February 6th, 2024
Community call update
Our literature search results

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

Replicated 13– as cohort definitions
○ 2 papers could not be replicated
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)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Alzheimer’s Disease</th>
<th>Lewy Body Dementia (LBD)</th>
<th>Frontotemporal Dementia (FTD)</th>
<th>Vascular Contributions to Cognitive Impairment and Dementia (VCID)</th>
<th>Mixed Dementias</th>
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<td><strong>Definition</strong></td>
<td>A progressive neurodegenerative disorder characterized by memory loss and cognitive decline.</td>
<td>A type of dementia associated with abnormal protein deposits in the brain known as Lewy bodies.</td>
<td>A group of disorders caused by progressive cell loss in the brain's frontal or temporal lobes.</td>
<td>Cognitive impairment caused by cerebrovascular problems that affect brain blood flow.</td>
<td>A condition featuring symptoms and pathological features of more than one type of dementia.</td>
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<td><strong>Pathognomonic Feature</strong></td>
<td>Amyloid plaques and neurofibrillary tangles in the brain.</td>
<td>Presence of Lewy bodies, abnormal aggregates of protein in neurons.</td>
<td>Prominent atrophy in frontal and/or temporal lobes of the brain.</td>
<td>Evidence of cerebrovascular disease contributing to cognitive impairment.</td>
<td>Combination of pathologies such as Alzheimer’s and vascular dementia.</td>
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<td><strong>Diagnostic Criteria</strong></td>
<td>Clinical diagnosis supported by imaging and biomarkers; exclusion of other dementias.</td>
<td>Clinical diagnosis based on core features, with possible biomarker support.</td>
<td>Diagnosis based on clinical presentation, imaging, and ruling out other causes.</td>
<td>Evidence of vascular disease via imaging, aligned with cognitive decline.</td>
<td>Clinical assessment and imaging to identify multiple types of dementia pathologies.</td>
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<td><strong>Characteristic Clinical Feature</strong></td>
<td>Memory loss, confusion, difficulty with problem-solving and language.</td>
<td>Fluctuating cognition, visual hallucinations, Parkinsonism.</td>
<td>Changes in behavior and personality, language difficulties.</td>
<td>Stepwise cognitive decline, history of strokes or vascular risk factors.</td>
<td>Symptoms that are not fully explained by one type of dementia alone.</td>
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<td>Gradual memory decline as an early and prominent feature.</td>
<td>Fluctuating cognitive symptoms and visual hallucinations.</td>
<td>Early changes in behavior or language, relative preservation of memory.</td>
<td>History of stroke or vascular disease, with stepwise decline.</td>
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Published studies varied in what they defined as the clinical condition 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"
Algorithms with validation

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


Received: 26 February 2019


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 Lange, MD, PhD, and Julie P W Bynum, MD, MPH.
How well can electronic health records from primary care identify Alzheimer’s disease cases?

Using SIDIAP data, we identified AD cases using algorithms that combined EHR, a method previously applied to identify dementia cases. 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 studies of incidence of AD, treated patients are considered to have the disease.

<table>
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<th>Algorithm</th>
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<td>A1</td>
<td>Diagnosed patients: have an ICD10 code for AD (F00 or G30).</td>
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<td>A2</td>
<td>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).</td>
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<tr>
<td>A3</td>
<td>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.</td>
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Validation of Claims Algorithms to Identify Alzheimer’s Disease and Related Dementias

Ellen P McCarthy, PhD, MPH, Chiang-Huei Chang, PhD, MS, Nicholas Titton, PhD, Mohammed U Kabebo, MS, Kenneth M Langa, MD, PhD, and Julie P W Bynum, MD, MPH

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<th>Observation Period</th>
<th>CCW</th>
<th>Bynum-EM</th>
<th>Bynum-Standard</th>
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<td>3 Years</td>
<td>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, 294.0, 294.10, 294.11, 294.20, 294.21, 294.8, 797</td>
<td>1 Year and 3 Years</td>
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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 unspecified 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-Egger 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

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.
  o Dx (2DX), RX (2RX), neurologist, inpatient vs. Outpatient,
  o 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