

Healthy Brain Aging: Consider the Possibilities

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Outline

- Landscape of Alzheimer's disease and other dementias
- Risk Related to Alzheimer's disease
 - Factors that are not modifiable
 - Factors that may be modifiable (cardiovascular risk factors, lifestyle risk factors and other related risk factors)
- Women and Alzheimer's
- What does this mean for you

Growing Epidemic in the United States

5.3

million Americans of **ALL** Ages
will have Alzheimer's in 2015

6

Of the top 10 killers,
Alzheimer's is the
only one that cannot
be prevented, cured
or even slowed.

TH LEADING
CAUSE OF DEATH
IN THE U.S.



Total cost of care for those with Alzheimer's,
with more than two-thirds paid by Medicare and Medicaid

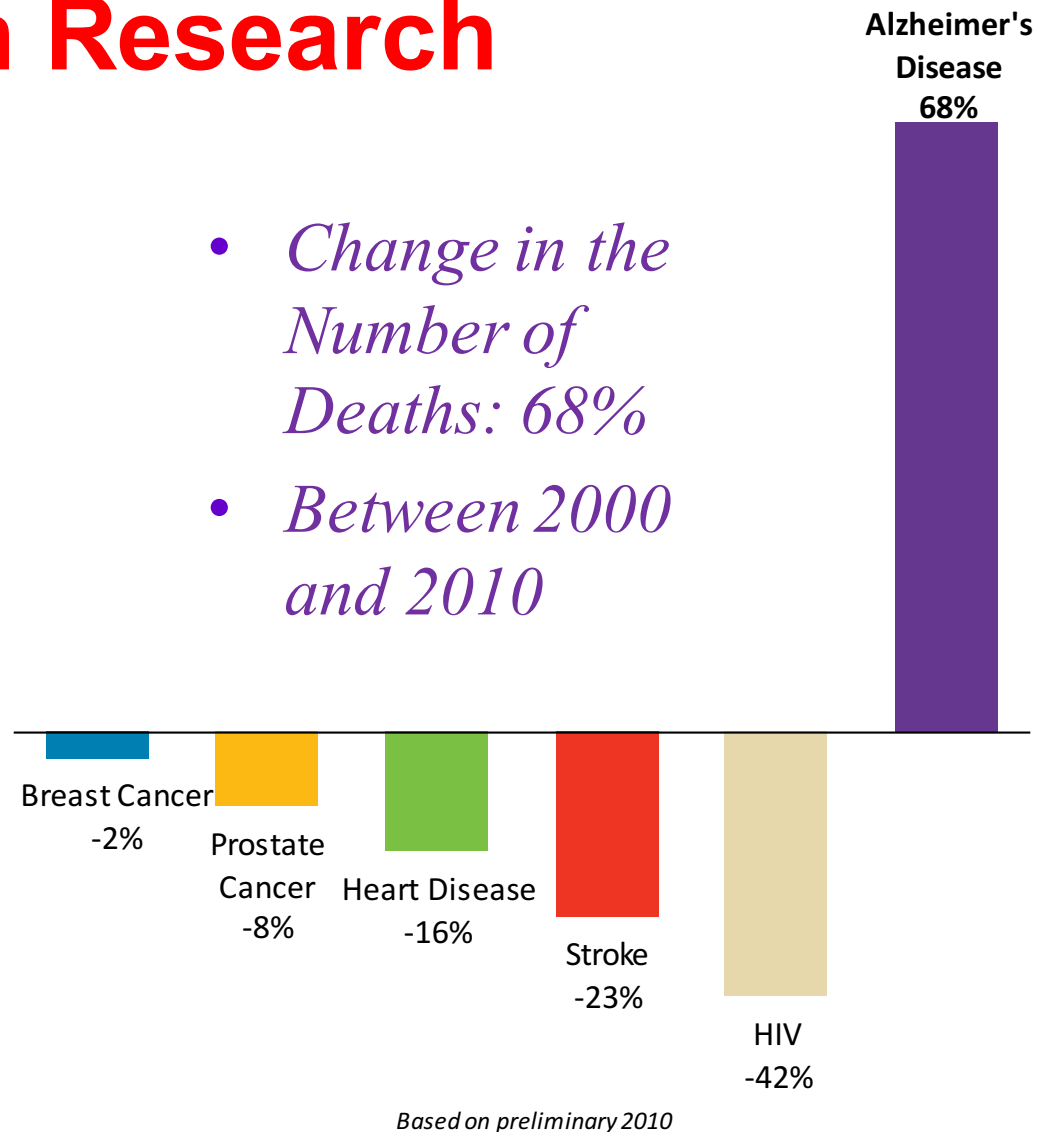
Source: Centers for Disease Control and Prevention (cdc.gov/nchs/fastats/leading-causes-of-death.htm)

Landscape of Alzheimer's

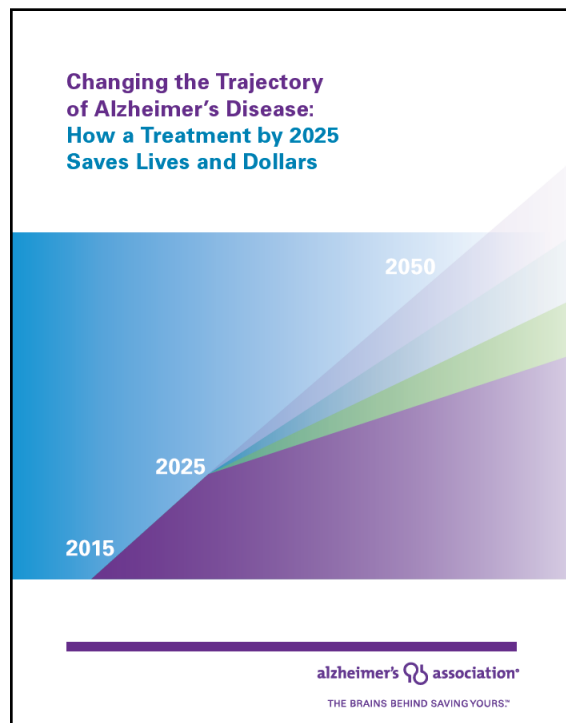
Hope In Research

- 6th leading cause of death across all ages
- 5th leading cause of death for those aged 65 and older
- Only cause of death among the top 10 in America without a way to prevent, cure or even slow its progression.

- *Change in the Number of Deaths: 68%*
- *Between 2000 and 2010*



Changing the Trajectory Report



DELAYED ONSET

If we develop a treatment by 2025 that delays the onset of Alzheimer's by just five years, then:

5.7
MILLION

people expected to develop Alzheimer's
would not in 2050.



Families
would save
\$87 billion in 2050.



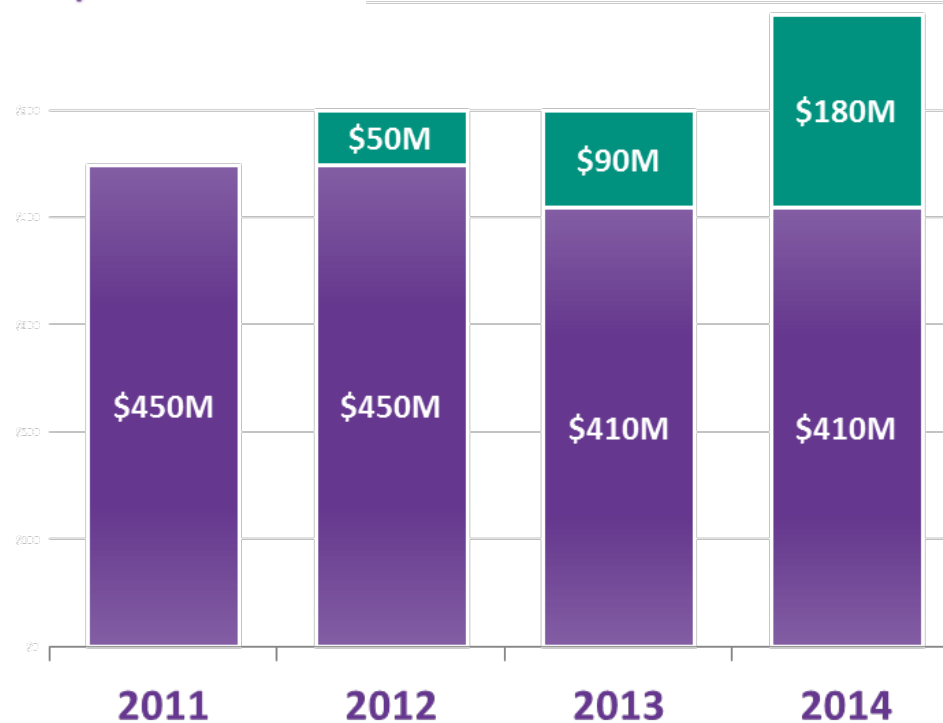
In total,
America would save
\$367 billion in 2050.

Federal Advocacy 2014

Challenge

Needed to move
past status quo
and on to growth

For that, no
substitute for
Congressional
engagement



\$350 million proposed by US Senate for Alzheimer's research

- US House of Representatives proposed a bill to increase funding for Alzheimer's research by \$300 million
- Senate increased to 350M
- If approved, biggest increase in Alzheimer's research funding ever.
- Be informed, get involved at alz.org/advocate



Alzheimer's Accountability Act

*Then... AAA requires the NIH to submit this Alzheimer's budget *directly* to Congress and the President.*

With comment only from the Secretary of HHS and the Alzheimer's Advisory Council.



Global Funder in Alzheimer's Research

- Currently funding over \$80 million to more than 350 active projects in 21 countries
- More than \$355 million since our first award
- Most Impactful Non-Profit Funder of AD

Thompson Reuters Web of Science, 2014

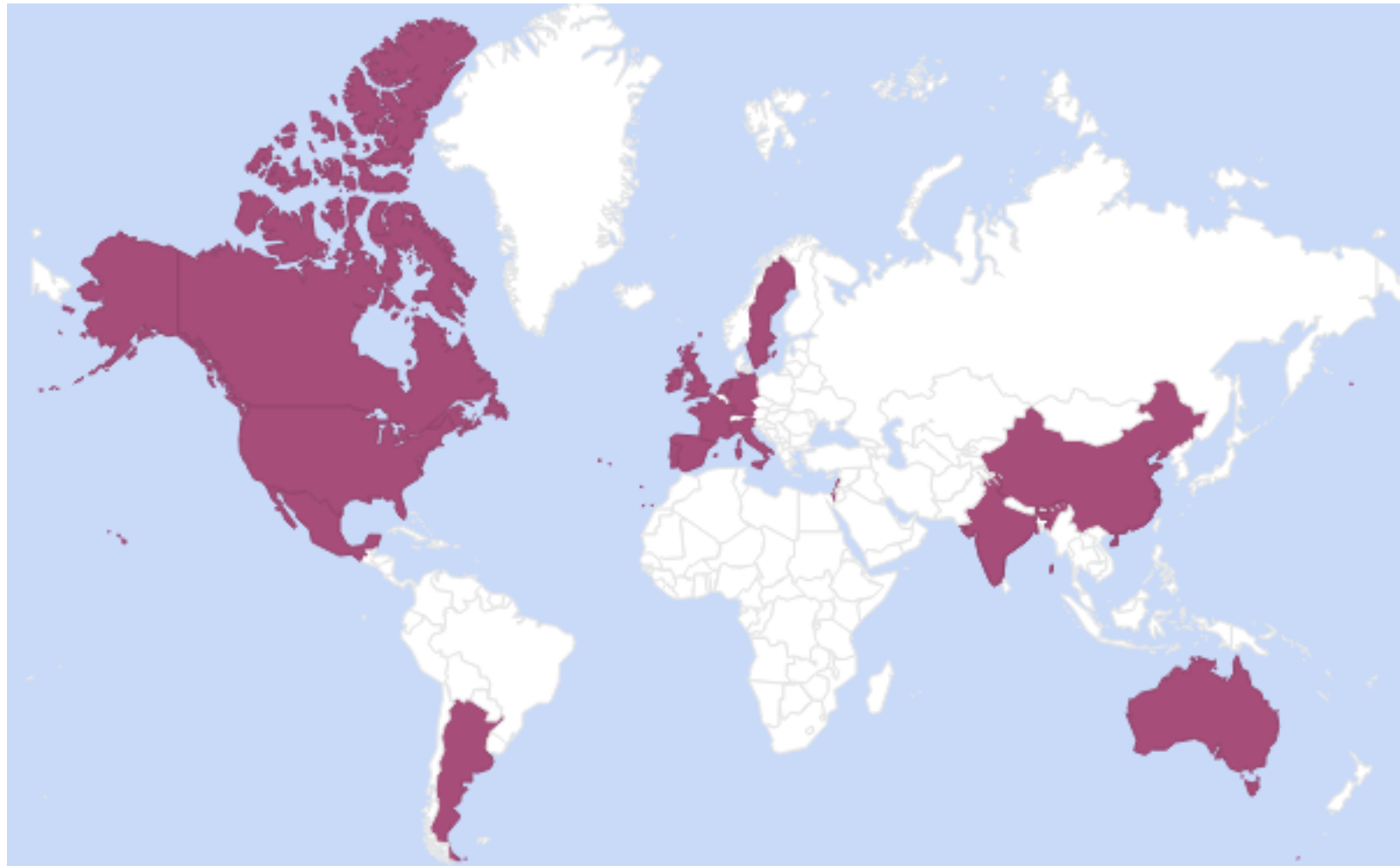


LOCAL Funder of Alzheimer's Research

- \$5.32 million to 28 awards since 1993 funded in Orange County
- Currently active - 6 awards \$850,000

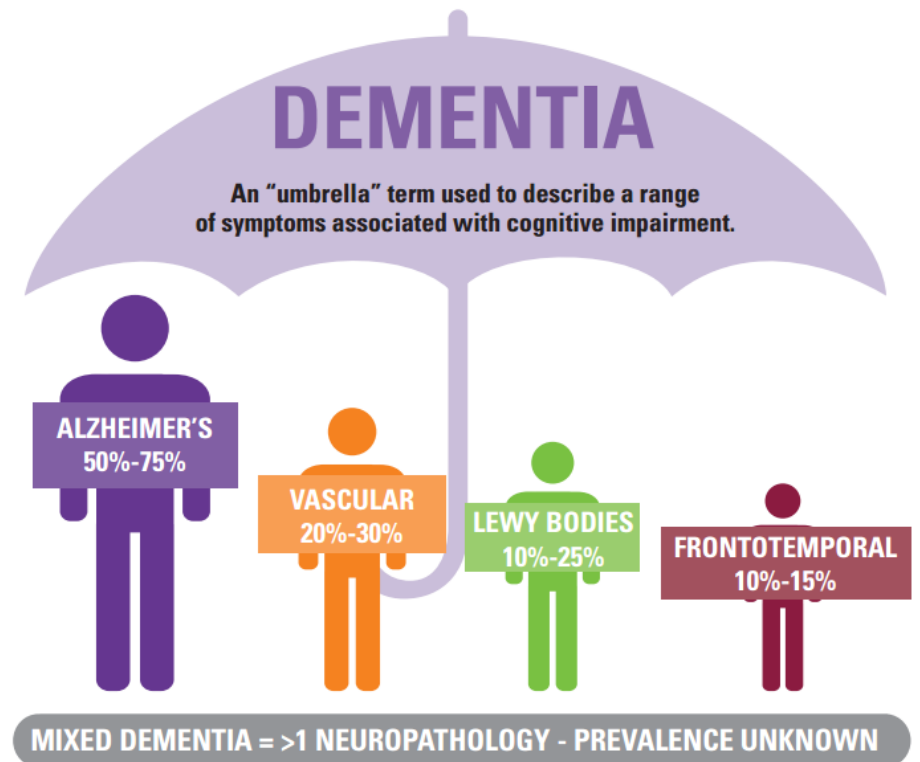


Global Funder in Alzheimer's Research



Dementia & Alzheimer's disease

- Dementia is the loss of memory due to changes in the brain
- Alzheimer's is most common form
- Biomarkers increase certainty of diagnosis, but definitive diagnosis by autopsy only
- Many mixed cases
- Many memory disorders reversible, not true dementia



What is Cognitive Aging

Key Features

Inherent in humans and animals as they age

Occurs across the spectrum of individuals as they age regardless of initial cognitive function

Highly dynamic process with variability within and between individuals

Includes some cognitive domains that may not change, may decline, or may improve with aging, and there is the potential for older adults to strengthen some cognitive abilities

Only now beginning to be understood biologically yet clearly involves structural and functional brain changes

Not a clinically defined neurological or psychiatric disease and does not inevitably lead to neuronal death and neurodegenerative dementia (such as in Alzheimer disease)

Blazer et al. JAMA. 2015;313(21):2121-2122

Cognitive Function, By Age

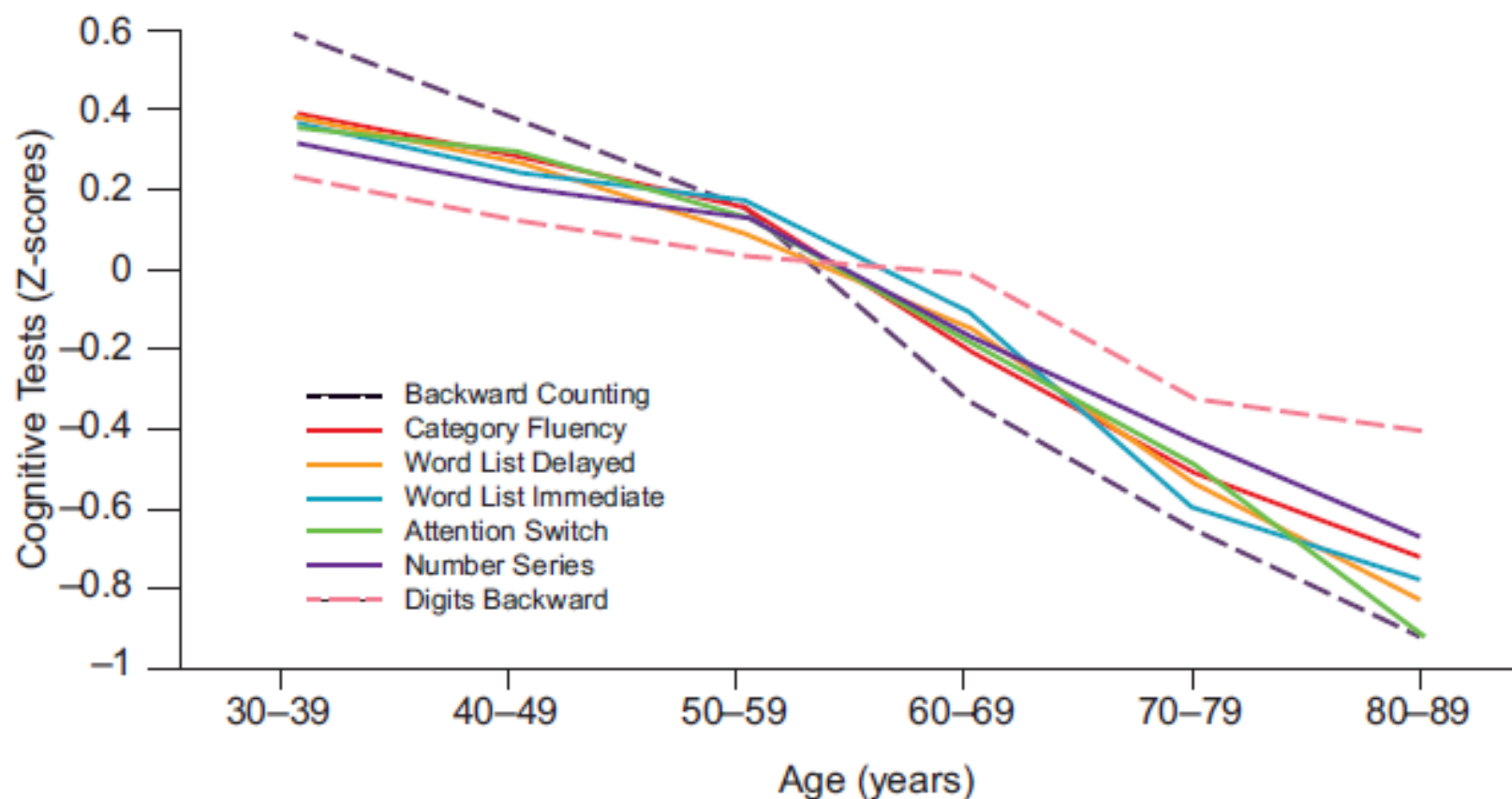


FIGURE 3-2 Differences in cognitive functioning by age based on different cognitive tests, Midlife in the United States Study II (MIDUS II), N = 4,268, United States, 2004–2006.

Developing Brain Gives Clues to Brain Change with Age

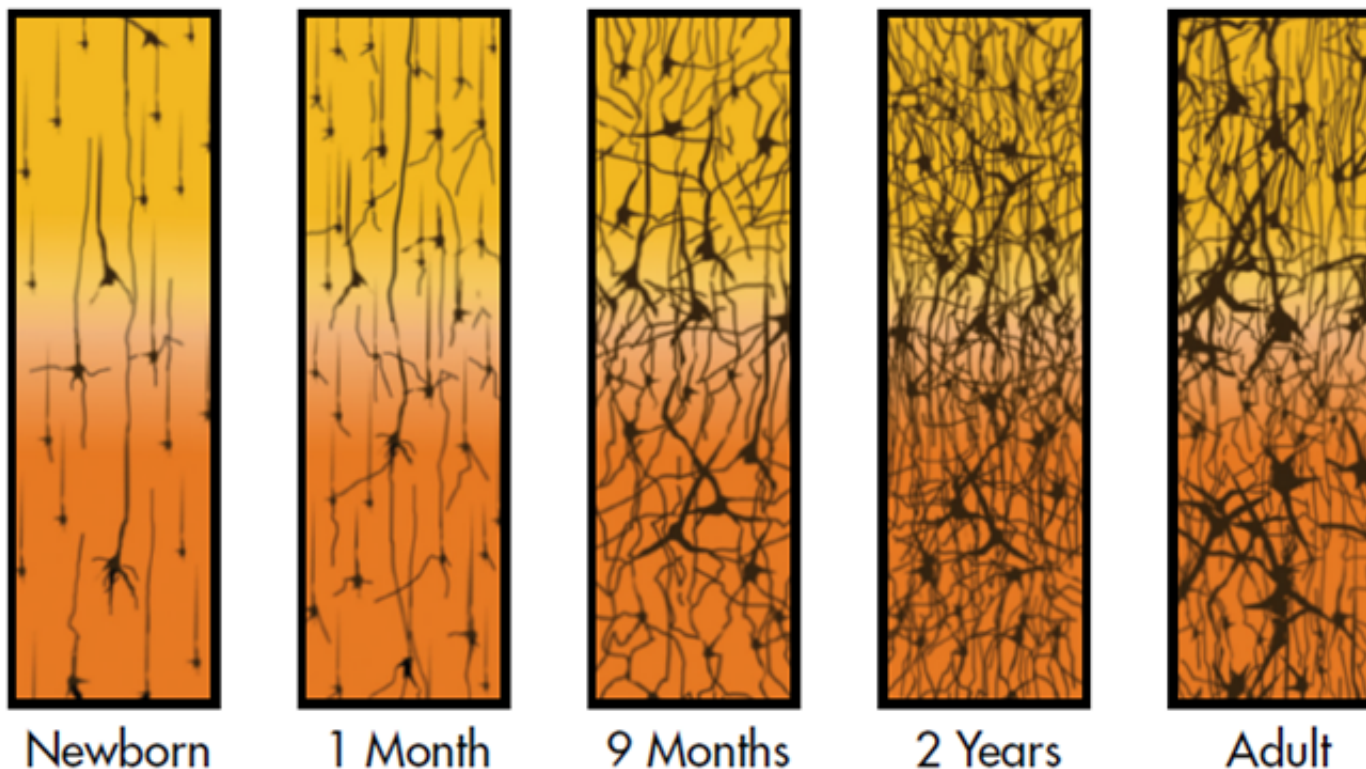


FIGURE 3:
Synapse Density
Over Time

Source: Corel, J.L.
The postnatal
development of the
human cerebral cortex.
Cambridge, MA:
Harvard University
Press; 1975.

Age Related Changes

- Many changes of our bodies as we age, including our brains
- Examples of changes in brain with age:
 - Shrinkage of specific parts of brain, especially prefrontal cortex, hippocampus.
 - Changes in how brain cells communicate.
 - Changes in the brain's blood vessels/ blood flow.
 - Damage by free radicals increases.
 - Increase in inflammation.

Adapted from NIA/NIH's Alzheimer's
Disease: Unravelling the Mysteries

Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective

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^a*Division of Public Policy, Alzheimer's Association, Washington, DC, USA*

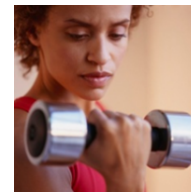
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^d*President & CEO, Alzheimer's Association, Chicago, IL, USA*

Statement of Evidence: Modifiable Risk Factors for Cognitive Decline & Dementia

- (1) Regular physical activity and management of cardiovascular risk factors (diabetes, obesity, smoking, and hypertension) have been shown to reduce the risk of cognitive decline and may reduce the risk of dementia;
- (2) Healthy diet and lifelong learning/cognitive training may also reduce the risk of cognitive decline;
- (3) There are still many unanswered questions and significant uncertainty with respect to the relationship between individual risk factors and dementia.



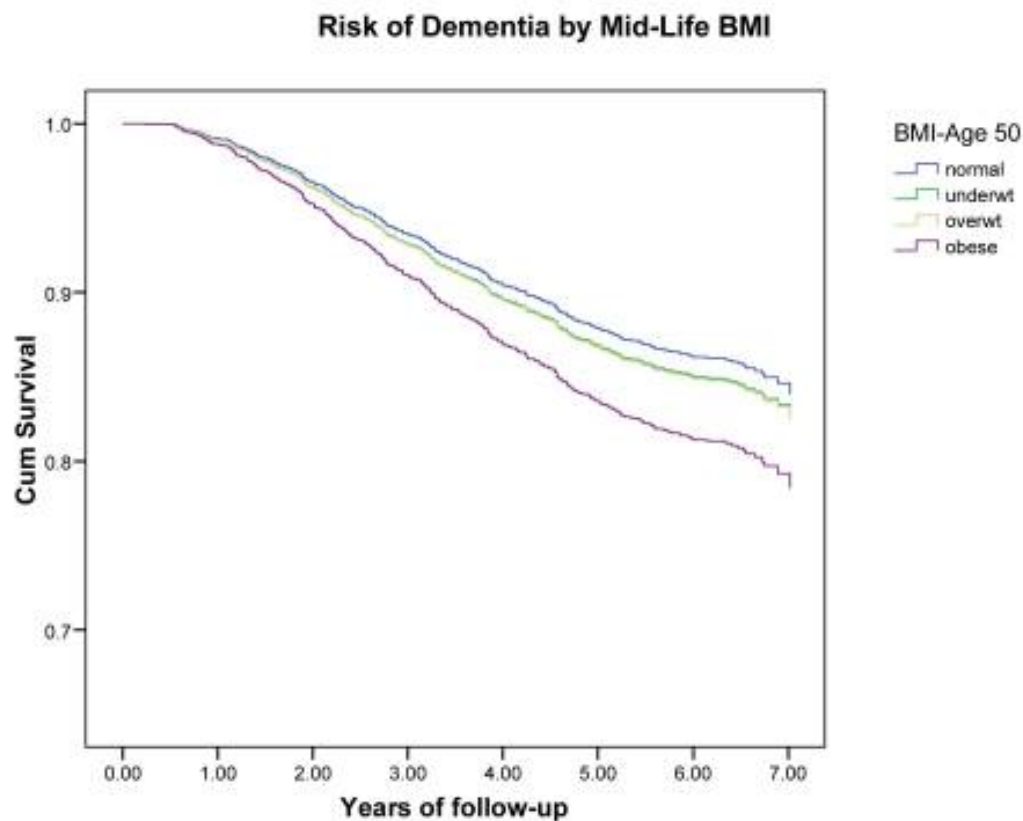
Risk Related to Cognitive Decline:

Possibly Able to Modify Behaviors

- Cardiovascular Risk Factors:
 - Diabetes
 - Mid-Life Obesity
 - Mid-Life Hypertension
 - Cholesterol

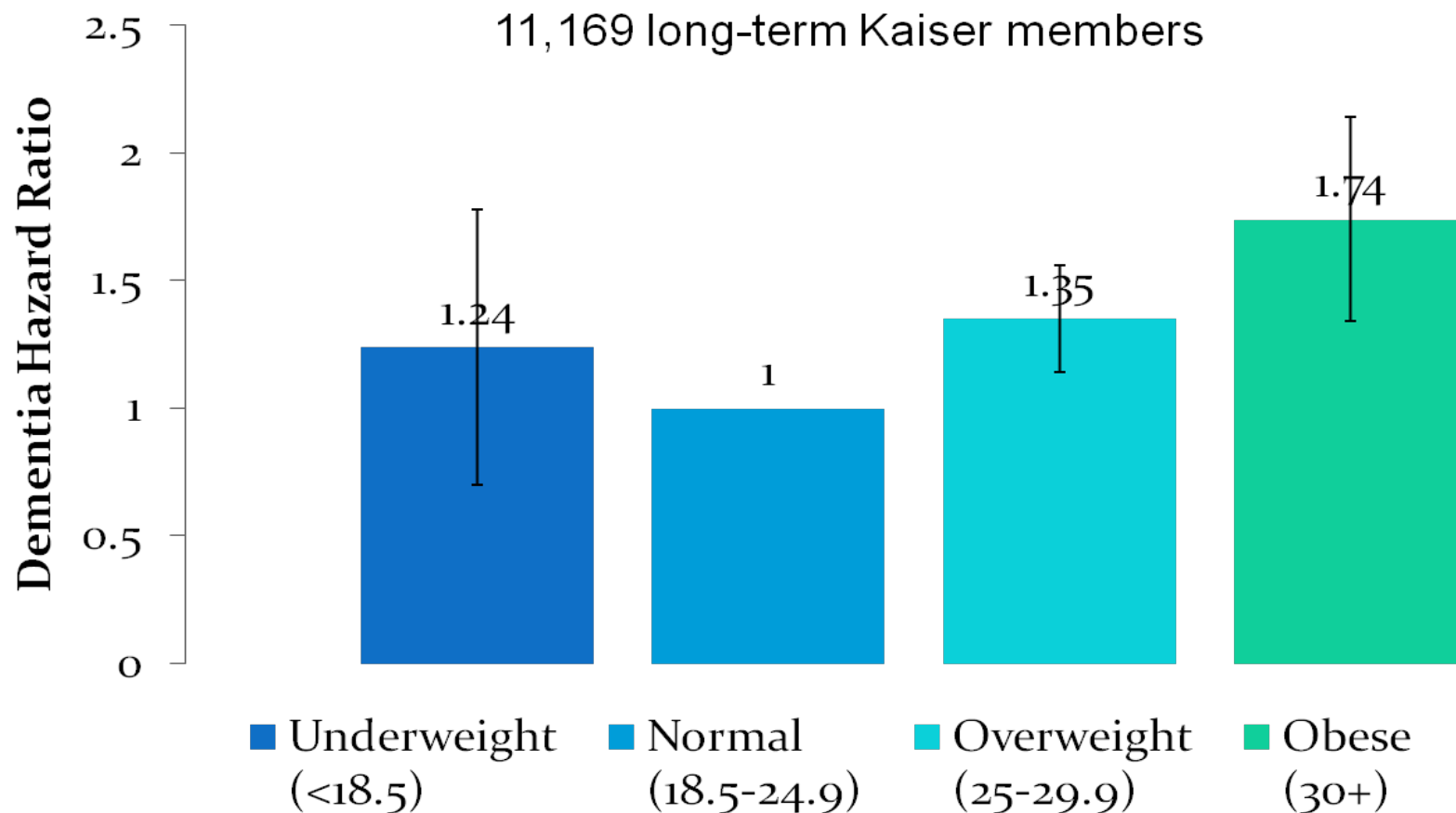


Cardiovascular Risk Factors: Mid-Life Obesity



- 10+ studies = mid-life obesity associated with increased risk of dementia
- Mid-life obesity measured by BMI

Cardiovascular Risk Factors: Mid-Life Obesity



Cardiovascular Risk Factors: Mid-Life Hypertension and Cholesterol

- Mid-life hypertension or cholesterol relationship with cognitive decline/ dementia not consistent
- Several studies have shown hypertension medications may reduce cognitive decline

National Cholesterol Education Program Cholesterol Guidelines			
	Desirable	Borderline High	High
Total Cholesterol	Less than 200	200 - 239	240 and higher
LDL Cholesterol (the "bad" cholesterol)	Less than 130	130 - 159	160 and higher
HDL Cholesterol (the "good" cholesterol)	50 and higher	40 - 49	Less than 40
Triglycerides	Less than 200	200 - 399	400 and higher

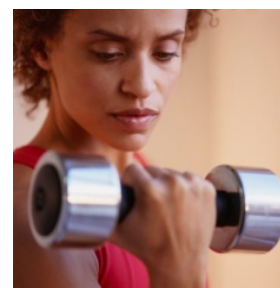
<http://www.eqpdi.com/2014/02/do-you-understand-your-cholesterol.html>



Risk Related to Cognitive Decline:

Possibly Able to Modify Behaviors

- Lifestyle Risk Factors:
 - Current Smoking
 - Physical Activity
 - Diet
 - Cognitive training/ lifelong learning

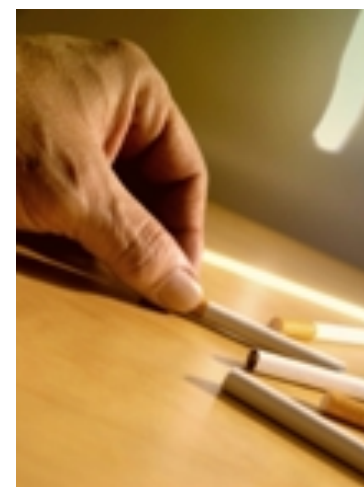


Lifestyle Risk Factors: Current Smoking

- Over 25 studies (n>50,000) show current smoking linked to increased risk of cognitive decline and possibly increased risk of dementia

		Current vs. never	Ex-smoker vs. never	Ever vs. never
Any dementia	Number of studies	5 ^{29,30,37,44,50}	5 ^{29,30,37,44,50}	2 ^{38,40}
	Pooled RR (95% CI)	1.20 (0.96-1.44)	0.87 (0.72-1.02)	1.22 (0.85-1.60)
	Heterogeneity Higgins' I ²	14.6%	43.3%	0.0%
AD	Number of studies	6 ^{29,30,33,35,40,45}	6 ^{29,30,33,35,40,45}	4 ^{38,39,41,45}
	Pooled RR (95% CI)	1.52 (1.18-1.86)	0.94 (0.76-1.12)	1.55 (1.15-1.95)
	Heterogeneity Higgins' I ²	0.0%	23 %	0%
VaD	Number of studies	3 ^{29,33,35}	3 ^{29,33,35}	None
	Pooled RR (95% CI)	1.46 (0.96-1.97)	0.97 (0.52-1.42)	n/a
	Heterogeneity Higgins' I ²	24.2%	0.0%	n/a

Review of meta-analyses to date. Adapted from 2014 World Alzheimer's Report, Alzheimer's Dementia International, pg 47.

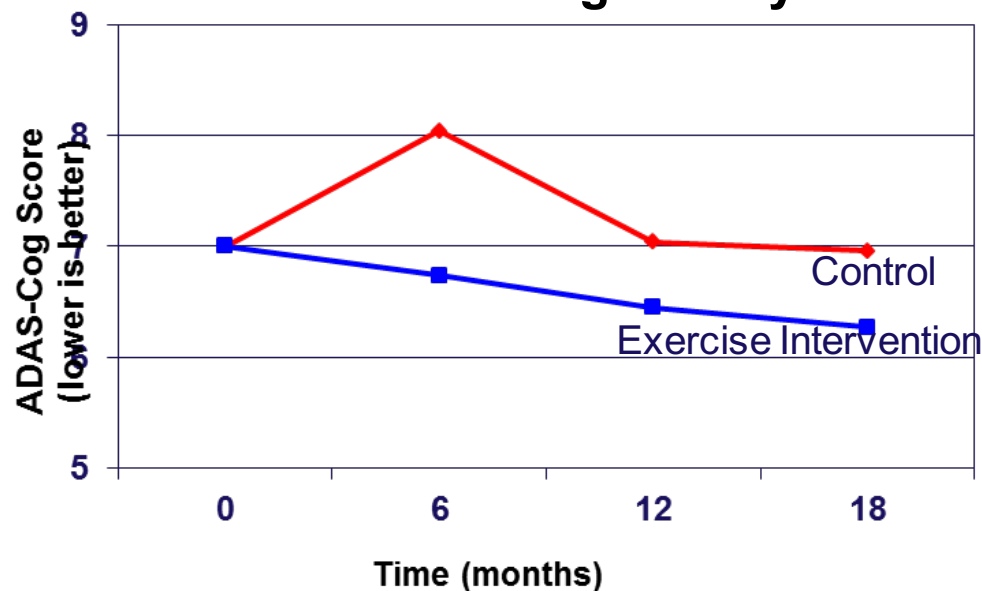


Lifestyle Risk Factors: Physical Activity

- Numerous studies suggest physical activity decreases risk of cognitive impairment and may possibly reduce risk of dementia
- ADCS launching exercise intervention for individuals with MCI (Baker/ Cotman)

Exercise Improves Cognition in Older Adults with MCI

170 adults age ≥ 50 yrs



Lifestyle Risk Factors: Diet



- Limited, conflicting information on role of diet
- For example, Mediterranean diet has shown positive risk reduction effects
- Alcohol consumption in older adults may decrease the risk of cognitive decline and dementia

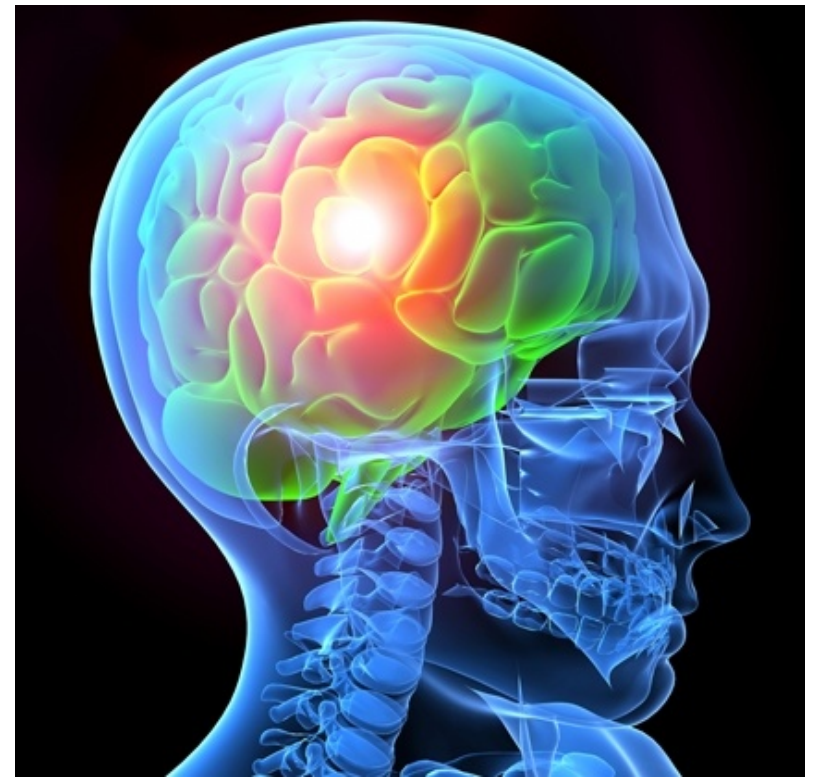
Risk Related to Cognitive Decline & Dementia

Years of formal education

People with fewer years of formal education or reduced literacy are at a higher risk for dementia than those with more years of formal education.

Head Injury:

Moderate or severe traumatic brain injury have been shown to increase the risk of developing certain types of dementia



Lifestyle Risk Factors: Cognitive Training / Lifelong Learning

- More than 35 large, rigorous studies of mental engagement/cognitive training show improvements in immediate and delayed recall
- Unclear whether benefit due to cognitive intervention.
- “Recipe” for any successful engagement is unknown.

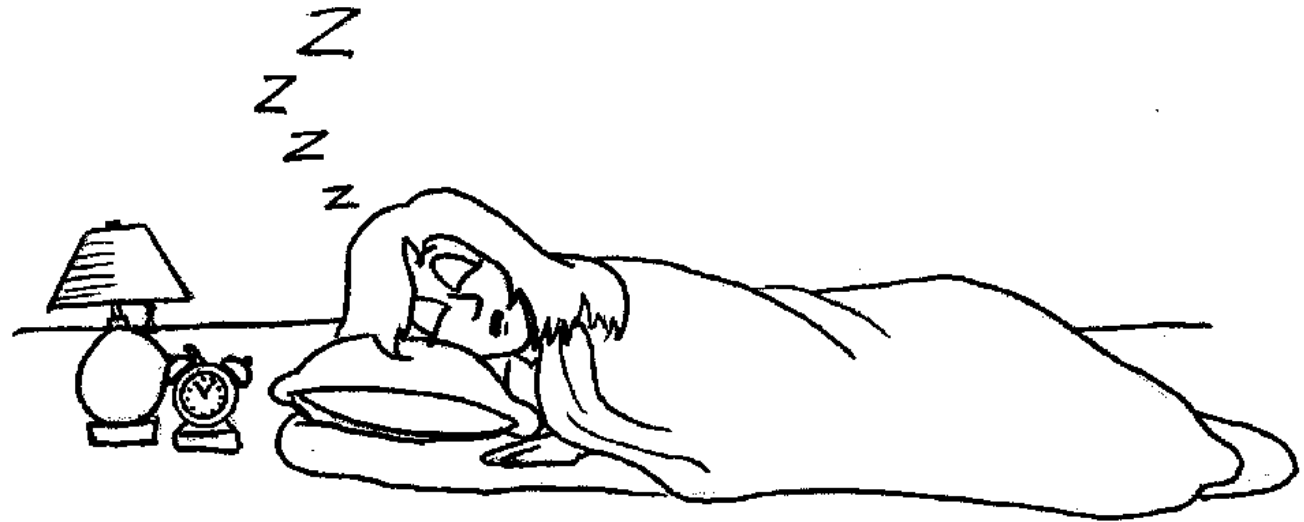


www.kinkonauts.com

Risk Related to Alzheimer's:

Possibly Able to Modify Behaviors

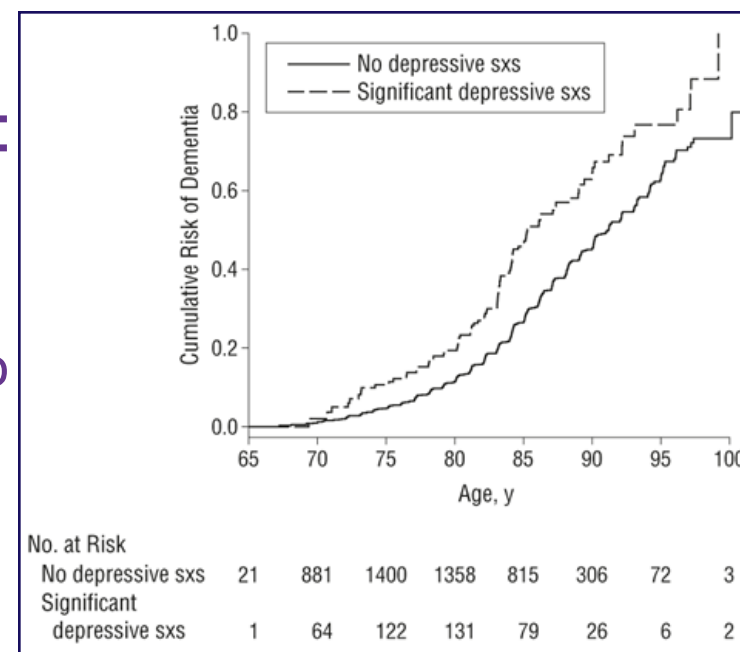
- Other Risk Factors:
 - Depression
 - Sleep



Other Risk Factors:

Depression

- 1 in 5 individuals will have depressive symptoms in a lifespan
- Depressive symptoms and dementia:
 - After someone diagnosed or in reaction to early cog. decline
 - May impair cognitive function and lead to “pseudodementia”
 - May be a risk factor or early symptom of dementia
- Nearly 20 studies with combined > 100,000 individuals show history of depression increases risk for dementia



Li, G et al. JAMA Psychiatry 2011, 68 (9)

Byers AL and Yaffe K, Nat Rev Neurol 2011, 7 (6).

Other Risk Factors:

Sleep

- More than three dozen randomized controlled trials of mental engagement/cognitive training interventions show improvements in immediate and delayed recall among those in the treatment group compared with the control group.
- A systematic review of observational studies reached similar conclusions.
- Unclear whether benefit due to cognitive intervention.
- Most studies in this area of research fairly small, the data overall are inconclusive, and (as with physical activity) the “recipe” for any successful engagement is unknown.

Factors that Increase/ Decrease Risk of Cognitive Decline

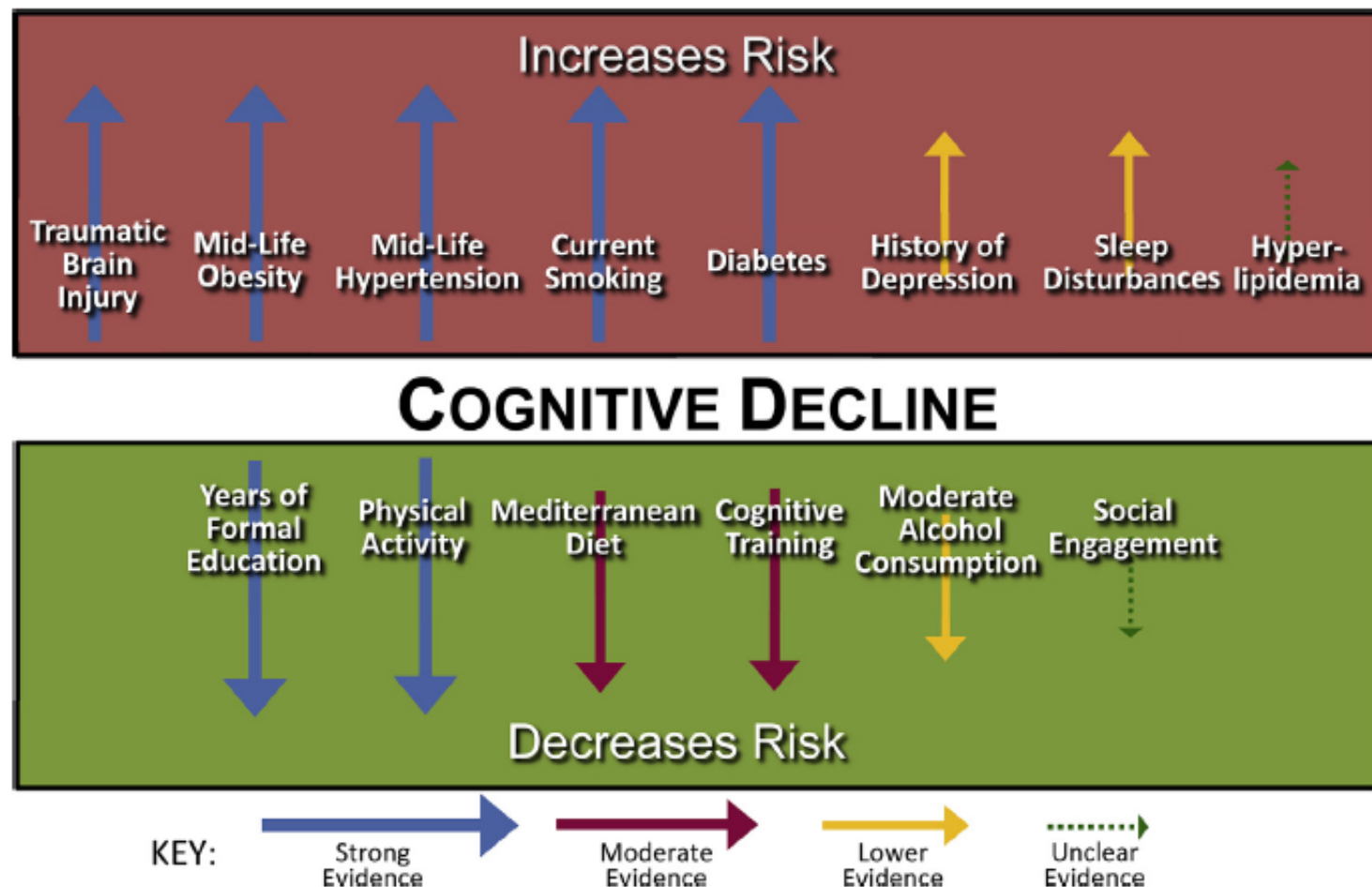


Fig. 1. Strength of evidence on risk factors for cognitive decline.

Factors that Increase/ Decrease Risk of Dementia

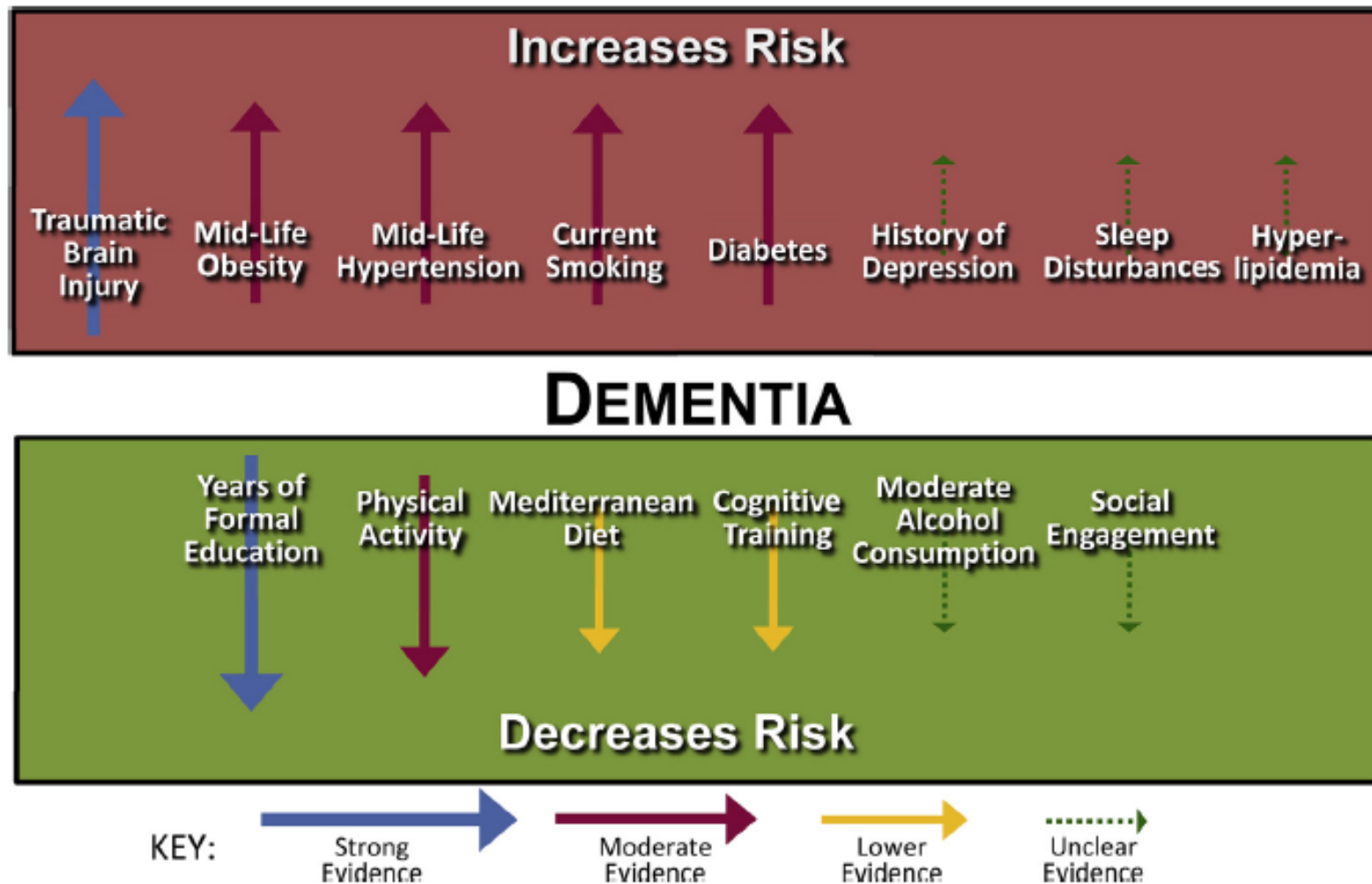


Fig. 2. Strength of evidence on risk factors for dementia.

FINGER Study: Receptacle of Lifestyle Interventions for Cognition



- Gold standard of testing any type of therapy or intervention – Randomized Control Trial (RCT)
- Large, rigorous study of 1,200 individuals
 - Half received intervention and half received standard of care
- First solid evidence that recipe of lifestyle interventions reduces cognitive decline
- Needs to be replicated in more diverse populations

ALZHEIMER'S DISEASE

is impacting

FAR TOO

MANY

WOMEN

3.2

million living with
ALZHEIMER'S

60%

OF CAREGIVERS

alzheimer's  association®

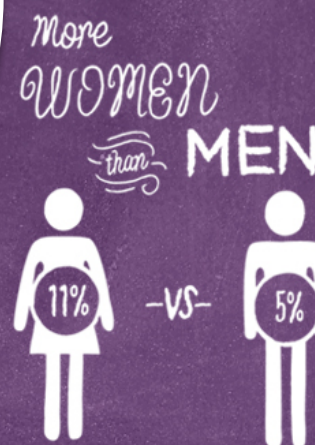
THE BRAINS BEHIND SAVING YOURS.™

OVER
60%
of
ALZHEIMER'S AND DEMENTIA
— CAREGIVERS —
are WOMEN

IN HER 60's
A woman's estimated lifetime
RISK OF DEVELOPING
ALZHEIMER'S
IS
1 IN 6
FOR BREAST CANCER IT IS
1 IN 11

WOMEN
ARE AT THE EPICENTER
of the
ALZHEIMER'S
EPIDEMIC

TODAY, $\frac{2}{3}$
NEARLY
... of ...
AMERICANS
LIVING WITH ALZHEIMER'S
are WOMEN



STOPPED WORKING
TO PROVIDE CARE FOR
Someone with
ALZHEIMER'S

Two-Thirds of Care Partners are Women (~10 million)

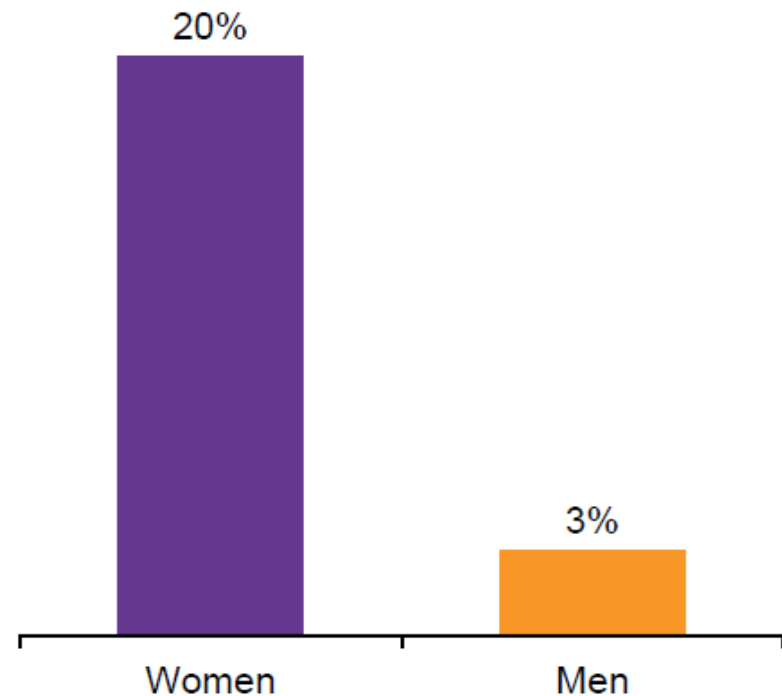
- Almost half express providing care is physically stressful (2x more than males)
- 62% of women find providing care emotionally stressful
- Providing care is isolating, but for women, this is more commonly linked to depression



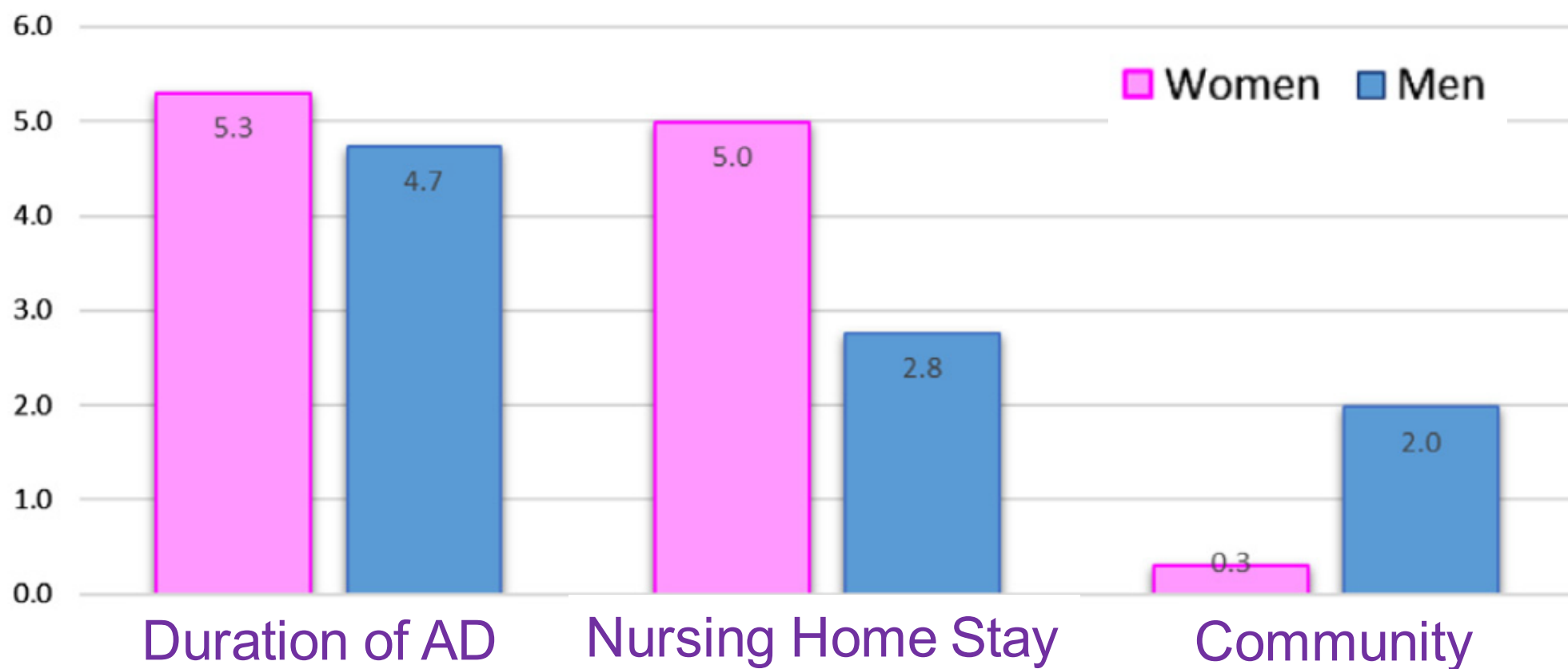
Impact of Caregiving on Women in the Workplace

- 20% from full time to part time employment
- 19% quit work as a result of caregiving
- 18% took leave of absence from work
- 10% lost job benefits
- 17% feel they were penalized as a result of caregiving duties

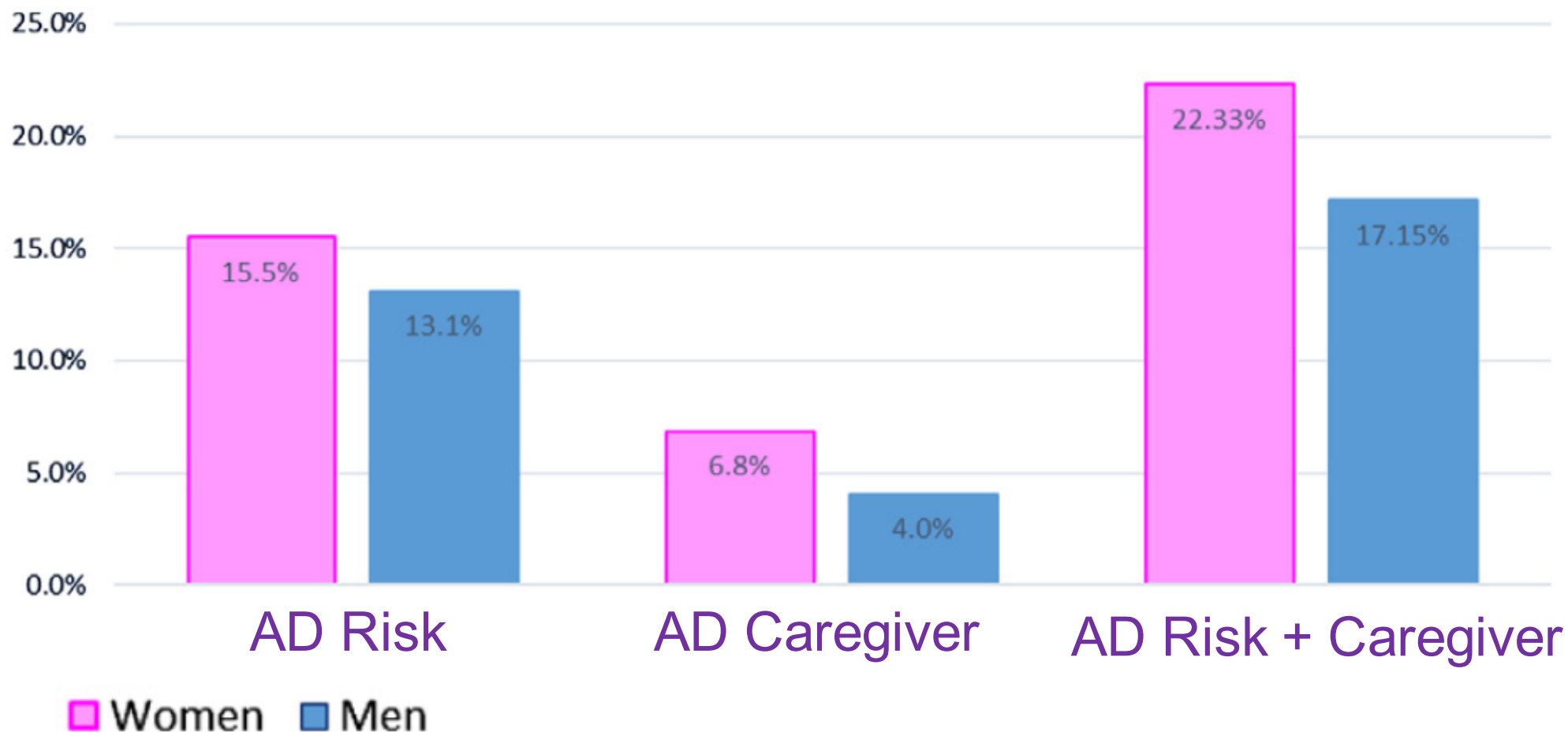
Percentage of Working Alzheimer's Caregivers Who Have Gone from Full-Time to Part-Time Work



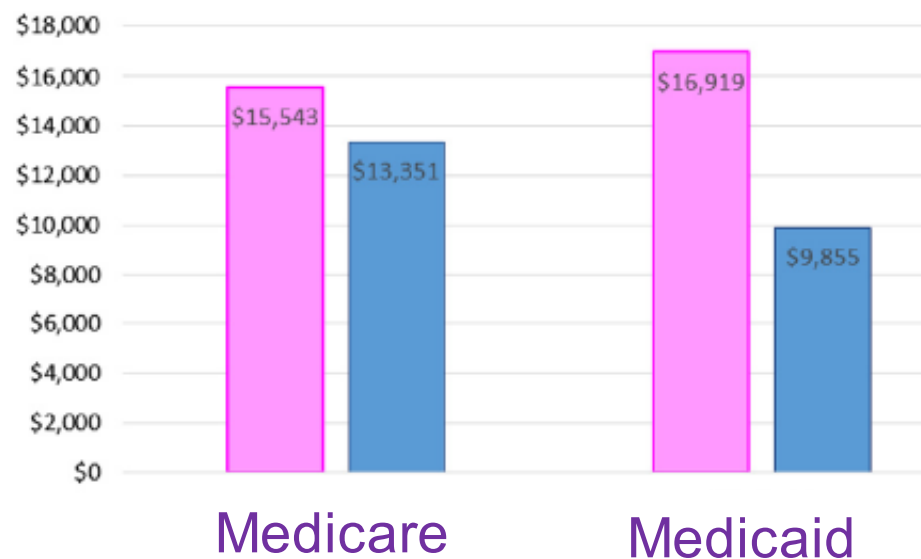
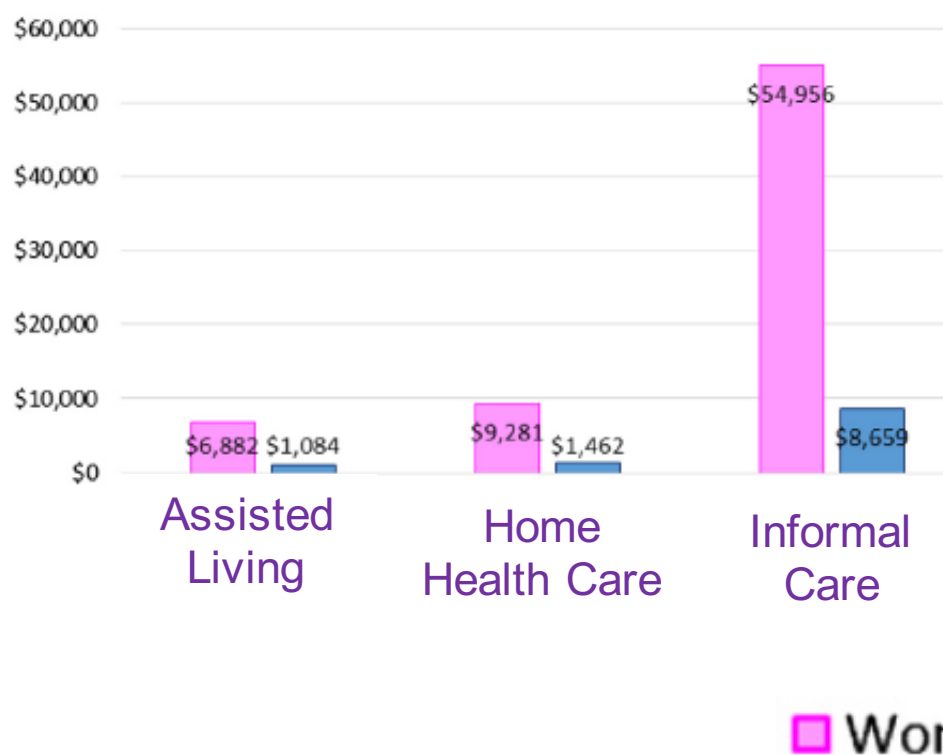
Duration & Course of Illness Different for Men and Women



Lifetime Risk is Greater for Women



Lifetime Out of Pocket, Informal & Third Party Costs Greater for Women



Further evidence that women are the epicenter of the Alzheimer's epidemic:

- **More women are living with Alzheimer's disease.**
 - Duration of the disease for women is also longer than for men.
 - Women are more likely to live in a nursing facility than men.
- **Women bear the burden of caregiving more than men.**
- **Women bear a greater economic burden from Alzheimer's.**
 - Women more likely to be lower-income & rely on Medicaid than men.
 - As caregivers, women are more likely drain finances than men.



What should I be doing now?



In Summary ...

- Cognitive decline as we age; this is not Alzheimer's disease or dementia
- Regular physical activity & management of cardiovascular risk factors (e.g. diabetes, obesity, smoking, and hypertension) have been shown to reduce the risk of cognitive decline and may reduce the risk of dementia.
- Healthy diet and lifelong learning/cognitive training may also reduce the risk of cognitive decline.



Alzheimer's Association Research Website

alz.org® | research center
advancing alzheimer's research worldwide

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Text Size [A](#) [A](#) [A](#)

A future without Alzheimer's

The race is on. Alzheimer's and related dementias research is a dynamic field, and momentum builds each year. This site is for [professional researchers](#) and anyone interested in following the [progress in research](#). The Alzheimer's Association has been involved in every major advancement in Alzheimer's and related dementias research since the 1980's and is a [leader in the global fight](#) for a world without Alzheimer's.



Discovering tomorrow's treatments

The Alzheimer's treatment horizon has never looked brighter. More potential treatments are in development than ever before as a result of 30 years of accelerating insight and identification of promising targets for intervention. The Alzheimer's Association is committed to sustaining this pace of discovery. [Learn more](#)

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ALZHEIMER'S
STARTS
WITH YOU

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