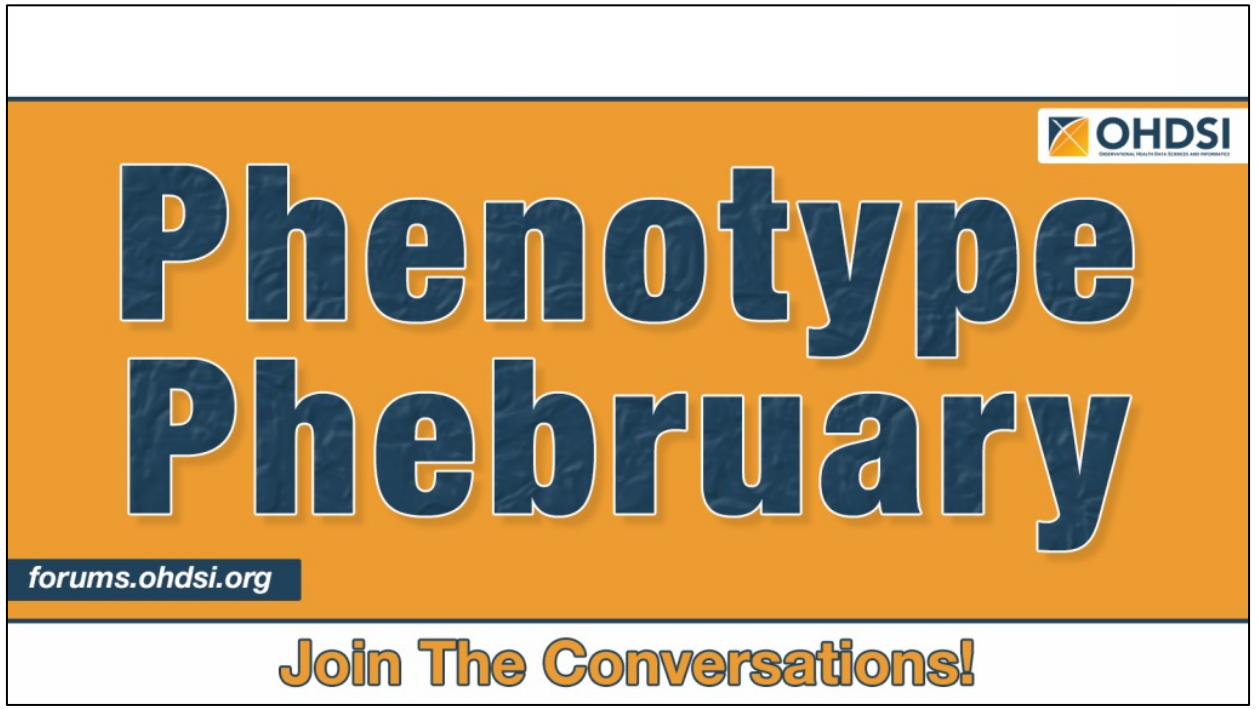
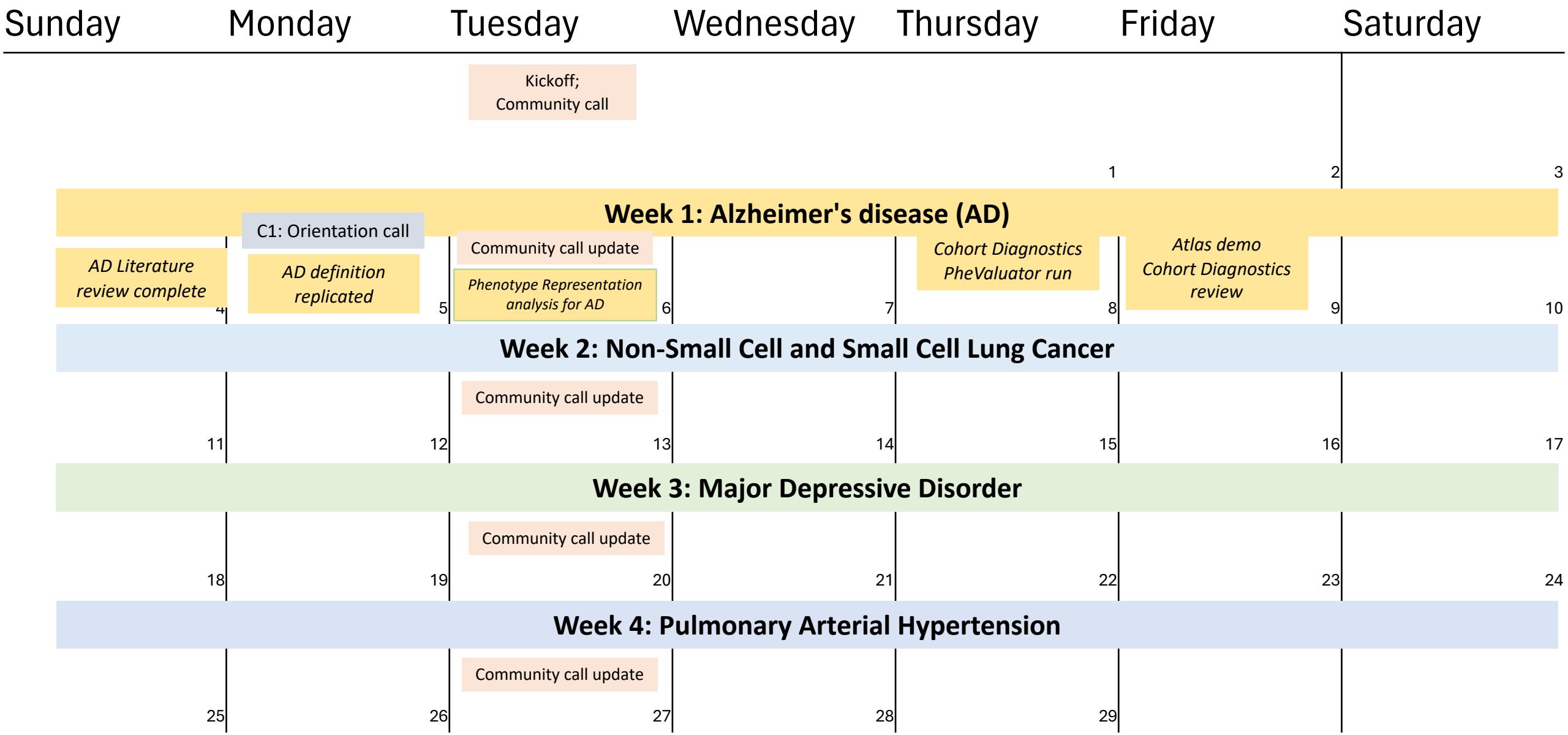
2024 Edition



February 6th, 2024

Community call update

Phenotype Phebruary 2024 Calendar



Our literature search results

- Query: 200 papers
- Filter by calendar year
- Post review: 20 paper

summary-AlzheimerD-set.txt

```
1: Nicholas LH, Langa KM, Bynum JPW, Hsu JW. Financial Presentation of Alzheimer
Disease and Related Dementias. JAMA Intern Med. 2021 Feb 1;181(2):220-227. doi:
10.1001/jamainternmed.2020.6432. Erratum in: JAMA Intern Med. 2021 Feb
1;181(2):296. PMID: 33252621; PMCID: PMC7851732.

2: Pourhadi N, Mørch LS, Holm EA, Torp-Pedersen C, Meaidi A. Menopausal hormone
therapy and dementia: nationwide, nested case-control study. BMJ. 2023 Jun
28;381:e072770. doi: 10.1136/bmj-2022-072770. Erratum in: BMJ. 2023 Jun
29;381:p1499. PMID: 37380194; PMCID: PMC10302215.

3: McCarthy EP, Chang CH, Tilton N, Kabeto MU, Langa KM, Bynum JPW. Validation
of Claims Algorithms to Identify Alzheimer's Disease and Related Dementias. J
Gerontol A Biol Sci Med Sci. 2022 Jun 1;77(6):1261-1271. doi:
10.1093/gerona/glab373. PMID: 34919686; PMCID: PMC9159657.

4: Beason-Held LL, Kerley CI, Chaganti S, Moghekar A, Thambisetty M, Ferrucci L,
Resnick SM, Landman BA. Health Conditions Associated with Alzheimer's Disease
and Vascular Dementia. Ann Neurol. 2023 Apr;93(4):805-818. doi:
10.1002/ana.26584. Epub 2023 Jan 18. PMID: 36571386.

5: Manemann SM, Knopman DS, St Sauver J, Bielinski SJ, Chamberlain AM, Weston
SA, Jiang R, Roger VL. Alzheimer's disease and related dementias and heart
failure: A community study. J Am Geriatr Soc. 2022 Jun;70(6):1664-1672. doi:
10.1111/jgs.17752. Epub 2022 Mar 18. PMID: 35304739; PMCID: PMC9177760.
```

- Replicated 13– as cohort definitions
  - 2 papers could not be replicated

15489	[PhePheb] Alzheimers disease per Riedel 2022
15490	[PhePheb] Alzheimers disease per Imfeld, 2013
15488	[PhePheb] Alzheimer disease per Chen 2020
15487	[PhePheb] Alzheimer dementia per Grande 2020
15486	[PhePheb] Alzheimers disease per Harris JAD 2023
15483	[PhePheb] 27 CCW Alzheimers disease and related disorders or senile dementia Bynum-standard revision
15482	[PhePheb] 27 CCW Alzheimers disease and related disorders or senile dementia - Bynum-EM revision
15481	[PhePheb] 27 CCW Alzheimers disease and related disorders or senile dementia
15480	[PhePheb] 27 CCW Alzheimers disease
15478	[PhePheb] 30 CCW Alzheimers disease

What we learned about Alzheimer so far

- Variation in terminology
- Variation in use of diagnose codes
- Variation in inclusion criteria (logic)

Shift in terminology: Alzheimer's disease (AD) or Alzheimer's Disease Related Dementia (ADRD)

- ADRD is umbrella Term: AD and related conditions like vascular, Lewy body, frontotemporal dementia.
- ADRD Background: Introduced by Law, the National Alzheimer's Project Act (NAPA) passed by US Congress in 2011.
  - Inclusivity: Recognizes the spectrum of dementia-related disorders beyond Alzheimer's.
- Usage
  - Increasing use in health research and policy.
  - Not used in clinical practice because of diagnosis specificity (physicians diagnose specific types of dementia rather than using the broad term ADRD)

Condition	Alzheimer's Disease	Lewy Body Dementia (LBD)	Frontotemporal Dementia (FTD)	Vascular Contributions to Cognitive Impairment and Dementia (VCID)	Mixed Dementias
Definition	A progressive neurodegenerative disorder characterized by memory loss and cognitive decline.	A type of dementia associated with abnormal protein deposits in the brain known as Lewy bodies.	A group of disorders caused by progressive cell loss in the brain's frontal or temporal lobes.	Cognitive impairment caused by cerebrovascular problems that affect brain blood flow.	A condition featuring symptoms and pathological features of more than one type of dementia.
Pathognomonic Feature	Amyloid plaques and neurofibrillary tangles in the brain.	Presence of Lewy bodies, abnormal aggregates of protein in neurons.	Prominent atrophy in frontal and/or temporal lobes of the brain.	Evidence of cerebrovascular disease contributing to cognitive impairment.	Combination of pathologies such as Alzheimer’s and vascular dementia.
Diagnostic Criteria	Clinical diagnosis supported by imaging and biomarkers; exclusion of other dementias.	Clinical diagnosis based on core features, with possible biomarker support.	Diagnosis based on clinical presentation, imaging, and ruling out other causes.	Evidence of vascular disease via imaging, aligned with cognitive decline.	Clinical assessment and imaging to identify multiple types of dementia pathologies.
Characteristic Clinical Feature	Memory loss, confusion, difficulty with problem-solving and language.	Fluctuating cognition, visual hallucinations, Parkinsonism.	Changes in behavior and personality, language difficulties.	Stepwise cognitive decline, history of strokes or vascular risk factors.	Symptoms that are not fully explained by one type of dementia alone.
Distinguishing Trait	Gradual memory decline as an early and prominent feature.	Fluctuating cognitive symptoms and visual hallucinations.	Early changes in behavior or language, relative preservation of memory.	History of stroke or vascular disease, with stepwise decline.	Mixed presentation of symptoms, not typical of one single dementia type.
Promising Treatments in Research	Research on anti-amyloid and tau therapies, neuroprotective agents.	Studies on alpha-synuclein inhibitors, neuroprotective strategies.	Research focuses on tau protein inhibitors and behavioral management.	Emphasis on vascular health, managing risk factors, neuroprotective drugs.	Combination therapies targeting multiple pathological processes.

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Condition	Alzheimer's Disease	Lewy Body Dementia (LBD)	Frontotemporal Dementia (FTD)	Vascular Contributions to Cognitive Impairment and Dementia (VCID)	Mixed Dementias
Defini	A progressive neurodegenerative	A type of dementia associated with abnormal	A group of disorders		A condition featuring symptoms and
Pathog					
Diagnc					
Charac Featur					
Disting					
Promising Treatments in Research	Research on anti-amyloid and tau therapies, neuroprotective agents.	Studies on alpha-synuclein inhibitors, neuroprotective strategies.	Research focuses on tau protein inhibitors and behavioral management.	Emphasis on vascular health, managing risk factors, neuroprotective drugs.	Combination therapies targeting multiple pathological processes.

Published studies varied in <u>what they defined as the clinical condition</u> with

- **older studies focusing on AD and**
- **more recent ones broadening the scope to ADRD.**

However, there was no consistency in how the specific conditions under ADRD were grouped.

"AD" was used both as "A. disease" and "A. Dementia"

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Algorithms with validation

Europe

ORIGINAL RESEARCH

How well can electronic health records from primary care identify Alzheimer's disease cases?

Fulltext | Metrics | Get Permission | Cite this article

Authors Ponjoan A, Garre-Olmo J, Blanch J, Fages E, Alves-Cabratosa L, Martí-Lluch R, Comas-Cufí M, Parramon D, García-Gil M, Ramos R

Received 26 February 2019

US

J Gerontol A Biol Sci Med Sci. 2022 Jun; 77(6): 1261–1271.
Published online 2021 Dec 17. doi: 10.1093/gerona/glab373

PMCID: PMC9159657
PMID: 34919686

Validation of Claims Algorithms to Identify Alzheimer's Disease and Related Dementias

Ellen P McCarthy, PhD, MPH, Chiang-Hua Chang, PhD, MS, Nicholas Tilton, PhD, Mohammed U Kabeto, MS, Kenneth M Langa, MD, PhD, and Julie P W Bynum, MD, MPH

Europe

ORIGINAL RESEARCH

How well can electronic health records from primary care identify Alzheimer's disease cases?

Fulltext | Metrics | Get Permission | Cite this article

Using SIDIAP data, we identified AD cases using algorithms that combined EHR, a method previously applied to identify dementia cases.[10,19] We followed Imfeld et al 2013 to define three algorithms that combine information about diagnoses and pharmacological treatment to identify AD cases (Table 1). We considered treated patients as cases because in

Algorithm	Definition of AD case
A1	Diagnosed patients: have an ICD10 code for AD (F00 or G30).
A2	Diagnosed or treated patients: have a code for AD (ICD10: F00 or G30) or for prescription or billing of anti-dementia drugs (ATC: N06DA, N06DX01).
A3	Diagnosed or treated patients without previous conditions: have a code for AD (ICD10: F00 or G30) or for prescription or billing of anti-dementia drugs (ATC: N06DA, N06DX01). Treated patients were included if they had no code of dementia diagnosis or had a code of unspecified dementia (F03), and were excluded if they had a code for: a specific subtype of dementia such as Lewy bodies dementia, vascular or frontotemporal dementia (ICD10: F01, F02); Parkinson (ICD10: G20-G22); anti-Parkinson drugs (ATC: N04); or cerebrovascular disease (ICD10:I60- I69, G45, G46) within two years prior to AD diagnosis.

J Gerontol A Biol Sci Med Sci. 2022 Jun; 77(6): 1261–1271.
Published online 2021 Dec 17. doi: 10.1093/gerona/glab373
PMCID: PMC9159657
PMID: 34919686

US

Validation of Claims Algorithms to Identify Alzheimer's Disease and Related Dementias

Ellen P McCarthy, PhD, MPH, Chiang-Hua Chang, PhD, MS, Nicholas Tilton, PhD, Mohammed U Kabeto, MS, Kenneth M Langa, MD, PhD, and Julie P W Bynum, MD, MPH✉

	CCW	Bynum-EM	Bynum-Standard
Observation Period	3 Years	1 Year and 3 Years	1 Year and 3 Years
ICD-9-CM Diagnosis Codes	331.0, 331.11, 331.19, 331.2, 331.7, 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, 294.0, 294.10, 294.11, 294.20, 294.21, 294.8, 797	331.0, 331.11, 331.19, 331.2, 331.7, **331.82, 331.89,** 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, **290.8**, 294.0, 294.10, 294.11, 294.20, 294.21, 797	331.0, 331.11, 331.19, 331.2, 331.7, **331.82, 331.89,** 290.0, 290.10, 290.11, 290.12, 290.13, 290.20, 290.21, 290.3, 290.40, 290.41, 290.42, 290.43, **290.8**, 294.0, 294.10, 294.11, 294.20, 294.21, 797
Claims Files and Qualifying Claims			
MEDPAR	Any inpatient or SNF claim	Any inpatient or SNF claim	Any inpatient or SNF claim
Home Health Agency	Any claim*	Any claim	Any claim
Hospice		Any claim	Any claim
HOF for outpatient medical services	Any claim*	Includes only claims from Rural Health Clinics, Federally Qualified Health Centers, and Critical Access Hospitals—Payment Option	Includes only claims from Rural Health Clinics, Federally Qualified Health Centers, and Critical Access Hospitals—Payment

View PDF EN

Bynum ADRD Algorithms

We evaluated whether modifications to the CCW algorithm improved classification of ADRD status by (a) shortening the observation period from 3 years to 1 year; (b) adding diagnosis codes for dementia with Lewy Bodies (331.82), other cerebral degeneration (331.89), and other nonspecified senile psychosis (290.8) based on discussion with experts in the field; and (c) modifying the claims input files by adding hospice claims and including only encounters in the hospital outpatient file (HOF) by underserved populations who receive care from Federally Qualified Health Centers, Rural Health Centers, and Critical Access Hospitals under payment option II.

We then constructed 2 new algorithms designed to address the potential for low specificity of the CCW algorithm (Table 1). In both algorithms, individuals are flagged with dementia if there is at least one qualifying claim for hospital inpatient, skilled nursing facility, home health care, or hospice service. In the first algorithm (Bynum-EM), beneficiaries could additionally be flagged if they had at least one claim for a face-to-face patient visit by a physician or other clinician determined by Berenson-Eggers Type of Service codes for "evaluation and management" (EM) services in the Carrier file or a qualifying visit in the HOF file. The second algorithm (Bynum-Standard) mimics other comorbidity algorithms by requiring 2 claims for any type of service in the Carrier file or qualifying HOF encounters by underserved populations described above that were at least 7 days apart to account for potential misclassification resulting from "rule out" diagnoses (15–17).

We ended up with 13 replicated definition

Article	Author	Citation	Year	Country	Validation	link to full text	Atlas ID
41	Imfeld	Epilepsia. 2013 Apr;54(4):700-7.	2013	UK	confirmed in 79%	https://jnj.sharepoint.com/teams/epi/Shared%20Documents/References/Alzheimers/Imfeld%20Epilepsia.%202013.pdf	15490
62	Grande	Dement Geriatr Cogn Disord. 2020;49(4):384-389	2020	Italy		Grande Dement Geriatr Cogn Disord. 2020.pdf	15487
43	McCarthy	J Gerontol A Biol Sci Med Sci. 2022 Jun 1;77(6):1261-1271. doi: 10.1093/gerona/gla	2022	US	3 yr period Sensitivity (95% CI) Specificity (95% CI) PPV (95% CI) NPV (95% CI) (1) 52.2	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9159657/	15478, 15480, 15481, 15482, 15483,
49	Riedel	Pharmacoepidemiol Drug Saf. 2022 May;31(5):546-555	2022	Germany		Riedel Pharmacoepidemiol Drug Saf. 2022.pdf	15489
57	Chen	PLoS Med. 2022 Mar 17;19(3):e1003941. doi:	2022	UK		https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8929585/	15488
51	Harris	A Claims-Based Cohort Study using Propensity Score	2023	US		https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10578243/	15486
53	Ponjoan	Clin Epidemiol . 2019 Jul 5:11:509-518. doi: 10.2147/CLEP.S206770. eCollection 2019.	2019	spain	PPV was 74.8 (95% CI: 73.1–76.4) for algorithm A1 (AD diagnoses), and 72.3 (95% CI: 70.7–73.9) for algorithm A3 (diagnosed or treated patients without	https://www.dovepress.com/how-well-can-electronic-health-records-from-primary-care-identify-alzh-peer-reviewed-fulltext-article-CLEP#T0002	15007

1 Dx vs (1 IP or 2 OP or 3 OP) vs (2 Dx or 2 Rx or (1Dx and 1Rx). Some required neurologist and some included procedures.

codes between AD and ADRD are different (and choice of codes to include vary within papers on ADRD)

What we learned about Alzheimer so far

- From Alzheimer's disease (AD) to Alzheimer's Disease Related Dementia (ADRD)
- At least 4 published articles discussing validation of AD/ADRD/Dementia algorithms (from US and Europe)
- A body of literature from Medicare
- Replicated 13 definitions.
  - Dx (2DX), RX (2RX), neurologist, inpatient vs. Outpatient,
  - Codes between AD and ADRD are different, and choice of codes varied from including general terms like "Senile degeneration of brain, not elsewhere classified" to limit to a single code of Alzheimer's disease
- Validation studies reporting PPV ranging from 50% TO 95% and sensitivity from 30-85%

Next steps

- Study package
  - Will include Cohort Diagnostics and Cohort Incidence
  - Currently being developed and tested within JNJ infrastructure
  - Once documented, will be available as R-package OHDSI-studies GitHub repository.
  - Data partners: Open for data partners to contribute

- Literature scan for other conditions
  - Contributors for lung cancer, depression and PAH selected