Implications of a Biologically Based Definition of Alzheimer’s Disease
NAPA 7-25-17

Clifford R Jack Jr MD
Prof. of Radiology and Alexander Family Professor of Alzheimer's Disease Research
Dept. Radiology, Mayo Clinic, Rochester, MN

What is Alzheimers disease (AD)?

- Symptoms (syndrome) vs disease
  - Shortness of breath vs heart, lung disease
  - Effect vs cause
- Dementia vs Alzheimer's disease
  - Dementia – progressive loss of cognitive ability leading to significant functional impairment (loss of independence)
- Alzheimers disease
  - Plaques
  - Tangles
  - Inflammation
  - Loss of neurons
Diagnosis of Alzheimer's disease

- Historic diagnosis (McKhann et al 1984): clinico-pathologic
  - Definite at autopsy
  - Probable or possible in life – syndromal definition
  - Definition “creep”
- Problems
  - Not all “AD” syndrome is AD (20%)
  - Some non AD syndromes are AD
  - Many AD are asymptomatic (up to 40%, depends on age)
- Solution - biomarkers

What is a biomarker?

- A measure of pathologic change that can be obtained in the living subject – biomarkers are proxies for specific pathologic changes in the brain
- Accepted Alzheimer's biomarkers are imaging or biofluid (CSF)*
Biomarkers are proxies for AD pathologic changes

*Measures of brain Aβ deposition – amyloid plaques*
- Amyloid PET
- CSF AB 42

*Measures of neurofibrillary tangles - pathologic tau*
- CSF phospho tau
- Tau PET

*Measures of neurodegeneration*
- FDG PET
- CSF total tau
- Structural MRI

**Amyloid PET - plaques**

Cognitively unimpaired  demented
Diagnosis of Alzheimer’s disease

  - Definite at autopsy
  - Probable or possible in life – syndromal definition

- Problems – treatment discovery and application
  - Not all “AD” syndrome is AD (20%)
  - Some non AD syndromes are AD
  - Many AD are clinically asymptomatic (up to 40%, depends on age)
85 yo F, progressive memory problem, demented, clinical diagnosis “Alzheimer's disease”

Cognitively unimpaired, 67 yo, M
Implications of biologically based (biomarker based) definition of Alzheimer's disease

- Specificity of biomarkers – AD treatment for those with AD
  - Clinical trials
  - Clinical practice
- Sensitivity of biomarkers – Prevention -- can not “treat” something that does “not exist”
  - Clinical trials
  - Clinical practice
- Prevalence - higher

NIA-AA Research Framework: Towards a Biological Definition of Alzheimer’s Disease

Clifford R. Jack, Jr. M.D., David A. Bennett, M.D., Kaj Blennow, M.D., Ph.D., Maria C. Carrillo, Ph.D., Billy Dunn, M.D., Cerise Elliott, Ph.D., Samantha Budd Haeberlein, Ph.D., David Holtzman, M.D., Ph.D., William Jagust, M.D., Frank Jessen, M.D., Jason Karlawish, M.D., Enchi Liu, Ph.D., Eliczer Masliah M.D., Jose Luis Molinuevo, M.D., Thomas Montine, M.D., Creighton Phelps, Ph.D., Katherine P. Rankin, Ph.D., Christopher Rowe, M.D., Laurie Ryan, Ph.D., Philip Scheltens, M.D., Eric Siemers, M.D., Nina Silverberg, Ph.D., Heather M. Snyder, Ph.D., Reisa Sperling, M.D.
July 28, 2017 -- Advisory Council Meeting #25

The meeting was held on Friday, July 28, 2017, in Washington, DC. The Advisory Council spent the morning discussing information gaps across the three areas of research, clinical care, and long-term services and supports. There was also a presentation on the recently released National Academy of Sciences, Engineering, and Medicine (NASEM) report on preventing cognitive decline. Additional presentations included a presentation on planning and progress towards the October Care and Services Summit and federal workgroup updates. Material available from this meeting is listed below and is also available at https://aspe.hhs.gov/advisory-council-alzheimers-research-care-and-services-meetings#Jul2017.

Comments and questions, or alerts to broken links, should be sent to napahhs.gov.

General Information

<table>
<thead>
<tr>
<th>Agenda</th>
<th>[HTML Version]</th>
<th>[PDF Version]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meeting Announcement</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Meeting Summary</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Public Comments</td>
<td>[HTML Version]</td>
<td></td>
</tr>
</tbody>
</table>

Presentation Slides

<table>
<thead>
<tr>
<th>2017 National Plan Update and Non-Federal Recommendations</th>
<th>[HTML Version]</th>
<th>[PDF Version]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Services Subcommittee Federal Update</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>CommunityRx for Community-Residing People with Dementia and Their Caregivers</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Dementia Caregiving in the U.S.</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Development of the FY 19 NIH Bypass Budget for Alzheimer's Disease and Related Dementias</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Implications of a Biologically Based Definition of Alzheimer's Disease</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Increasing Opportunities for Choice and Control for Persons with Dementia</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Interventions to Prevent or Slow Cognitive Decline, MCI and Dementia in Individuals without Dementia</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
<tr>
<td>Living Alone With Dementia</td>
<td>[HTML Version]</td>
<td>[PDF Version]</td>
</tr>
</tbody>
</table>
Long-Term Services and Supports Committee Update [HTML Version] [PDF Version]
Managing Chronic Conditions in People Living with Dementia [HTML Version] [PDF Version]
Preventing Cognitive Decline and Dementia [HTML Version] [PDF Version]
Research Summit on Dementia Care [HTML Version] [PDF Version]
The Many Challenges of Alzheimer's Disease [HTML Version] [PDF Version]

Videos

Welcome thru Clinical Care [Video]
LTSS Research [Video]
Public Comments thru Federal Workgroup Updates [Video]
Recommendations thru Adjourn [Video]

Last Updated: 06/27/2018