The Alzheimer’s and Dementia Research Landscape

Rebecca Edelmayer, Ph.D.
Sr. Director, Scientific Engagement
Medical & Scientific Relations
Our Time Today

1. About Alzheimer’s & Dementia
2. Understanding Risk
3. Early Detection and Diagnosis
4. Treatment Pipeline
5. How You Can Get Involved
2024 ALZHEIMER’S DISEASE FACTS AND FIGURES

NEARLY 7 MILLION AMERICANS ARE LIVING WITH ALZHEIMER’S

THE LIFETIME RISK FOR ALZHEIMER’S AT AGE 45 IS

1 in 5 for women

1 in 10 for men

Older Black Americans are 2X AS LIKELY to have Alzheimer’s or other dementia than Whites.

BETWEEN 2000 AND 2021, DEATHS FROM HEART DISEASE HAVE DECREASED 2.1% WHILE DEATHS FROM ALZHEIMER’S DISEASE HAVE INCREASED 141%.

1 in 3 seniors dies with Alzheimer’s or another dementia

IT KILLS MORE THAN BREAST CANCER AND PROSTATE CANCER COMBINED

Older Hispanic Americans are 1.5X AS LIKELY to have Alzheimer’s or other dementia than Whites.
What is Dementia?

- Dementia is a collection of symptoms related to cognitive decline.
  - This can include:
    - Cognitive symptoms
    - Behavioral symptoms
    - Psychological symptoms
- Alzheimer’s is the most common cause of dementia.
- Not everyone with cognitive decline has dementia. Some causes of cognitive decline are reversible.
The Hallmarks of Alzheimer's

1. Plaques
   - Made up of **beta amyloid**

2. Tangles
   - Made up of **tau**

3. Brain Cell Death
   - Healthy brain
   - Advanced Alzheimer's
Alzheimer’s Disease is a Continuum

Asymptomatic
No symptoms but biological changes may be occurring in the brain up to 20 years before symptoms start

MCI* due to Alzheimer’s Disease
Symptoms of cognitive decline appear

Mild
Symptoms interfere with some daily activities

Moderate
Symptoms interfere with many daily activities

Severe
Symptoms interfere with most/all daily activities

MCI = Mild Cognitive Impairment is an early stage of memory loss or other cognitive ability loss that may develop into dementia
What May Impact Risk of Cognitive Decline or Dementia?

- Constellation of reasons may be fundamental and unique to everyone
- Social determinants of health may impact some or all of these factors
- Strength of our understanding is different across risk factors
- Need to study risk from ALL angles
Reducing Risk of Dementia

- Positive, everyday actions can make a difference in brain health, even lowering the risk of cognitive decline and possibly Alzheimer's and dementia.
- Up to 40% of dementia cases could be prevented or delayed by targeting modifiable risk factors.
- Research suggests combining multiple healthy factors may be the most impactful.
Early Detection and Diagnosis
Benefits of an Early and Accurate Diagnosis

Medical Benefits
- Access to current treatments
- An opportunity to participate in clinical trials
- A chance to prioritize health, including making lifestyle changes

Emotional and Social Benefits
- More time to plan for the future, access resources
- Time to plan end-of-life decisions

Financial Benefits
- Cost savings for families
- Cost savings for the U.S. government
How is Alzheimer’s Currently Diagnosed?

There is no single test that can determine if a person is living with Alzheimer’s disease or another dementia. Doctors use a combination of diagnostic tools combined with medical history to make an accurate diagnosis.
What is a Biomarker?

A biomarker is a biological marker that measures change.

Biomarkers are reliable predictors and indicators of disease and disease progression.

For example:

- Glucose is a biomarker for insulin resistance and diabetes.
- Cholesterol is a biomarker for heart disease

Uses of biomarkers in Alzheimer’s disease include:

**Diagnostic:** used to determine diagnosis

**Enrichment:** used to determine entry into a clinical trial

**Prognostic:** used to determine course of illness

**Predictive:** used to track outcomes and side effects of treatments
Biomarker Development for Hallmark Brain Changes

1906
Amyloid and Tau Pathology

Late 1990s
CSF A\(\beta\), Tau, p-Tau

Mid-late 2000s
Amyloid PET

Mid-late 2010s
Tau PET

2020s
Plasma A\(\beta\), Tau, p-Tau
Modernizing the Diagnosis

Cognitively Unimpaired  Alzheimer’s Dementia

Biomarkers  History & Cognition

Cognitive function

Preclinical  MCI  Dementia

Aging

years or more before symptoms appear, the brain changes of Alzheimer's may begin.

Adapted from Reisa Sperling, BWH, MGH
Why is Early Detection so Important? Understanding the Treatment Landscape
## FDA-Approved Therapies for Alzheimer's

<table>
<thead>
<tr>
<th>Year</th>
<th>Therapy</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1906</td>
<td>First description</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>donepezil (Aricept)</td>
<td>Treat Symptoms: Cognition and Function</td>
</tr>
<tr>
<td>2000</td>
<td>rivastigmine (Exelon)</td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>galantamine (Razadyne)</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>memantine (Namenda)</td>
<td>Slow Disease Progression: Cognition, Function and Behavior</td>
</tr>
<tr>
<td>2004</td>
<td>memantine + donepezil (Namzaric)</td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>suvorexant* (Belsomra)</td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td>aducanumab (Aduhelm)</td>
<td></td>
</tr>
<tr>
<td>2023</td>
<td>lecanemab (Leqembi)</td>
<td></td>
</tr>
<tr>
<td>2023</td>
<td>brexipiprazole (Rexulti)</td>
<td></td>
</tr>
<tr>
<td>2024</td>
<td>donanemab (Kisunla)</td>
<td></td>
</tr>
</tbody>
</table>

* Suvorexant approved for insomnia, but trials show it is safe and effective in an Alzheimer's disease population.
2024 Alzheimer’s Drug Development Pipeline

Unique therapies

Clinical Trials for Alzheimer’s disease as registered on clinicaltrials.gov

New agents have entered the pipeline in the past year

Total number of participants needed to populate all currently active trials (Phases 1, 2 and 3)

Targets of agents currently in clinical trials include:

- 76% disease modification
- 12% cognitive enhancement
- 13% behavioral and neuropsychiatric symptoms
- 75% novel disease processes
- 25% amyloid & tau

Adapted from Cummings J. et al. 2024

* As of April 2024
Get Involved in Research

• TrialMatch is a free clinical studies matching service designed to provide a customized list of potential study matches to each user.

• Healthy and cognitively impaired people from all backgrounds are needed to participate in Alzheimer’s and dementia research.

*Over 370,000 users and includes 750+ clinical studies around the world.

731 Alzheimer’s Disease
351 Mild Cognitive Impairment
36 Vascular Dementia
110 Other Dementia

*as of March 2024
New Era of Research, Treatment and Care…

A combination of sustainable risk reduction strategies and powerful effective treatments

Adapted from R. Petersen, Neurology 2018 91(9)
In Summary...

- Exciting time in research
- New tools for detection and diagnosis
- New approved treatments and more in the pipeline
- Strategies for risk reduction

It is a NEW ERA of Research, Diagnosis, Treatment & Care