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

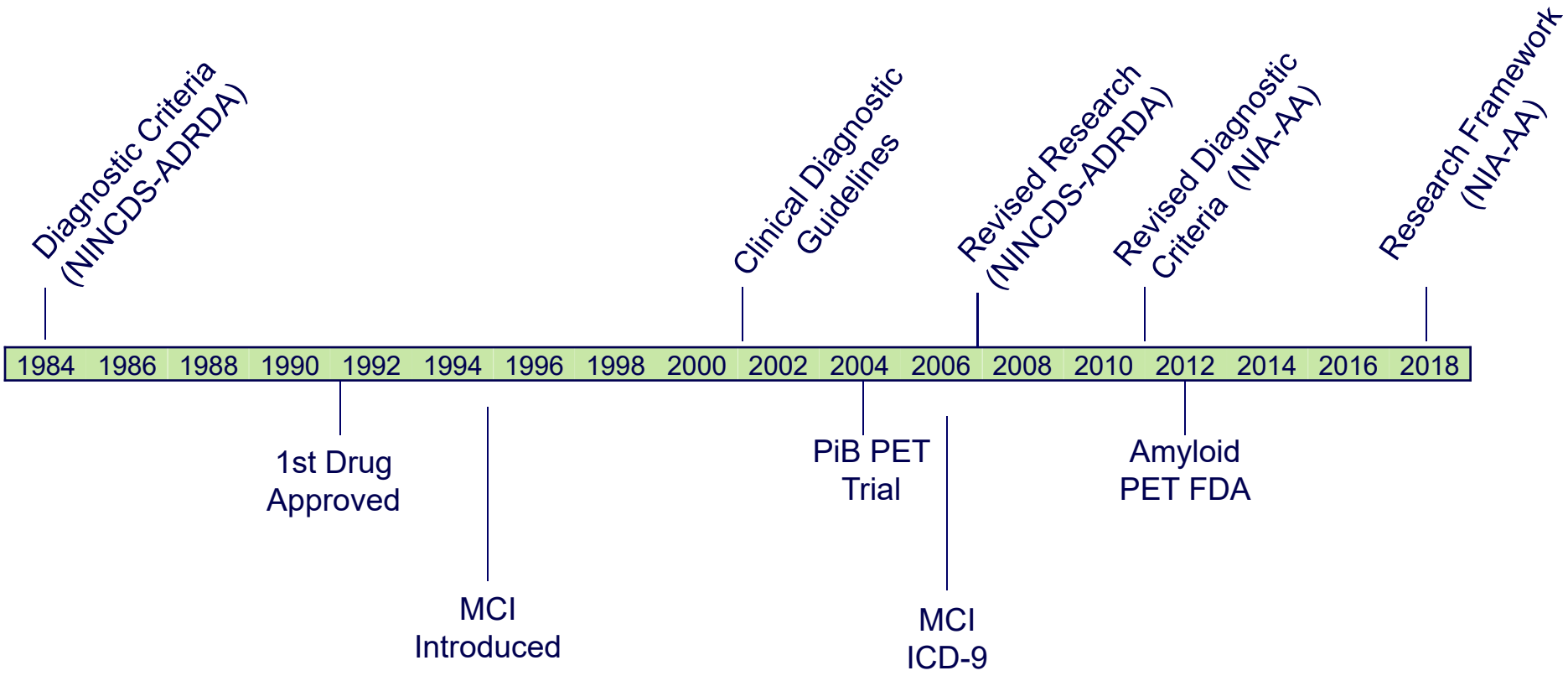
Use Cases for Population Prevalence

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

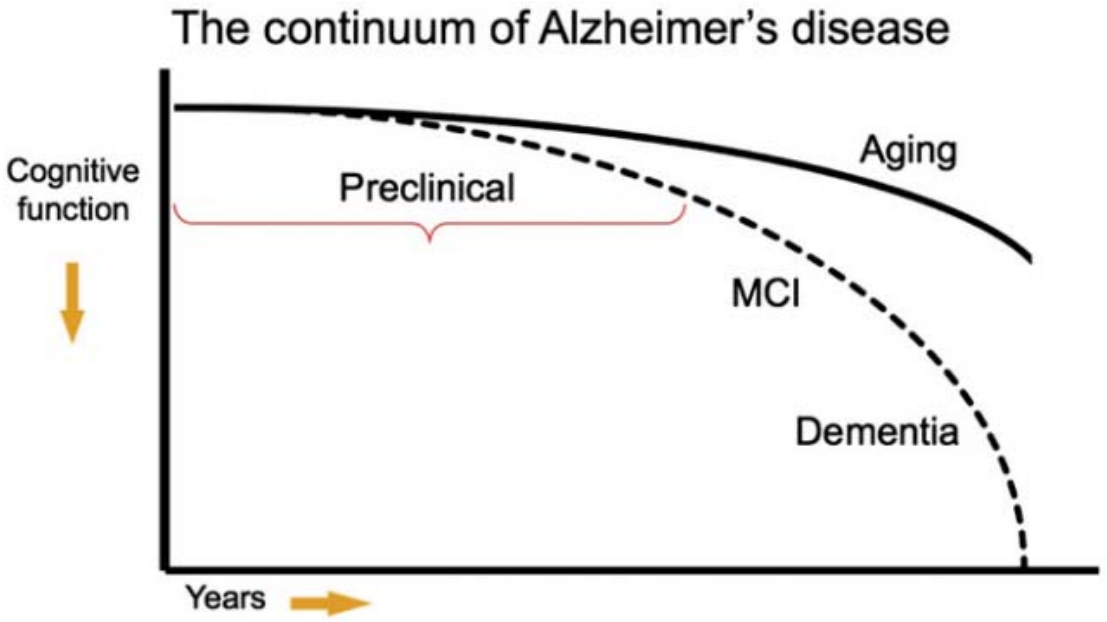
Population Surveillance Data

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

Evolving Diagnosis Definitions



2011 NIA-AA Diagnostic Guidelines



- Clinically observable syndromes:

  Dementia (AD vs all-cause) and MCI

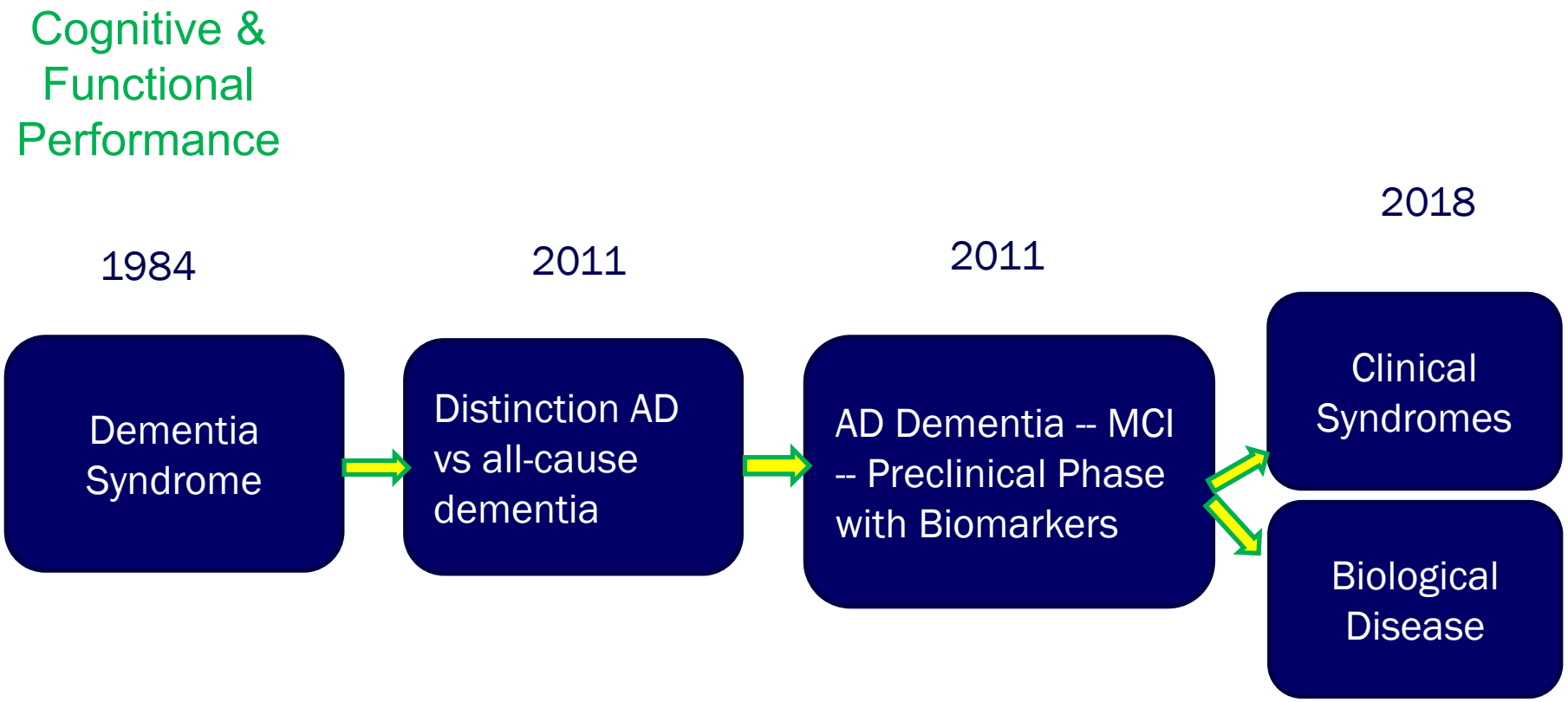
- Preclinical Phase - biomarkers/pathophysiologic

Source: Sperling et al, *Alzheimer's and Dementia*, 2011.

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:
    - **A**myloid deposition;
    - pathological **T**au protein;
    - and **N**eurodegeneration

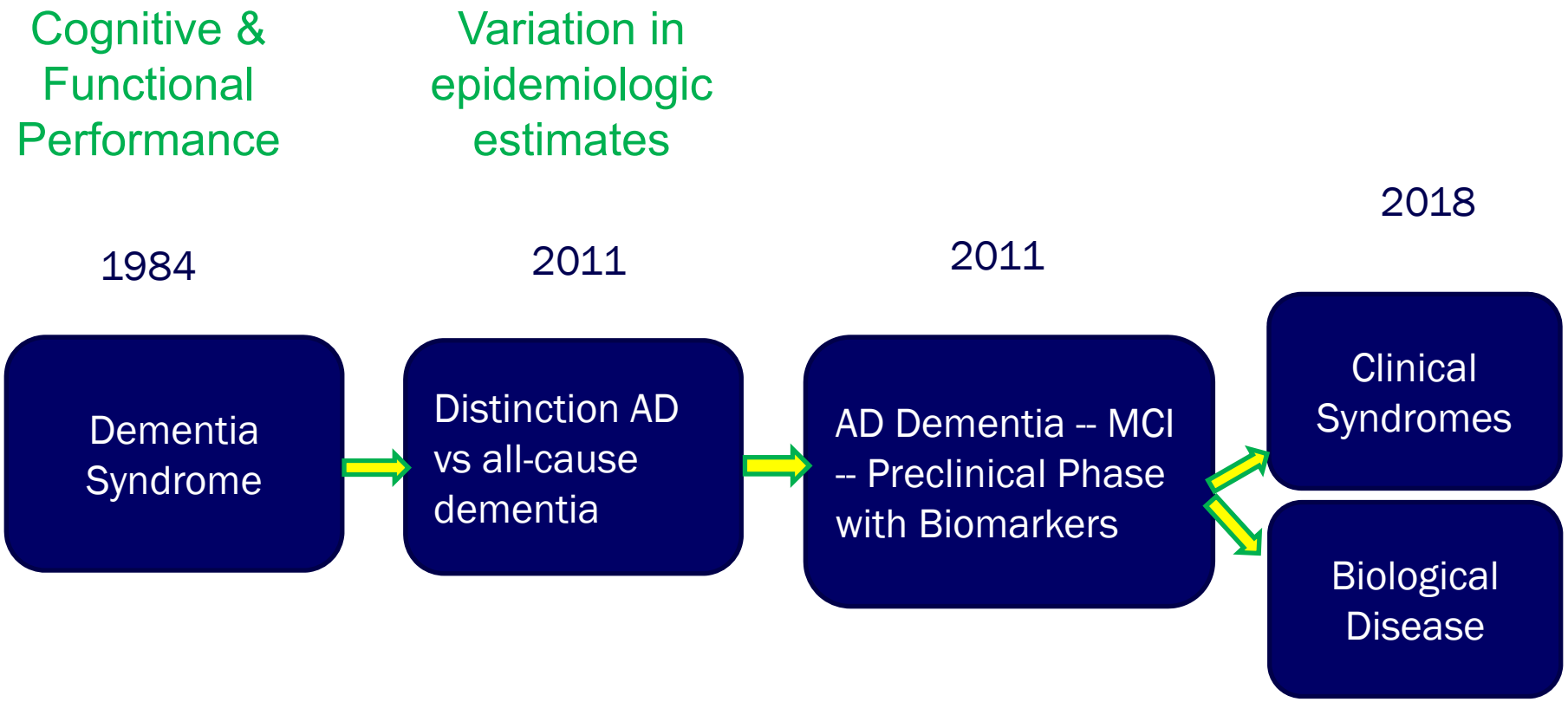
Population prevalence: Which construct



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

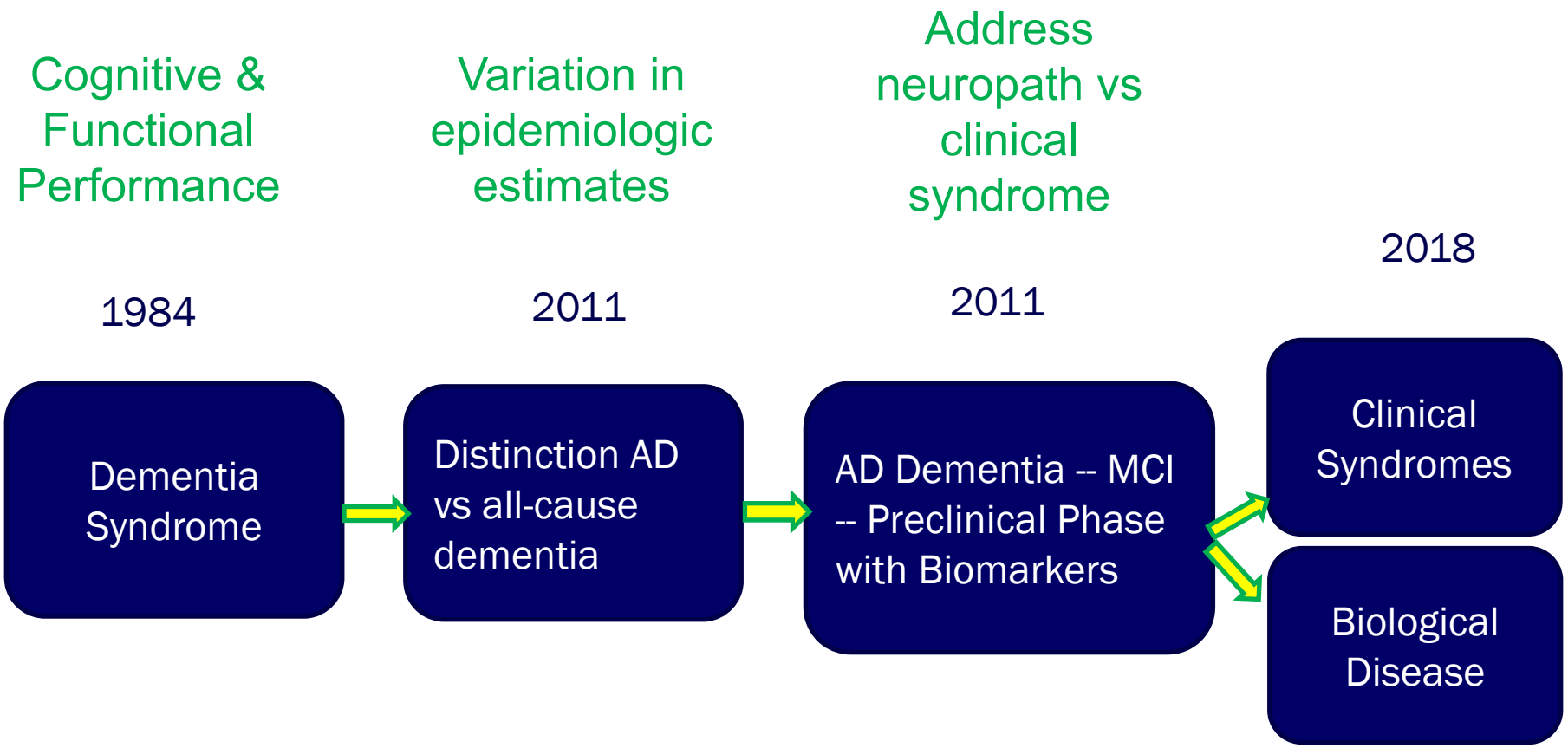
Population prevalence: Which construct



Epidemiologic data limits and challenges

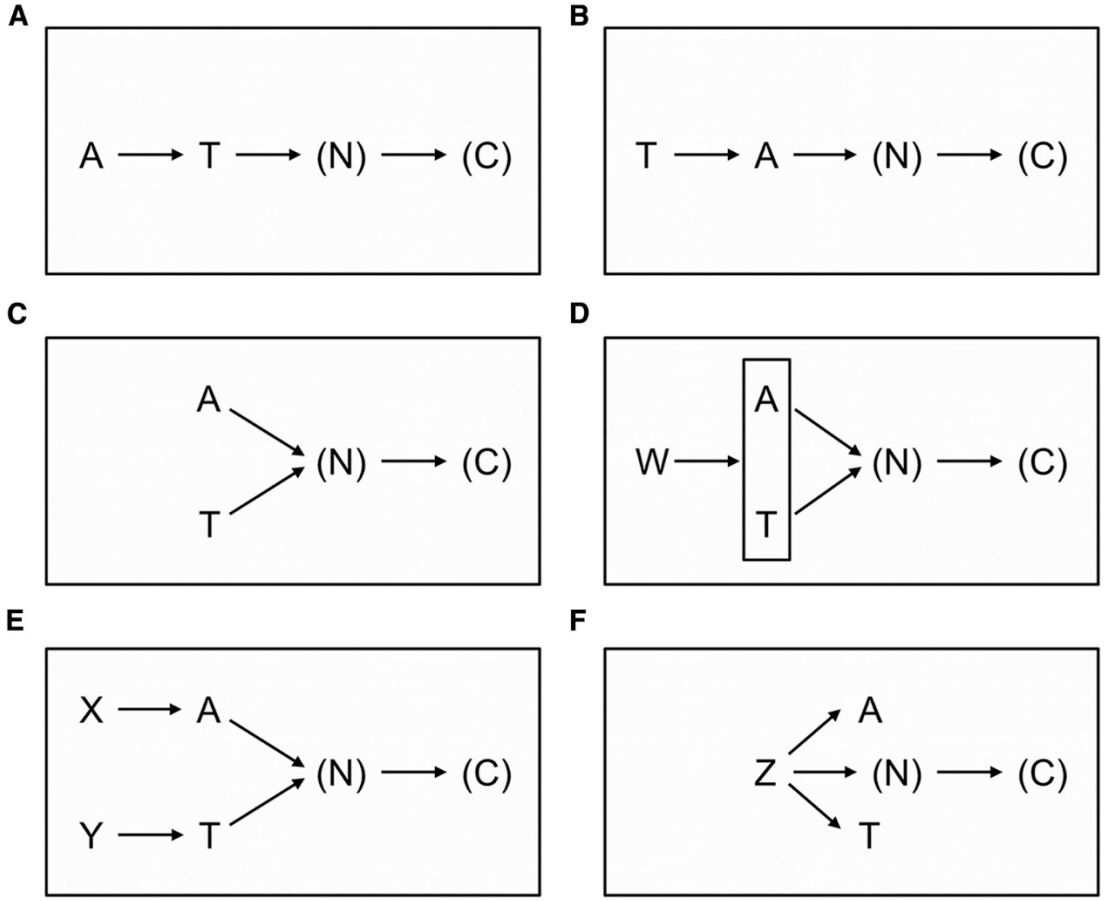
- National representation size necessitates instruments over more accurate in-person assessment
- Variation in method and population leads to variation in estimates (harmonization needed)
- Uneven recruitment of certain groups
- Ability to generate geographically-specific measures limited

Population prevalence: Which construct



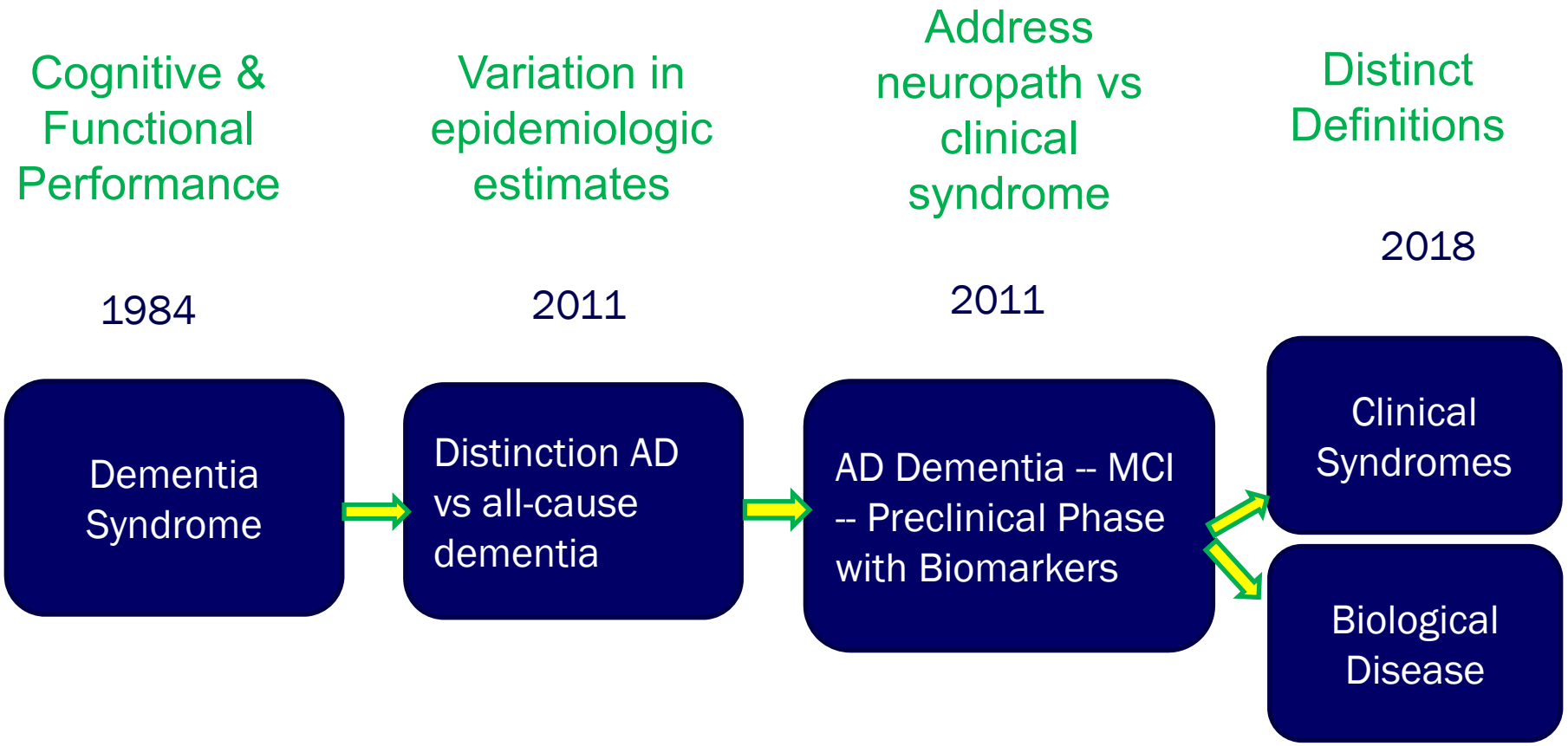
Combining the Biomarkers and Clinical Syndrome into Explanatory Models

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



Jack, Alz&Dem 2018

Future population prevalence: Which construct



Question: Population surveillance of Biological Disease?

Biomarkers
NIA-AA Research Framework Defining Disease

A= amyloid
T= tau
N= neurodegeneration

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N)-	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

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

Biomarker Challenge

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:

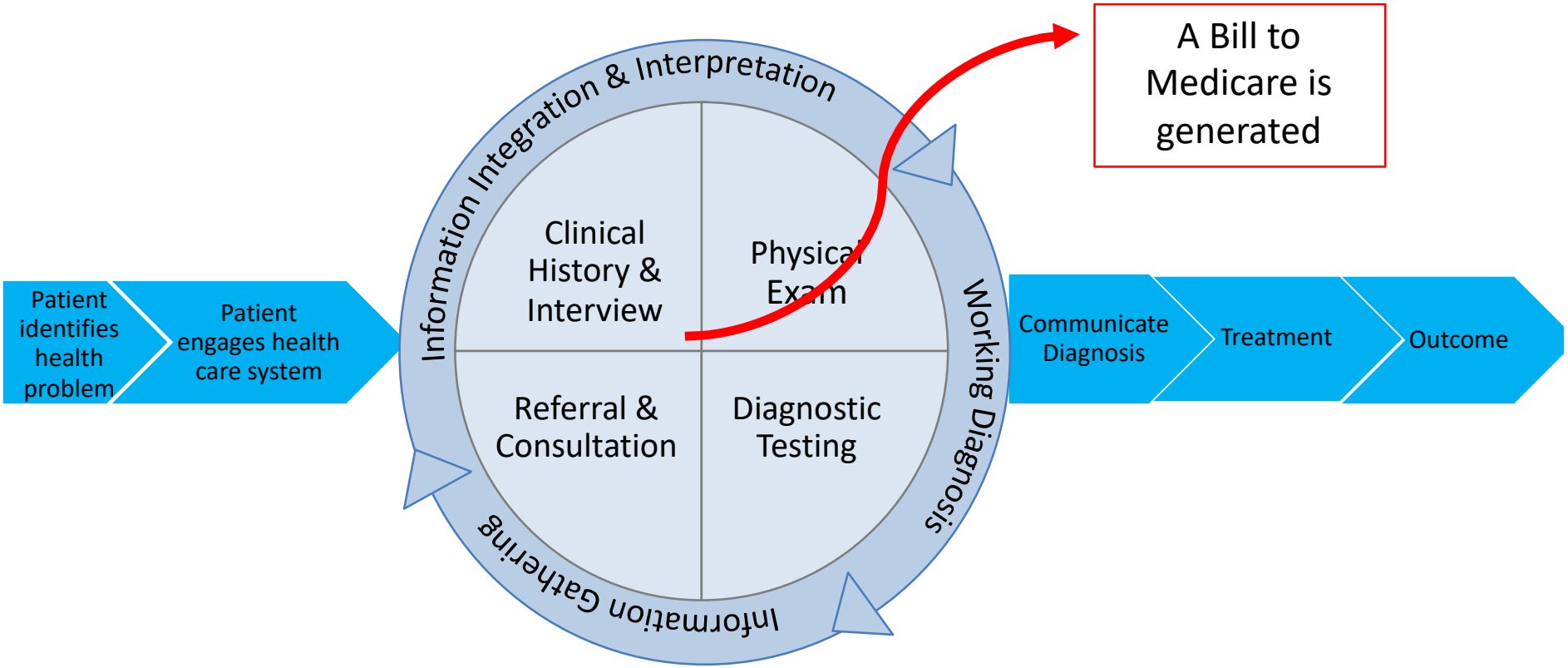
- Medicare Fee-for-Service (CMS)
- Medicare Advantage (CMS)
- Commercial Insurance (OPTUM, Sentinel/DRN)
- Medicaid (CMS, state)
- Minimum Dataset/OASIS (CMS)

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



National Academy of Medicine, 2014

Case Finding in Clinical Practice

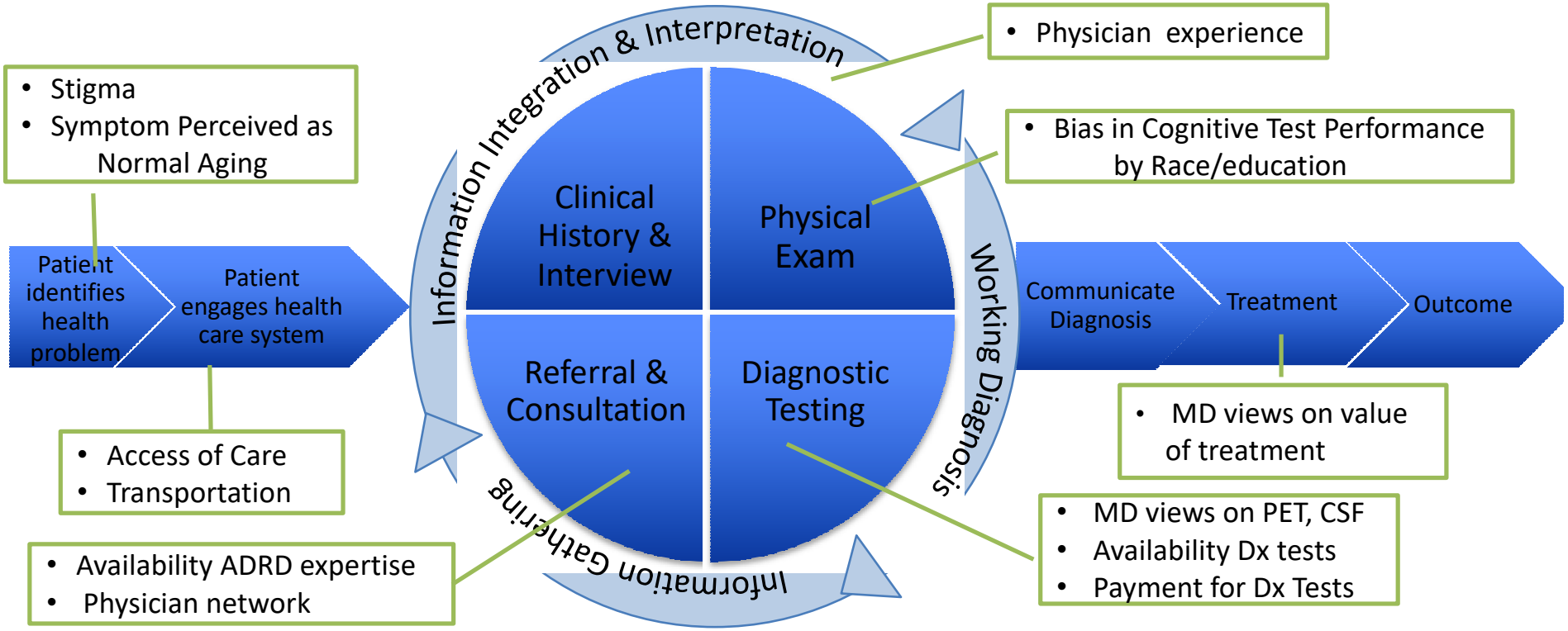
- 62% un-detected dementia in community

  (Lang et al. 2017 Metanalysis. 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



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

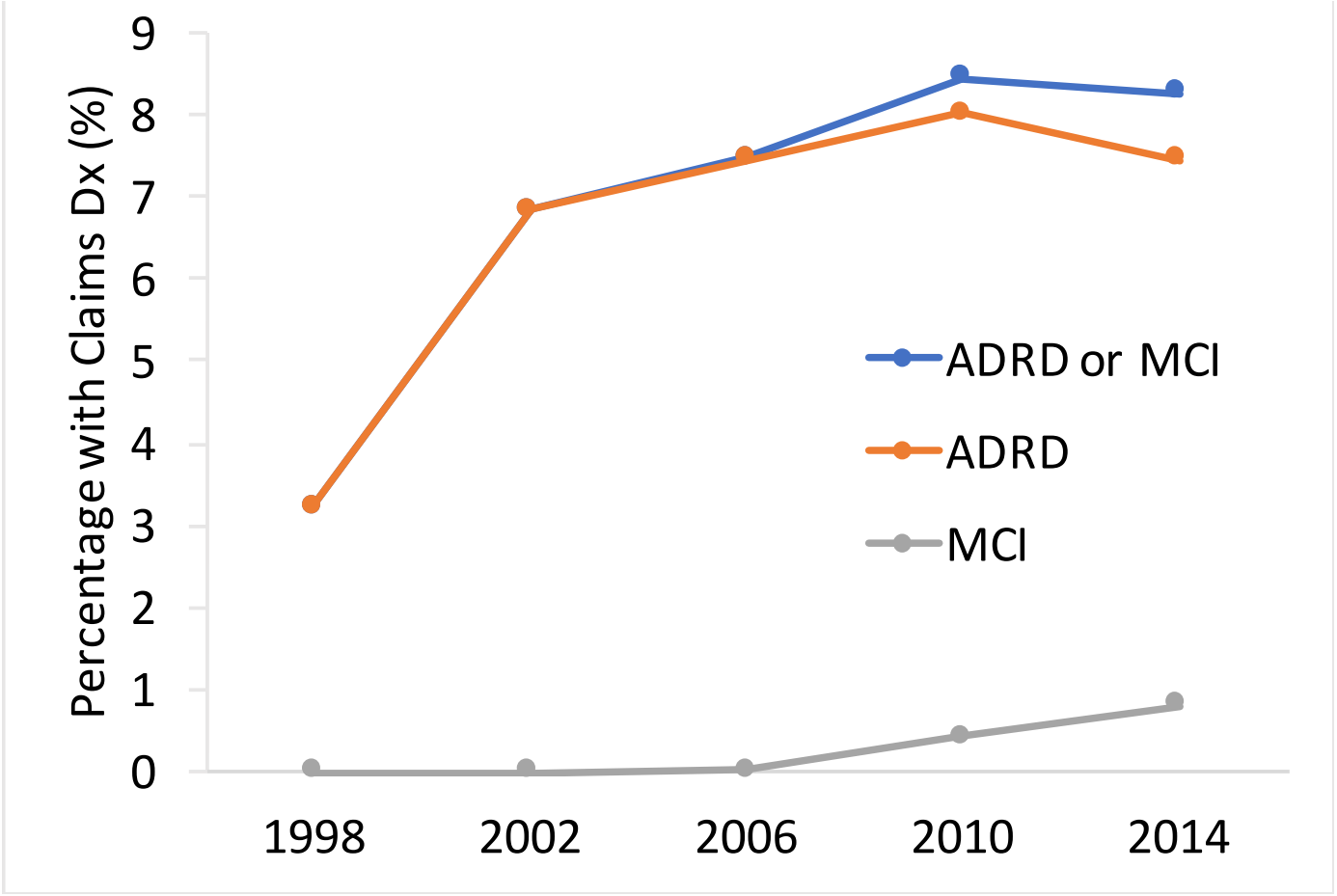
Algorithm Performance: Slide 1 of many

Author	Year Publish (data)	Sample	Findings	Gold Standard
Newcomer	1999 (1991-2)	MADDE N=5379, AD care management demonstration project	19% sensitive (2 claims in 1 yr) 31% sensitive (1 claim 1 yr)	Referring physician diagnosis (weak)
Taylor	2002 (1991-95)	CERAD n=417 registry enrolled, used 5 yrs claims	*Sensitivity:* 87% dementia 78% AD	NINCDS-ADRDA criteria at 23 research sites
Pressley	2003	National Survey N=5089 NLTCS community survey: SPMSQ, self-report dx, claim 1 or 5 yrs	Finding: Poor agreement between sources	None
Ostbye	2008 (1993-5)	National Survey AHEAD n=7974 TICs or IQCODE, 5yrs claims, death certificate	Finding: Poor agreement between sources	None
Taylor	2009 (2001-3)	National sample ADAMS n=758 cases & controls Clinical assessment, all claims available 1993-2005	*Sensitivity:* .85 dementia; .64 AD *Specificity:* .89 dementia; .97 AD	Research team clinical assessment: NI, CIND, Dementia

Survey Name	Future Linkages	Studied Expected to be Linked with CMS Data by end of 2019
Health and Retirement Study (HRS)		x
National Long Term Care Survey (NLTCS)		x
Dynamics of Health, Aging, and Body Composition (Health ABC)		x
National Social Life, Health, and Aging Project (NSHAP)		x
Wisconsin Longitudinal Study (WLS)		x
Panel Study of Income Dynamics (PSID)		x
Baltimore Longitudinal Study of Aging (BLSA)		x
Long-Life Family Study Data Management and Coordinating Center (LLFS)		x
Predictors of Severity of Alzheimer's Disease Study (PSAD)		x
Rush Alzheimer's Disease Center (RADC)		x
National Health and Aging Trends Study (NHATS)		x
Project Talent Health and Wellness Study		x
Care Ecosystem		x
Useful Field of View Training (UFOVT)	x	
Add Health Parent Study (AHPS)	x	
Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE)	x	
Understanding America Study (UAS)	x	
Aging with Pride: National Health, Aging, and Sexuality/Gender Study (NHAS)	x	
Midlife Development in the U.S. (MIDUS)	x	
Diabetes Prevention Program (DPP)	x	
High School & Beyond (HS&B) Midlife Follow-up Study	x	
Chicago Health and Aging Project (CHAP) study	x	

Trend in ADRD & MCI Clinically Diagnosed Prevalence

Now: ICD 9 to ICD 10



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

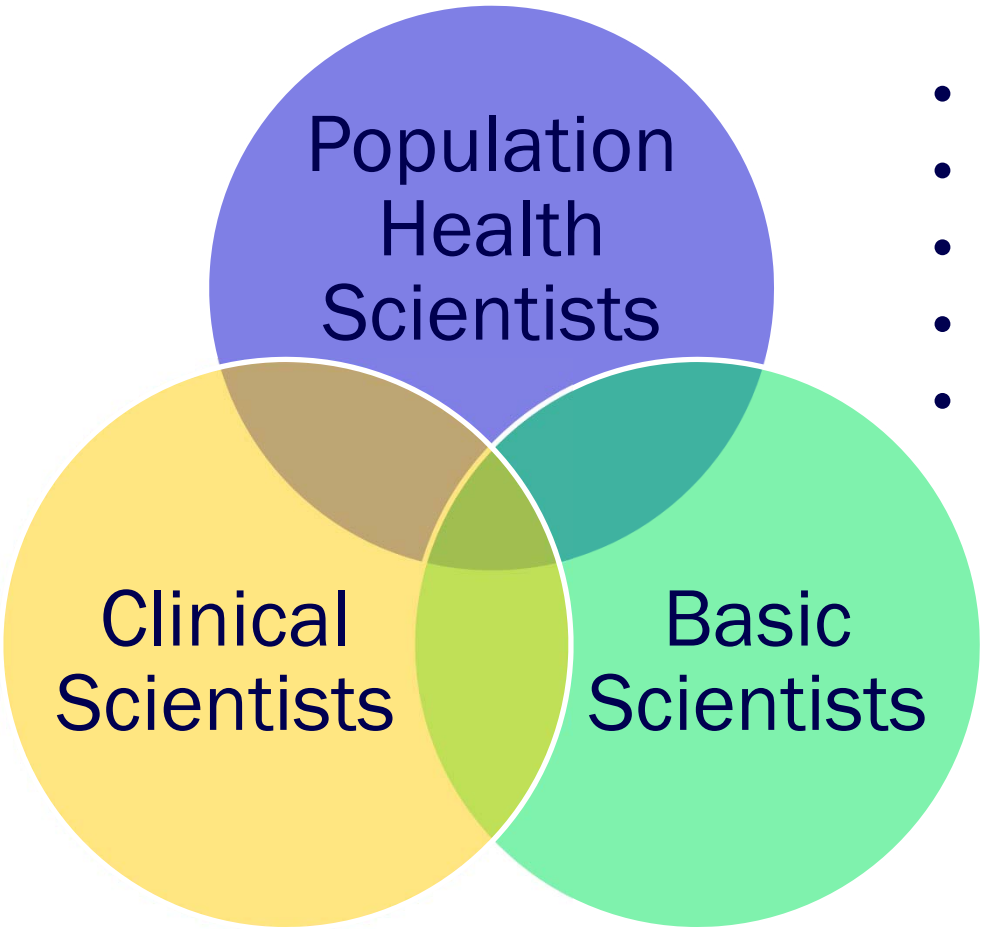
Non-Alzheimer's Forms of Dementia

- 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
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Proposed Paper Outline

- Definition of Disease & Evolution over Time
- Overview Data Types – Fitness for Purpose
- Epidemiologic data current state
- Administrative data current state
- Combined Data
- Biomarker-based Disease
- Non-traditional data sources
- Representativeness and Pitfalls
- Non-AD Forms of Dementia
- Recommendations