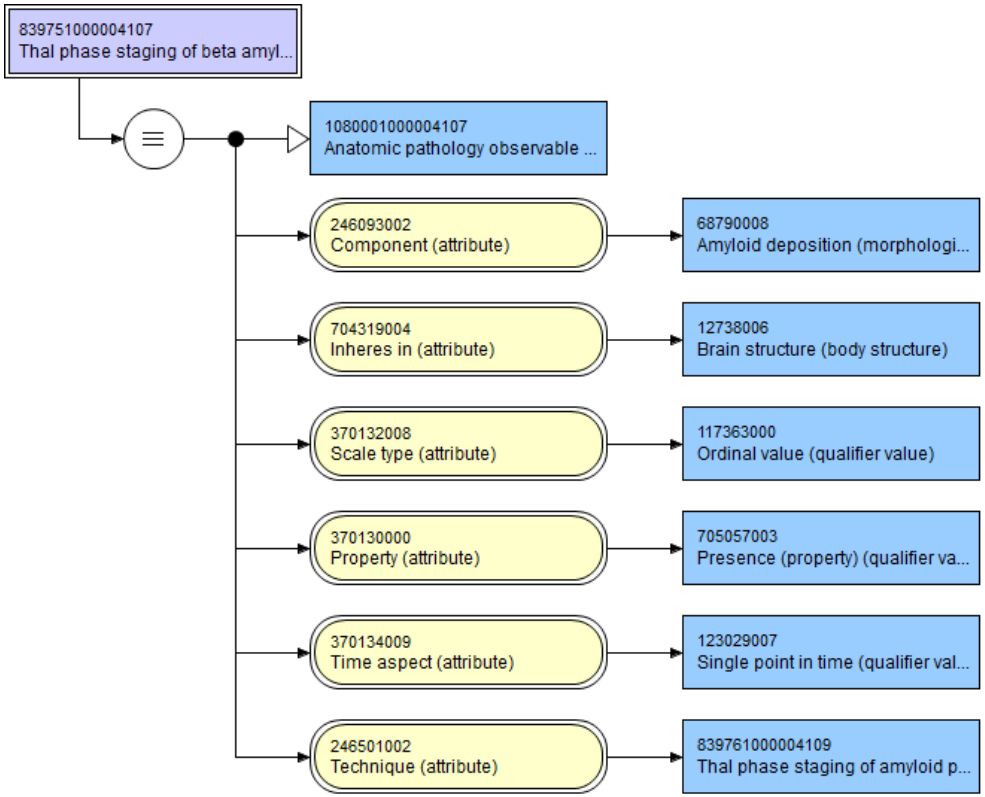
- Cholinesterase inhibitors:
  - Donepezil(Aricept) 10 mg oral tablet
  - RXNORM: 997223
  - SNOMED CT: 323365007
- Anti-psychotics
- Antidepressents
- Bipolar treatments
- Parkinsons therapies
- >2900 medications; US pharmacopoeia complete in RXNORM; well-represented in SNOMED CT

CNS Autopsy

National Association for Alzheimers Coordinating Center (U Washington) Neuropathology Data Set v10

- Data dictionaries published and maintained since 2006 but no reference coding standards
- 90+ data items aligned with revision of NIA-AA criteria(2014)
- No ONC LOINC, SNOMED CT or ICD* data encoding

Observable:
Thal phase staging of beta amyloid plaques in brain



Rüb U, Stratmann K, Heinsen H, Turco DD, Seidel K, Dunnen Wd, Korf HW. The Brainstem Tau Cytoskeletal Pathology of Alzheimer's Disease: A Brief Historical Overview and Description of its Anatomical Distribution Pattern, Evolutional Features, Pathogenetic and Clinical Relevance. Curr Alzheimer Res. 2016;13(10):1178-97.

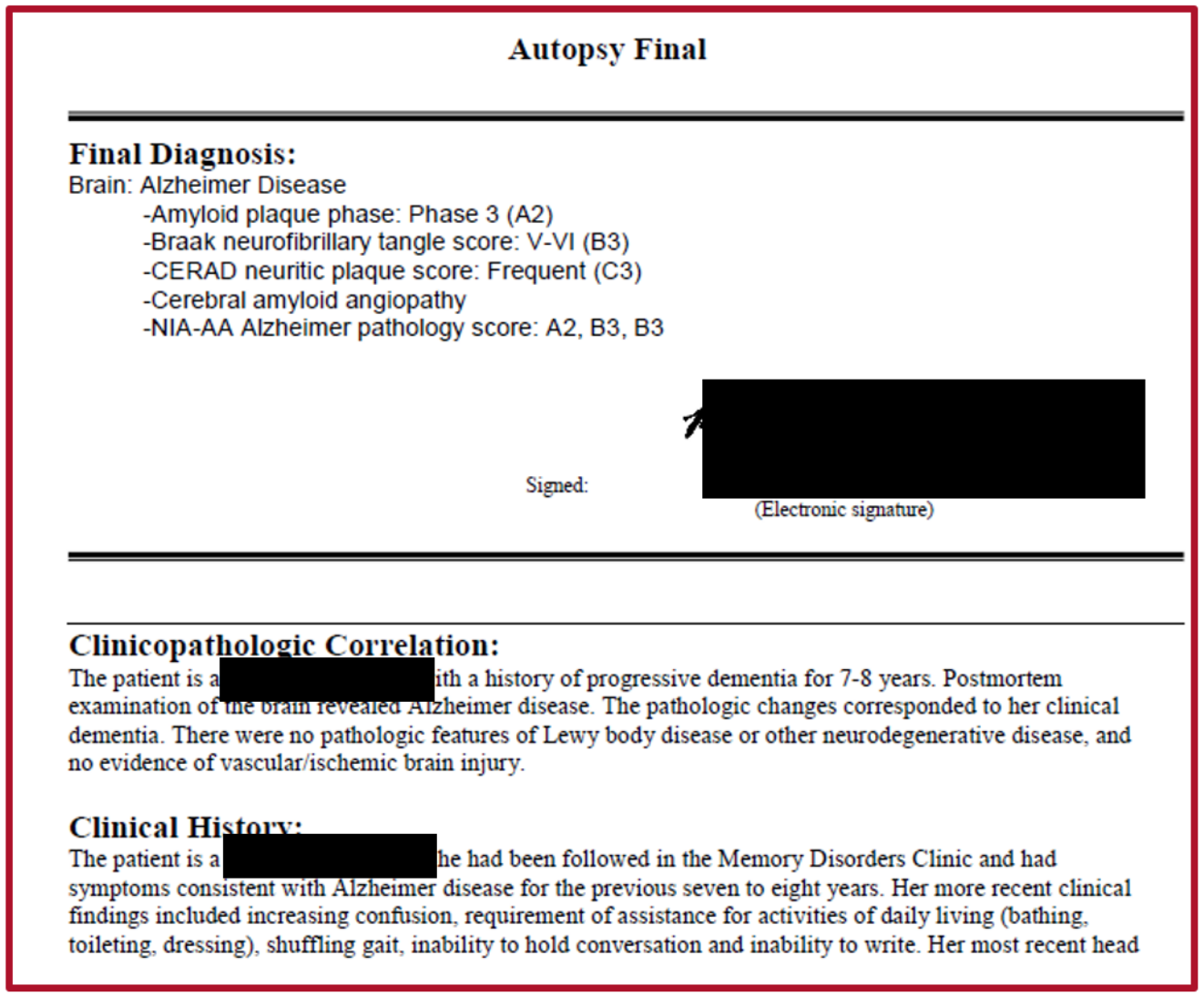
Terminology Review and Development

	SNOMED CT	LOINC	TOTAL
Clinical Assessment	(18 Neb Observables)	37	148
Clinical Biomarkers	Most as Procedures	88	16
Therapies	100% Subst/PharmProd	--	2915
Autopsy	(82 Neb Observables)	0	82
Diagnoses	(29 Neb ClinFind) 40 ClinFind	--	69

(Nebraska Lexicon extension concepts developed for project)

Validation:
50 autopsy cases with dementia

Obse	
Thal p	
Braak	
CERA	
Weigl	s
Prese	/48
Prese	/42
Prese	/38
Prese	/35
...tota	



Autopsy Final

Final Diagnosis:

Brain: Alzheimer Disease

-Amyloid plaque phase: Phase 3 (A2)
-Braak neurofibrillary tangle score: V-VI (B3)
-CERAD neuritic plaque score: Frequent (C3)
-Cerebral amyloid angiopathy
-NIA-AA Alzheimer pathology score: A2, B3, B3

Signed: [redacted]
(Electronic signature)

Clinicopathologic Correlation:

The patient is a [redacted] ith a history of progressive dementia for 7-8 years. Postmortem examination of the brain revealed Alzheimer disease. The pathologic changes corresponded to her clinical dementia. There were no pathologic features of Lewy body disease or other neurodegenerative disease, and no evidence of vascular/ischemic brain injury.

Clinical History:

The patient is a [redacted] he had been followed in the Memory Disorders Clinic and had symptoms consistent with Alzheimer disease for the previous seven to eight years. Her more recent clinical findings included increasing confusion, requirement of assistance for activities of daily living (bathing, toileting, dressing), shuffling gait, inability to hold conversation and inability to write. Her most recent head

Validation:
50 autopsy cases with dementia

Observable entity	Median
Thal phase staging beta amyloid plaques in brain	Stage 3-4
Braak stage neurofibrillary degeneration in brain	Stage 4
CERAD score for neuritic plaques in brain	Moderate-Frequent
Weight of whole brain	1243 grams
Presence of meningeal pathology	Present 15/48
Presence of atherosclerosis	Present 24/42
Presence of cerebral cortical atrophy of brain on gross exam	Present 35/38
Presence ventricular dilatation on gross exam	Present 24/35
…total of 82 data items	

Final Diagnoses:
50 autopsy cases with dementia

SNOMED CT	Fully Specified Name	#
481291000004108	Intermediate level Alzheimers neuropathology changes (disorder)	23
481311000004107	High level Alzheimers neuropathology changes (disorder)	13
230724001	Cerebral amyloid angiopathy (disorder)	8
278849000	Cerebral atrophy (disorder)	8
62914000	Cerebrovascular disease (disorder)	8
80098002	Diffuse Lewy Body Disease	7
471041000004103	Low level Alzheimers neuropathology changes (disorder)	6
256081000004103	Alzheimers type II astrocytosis neuropathologic changes (finding)	5
2032001	Cerebral edema (disorder)	5

Conclusions

- Computable phenotyping in AD is a major challenge due to the paucity of coded data
- Significant SNOMED CT terminology development is required to support clinical assessment, neuroanatomical reporting and diagnostic granularity for clinical care and research in Alzheimers Dementia
- Both SNOMED CT and LOINC are insufficient for capturing datasets supporting cognitive assessment tools and neuroanatomical autopsy

Questions?

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