Risk Factors for Alzheimer’s and Dementia

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alzheimer's association®
Our Time Today…

• Prevalence of Alzheimer’s Disease
• Diversity in Research
• Risk Factors
• Latest Advances in Clinical Trials, Treatments and Lifestyle Interventions
Prevalence and Incidence

Projected Number of People Age 65 and Older in the U.S. Population with Alzheimer's Dementia

<table>
<thead>
<tr>
<th>Year</th>
<th>Millions of people with Alzheimer's</th>
<th>Ages 65-74</th>
<th>Ages 75-84</th>
<th>Ages 84+</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>4.7</td>
<td></td>
<td></td>
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<tr>
<td>2020</td>
<td>5.8</td>
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<tr>
<td>2030</td>
<td>8.4</td>
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<tr>
<td>2040</td>
<td>11.6</td>
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<tr>
<td>2050</td>
<td>13.8</td>
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Every 65 seconds, someone in the United States develops Alzheimer's disease.
Impact of Alzheimer’s

Alzheimer’s disease is the 6th leading cause of death in the United States among all Americans.

Alzheimer’s disease is the 5th leading cause of death in the United States among 65+ and women of all ages.
Gender and Racial Differences in Alzheimer’s Prevalence

- Almost two-thirds of Americans with Alzheimer’s are women.
- Older African Americans and Hispanics are more likely, on per-capita basis, than older whites to have Alzheimer’s.
  - Mostly due to health, lifestyle and socioeconomic risk factors

*2019 Alzheimer’s Disease Facts and Figures
Studying Dementia from All Angles

First data on dementia prevalence in LGB seniors

- Study of more than 4,300 LGB people 60+
- 8% diagnosed with dementia
- Younger on average (69 years old)
- Number expected to double by 2040
- Unique challenges
  - Greater exposure to risk factors
  - More likely to age without spouses, partners or children
  - Lower rates of access to care
- Working with SAGE, the Association calls for culturally competent care and support services
Importance of Diversity in Clinical Trials

• < 5% of trial participants are ethnoracial groups
• Increased modifiable risk factors for AD
• African Americans less likely to participate in clinical trials and have higher drop out rates in AD trials
Diversity in Clinical Trials.....

• Allows the results to be a representation of the general public
• To investigate potential biological differences across diverse groups and their effects on drug efficacy and adverse events
• To identify socio-economic, behavioral and cultural risk factors
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**
Modernizing the Diagnosis

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

Adapted from Clifford Jack, Mayo Clinic
Biology Impacts Behavior

β-Amyloid plaques

Brain cell death

Tau tangles

Adapted from Gil Rabinovici, UCSF
The Role Our Genes Play in Alzheimer’s

Relatively rare: 1-3% of all cases of Alzheimer’s

Deterministic Risk

APOE

Chromosome 19

19q13.2

APOE2

APOE3

APOE4

*Alzheimer's disease

Adapted from DIAN-TU website; Lambert et al 2013 Nature Genetics; Ortiz et al 2015 Alzheimer's Disease: Challenges for Future; Stritmatter et al., 1993; Corder et al., 1993
Factors that Affect Risk of Cognitive Decline

Fig. 1. Strength of evidence on risk factors for cognitive decline.
Factors that Affect Risk of Dementia

Fig. 2. Strength of evidence on risk factors for dementia.
Focus on Prevention

THE LANCET

The Lancet Commission on dementia

"Effective dementia prevention, intervention, and care could transform the future for society and vastly improve living and dying for individuals with dementia and their families. Acting now on what we already know can make this difference happen."

A Commission by The Lancet

alzheimer's association

Global Dementia May be Preventable

The Lancet 2017 390, 2673-2734
DOI: (10.1016/S0140-6736(17)31363-6)
Possibility of Prevention
DIAN TU Trials

• Testing therapeutics on individuals with genetically-based, younger-onset Alzheimer’s and to expand biomarker use.

• **DIAN TU Next Generation (NexGen) Study**
  – Uses innovative trial designs to accelerate timelines
  – Incorporates amyloid and tau imaging and other emerging biomarkers

• **DIAN TU Dose Escalation Study**
  – Part of the DIAN-TU Next Generation Study
  – Increasing the dose of the experimental anti-amyloid therapy (Solanezumab) to maximize its therapeutic benefit.

• **Study results expected to be reported in 2020**
In DIAN individuals, 2.5+ hrs/ week of moderate exercise linked to less brain changes and more benefits for cognition, function.

Published in *Alzheimer's & Dementia*
Nearly a quarter of a million Americans
Understudied population

- 600 participants, under 65 years of age
- No known AD-causing mutations
- Observational Study: Disease progression
- Followed for at least 2 years
- Illuminating similarities and differences with late onset AD
- Battery of data
  - MRI, PET imaging, CSF, blood, and genetics
  - Cognitive and behavioral measures
- Less likely to have other medical conditions that complicate clinical trials
A4 – Treatment Trial (n=1000)
- Cognitively normal
- Amyloid PET Positive (+)
- Anti-amyloid therapy (Solanezumab), Dose escalated, Trial lengthened (4½ yrs)

LEARN – Observational Trial, Natural History Study (n=500)
- Companion study to A4, 1st of its kind
- Cognitively normal, determining rate of cognitive decline
- Screen failed A4: amyloid PET (-)
- Biomarkers: Tau PET Scans to determine relationship with cognitive decline
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

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levalahti, Satu Ahtiluoto, Riitta Antikainen, Lars Backman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Joana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilkka Soininen, Mila Kivipelto

- 1260 participants, ages 60-77
- 1st large-scale study to report multidomain intervention can be beneficial
Does a recipe that combines lifestyle interventions prevent or delay cognitive decline?

U.S. POINTER will evaluate two healthy lifestyle interventions:

- Physical Exercise
- Nutritional Counseling & Modification
- Cognitive & Social Stimulation
- Improved Self-Management of Health Status
Combining multiple healthy lifestyle factors may be more impactful for reducing dementia risk

- Healthy diet
- Moderate to vigorous physical activity
- Light to moderate alcohol intake
- Smoking
- Cognitive stimulation

4 or 5 → 59% lower risk of Alzheimer’s dementia
2 or 3 → 39% lower risk
May even offset risk associated with genetics
Sleep Research at AAIC 2019

- Use of sleep medication, especially in people who do not have sleep disturbances, may increase risk for dementia
- However poor sleep is a risk factor for Alzheimer’s and also worsens cognitive function in all people
- A drug trial focused on improving irregular sleep patterns showed positive preliminary benefit
- Other research focused on behavioral sleep interventions such as light therapy and physical activity
- The Alzheimer’s Association offers a variety of coping strategies for sleep issues and sun downing on our website, alz.org
A Woman’s Reproductive History and Risk for Dementia

• 14,500+ women members of Kaiser Permanente Northern California

• Dementia risk studied:
  – Having 3+ children, decreased risk
  – History of miscarriage, increased risk
  – Longer reproductive period, decreased risk

• Smaller study out of UK
  – Total months pregnant, decreased risk
Reproductive History Across the Lifespan and Dementia Risk

• Mechanisms are unknown and more research is clearly needed

• Possible explanations
  – Nutrition, both lifespan and during pregnancy
  – Immune system changes during pregnancy, which may be persistent
  – Changes in vascular system
  – Hormonal changes
  – Other biological or social factors
Alzheimer’s Risk, Progression and Resilience Differs by Sex

• New research suggests sex-specific differences may inform unique risk profiles and define the biology behind Alzheimer’s

• 11 novel sex-specific risk genes for Alzheimer’s disease

• Differences in the structural and functional connections in the brains of women that might contribute to accelerated spread of abnormal tau protein

• Women who participated in the paid labor force showed slower rates of memory decline in late-life
10 Ways to Love Your Brain

START NOW

It’s never too late or too early to incorporate healthy habits.
A WORLD WITHOUT ALZHEIMER'S DISEASE.

OUR VISION

ALZ.ORG