Introduction to Alzheimer’s Disease, and Use of AD8 for Community Screening

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Who We Are: Knight Alzheimer’s Disease Research Center

- Part of Washington University School of Medicine.
- Memory and Aging Project (MAP) is the research office where all participants come for their annual assessments of memory and thinking.
- Led by Principal Investigator John C. Morris, MD.
- MAP began in August 1979 when our first participant was evaluated.
- All participant assessments are supported with funding (grants) from the National Institutes of Health.
- Special procedures (e.g., brain scans, lumbar punctures) may be done elsewhere on the Washington University School of Medicine campus.
Program Overview

- Part One: Dementia and Alzheimer’s Disease (AD) Overview
  - Prevalence and Impact
  - Importance and Benefits of Early Detection
  - Risk
  - Available Treatments

- Part Two: Screening for Dementia in Community Settings

- Part Three: AD8 Dementia Screening Interview
Part One

Dementia and Alzheimer’s Disease (AD) Overview
AD Pathologic Hallmarks

- Plaques (diffuse, neuritic, CAA) (Aβ)
- Neurofilbrillary tangles (NFT) (tau)
- Neuronal and synaptic dysfunction and loss, Atrophy of the brain
- Inflammation
“Alzheimer disease” (AD) refers to the neurodegenerative brain disorder, regardless of clinical status, representing a continuous process of synaptic and neuronal deterioration.

AD has two major stages:
- Preclinical (presymptomatic; asymptomatic), undetectable by current clinical methods
- Symptomatic (clinical)

Symptomatic AD is defined by intraindividual cognitive decline, from subtle to severe, that interferes with daily function, and can be subclassified on symptom severity:
- Incipient (prodromal; mild cognitive impairment)
- Dementia

Intraindividual Decline, Not Test Score, Marks Alzheimer Dementia

Courtesy of Martha Storandt
Dementia

- **Definition:** An acquired syndrome of decline in memory and other cognitive domains sufficient to affect daily function

- **Detection:**
  - Intra-individual change: Informant observations about decline in previously established cognitive and functional abilities
  - Inter-individual differences: Cognitive test performance compared with age- and education-matched norms
Dementia vs. Alzheimer’s Disease

- Dementia is a general term that describes a progressive change in memory and thinking abilities that interfere with everyday activities.
- Alzheimer’s disease is the most common cause of dementia. Other causes include strokes, Parkinson’s disease, Pick’s disease.
- All Alzheimer’s disease is dementia but not all dementia is Alzheimer’s disease. “Chevy is a type of car, but not the only type of car.” One type of dementia is not “better” or “worse” than another type.
- What we are proposing to do today is to detect the presence of a possible dementia. It is up to the client’s physicians to make a formal diagnosis of Alzheimer’s disease or other cause of dementia.
National Population: Notice the increase in the elderly as baby-boomers age

Source: U.S. Census Bureau
The Epidemic of AD

● Scope
  – 4 million Americans now affected; will double by 2025

● Impact
  – Emotional, physical, financial toll on caregivers; most AD care provided by family (24/7)
  – 3rd most expensive, after heart disease and cancer
  – By 2015, annual costs to Medicare will be $189 billion (from $91 billion in 2005)

● Change perceptions
  – AD presents urgent, unmet needs (like cancer or AIDS); must balance risks of potential new therapies with benefits
  – Fund cure and care
Stages of Alzheimer Dementia (Clinical Dementia Rating)

- **CDR 0** (normal)
  - Insidious onset
  - “Forgetful”; repetitious; impaired decisional abilities; independent in self-care; looks and acts “normal”, can perform some IADLs but often impaired to some degree
  - Only highly learned material recalled; little or no pretense of IADLs; disruptive behaviors; supervised BADLs
  - Oriented only to self; requires full care for BADLs; akinetic mutism

Course of Dementia
7-10 yr
Candidate Risk & Protective Factors

Increased Risk
- Susceptibility genes
- Insulin resistance; metabolic syndrome; CVD risk factors
- Inflammatory markers

Decreased Risk
- Protective genes
- Mediterranean diet: high intake of fish, vegetables, fruits, cereal, unsaturated fatty acids [olive oil], and low intake of meat/poultry, dairy products, and saturated fatty acids
- Moderate alcohol intake
- Engaged lifestyle (physical, cognitive, social)
Currently Approved Symptomatic Treatments for AD

- **Cholinesterase inhibitors** target the cholinergic system
  - Donepezil (Aricept®)
  - Rivastigmine (Exelon®)
  - Galantamine (Razadyne®)

- **NMDA receptor antagonist** targets the glutamatergic system
  - Memantine (Namenda®)
Part Two

Screening for Dementia in Community Settings
Screening for Dementia in Community Settings - Objectives

- Review symptoms of AD and compare across disease progression
- Review the indications for evaluating older adults for cognitive disorders
- Describe use and interpretation of AD8 scores
- Review what to do with a “positive” screening test
Indications for Evaluation of AD

- Difficulty in learning and retaining new information
- Difficulty in performing complex tasks
- Impaired reasoning ability
- Problems with orientation and spatial abilities
- Language difficulties
- Depression or anxiety in old age
- Behavioral or personality changes

Know the 10 Signs – 10 signs that highlight change and encourage discussion with a physician
alz.org/10signs
**AD Is Underdiagnosed**

- Early Alzheimer’s disease is subtle—it is easy for family members and physicians to miss the initial signs and symptoms
- Many patients remain undiagnosed
- Undiagnosed AD patients often face avoidable social, financial, and medical problems
- Early diagnosis and appropriate intervention may lessen disease burden
- Laboratory tests of biological markers indicating likelihood of AD are not available for general clinical use
Barriers to Diagnosis

- Misidentification of early stages of dementia as part of “normal” aging
- Social skills often maintained early in disease
- Denial and lack of insight by patient
- Social stigma associated with diagnosis
- Lack of definitive screening and diagnostic tests
- A “positive” screening begins the process of seeking a diagnosis and support, and a positive screen is **NOT** the same as diagnosis
- False positives and false negatives may occur
Benefits of Early Recognition and Treatment

- Allows patients to participate in care plan at a time when they may still be able to express their needs and wishes
- Facilitate caregiver and family participation
- May slow progression of disease
- Offers potential for functional stabilization and independence
- Ease caregiver burden
The diagnosis of Alzheimer disease (AD) and related disorders remains clinical.

Founded on:
- intra-individual decline in cognition
- interference in accustomed daily activities.

Physician Most Likely to Be Consulted for AD-related Problems

- Family Physician/Internist: 83%
- Neurologist: 7%
- Psychiatrist: 5%
US Health Care Reform Encourages Early Detection

- On March 23, 2010 the US Health Care Reform bill was signed into law, and took effect in 2011.
- It includes a provision that ensures Medicare beneficiaries an Annual Wellness Visit that includes cognitive impairment detection/screening.
- Missouri State Alzheimer’s Disease Task Force submitted recommendations to the governor in 2012 strongly encouraging the use of the AD8 as a consistent assessment tool to identify people in the early stages of dementia.
Recent Changes

- Congress expanded Medicare coverage under part B to include an “Annual Wellness Visit providing Personalized Prevention Plan services”
- The visit includes a health risk assessment (HRA) with the physician, and creates Personalized Prevention Plans for beneficiaries that will be updated following each visit
Problems with Performance Testing

- Brief tests may be:
  - insensitive to the early stages of dementia (MMSE)
  - culturally biased (MMSE)
  - weighted towards memory impairment (SBT)
  - Missing non-memory domains (SBT)

- Comparison with normative values may:
  - not detect very mild decline in high functioning individuals.
  - falsely detect dementia in individuals with life-long poor cognitive function

- Offer no sense of change from prior status or interference with social or occupational functioning

- Formal neuropsychological evaluations have less bias but require extensive training and are lengthy to administer and score
Part Three

AD8: A Brief Informant Interview to Detect Dementia
Desired Attributes of a Brief Scale

- Predictive of early dementia
- Inexpensive
- High face validity
- Reliable, sensitive and specific
- Brief
- Easy to administer and score
- Socially acceptable
- Culturally sensitive
Time Considerations

- Given the brief period available to primary care physicians, instrument must be able to be completed in a short period of time (ideally in 2-3 minutes).

- Mini-Mental State Exam takes about 7-10 minutes to administer, the Short Blessed Test about 5-7 minutes, but both may be insensitive.

- There will likely be some acceptable time trade-off to the clinician, forsaking power in order to keep the inventory brief.
Informant Assessment – AD8

- Detect change in individuals compared to previous level of function
  - No need for baseline assessment
  - Patients serve as their own control
  - Not biased by education, race, gender

- Brief (< 2 min), Yes/No format
  - 2 or more “Yes” answers highly correlated with presence of dementia

Galvin JE et al, Neurology, 2005
<table>
<thead>
<tr>
<th>Problem</th>
<th>YES, A change</th>
<th>NO, No change</th>
<th>N/A, Don’t know</th>
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</thead>
<tbody>
<tr>
<td>Problems with judgment (e.g. falls for scams, bad financial decisions, buys gifts inappropriate for recipients)</td>
<td></td>
<td></td>
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<tr>
<td>Reduced interest in hobbies/activities</td>
<td></td>
<td></td>
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<tr>
<td>Repeats questions, stories or statements</td>
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<tr>
<td>Trouble learning how to use a tool, appliance or gadget (e.g. VCR, computer, microwave, remote control)</td>
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<td>Forgets correct month or year</td>
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<tr>
<td>Difficulty handling complicated financial affairs (e.g. balancing checkbook, income taxes, paying bills)</td>
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<td>Difficulty remembering appointments</td>
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<tr>
<td>Daily problems with thinking and/or memory</td>
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**TOTAL AD8 SCORE**

Galvin JE et al, Neurology, 2005
To test how well the AD8 performs as a self-rating tool, we compare the AD8 administered to the participant compared with informant and clinician impression of cognitive status.

In real life settings, informants are not always available.
AD8 Scores by CDR and Rater

<table>
<thead>
<tr>
<th>CDR</th>
<th>N</th>
<th>CS</th>
<th>S</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>149</td>
<td>0.64 (1.19)</td>
<td>1.01 (1.52)</td>
</tr>
<tr>
<td>0.5</td>
<td>102</td>
<td>3.49 (2.32)</td>
<td>2.80 (2.19)</td>
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<tr>
<td>1</td>
<td>50</td>
<td>6.64 (1.74)</td>
<td>2.40 (2.51)</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>6.22 (2.66)</td>
<td>3.00 (2.66)</td>
</tr>
</tbody>
</table>

Intraclass Correlation Coefficient (ICC) = 0.522; 95%CI: .41-.62

Discrimination:
- Informant AUC = .895 (95% CI: .86-.93)
- Participant AUC = .735 (95% CI: .68-.79)

Galvin JE et al, Arch Neurol, 2007
Combining the AD8 with Performance

- Which brief cognitive measures could be combined with the AD8 to increase the ability to detect individuals with even the mildest stages of dementia?

- Combine with neuropsychological battery:
  - MMSE, Short Blessed, Animal Fluency, Boston Naming, CERAD Word List (10-item) immediate and delayed recall, Logical Memory,Trailmaking A and B, Digit Symbol
Summary

- The AD8 is a brief, valid and reliable screening tool to detect cognitive impairment.

- The AD8 takes less than three minutes to complete and can be reliably administered either in-person or over the phone.

- The AD8 can be administered to an informant (or to the patient when an informant is not available)

- Dementia may be detected at the earliest stages by placing emphasis on intra-individual, rather than inter-individual comparisons regardless of culture, language or race.

- The AD8 is also applicable for community use to assist in providing individuals with products and services that are most appropriate to their needs.
Websites

- Alzheimer’s disease, including clinical trials
  - clinicaltrials.gov
  - www.alz.org
  - www.alzforum.org
  - www.alzheimers.org
  - www.hbo.com/docs (The Alzheimer Project)

- Washington University Alzheimer’s Disease Research Center (ADRC)
  - http://alzheimer.wustl.edu