Reducing Dementia Risk in At Risk Populations

April 8, 2025

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None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

This publication was made possible by NU58DP007507 from Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Department or CDC. [ECHO Idaho] [2025]





Disclosures

- I am a full-time employee of the Alzheimer's Association.
- Received grant funding from National Institutes of Health and Center for Disease Control and Prevention.
- Spouse is an employee in Abbott Labs in an unrelated field.

Alzheimer's Association

The Alzheimer's Association forges partnerships with all those with the shared commitment to end Alzheimer's and other dementia, including Alzheimer's organizations around the globe, the National Institutes of Health, National Institute on Aging, universities, corporations and the pharmaceutical, biotech and device industries. This and additional information can be found at www.alz.org/about/transparency.



Learning Objectives

- Describe the current landscape of what we know about prevalence and incidence across the U.S. and in populations that may have greater risk.
- Detail examples of modifiable risk factors for cognitive decline and dementia.
- Outline strategies being pursued to address modifiable risk factors, and the current state of this research.



Vision: A world without

Alzheimer's disease

and all other dementia.™



Our Research Strategy

Dynamic, Durable, Multi-dimensional, Multi-faceted



SEED

new ideas



\$430M

currently active



SPEED

the development of new therapies



1150 projects



SCALE

to accelerate the science



countries



2024
ALZHEIMER'S DISEASE
FACTS AND FIGURES



7 MILLION

AMERICANS ARE LIVING
WITH ALZHEIMER'S

1 IN 3

SENIORS DIES WITH ALZHEIMER'S OR ANOTHER DEMENTIA

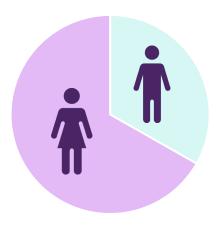
BREAST CANCER AND PROSTATE CANCER

COMBINED

OVER 11 MILLION
AMERICANS PROVIDE
UNPAID CARE
FOR PEOPLE WITH ALZHEIMER'S

OR OTHER DEMENTIAS

What We Know about Prevalence and Incidence



Almost **two-thirds** of Americans with Alzheimer's are **women.**



Older Black and Hispanic
Americans are
disproportionately more
likely than older Whites to
have Alzheimer's or other
dementias.

Prevalence of cognitive impairment approx 54% in American Indians aged 70-95

35% Mild Cognitive Impairment; 10% dementia

Significant impact of cardiovascular disease, hypertension & diabetes

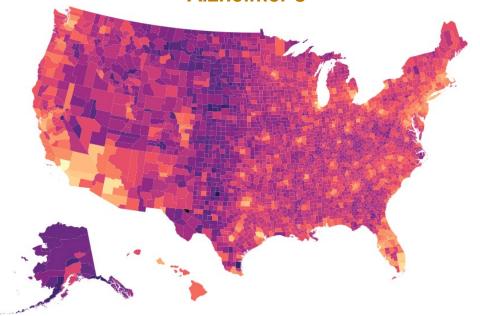
Opportunities to address risk factors such as hypertension & diabetes

Need for culturally sensitive screening tests



US County Dementia Level Prevalence

Estimated number of people living with Alzheimer's



This is the **first ever county-level** estimates of the **prevalence** of Alzheimer's dementia in people 65 and older

They found the **highest** U.S. prevalence of Alzheimer's are in the East and Southeastern regions

Demographic characteristics including older

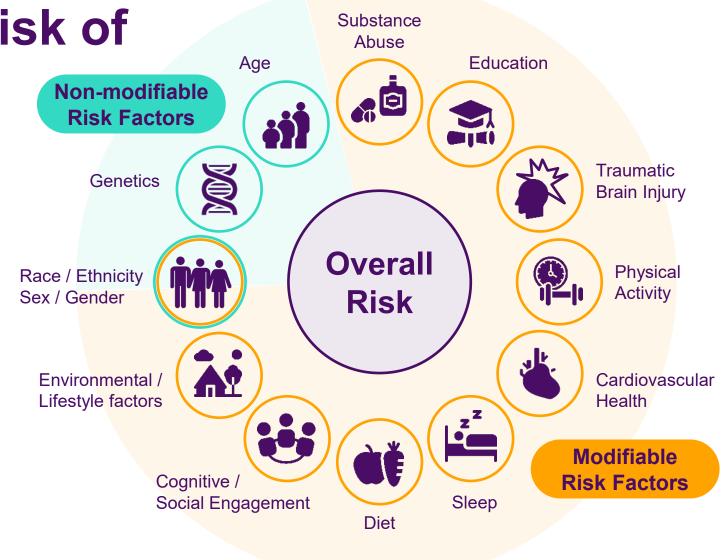
average and higher percentages of Black and **Hispanic** residents may explain elevated prevalence

First ever county level prevalence for Alzheimer's will help public health programs better understand and pinpoint areas of high risk and need



What May Impact Risk of Cognitive Decline Non-more Risk From the Control of the

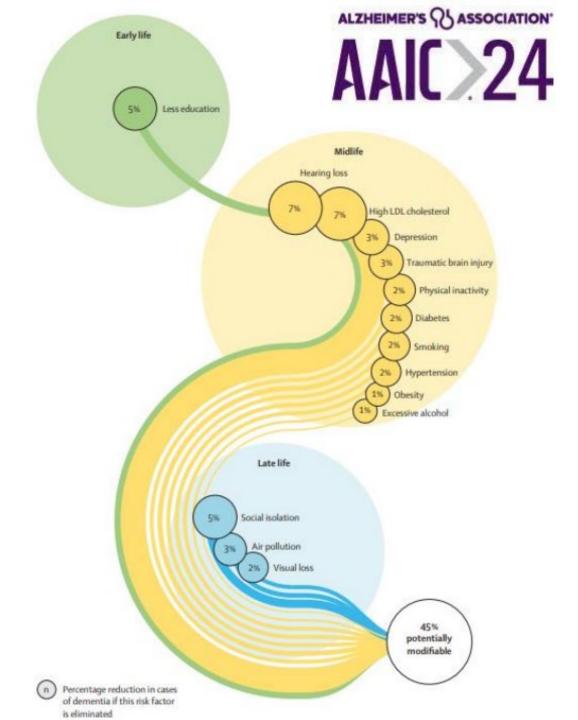
- Constellation of reasons may be fundamental; each person's risk is unique to their lived experience
- Environment may impact one or more of these
- Strength of our understanding is different across risk factors
- Need to study risk from ALL angles

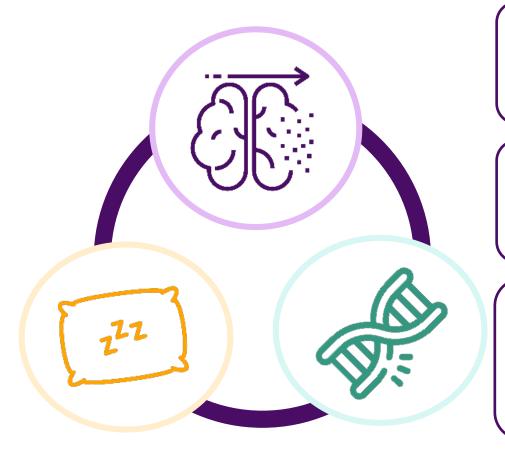


Focus on Risk Reduction

THE LANCET

Suggests 14 modifiable risk factors, if eliminated, would have impact on nearly 50% of all dementia worldwide.





Studies indicate that those who report short sleep in mid life have an increased risk of developing dementia 25-30 years later.

Poor sleep is associated with changes in Alzheimer's biomarkers including amyloid and tau.

Recent (small) study showed treatment of sleep disturbances reduced the levels of Alzheimer's-related biomarkers. Possible strategy for prevention

Strong Links to Vascular Health

- Confounding factors
 - Midlife Hypertension
 - Midlife Obesity
 - Diabetes
 - Smoking
 - Physical Activity
 - Sleep Quality
- Possible Mechanisms
 - Arterial stiffness
 - Endothelial dysfunction
 - Oxidative damage
 - Inflammation

Hypertension Oxidative damage, metabolic dysfunction and exacerbates mechanisms Cellular accumulation of inflammation drive brain atrophy, demylenation non-heme iron outside of of aging to accelerate and decline in neurotransmission binding complexes produce ROS cognitive decline and increase dementia risk Systemic Oxidative Inflammation Damage IL-6, IL-1β, ROS Production TNFa, CRP Bioactivity Neuroinflammation acts reciprocally to Oxidative damage iron homeostasis to increase causes metabolic oxidative damage; impairs dysfunction; cerebrovascular function mitochondria upregulate unbound iron to compensate for energetic failure Age, hypertension, and Autonomic cerbrovascular disease increase High blood pressure & low heart rate variability Dysregulation risk for vascular injury; cerebral impair endothelial function; exacerbate iron Decrease microbleeds cause focal dyshomeostasis, metabolic dysfunction Blood Pressure oxidative damage Control Target organ damage by oxidative stress and inflammation contribute to pre-clinical hypertension

Daugherty, Seminars in Cell and Developmental Biology, https://doi.org/10.1016/j.semcdb.2021.03.002

Seminars in Cell and Developmental Biology xxxx (xxxxx) xxxx

A.M. Daugherty

Obesity as a Risk Factor for Cognitive Decline and Cognitive Impairment

IMPACT

- Mid-life obesity is associated with:
 - Concurrent relative deficits of cognitive function
 - Increased rates of cognitive decline
 - Increased risks (50-90%) for dementia
- Late-life obesity: relationships are less clear
 - Obesity paradox
 - Survivorship bias
 - Later-life weight loss / frailty

MECHANISMS

- Inflammation
- Risk factors for vascular disease
- Hypertension, Insulin resistance, Dyslipidemia
- Accelerated aging
- Disruption of energy metabolism

Obesity <u>Prevention</u> as a Means to Reduce Risk: <u>Strategies</u>

Hearing Aid Intervention Shows Benefit

For Some



Previous research identified hearing loss as potentially largest dementia risk factor that can be addressed with existing tools

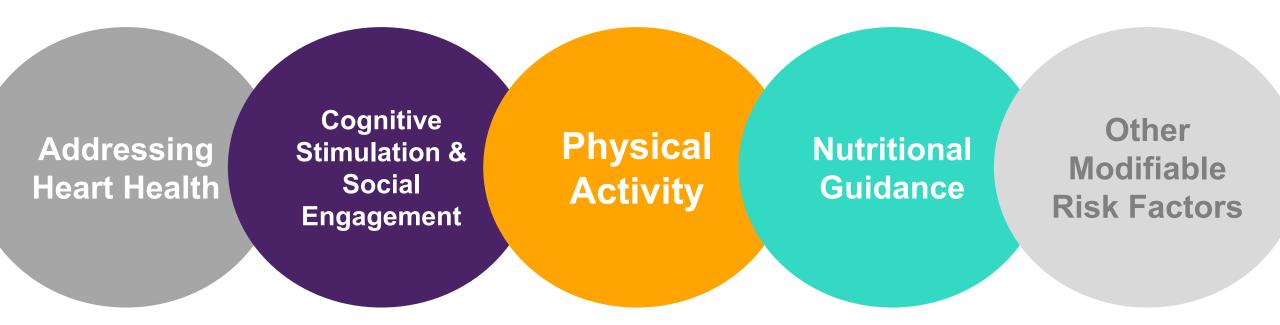
ACHIEVE study was a **3-year intervention** with **hearing aids** to investigate reduction in long-term cognitive changes

In total study population, there was no benefit of the intervention on cognitive decline. For a subgroup at risk of cognitive decline, the intervention cut decline in half

Take home message: Strategies to reduce cognitive decline risk will likely need to **target more than one** risk factor for success



Synergy: Multi-Component Interventions

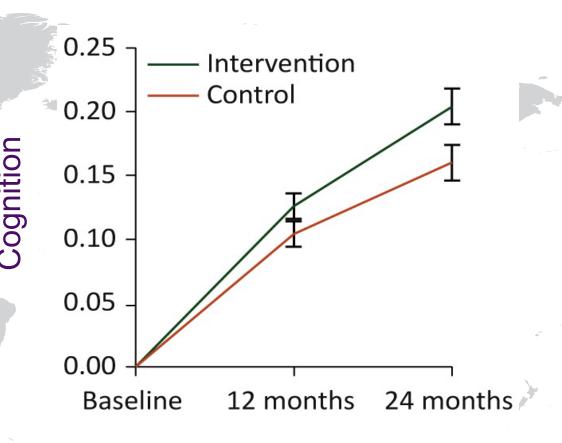


The FINGER Study: Design and Outcome



- 1260 cognitively healthy 60-77 year old adults, at increased risk for cognitive decline
- 2 year multi-domain study of Lifestyle Intervention vs. Usual Care
 - Nutrition
 - Exercise
 - Cognitive training
 - Vascular risk monitoring

Results of the large, long-term, randomized controlled **FINGER Study** suggested that a multi-domain intervention could **improve or maintain cognitive functioning in an at-risk population.**



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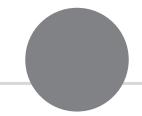


A Landmark Study for the US and Global Community



Participants

Older adults (60-79 years, no objective cognitive impairment) at increased risk for cognitive decline



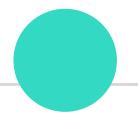
Study Design

Large, randomized controlled trial testing the effects of lifestyle intervention on cognitive function



Multi Domain

Self-guided and
Structured
Interventions:
Physical Activity,
Nutrition, Cognitive
Exercise, Medical
Monitoring



Robust Data Collection

Clinical, Biofluid, Genetic, Imaging, Sleep, Microbiome, Neurovascular

















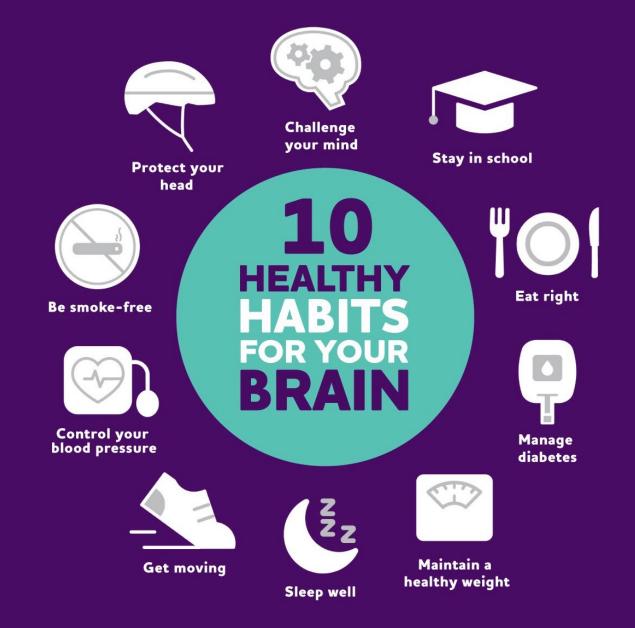
TRIAL RESULTS EXPECTED



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Vision: A world without

Alzheimer's disease

and all other dementia.™

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More info: alz.org

Contact: hsnyder@alz.org

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