Advancing the Science: Alzheimer’s and Dementia Research

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Our Time Today…

- Landscape of Alzheimer’s and Dementia Science
- Biomarkers are Changing the Game
- Latest Advances in Clinical Trials, Treatments and Lifestyle Interventions
Dementia is a Syndrome

- Dementia is a collection of symptoms related to cognitive decline
- Can include cognitive, behavioral and psychological symptoms
- Due to biological changes in the brain
- Alzheimer’s is most common cause
- Mixed dementia is very prevalent
- Some causes of cognitive decline are reversible and not truly dementia

Continuum of Cognitive Impairment

- Impairment does not interfere with activities of daily living
- Impairment in two or more cognitive functions that interfere with activities of daily living

MCI is a known risk factor for dementia

Everyone who experiences dementia passes through MCI

When you prevent new cases of MCI, you are preventing new cases of dementia
**Hallmarks of Alzheimer’s Disease**

- **Neuritic Plaques**: Extracellular deposits of beta-amyloid
- **Neurofibrillary Tangles**: Intracellular deposits of hyperphosphorylated tau
- **Neurodegeneration Cortical Atrophy**
  - Healthy Brain
  - Advanced Alzheimer’s

**Risk Factors**

- **Ages of People with Alzheimer's Dementia, 2019**
  - <65 years: 0.2 million (3%)
  - 65-74 years: 0.9 million (16%)
  - 75-84 years: 2.6 million (45%)
  - 85+ years: 2.1 million (36%)

Created from data from Hebert et al.\(^2,51\)

**Alzheimer’s is not typical aging**

- **Age**
- **APOE-e4 gene**
- **Family history**
  - Genetics
  - Shared environmental & lifestyle factors
- **Cardiovascular disease**
  - Hypertension, diet, diabetes, smoking
- **Social & cognitive stimulation**
- **Education**
- **Traumatic brain injury**
**Available Therapies**

Disease modification versus symptomatic benefit in the treatment of Alzheimer's Disease

- Currently, there are no therapies that can cure Alzheimer's
- Some drugs are available to temporarily improve symptoms

**Impact of Alzheimer's**

**IN 2019**, Alzheimer's and other dementias will cost the nation $290 BILLION

**BY 2050**, these costs could rise as high as $1.1 TRILLION

MORE THAN 16 MILLION AMERICANS provide unpaid care for people with Alzheimer's or other dementias

ALZHEIMER'S DISEASE IS THE 6TH leading cause of death in the United States

5.8 MILLION Americans are living with Alzheimer's

BY 2050, this number is projected to rise to nearly 14 MILLION
We Advocate

Alzheimer’s and Related Dementia Research Funding at the NIH

Alzheimer’s Association Global Research Investment

$165 million
450+ projects
25 countries
Moving the Needle on Research

Our Research Priority Areas
Inform the Structure of our Grant Program and Global Collaborative Partnerships

Exciting Time in Research
The Hunt for Biomarkers

- Biological marker to measure change
- Reliable predictor and indicator of disease and disease progression
  - Glucose for insulin resistance and diabetes
  - Cholesterol for heart disease
- Uses in Alzheimer’s disease include:
  - **Diagnostic**: determining diagnosis
  - **Enrichment**: reinforcing entry criteria into a clinical trial
  - **Prognostic**: determining course of illness
  - **Predictive**: treatment outcomes and safety assessment

Biomarkers Are Changing the Game

- **Saliva Biofluid**
- **Amyloid-β PET**
- **Tau PET Imaging**
- **Blood Test**
- **Optical Evaluation**
- **CSF – Lumbar Puncture**
Modernizing the Diagnosis

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

Adapted from Clifford Jack, Mayo Clinic

RESULTS OF THE IDEAS STUDY JUST PUBLISHED IN JAMA APRIL 2, 2019

National study on utility of amyloid PET scans
~18,500 Medicare beneficiaries
With mild cognitive impairment (MCI) or dementia of uncertain cause

Aim 1: Impact of scan on management plan at 3 months
Aim 2: Impact on major medical outcomes at 12 months

Two-thirds of participants had a change in their diagnosis and/or care management as a result of their PET scan results
Detect NfL (neurofilament light) in blood in DIAN patients before symptoms occur
Identified 10 blood proteins plus age and APOE4 status, aligned with brain amyloid build up with high accuracy in individuals who were cognitively unimpaired
C2N Diagnostics announced FDA breakthrough status and pivotal PARIS trial
PARIS trial is an IDEAS add-on study: Plasma Test for Amyloid Risk Screening

Progress Toward More Effective Treatment By 2025
Medicines
Lifestyle/ Behavior
How A Potential Therapy is Developed

Current Landscape of Clinical Trials for Alzheimer’s & Dementia

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>As of Jan. 2019</th>
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<tbody>
<tr>
<td>97</td>
<td>167</td>
<td>56</td>
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Always a Need for Participants

Please note that an agent or device may be associated with more than one active clinical trial.
Progress Toward More Effective Treatment By 2025

Medicines

Anti-Amyloid Trials In The News

- Drug trial demonstrates:
  - Clearance of amyloid plaque
  - Suggested improvement of cognition
  - BAN2401 (Ph 3 Readout 2022)
  - Phase 3 confirmatory study to validate Phase 2b results

- Biogen and Eisai stop Phase 3 trial of Aducanumab
Diverse Therapeutic Mechanisms Under Investigation

- Environmental Mediated Factors
- Sleep & Circadian Rhythms
- Cell Death
- APOE & Lipid Neurobiology
- Presenilin Biology
- Proteinopathies
- Neuroendocrine
- Circuits and Synapses
- Amyloid Beta
- Tau
- Vascular Etiology
- Circuits and Synapses
- Genetics
- Immunity and Inflammation
- Metabolism and Bioenergetics
- Autophagy, Endocytosis, Membrane Trafficking

Research Focused on Non-cognitive Symptoms of Dementia

- Non-cognitive = behavioral and psychological symptoms
- A major quality of life problem for people living with dementia and their caregivers
- Ongoing studies focusing on therapies for
  - Agitation
  - Sleep disturbances
Progress Toward More Effective Treatment By 2025

Lifestyle & Behavior

In The News…SPRINT-MIND Study

Lowering blood pressure could cut risk factor for dementia

The New York Times
Study Offers Hint of Hope for Staving Off Dementia in Some People
People who received intensive treatment for hypertension were less likely to develop minor cognitive problems than those receiving standard treatment.
The SPRINT-MIND Study
First Study to Demonstrate Reduction of New Cases of Cognitive Impairment

- 9,000+ people, Over age 50, All-cause dementia risk
- Standard vs. Intensive Blood Pressure Intervention
- Intensive treatment 120 systolic vs. 140 systolic
  - 19% reduced risk for MCI
  - 17% reduced risk for dementia * Not Statistically Significant
  - 15% reduced combined risk for MCI and dementia
- Dramatic reduction of small vessel disease on MRI

SPRINT-MIND 2.0

- SEED 2.0 to clarify impact on dementia with 2 years additional follow up
- Over 7,000 will be contacted for additional follow up
- Initiate study NOW to allow for maximum participant retention
Why Is This Important?

There are things you can do to reduce your risk of MCI and dementia – especially regarding cardiovascular disease risk factors.

Immediate opportunity with life changing impact potential

FINGER Multidomain Intervention Trial

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial


- 1260 participants, ages 60-77
- 1st large-scale study to report multidomain intervention can be beneficial

Change in cognitive performance

![Graph showing change in cognitive performance during the 2-year intervention](image)
U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk

**Two year** multi-center randomized clinical trial

**Self-Guided** and **Structured** Lifestyle Groups

**2,000 Participants** at five U.S. sites

- Landmark study
- Uniquely positioned
  - Embedded in community systems
  - Ready for implementation if the intervention works
- Goal of 23% diversity
- Adults 60-79, with parent or sibling with memory loss or dementia
- There are several ancillary studies applying to NIH that would add imaging, sleep measures, monitoring of gut health, etc.
Changing the Trajectory of Alzheimer’s Disease

DELAYED ONSET
If we develop a treatment by 2025 that delays the onset of Alzheimer’s by just 5 years, then:

5.7 MILLION people expected to develop Alzheimer’s would not in 2050.
10 Ways to Love Your Brain

START NOW

It’s never too late or too early to incorporate healthy habits.

How to Get Involved in Research

*Over 350,000 Users as of Today*

250+ Clinical Studies

500+ Study Locations

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

Types of Studies Available

- Treatment - 106
- Diagnostic - 43
- Prevention - 12
- Quality of Life - 119
- Online - 17
In Summary …

• Alzheimer’s Association is a global leader for Alzheimer’s and dementia science

• Exciting time in research
  – New tools for detection and diagnosis
  – Growing diversity of therapies under investigation

• New research adding credibility to future therapy that combines drugs and modifiable risk factor interventions

• There is HOPE in research !!