Prevalence Measurement for Alzheimer’s Disease and Dementia: Current and Future

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Outline for Today

- Prevalence data diverse use and data sources
- Changing diagnostic categories impact on data collection
- Challenges of epidemiologic data and healthcare data
- Newer data sources
- Multi-use data for the future
Use Cases for Population Prevalence

- Public Health Surveillance
- Public Policy Development
- Research
  - Trends
  - Etiology/Risk Factors
  - Outcomes of Preventive Interventions
  - Disparities Reduction
Population Surveillance Data

• Epidemiological
  – Clinically-Adjudicated Diagnosis
  – Survey-instrument Assessment
• Clinical Process of Care Data
  – Billing/Claims
  – Electronic Health Record
• Biomarkers
• Non-Traditional Data
Evolving Diagnosis Definitions

- **Diagnostic Criteria (NINCDS-ADRDA)**
  - 1984
  - 1986
  - 1988
  - 1990
  - 1992
  - 1994
  - 1996
  - 1998
  - 2000
  - 2002
  - 2004
  - 2006
  - 2008
  - 2010
  - 2012
  - 2014
  - 2016
  - 2018

- **Clinical Diagnostic Guidelines**
  - PiB PET Trial

- **Revised Research (NINCDS-ADRDA)**
  - MCI Introduced

- **Revised Diagnostic Criteria (NIA-AA)**
  - 1st Drug Approved

- **Research Framework (NIA-AA)**
  - Amyloid PET FDA

- **MCI ICD-9**
Clinically observable syndromes:
- Dementia (AD vs all-cause) and MCI
- Preclinical Phase - biomarkers/pathophysiologic
2018 New NIA-AA Research Framework

• 2018 New NIA-AA Research Framework

  – AD biologically, by neuropathologic change or biomarkers, and treats cognitive impairment as a symptom/sign of the disease rather than the definition of the disease
    • Shift from “syndromal diagnosis” to “biological diagnosis”

  – AD diagnosis based on presence of biomarkers of:
    • \textbf{Amyloid} deposition;
    • pathological \textbf{Tau} protein;
    • and \textbf{Neurodegeneration}
Population prevalence: Which construct

Cognitive & Functional Performance

1984

Dementia Syndrome

2011

Distinction AD vs all-cause dementia

2011

AD Dementia – MCI -- Preclinical Phase with Biomarkers

2018

Clinical Syndromes

Biological Disease
Epidemiologic Data: Cognitive Performance

• Regional vs National vs International
  – Ex. Framingham vs MCBS vs ELSA

• Cognitive-specific vs General that include cognitive
  – Ex. CHAPS vs MESA

• In-person assessment with clinical consensus
  – Ex. ADAMS, Cache County

• Use reported diagnosis & proxies
  – Ex. MCBS

• Use of standardized instruments and proxies
  – Ex. HRS, NHATS
Population prevalence: Which construct

Cognitive & Functional Performance

Variation in epidemiologic estimates

1984

Dementia Syndrome

Distinction AD vs all-cause dementia

2011

AD Dementia – MCI -- Preclinical Phase with Biomarkers

2011

Clinical Syndromes

Biological Disease

1984

2011

2011

2018
Epidemiologic data limits and challenges

- National representation size necessitates instruments over more accurate in-person assessment
- Variation in method and population leads to variation in estimates (harmonization needed)
- Uneven recruitment of certain groups
- Ability to generate geographically-specific measures limited
Population prevalence: Which construct

Cognitive & Functional Performance

1984

Dementia Syndrome

Variation in epidemiologic estimates

2011

Distinction AD vs all-cause dementia

2011

AD Dementia – MCI -- Preclinical Phase with Biomarkers

Address neuropath vs clinical syndrome

2018

Clinical Syndromes

Biological Disease

Variation in epidemiologic estimates

Address neuropath vs clinical syndrome
Combining the Biomarkers and Clinical Syndrome into Explanatory Models

A = amyloid
T = tau
N = neurodegeneration
C = cognitive impairment

A → T → (N) → (C)
T → A → (N) → (C)
A → (N) → (C)
W → A → (N) → (C)
X → A → (N) → (C)
Y → T
Z → (N) → (C)

Jack, Alz&Dem 2018
Future population prevalence: Which construct

Cognitive & Functional Performance

Variation in epidemiologic estimates

Address neuropath vs clinical syndrome

Distinct Definitions

1984

Dementia Syndrome

Distinction AD vs all-cause dementia

AD Dementia – MCI -- Preclinical Phase with Biomarkers

Clinical Syndromes

Biological Disease

Question: Population surveillance of Biological Disease?
# Biomarkers

## NIA-AA Research Framework Defining Disease

<table>
<thead>
<tr>
<th>AT(N) Profiles</th>
<th>Biomarker Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-T-(N)-</td>
<td>Normal AD biomarkers</td>
</tr>
<tr>
<td>A+T-(N)-</td>
<td>Alzheimer’s pathologic change</td>
</tr>
<tr>
<td>A+T+(N)-</td>
<td>Alzheimer’s disease</td>
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<tr>
<td>A+T+(N)+</td>
<td>Alzheimer’s disease</td>
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<tr>
<td>A+T-(N)+</td>
<td>Alzheimer’s and concomitant suspected non Alzheimer’s pathologic change</td>
</tr>
<tr>
<td>A-T+(N)-</td>
<td>Non-AD pathologic change</td>
</tr>
<tr>
<td>A-T-(N)+</td>
<td>Non-AD pathologic change</td>
</tr>
<tr>
<td>A-T+(N)+</td>
<td>Non-AD pathologic change</td>
</tr>
</tbody>
</table>

A= amyloid  
T= tau  
N= neurodegeneration

Jack, Alz&Dem 2018
Biomarkers- Challenges for Epidemiology

– Categorization of “disease status” not yet stable
– Major groups have categorizations that are similar but not the same (NIA-AA 2018 and IWG 2014)
– Evolving technology (ex tau PET) difficult to anticipate what should be collected
– How to obtain population-based as opposed to clinic-based cohorts for assessment
Generalizability of Current Data

“The vast majority of [current imaging and biomarker] data...are from selected participants recruited through tertiary care dementia centers. There are limited data...from population-based studies. Therefore, incorporating biomarkers into these studies is highly warranted to increase our understanding of the biology of AD.

Importantly, there are less data from diverse populations.”

Source: Jack et al, Alzheimer’s and Dementia, 2018.
Billing/Claims Data Current State

Data collected in the process of payment for health care services with availability of a population denominator:

- Medicare Fee-for-Service (CMS)
- Medicare Advantage (CMS)
- Commercial Insurance (OPTUM, Sentinel/DRN)
- Medicaid (CMS, state)
- Minimum Dataset/OASIS (CMS)
Medicare Administrative Data

- Medicare is the health insurance for all Americans over age 65
- Diagnosis required for every service delivered except for medications
- Complete capture of services because necessary for payment
- Federal system so all data centralized
Challenge of Claims for Prevalence Measure

Conceptual Process of Diagnosis

Patient identifies health problem
Patient engages health care system

Information Integration & Interpretation
Clinical History & Interview
Referral & Consultation

Physical Exam
Diagnostic Testing

Working Diagnosis

 Communicate Diagnosis, Treatment, Outcome

- A Bill to Medicare is generated

National Academy of Medicine, 2014
Case Finding in Clinical Practice

• 62% undetected dementia in community
  (Lang et al. 2017 Meta-analysis. BMJ Open)
• Studies in Primary Care ≈ 50% undetected

1988 – O’Connor, England N=444
1995 – Callahan, USA N=3954
2000 – Olafsdottir, Sweden N=350
2000 – Valcour, USA N=297
2003 – Lopponen, Finland N=1260
2005 – Boustani, USA N=3340
2006 – Borson, USA N=371
2007 – Wilkens, USA N=411
Challenge of Claims for Prevalence Measure

- Stigma
- Symptom Perceived as Normal Aging

Patient identifies health problem

Patient engages health care system

- Access of Care
- Transportation

- Availability ADRD expertise
- Physician network

Information Integration & Interpretation

Clinical History & Interview

Physician Exam

Referral & Consultation

Diagnostic Testing

Working Diagnosis

- Physician experience

- Bias in Cognitive Test Performance by Race/education

Communicate Diagnosis

Treatment

Outcome

- MD views on value of treatment
- MD views on PET, CSF
- Availability Dx tests
- Payment for Dx Tests
Combined Epidemiologic & Claims Data

• Many epidemiological studies with objective cognitive measures have been linked to Medicare claims data

• Studies of accuracy of claims based on:
  – Patient registries
  – Regional epidemiological studies
  – National epidemiological studies
<table>
<thead>
<tr>
<th>Author</th>
<th>Year Publish (data)</th>
<th>Sample</th>
<th>Findings</th>
<th>Gold Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newcomer</td>
<td>1999 (1991-2)</td>
<td>MADDE N=5379, AD care management demonstration project</td>
<td>19% sensitive (2 claims in 1 yr)</td>
<td>Referring physician diagnosis (weak)</td>
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<td></td>
<td></td>
<td></td>
<td>31% sensitive (1 claim 1 yr)</td>
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<tr>
<td>Taylor</td>
<td>2002 (1991-95)</td>
<td>CERAD n=417 registry enrolled, used 5 yrs claims</td>
<td>Sensitivity: 87% dementia 78% AD</td>
<td>NINCDS-ADRDA criteria at 23 research sites</td>
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<tr>
<td>Pressley</td>
<td>2003</td>
<td>National Survey N=5089 NLTCS community survey: SPMSQ, self-report dx,</td>
<td>Finding: Poor agreement between sources</td>
<td>None</td>
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<tr>
<td></td>
<td></td>
<td>claim 1 or 5 yrs</td>
<td></td>
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<tr>
<td>Ostbye</td>
<td>2008 (1993-5)</td>
<td>National Survey AHEAD n=7974 TICs or IQCODE, 5yrs claims, death certificate</td>
<td>Finding: Poor agreement between sources</td>
<td>None</td>
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<tr>
<td>Taylor</td>
<td>2009 (2001-3)</td>
<td>National sample ADAMS n=758 cases &amp; controls Clinical assessment, all claims available 1993-2005</td>
<td>Sensitivity: .85 dementia; .64 AD Specificity: .89 dementia; .97 AD</td>
<td>Research team clinical assessment: NI, CIND, Dementia</td>
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<tr>
<td>Survey Name</td>
<td>Future Linkages</td>
<td>Studied Expected to be Linked with CMS Data by end of 2019</td>
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<td>-----------------------------------------------------------------------------</td>
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<tr>
<td>Health and Retirement Study (HRS)</td>
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<td>X</td>
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<td>National Long Term Care Survey (NLTCS)</td>
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<td>Dynamics of Health, Aging, and Body Composition (Health ABC)</td>
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<td>National Social Life, Health, and Aging Project (NSHAP)</td>
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<td>Wisconsin Longitudinal Study (WLS)</td>
<td></td>
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<td>Panel Study of Income Dynamics (PSID)</td>
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<tr>
<td>Baltimore Longitudinal Study of Aging (BLSA)</td>
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<td>Long-Life Family Study Data Management and Coordinating Center (LLFS)</td>
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<td>Predictors of Severity of Alzheimer’s Disease Study (PSAD)</td>
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<td>Rush Alzheimer’s Disease Center (RADC)</td>
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<td>National Health and Aging Trends Study (NHATS)</td>
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<td>Project Talent Health and Wellness Study</td>
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<td>Care Ecosystem</td>
<td></td>
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<td>Useful Field of View Training (UFOVT)</td>
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<td>Add Health Parent Study (AHPS)</td>
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<tr>
<td>Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE)</td>
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<td>Understanding America Study (UAS)</td>
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<td>Aging with Pride: National Health, Aging, and Sexuality/Gender Study (NHAS)</td>
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<td>Midlife Development in the U.S. (MIDUS)</td>
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<td>Diabetes Prevention Program (DPP)</td>
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<tr>
<td>High School &amp; Beyond (HS&amp;B) Midlife Follow-up Study</td>
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<tr>
<td>Chicago Health and Aging Project (CHAP) study</td>
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</tbody>
</table>
Trend in ADRD & MCI Clinically Diagnosed Prevalence

Now: ICD 9 to ICD 10

Percentage with Claims Dx (%)

<table>
<thead>
<tr>
<th>Year</th>
<th>ADRD or MCI</th>
<th>ADRD</th>
<th>MCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td></td>
<td>3.0%</td>
<td>0.5%</td>
</tr>
<tr>
<td>2002</td>
<td>8.0%</td>
<td>7.0%</td>
<td>0.5%</td>
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<tr>
<td>2006</td>
<td>8.0%</td>
<td>7.0%</td>
<td>0.5%</td>
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<tr>
<td>2010</td>
<td>8.5%</td>
<td>7.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>2014</td>
<td>8.5%</td>
<td>7.5%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Age Standardized Clinical Prevalence,
20% National FFS Medicare Sample aged 65 and older
Billing/Claims data limitations

- Dependent on care seeking
- Clinician expertise in diagnosis & billing pressures influence accuracy
- Changing diagnostic coding systems
- Changing clinical practice patterns
- Differences in practice norms across region
Combined Data – Epi/ Biomarker/Claims

• Objective measures of cognition + Biomarkers
  – Rush studies

• Objective measures of cognition + Claims
  – Nationally representative: HRS & NHATS
  – Regional representation: Increasing #s

• EHR + Claims/Assessments

• Claims, Objective measures + Biomarker
  – IDEAS trial (not pop’n representative)
  – HRS sample (N=100 with PET scan)
Electronic Health Data current state

- Many algorithms for detecting presence of or risk of development Alzheimer’s disease
  - Several published and many in the pipeline
  - Drawing on machine learning/text mining
- Similar drawbacks to claims
- Additional challenges
  - Lack of denominator
  - Comparability across EHRs
Non-Traditional Data

• Technology driven
  – Ex. hand writing analysis, eye movt, retinal scans
  – Some direct to consumer

• Financial data
  – Lauren Nicholas work on financial behavior as early marker
Non-Alzheimer’s Forms of Dementia

• Other Etiologies:
  – Vascular Dementia
  – Frontotemporal Dementia
  – Lewy Body Disease
  – Mixed forms

• Differentially effect specific groups
  – Stroke risk and race with vascular dementia
  – Younger age and frontotemporal dementia
Summary of Major Challenges - Priorities?

- **Representation**
  - Address disparities
- **Geographical-specificity**
  - Address environment
- **Incorporation of biomarkers**
  - Address etiology/risk factor
- **Dementia Type**
- **Accessibility of data**
  - Tradeoff accuracy for cost
  - Timeliness
  - Timelessness (stand up to change in science)
Closing: Where data needs align and diverge

Ranking Priorities for Multi-Use Data?

- Accuracy of diagnosis
- Representation of populations
- Biomarkers
- 
- 

Population Health Scientists

Clinical Scientists

Basic Scientists