



Alzheimer's Disease
Research Center

Healthy Brain Aging

Charles DeCari MD
Professor of Neurology

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Professor of Public Health Sciences and
Neurology



Dementia prevention, intervention, and care: 2020 report of the Lancet Commission



Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

Panel: Recommended strategies for dementia risk reduction

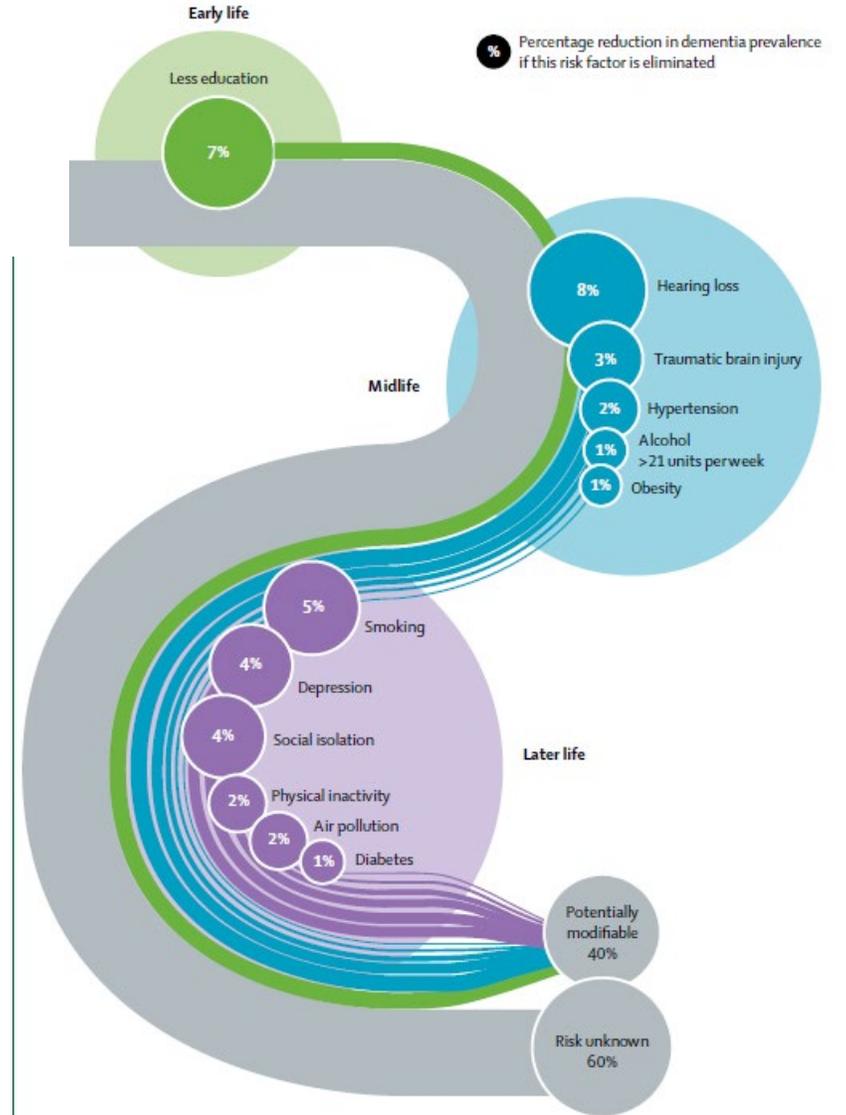
Risks are particularly high in more socially disadvantaged populations including in Black, Asian, and minority ethnic groups.

Population-wide

- Prioritise childhood education for all, worldwide
- Implement social public health policies that reduce hypertension risk in the entire population
- Develop policies that encourage social, cognitive, and physical activity across the life course for all (with no evidence for any specific activities being more protective)
- Scrutinise the risks for hearing loss throughout the life course, to reduce the risk of exposure to this risk factor
- Reduce the risk of serious brain trauma in relevant settings, including occupational and transport
- National and international policies to reduce population exposure to air pollution
- Continue to strengthen national and international efforts to reduce exposure to smoking, both for children and adults, and to reduce uptake and encourage cessation

Targeted on individuals

- Treat hypertension and aim for systolic blood pressure <130 mm Hg in midlife
- Use hearing aids for hearing loss; we need to help people wear hearing aids as many find them unacceptable, too difficult to use, or ineffective
- Avoid or discourage drinking 21 or more units of alcohol per week
- Prevent head trauma where an individual is at high risk
- Stopping smoking is beneficial regardless of age
- Reduce obesity and the linked condition of diabetes by healthy food availability and an environment to increase movement
- Sustain midlife, and possibly late-life physical activity



Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study

Miia Kivipelto, Tiia Nqandu, Tiina Laatikainen, Benqt Winblad, Hilka Soininen, Jaakko Tuomilehto

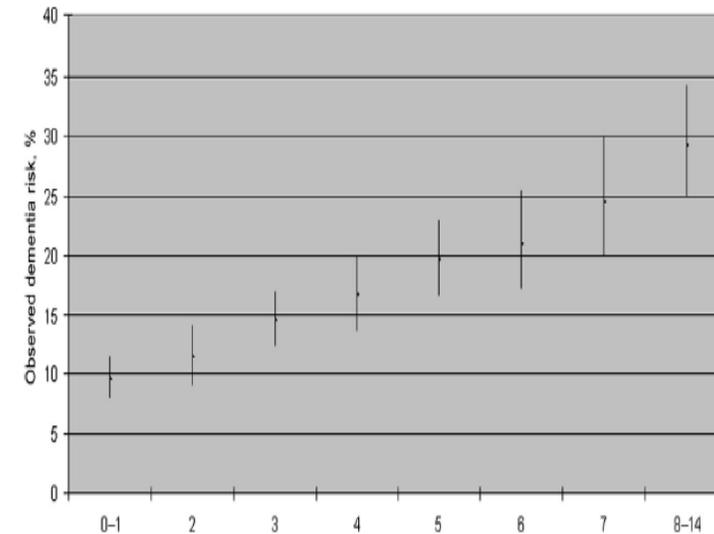
Lancet Neurol 2006; 5: 735-41

Midlife risk score for the prediction of dementia four decades later

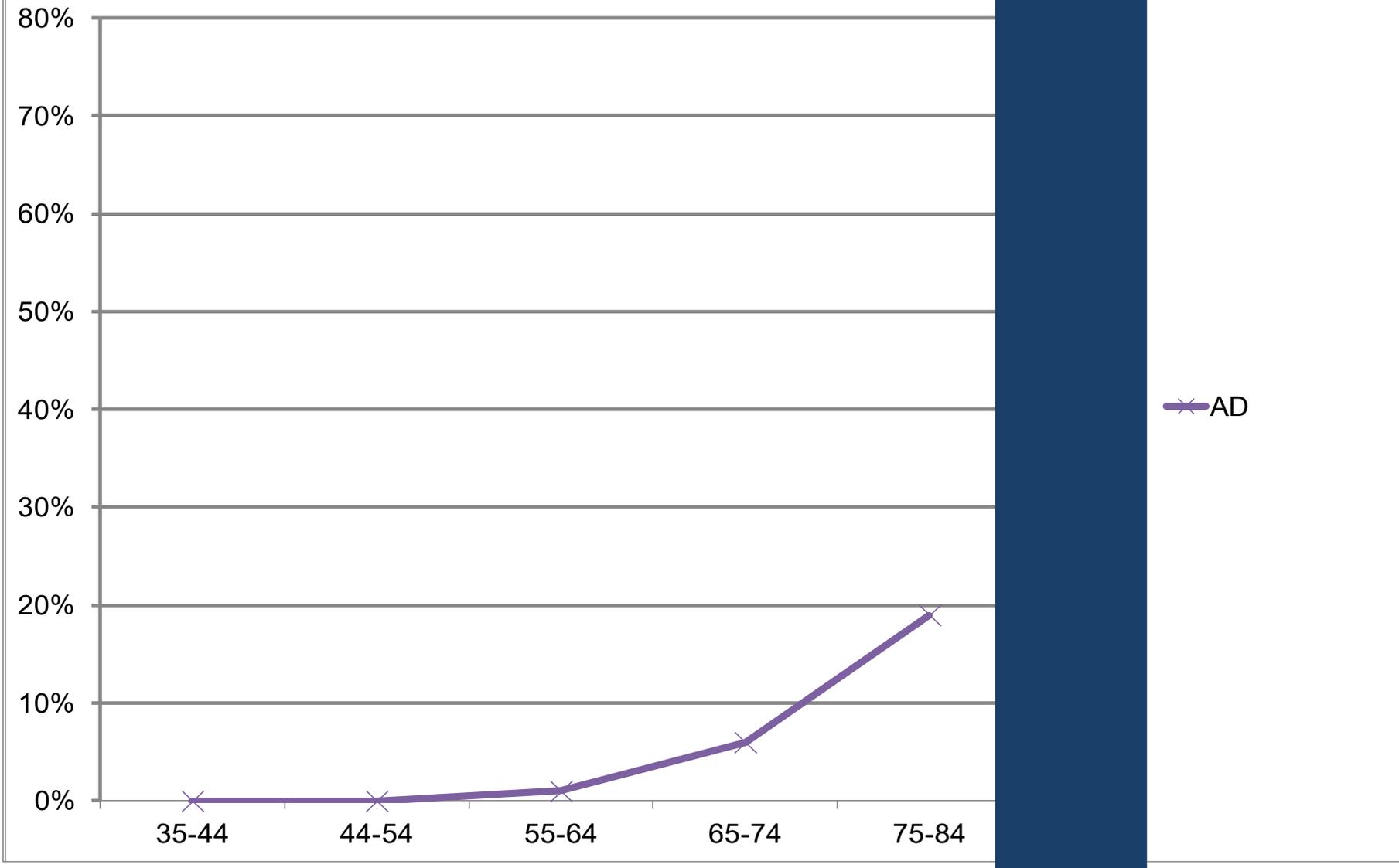
Lieza G. Exalto^{a,b}, Charles P. Quesenberry^a, Deborah Barnes^c, Miia Kivipelto^d,
Geert Jan Biessels^a, Rachel A. Whitmer^{b,*}

Alzheimer's & Dementia 10 (2014) 562-570

Step 1		Step 4		Step 2		Step 5		Step 3		Step 6		Predicted 40-year risk of dementia	
Age, y	Points	Cholesterol, mg/dL	Points	Education, y	Points	BMI, kg/m ²	Points	Sex	Points	Systolic blood Pressure, mm/Hg	Points	Total points	40-Year risk, %
40-46	0	<251	0	0-6	3	<30	0	Men	1	<140	0	0-1	10
47-53	3	≥251	2	7-9	2	≥30	2	Female	0	>140	2	2	11
54-55	4			>9	0							3	15
												4	17
												5	20
												6	21
												7	25
												8-14	29

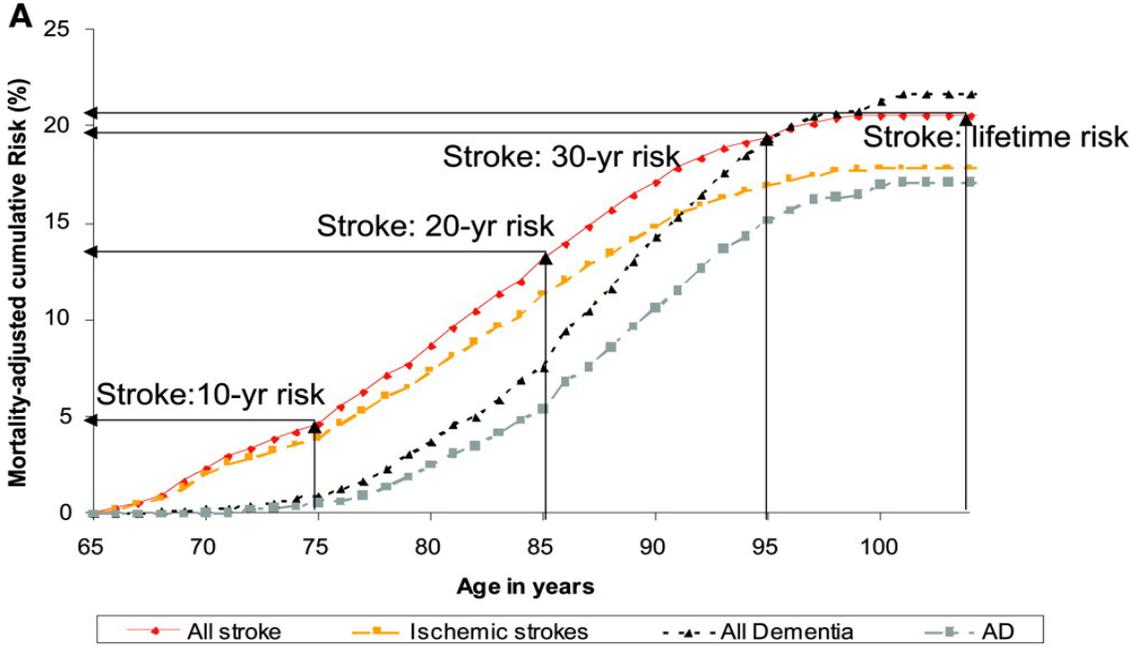


Age-Specific Prevalence of Vascular Disease and Brain Volume



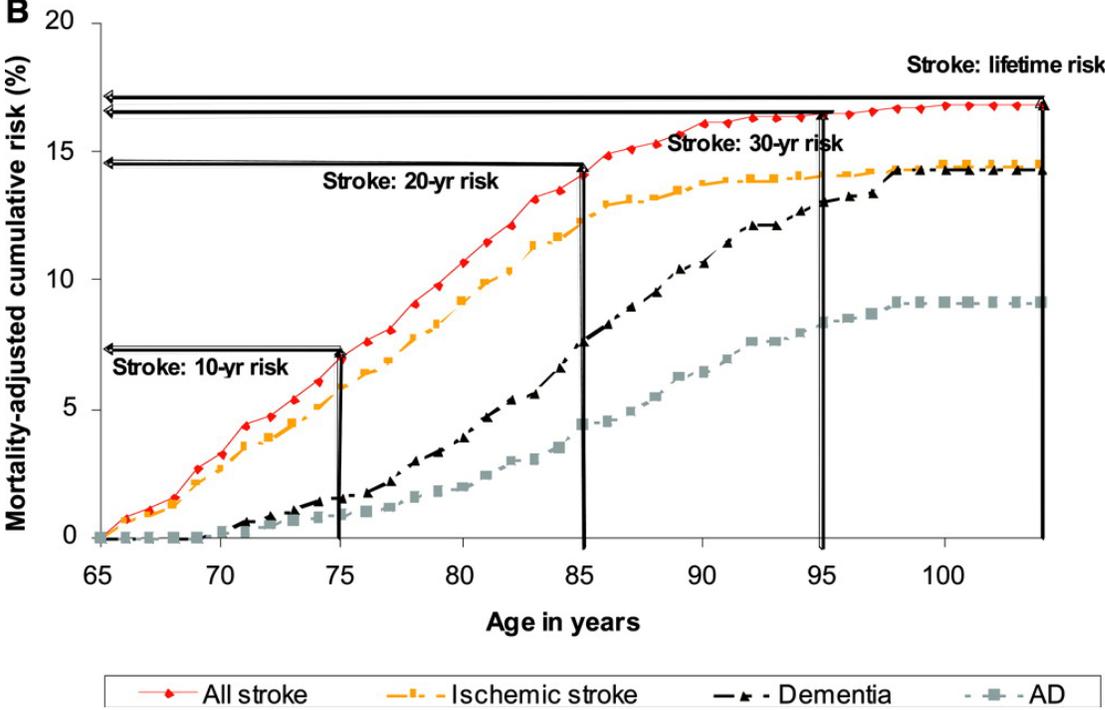
Future Risk of Stroke or Dementia at Age 65

Women

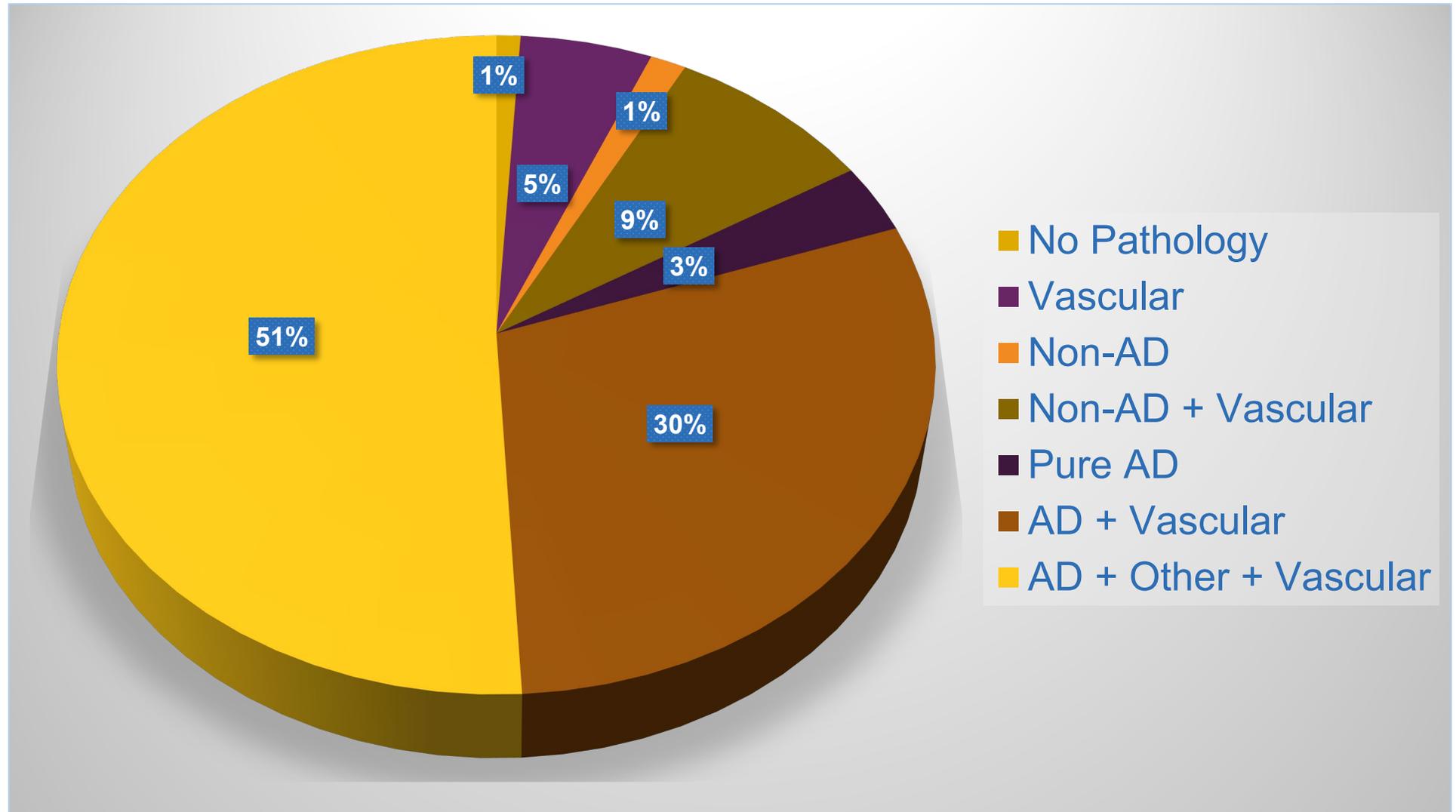


Seshadri, S. et al.
Stroke 2006;37:345-350

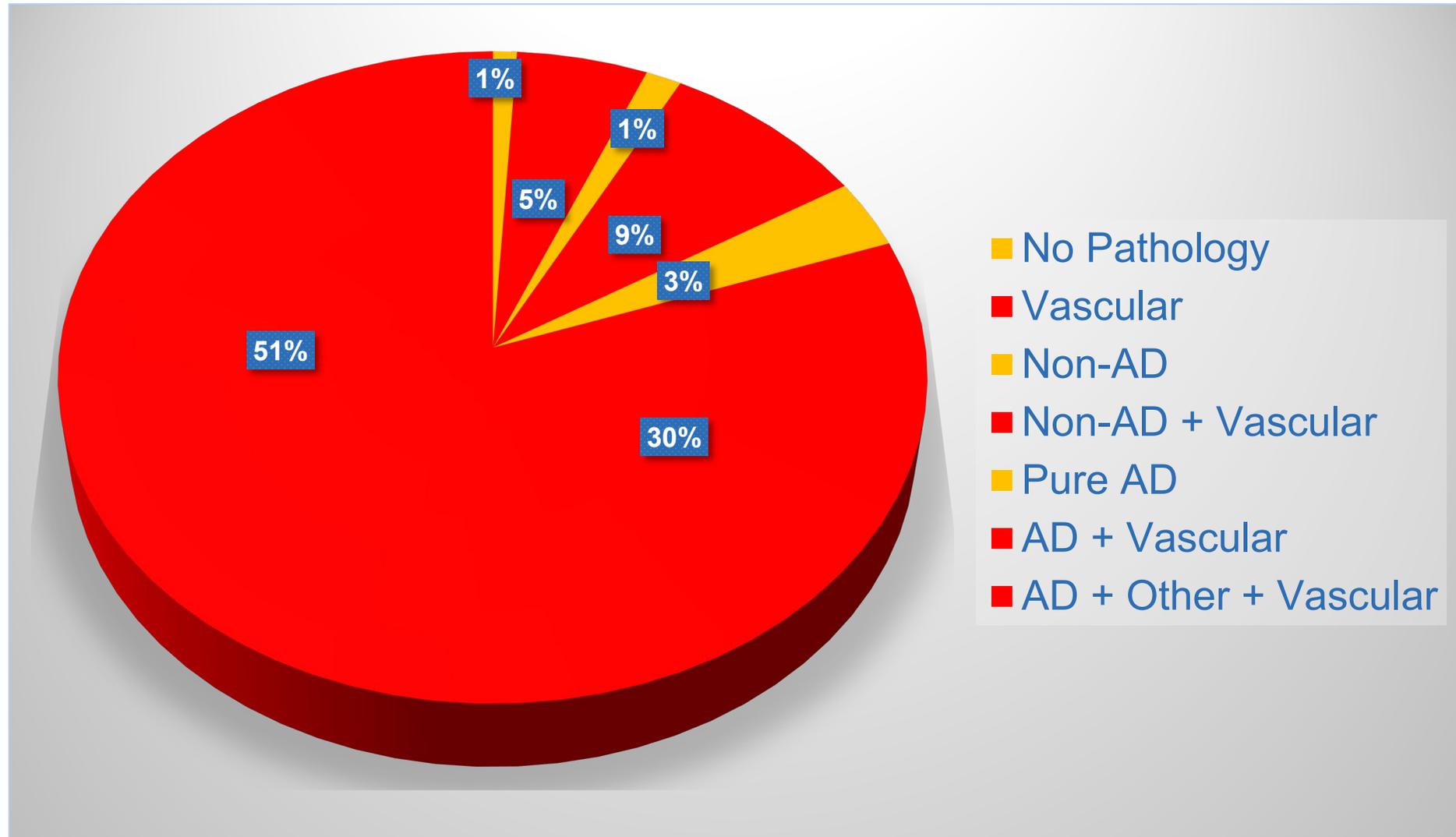
Men



Pathology of Dementia

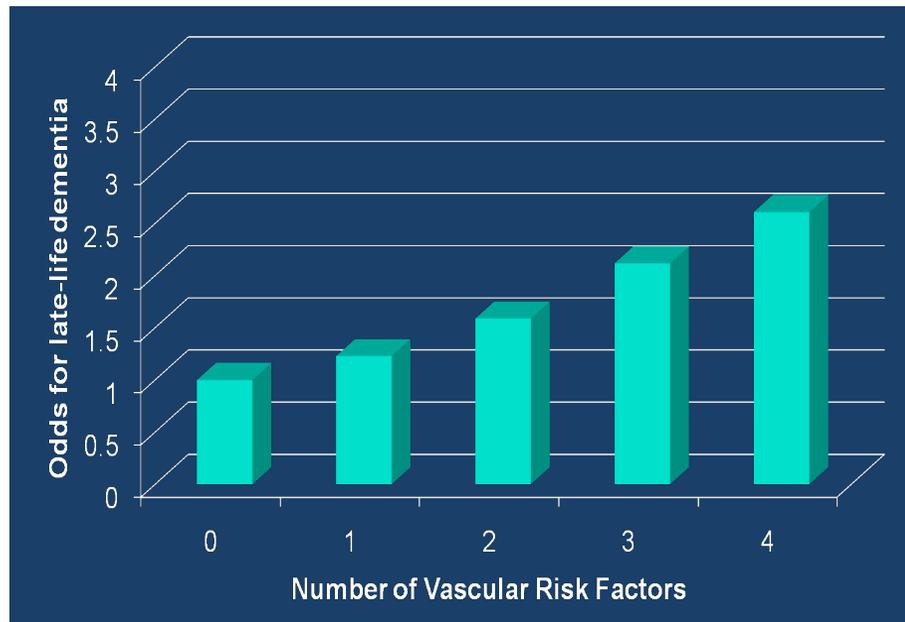


Vascular Pathology of Dementia

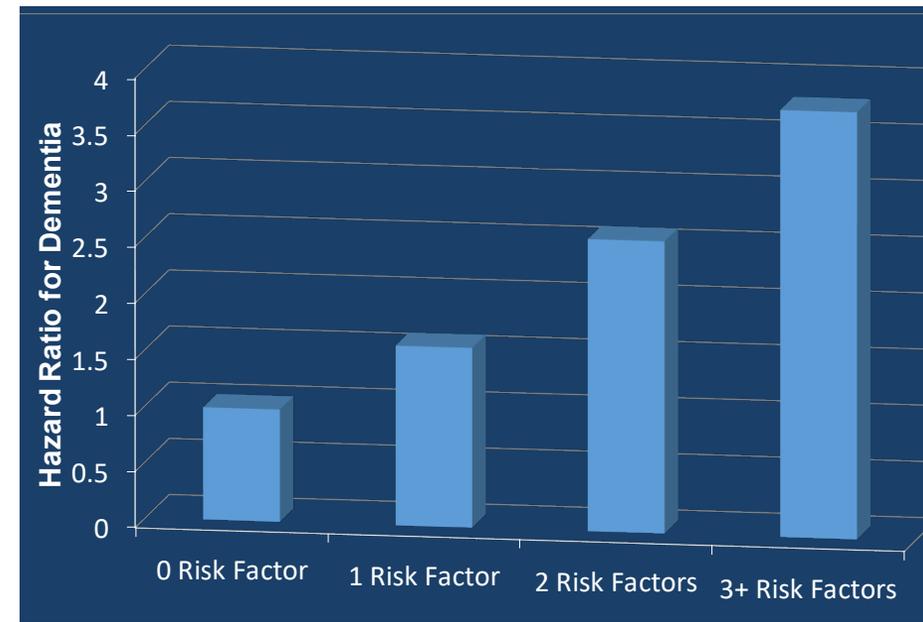


Increasing odds of Dementia with Number of Vascular Risk Factors

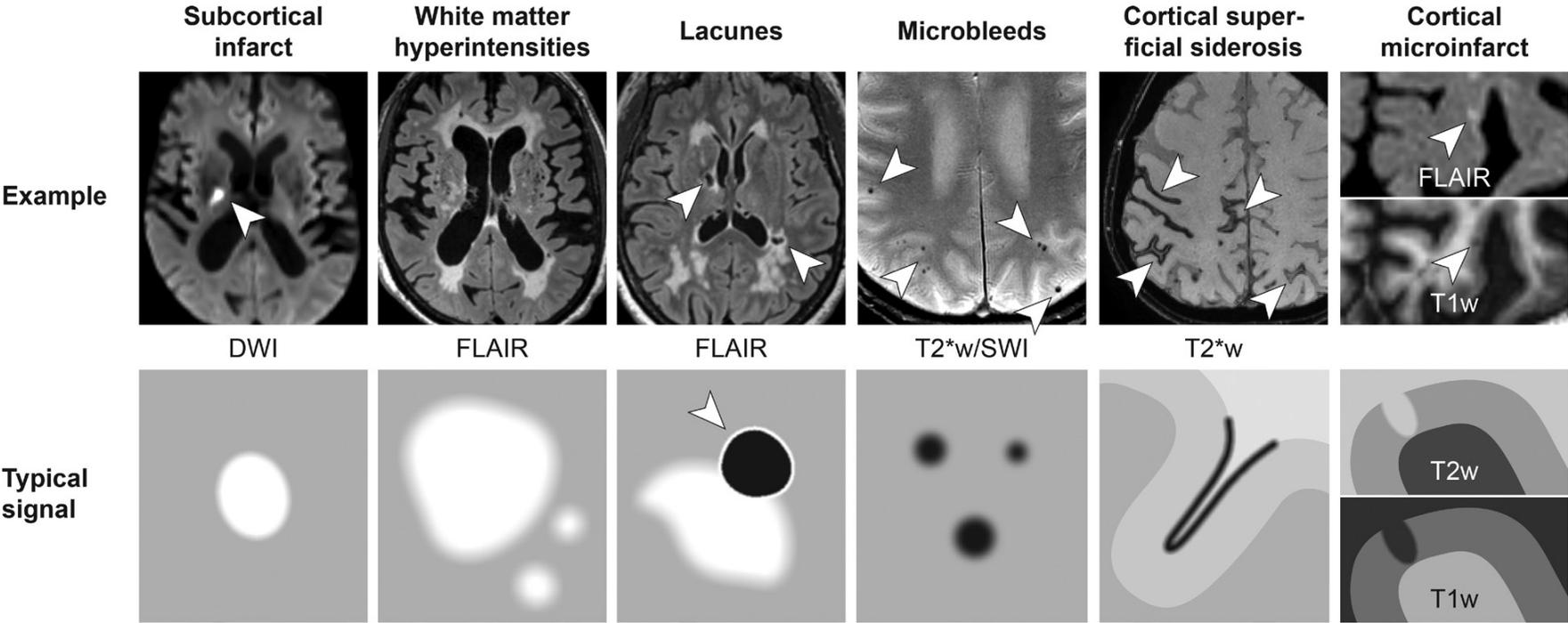
Whitmer, et al, Neurology, 2005
~74% Caucasian



Luchsinger, et al, Neurology 2005
~23% Caucasian

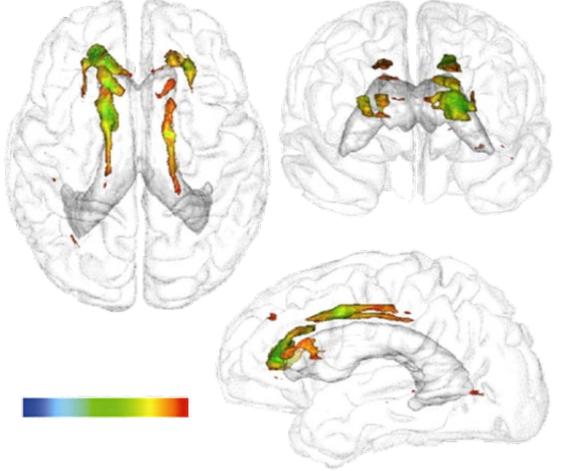


Imaging of Brain Vascular Disease

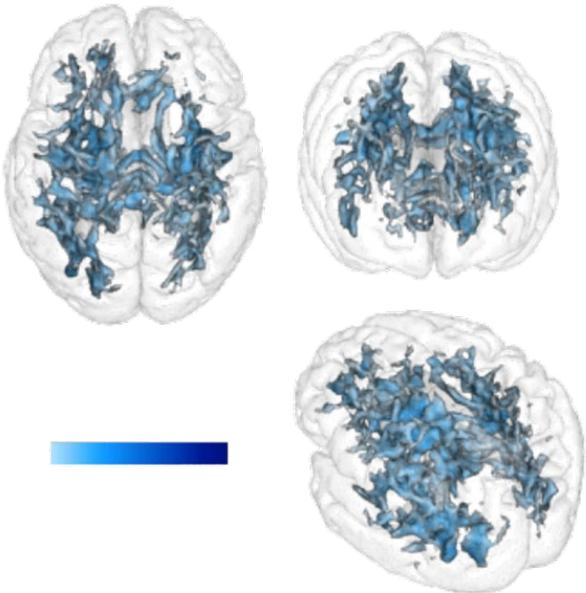
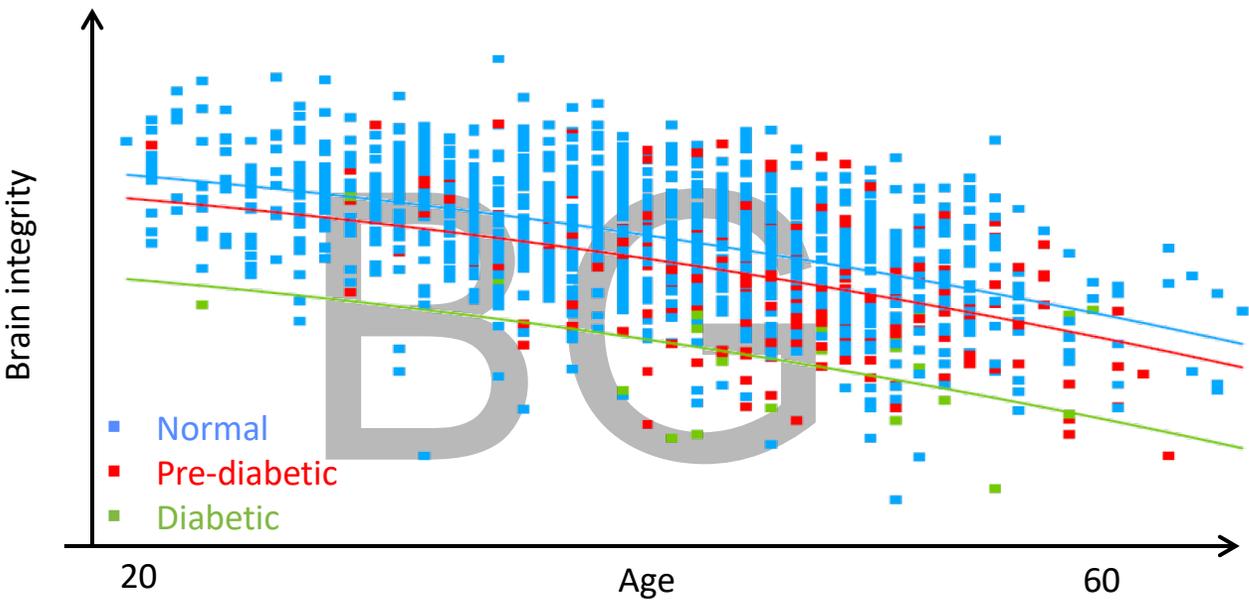


Vemuri, et al. Stroke, 2022

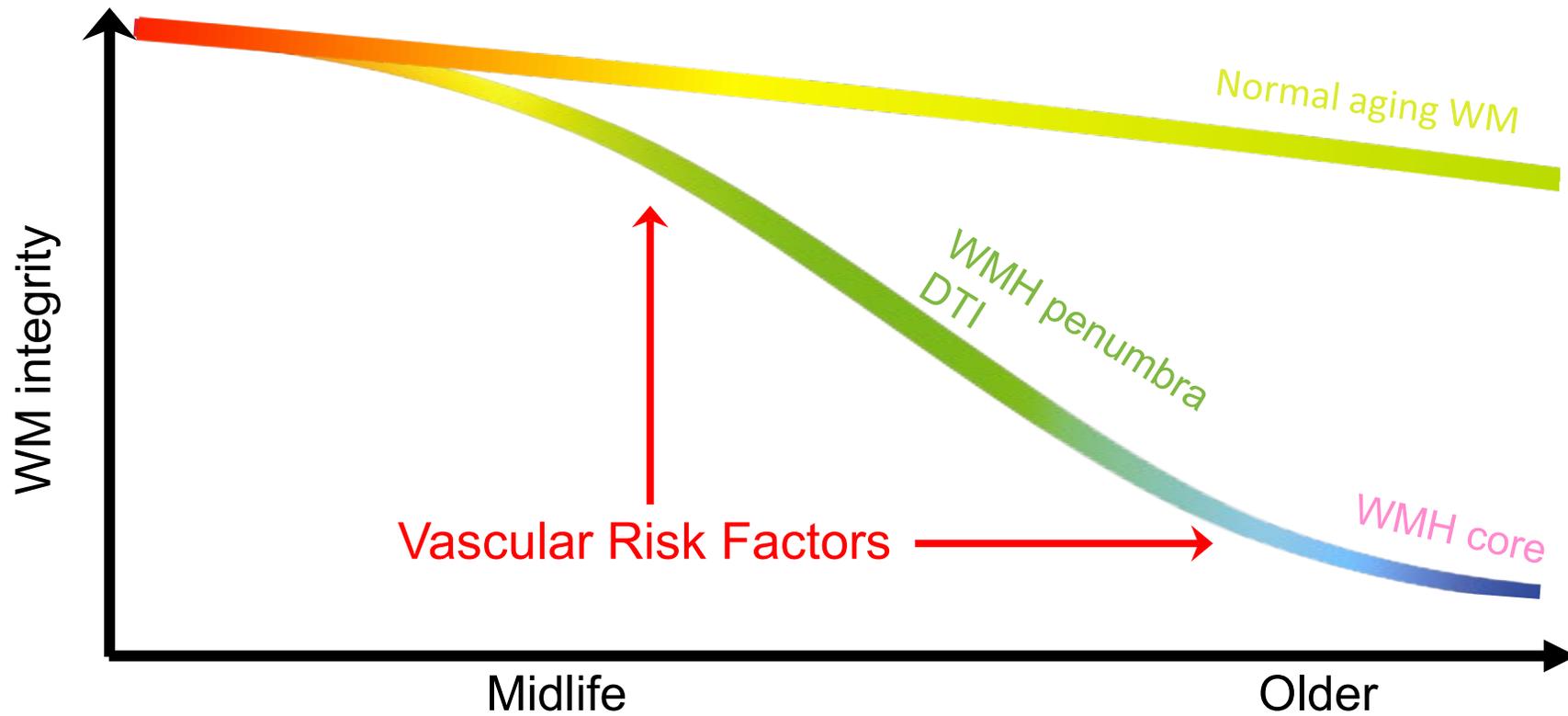
Vascular Brain Injury Begins Early



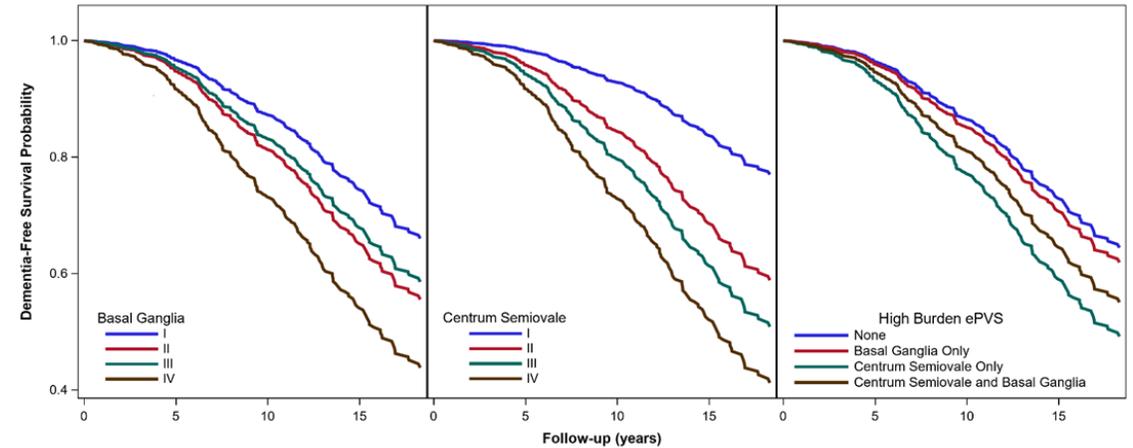
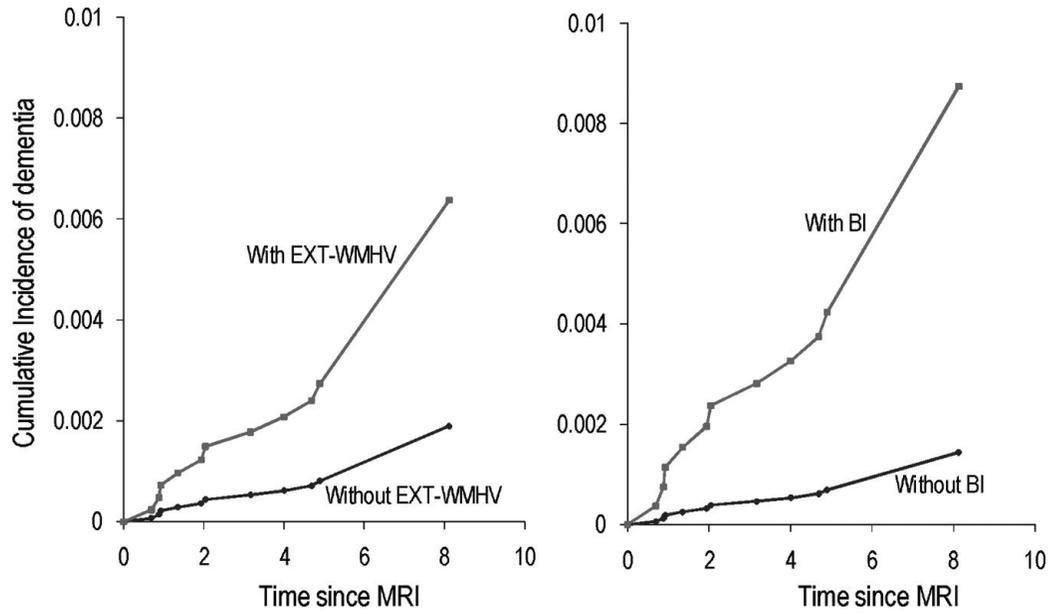
Maillard et al.,
Lancet Neurology, 2012
Weinstein et al.,
Neurology, 2015



Vascular Risk Factors Have Continuous Effects



Dementia Risk with MRI Individual Vascular Measures



CMB location	All-cause dementia Model 1, HR (95% CI)
Any	1.74 [1.00–3.01] $p = 0.049$
Lobar only	1.01 [0.46–2.23] $p = \text{n.s.}$
Lobar + mixed	1.48 [0.79–2.78] $p = \text{n.s.}$
Deep only	2.50 [1.00–6.30] $p = 0.05$
Deep + mixed	2.99 [1.52–5.90] $p = 0.002$

Debette et al, Stroke, 2010

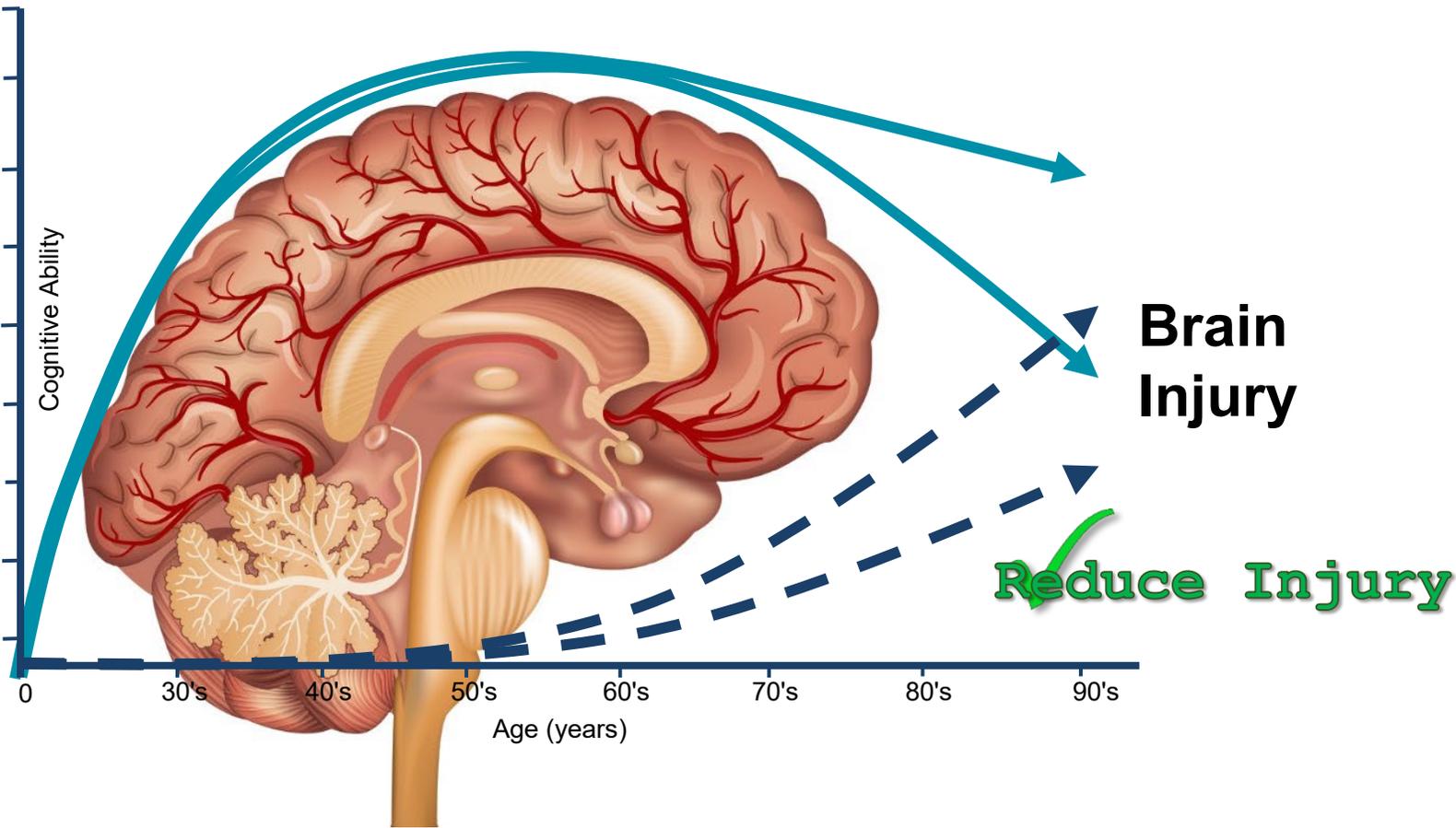
Romero et al, Neurobiology of Aging, 2017

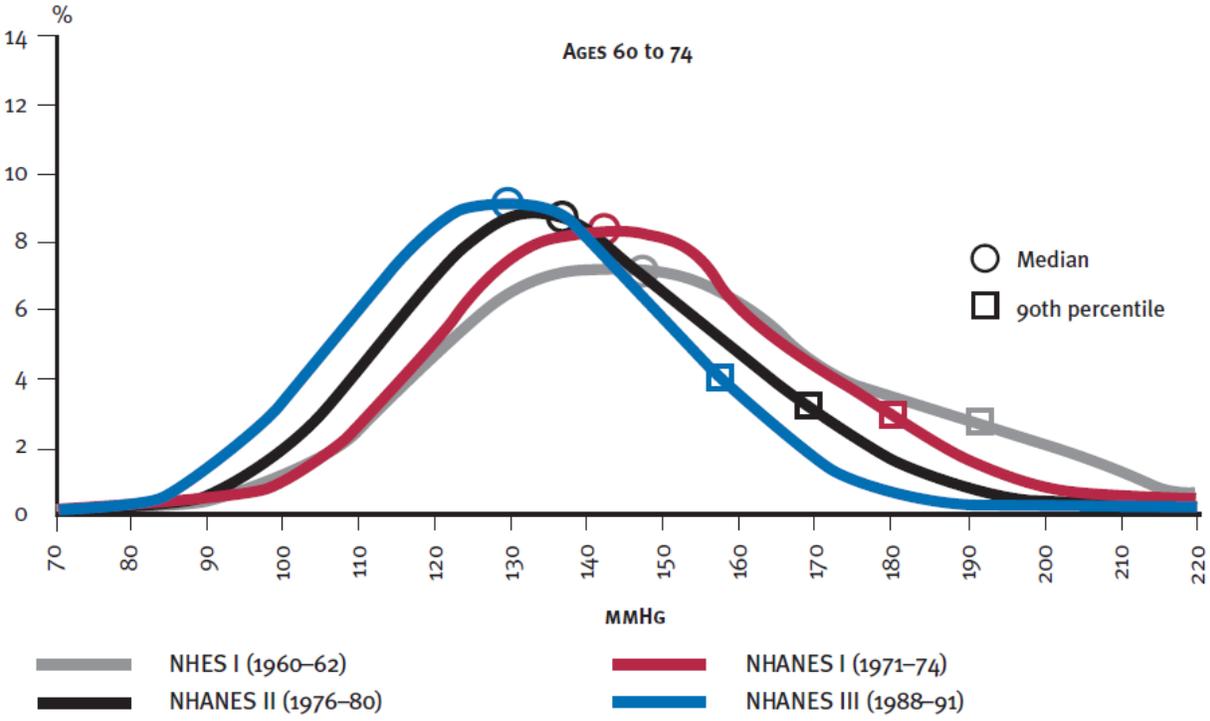
Romero et al, under review

Summary

- Vascular risk factors and consequential vascular disease is common to the aging process
- Vascular risk factors also increase risk for dementia
- Vascular pathology commonly accompanies Alzheimer's disease in dementia

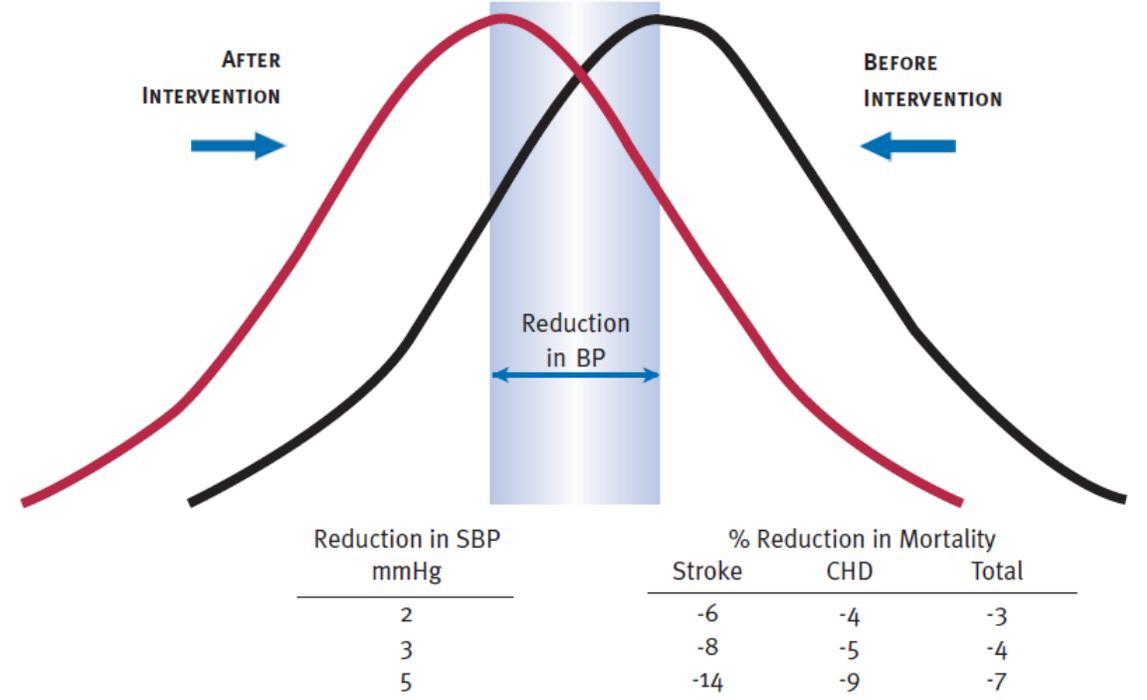
IMPROVING COGNITIVE AGING





NHANES, National Health and Nutrition Examination Survey; NHES, National Health Examination Survey

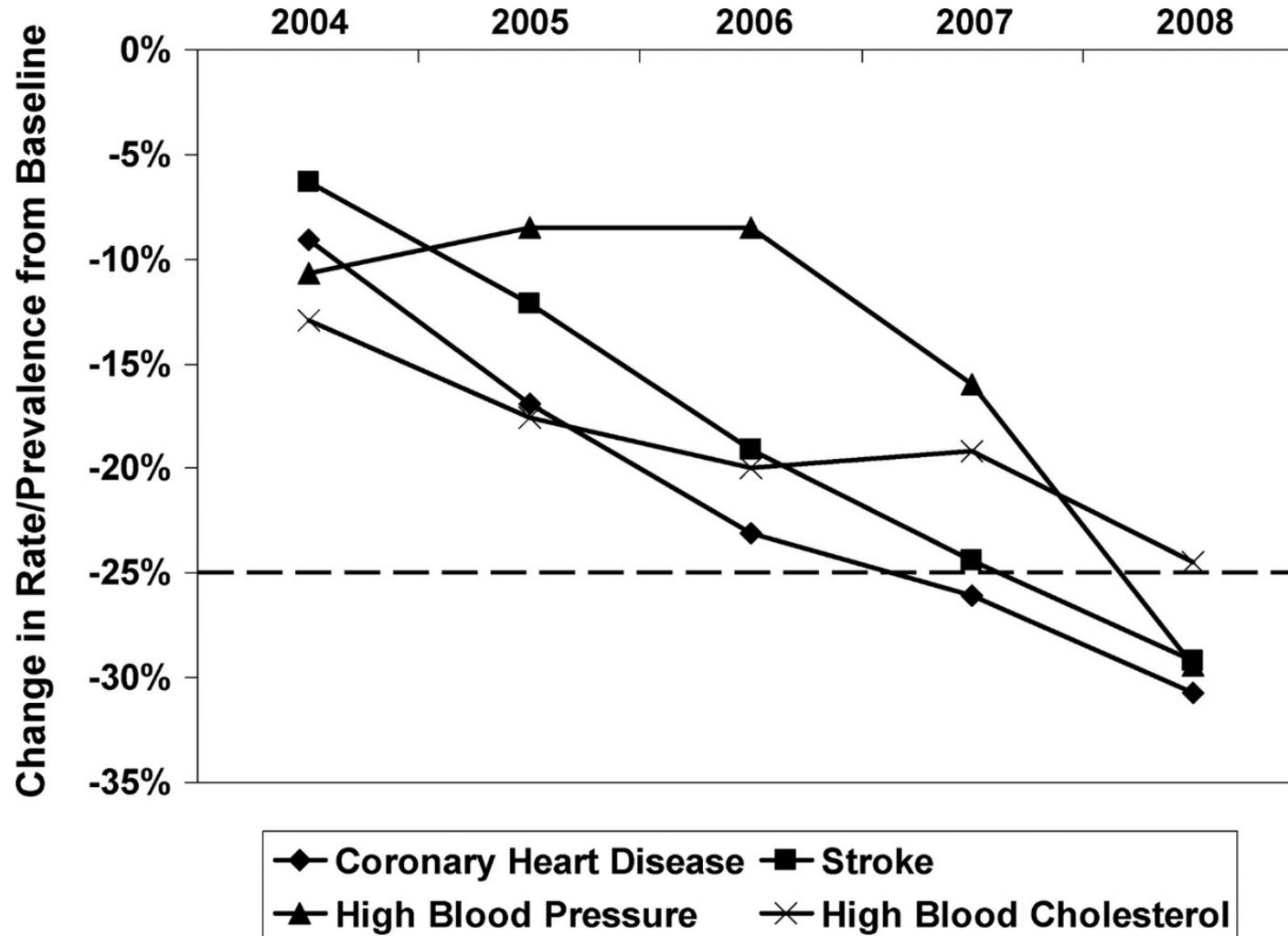
Source: Burt VL, et al. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US population. Data from the health examination surveys, 1960 to 1991. Erratum in: Hypertension 1996;7(5):1192.



BP, blood pressure; CHD, coronary heart disease; SBP, systolic blood pressure

Source: Whelton PK, et al. Primary prevention of hypertension: Clinical and public health advisory from The National High Blood Pressure Education Program. JAMA 2002;288:1882–8.

Trajectory of mortality rates from CHD and stroke, rate of uncontrolled high blood pressure, and prevalence of high blood cholesterol from 2004 to 2008.



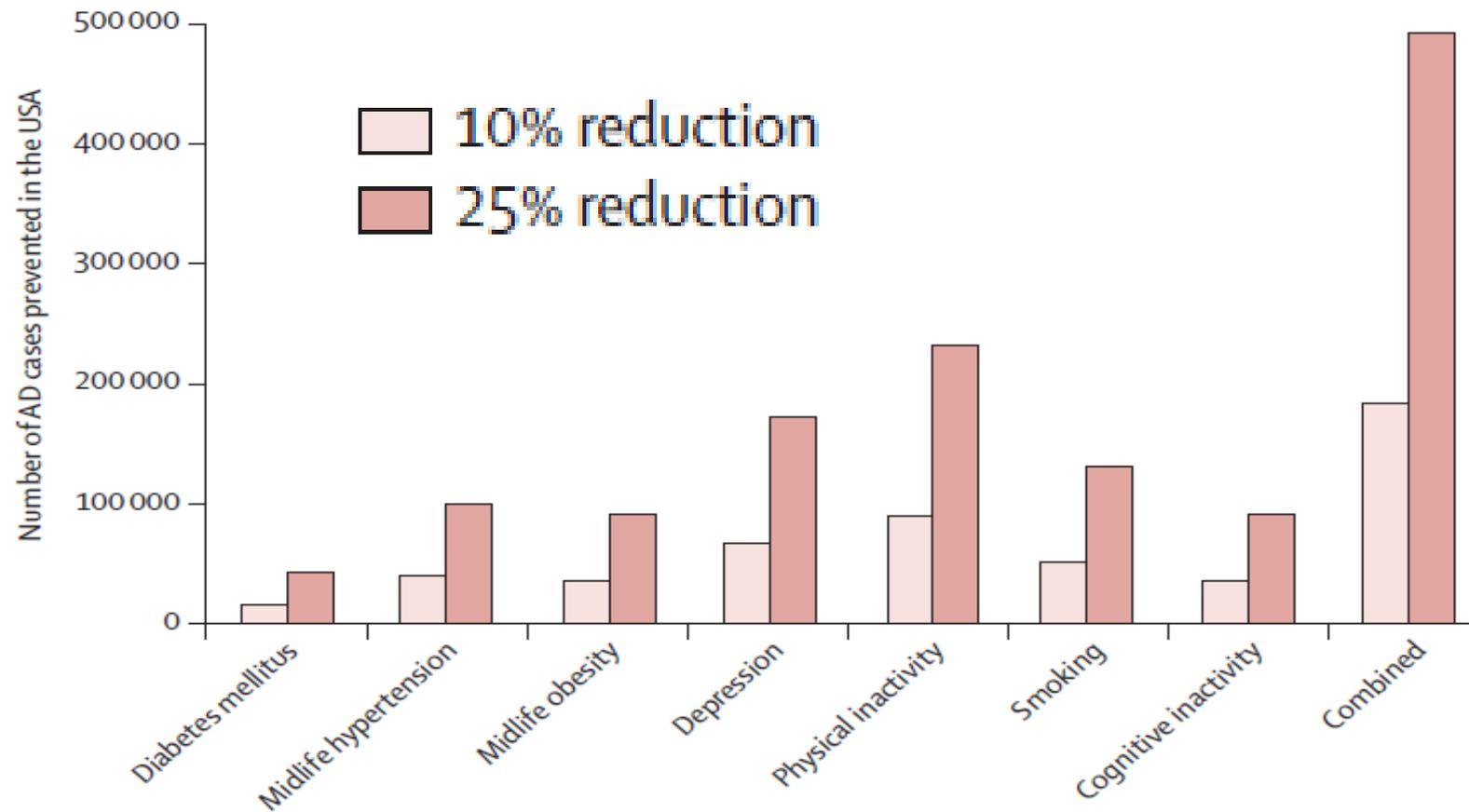
Donald M. Lloyd-Jones et al. *Circulation*. 2010;121:586-613

The projected effect of risk factor reduction on Alzheimer's disease prevalence



Deborah E Barnes, Kristine Yaffe

www.thelancet.com/neurology Vol 10 September 2011



Life's Essential 8: Updating and Enhancing the American Heart Association's Construct of Cardiovascular Health: A Presidential Advisory From the American Heart Association

Donald M. Lloyd-Jones, MD, ScM, FAHA, Chair; Norrina B. Allen, PhD, MPH, FAHA; Cheryl A.M. Anderson, PhD, MPH, MS, FAHA; Terrie Black, DNP, MBA, CRRN, FAHA; LaPrincess C. Brewer, MD, MPH; Randi E. Foraker, PhD, MA, FAHA; Michael A. Grandner, PhD, MTR, FAHA; Helen Lavretsky, MD, MS; Amanda Marma Perak, MD, MS, FAHA; Garima Sharma, MD; Wayne Rosamond, PhD, MS, FAHA; on behalf of the American Heart Association



A Few Words About Diet



Dietary habits show strongest evidence for causal effects on cardiovascular events, diabetes, and/or obesity



Recommend dietary pattern based on foods rather than nutrients



Inclusion of as few as possible elements with minimal overlap with each other while at the same time having some overlap with other relevant dietary guidelines

A Few Words About Sleep

It is not all about the length!

- Too short is bad
- Too long is bad

Its about the quality!

- Restful, deep sleep is best
- Awaking spontaneously is best

Its about the oxygen!

- Sleep apnea reduces oxygen to the brain
 - Repeated awakening
 - Day time sleepiness

Risk Factors for Sleep Apnea

- **Excess weight:** Fat deposits around your upper airway can obstruct your breathing
- **Neck circumference:** People with thicker necks might have narrower airways
- **A narrowed airway:** Tonsils or adenoids also can enlarge and block the airway, particularly in children.
- **Being male**
- **Being older**
- **Positive Family history**

Risk Factors for Sleep Apnea (cont'd)



USE OF ALCOHOL, SEDATIVES OR TRANQUILIZERS.

THESE SUBSTANCES RELAX THE MUSCLES IN YOUR THROAT, WHICH CAN WORSEN OBSTRUCTIVE SLEEP APNEA



SMOKING



NASAL CONGESTION



MEDICAL CONDITIONS: CONGESTIVE HEART FAILURE, HIGH BLOOD PRESSURE, TYPE 2 DIABETES AND LUNG DISEASES

Monitoring your Cardiovascular Health

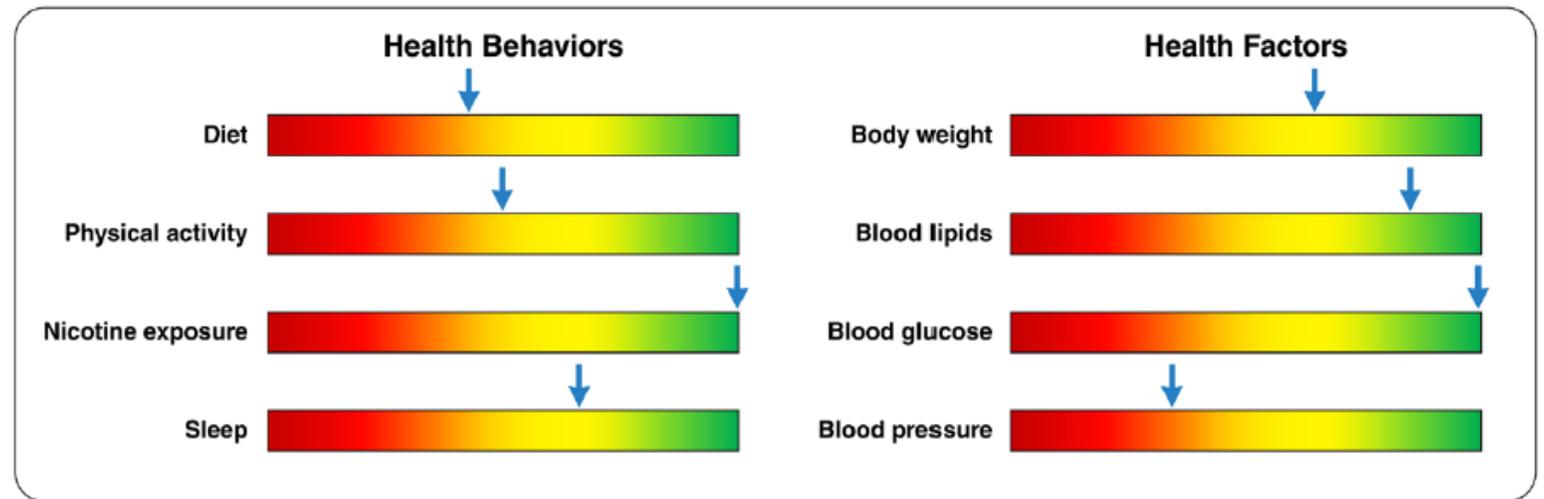
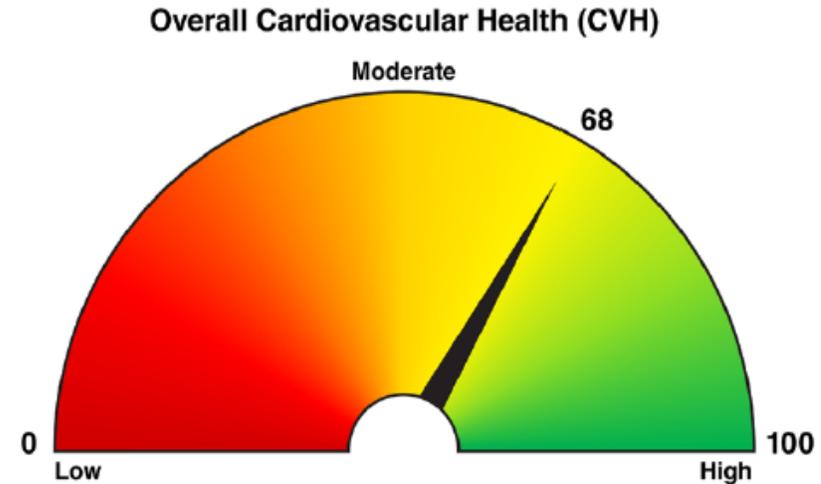


**GOOD HABITS BUILD
BETTER HEALTH**

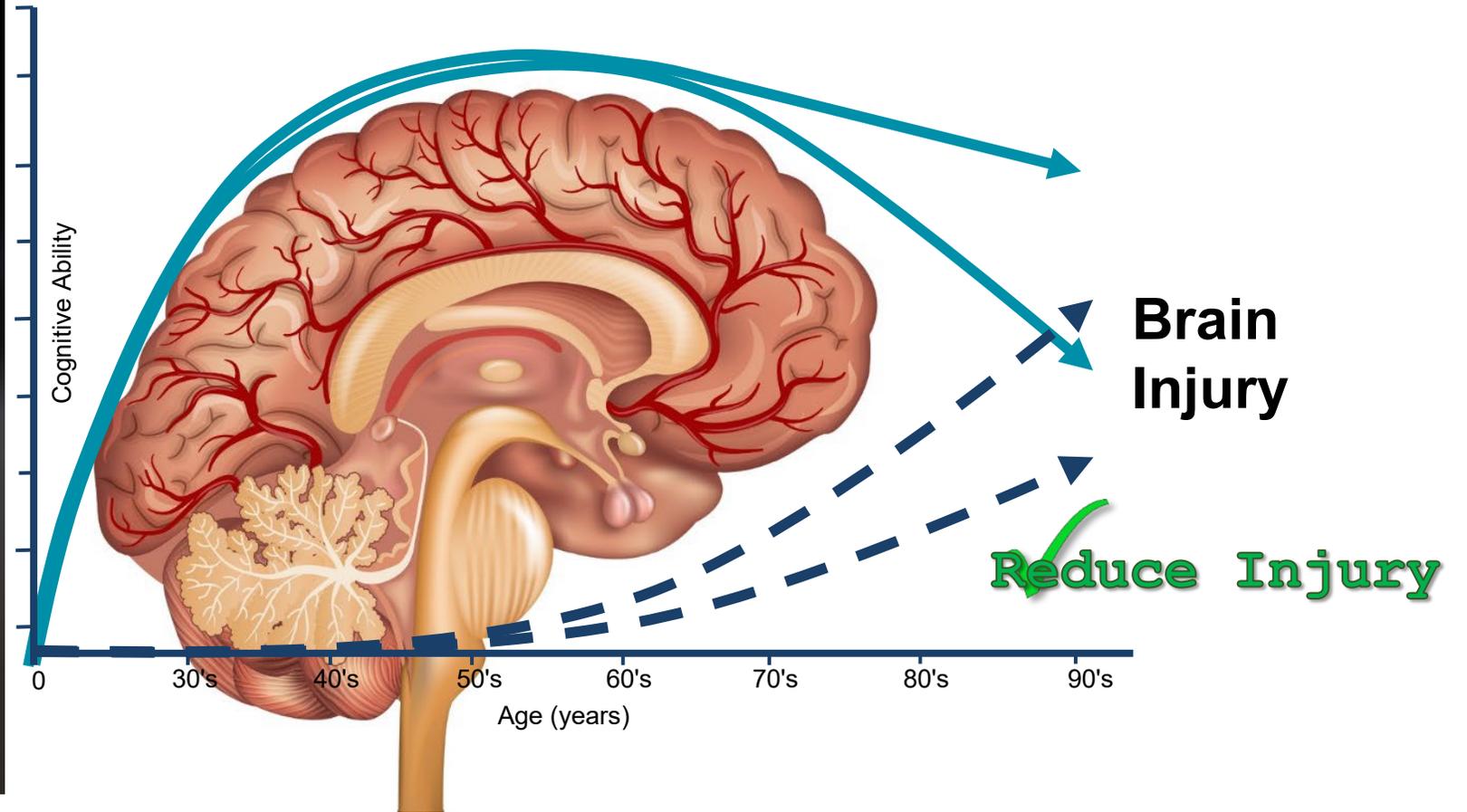
We've helped millions of people make healthier choices.

The AHA is the nation's oldest and largest voluntary organization dedicated to fighting heart disease and stroke. For nearly 100 years, we've been helping people like you live longer, healthier lives.

<https://mlc.heart.org/>



IMPROVING COGNITIVE AGING



Conclusions



Treatment of vascular risk factors and promotion of “vascular health” is likely to have a strong public health benefit to reduce late-life dementia



Current efforts to improve vascular health with “Life’s Essential 8” provide a public health opportunity to assess the efficacy of this approach

Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission



Gill Livingston, Jonathan Huntley, Kathy Y Liu, Sergi G Costafreda, Geir Selbæk, Suvarna Alladi, David Ames, Sube Banerjee, Alistair Burns, Carol Brayne, Nick C Fox, Cleusa P Ferri, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Noeline Nakasujja, Kenneth Rockwood, Quincy Samus, Kokoro Shirai, Archana Singh-Manoux, Lon S Schneider, Sebastian Walsh, Yao Yao, Andrew Sommerlad*, Naaheed Mukadam*

Prevention potential \approx 45%
14 modifiable risk factors



1. Diabetes
2. High blood pressure at midlife
3. Obesity at midlife
4. **High LDL cholesterol**
5. Physical inactivity
6. Depression
7. Smoking
8. Low education
9. Hearing loss
10. **Vision loss**
11. Traumatic Brain Injury
12. High alcohol consumption
13. Social isolation
14. Air pollution

Protective factors

- Healthy diet
- Education
- Physical activity
- Mental activity
- Social activity

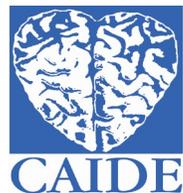
'Novel' risk factors

- Loneliness
- Hopelessness
- Stress
- Sleep disturbances
- Impaired oral health
- Infections? Covid-19?

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

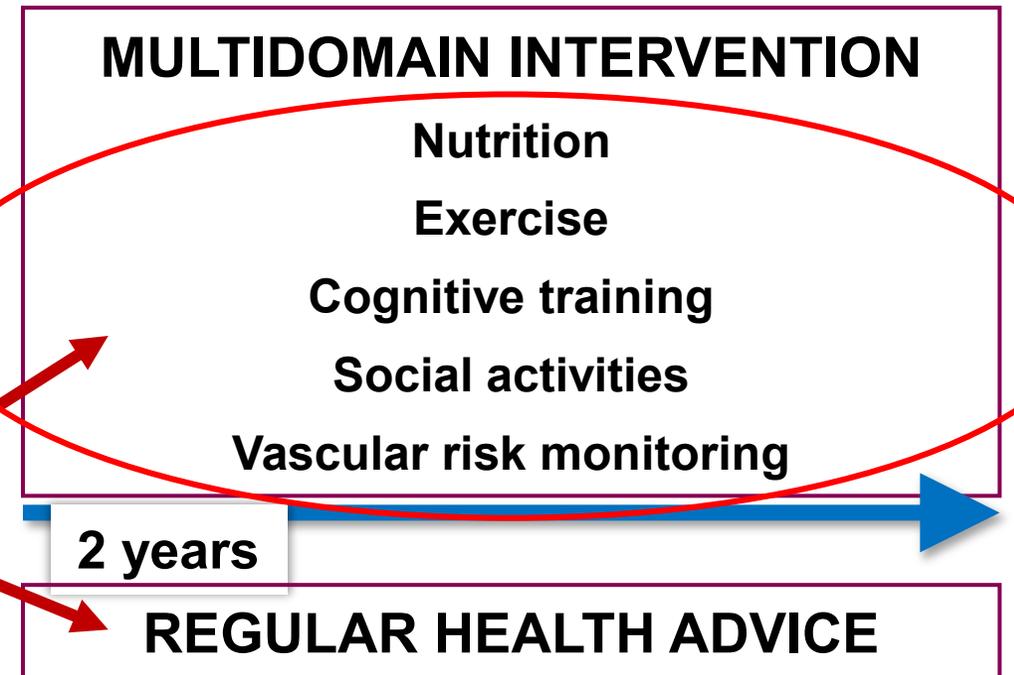
FINGER
Lancet 2015; 385: 2255-63

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälähti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilikka Soininen, Miia Kivipelto



Dementia Risk Score (midlife)

N = 1260
Age 60-77 years
At risk general population

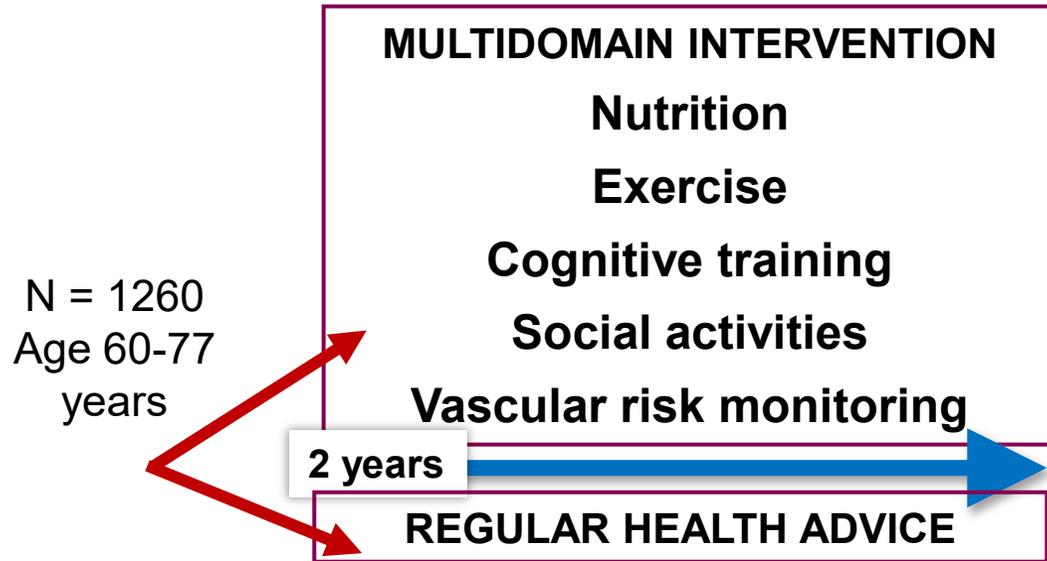


*Kivipelto et al., Lancet Neurology 2006
Alzheimer's and Dementia 2011*

Extended 5- & 7- & 11- year follow-up finished

The FINGER model for better brain health

FINGER



Dementia
risk score

Lancet 2015; JAMA Neurology 2018, Eur Ger Med 2017, JAMDA 2017, JAGS 2019; Alzheimer's Dementia 2021; European J Cardiology 2022, Alzheimer's Dementia 2022



Cognitive benefits



20% lower risk for cardiovascular events



30% lower risk for functional decline



60% lower risk for chronic diseases



Better health related quality of life



Reduced costs for healthcare



Health-economical benefits

A LANDMARK STUDY

**Completed
Recruitment**
March 2023



5
sites

2,111
participants

2
Self-Guided
or
Structured

2
Year
Intervention



1

What we set out to learn

Following the Evidence:

CALL TO ACTION

The FINGER results prompted the Alzheimer's Association to raise a key question: Can these lifestyle strategies protect brain health in older adults in other countries and settings ?



01



02



03

FINGER

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) showed that a multidomain lifestyle intervention improved cognitive function

U.S. POINTER

U.S. POINTER adapted and expanded the FINGER approach for the United States—where older adults live, eat, and receive care in many different ways

1 What we set out to learn



THE POINT OF POINTER

To understand whether lifestyle interventions can protect brain health and reduce risk of dementia in a large, diverse population of older adults in the United States—and whether varying levels of structure and support lead to different outcomes

2

What we did



U.S. POINTER LOCATIONS

5 Sites Across the United States



2

What we did



At Risk for Cognitive Decline, but Without Dementia

PARTICIPANT QUALIFICATIONS

 60 - 79 years old

+

 Does Not Exercise Regularly

+

 Suboptimal Diet (MIND Diet Score)

+ two or more of the following:

 70 + years old

 African American / Black or Native American Race; Hispanic Ethnicity

 Family History of Memory Impairment

 Cardiovascular Health Risk

2

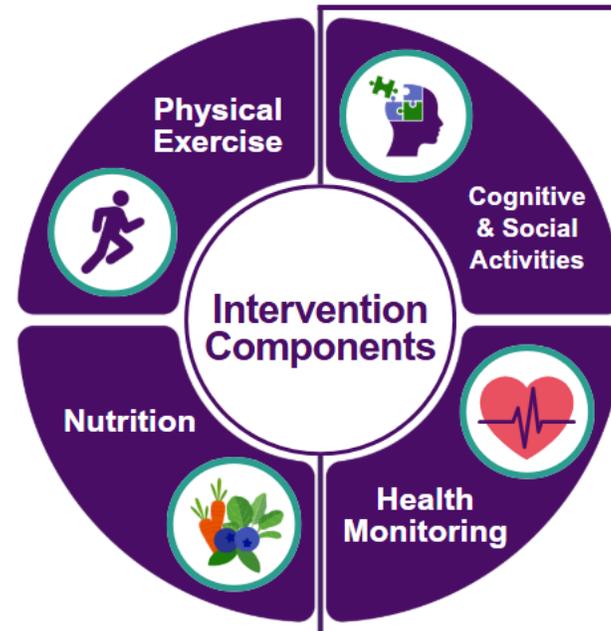
What we did



Participants Randomized into 2 Groups

LIFESTYLE INTERVENTIONS

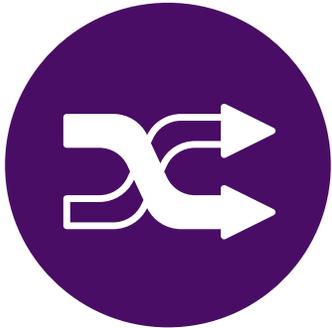
Self-Guided (SG)



Structured (STR)

2

What we did



SG

6 facilitated peer team meetings over 2 years with general support from study navigator



Education & General Support

Met with study navigator 3 times per year to receive:

- Healthy lifestyle education
- Tangible tools to facilitate self-guided plans
- General support to encourage physical activity, a healthy diet, and cognitive and social stimulation



Health Monitoring

Blood laboratory results and blood pressure measurements were provided at clinic assessment visits

STR

38 facilitated peer team meetings over 2 years, with education, goal-setting, accountability and support from study interventionist and navigator



Physical Exercise

Aerobic, resistance, and stretching & balance exercise primarily at a community facility



Nutrition

Encouragement to follow the MIND diet, with extra support through telephone contacts with the interventionist



Cognitive and Social Challenge

Home-based computer cognitive training and regular participation in intellectually & socially engaging activities



Guideline-Based Health Coaching

Medical advisor appointments every 6 months for goal-setting, and to review monthly blood pressure measurements and blood laboratory results provided at clinic visits

2

What we did



POINTER Rx



Aerobic: 4 days/week,
30-35 min/session

Resistance: 2 days/week,
15-20 min/session

Stretch/Bal: 2 days/week,
10-15 min/session



MIND diet: Score \geq 9.5



BrainHQ: 3 times/week,
15-20 min/session



Labs: Biannual review

STR

38 facilitated peer team meetings over 2 years, with education, goal-setting, accountability and support from study interventionist and navigator



Physical Exercise

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WHAT'S ON THE **MIND DIET?**

 AT LEAST **THREE SERVINGS** OF WHOLE GRAINS EACH DAY

AT LEAST ONE DARK GREEN SALAD AND ONE OTHER VEGETABLE EACH DAY



BERRIES AT LEAST TWICE A WEEK

 AT LEAST A ONE-OUNCE SERVING OF NUTS EACH DAY 


BEANS OR LEGUMES AT LEAST EVERY OTHER DAY

POULTRY AT LEAST TWICE A WEEK




FISH AT LEAST ONCE A WEEK

NO MORE THAN ONE TABLESPOON A DAY OF BUTTER OR MARGARINE; CHOOSE OLIVE OIL INSTEAD



CHEESE, FRIED FOOD AND FAST FOOD NO MORE THAN ONCE A WEEK

PASTRIES AND SWEETS LESS THAN FIVE TIMES A WEEK 

2

What we did

**PRIMARY
OUTCOME**

Change in Cognitive Function Over 2 Years



Each group followed the intervention for 2 years, and cognitive function was measured every 6 months using memory and other thinking tests

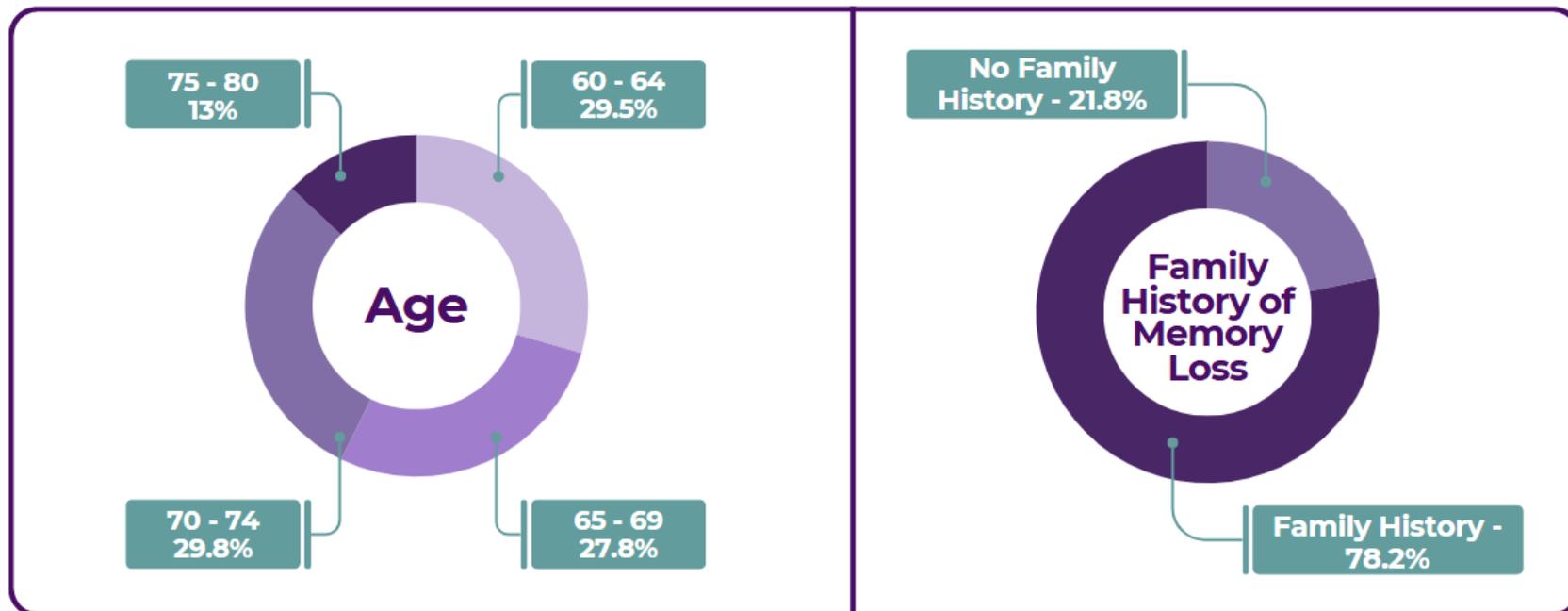
2

What we did



2111 Older Adults from Diverse Groups

PARTICIPANT CHARACTERISTICS

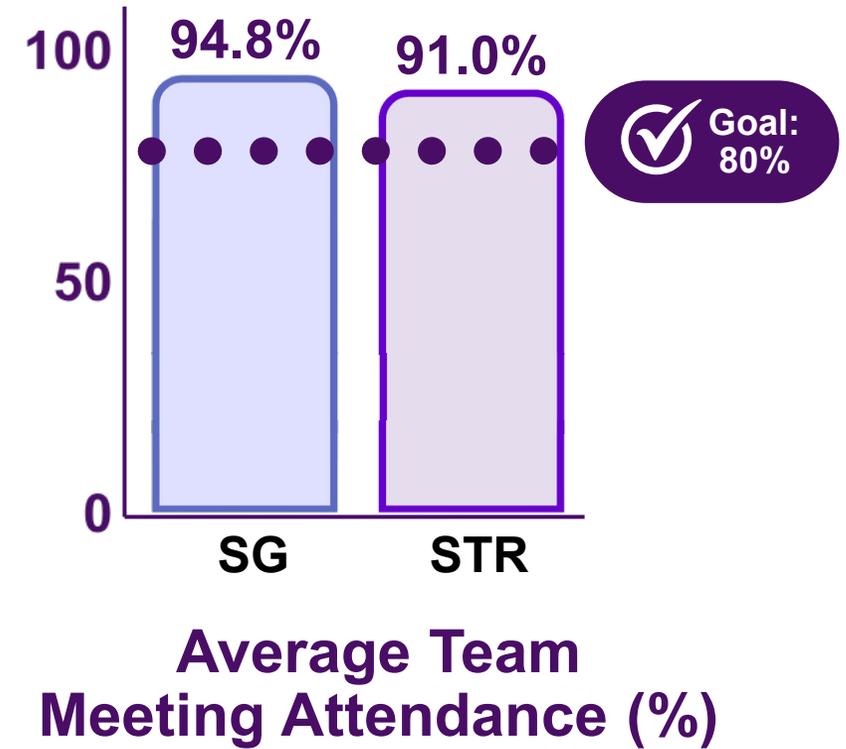


3

What we found

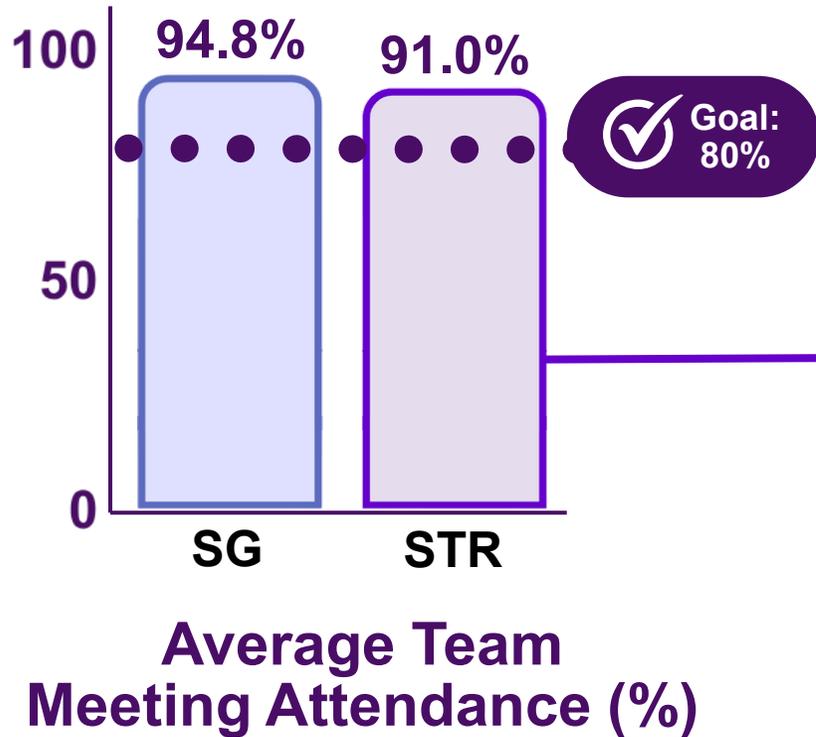
89% of all participants completed the last clinic assessment

Both groups did well in following the POINTER interventions



3

What we found



For participants in the Structured intervention:



The average number of very active Fitbit minutes per week was 86 minutes (goal was 90 minutes)

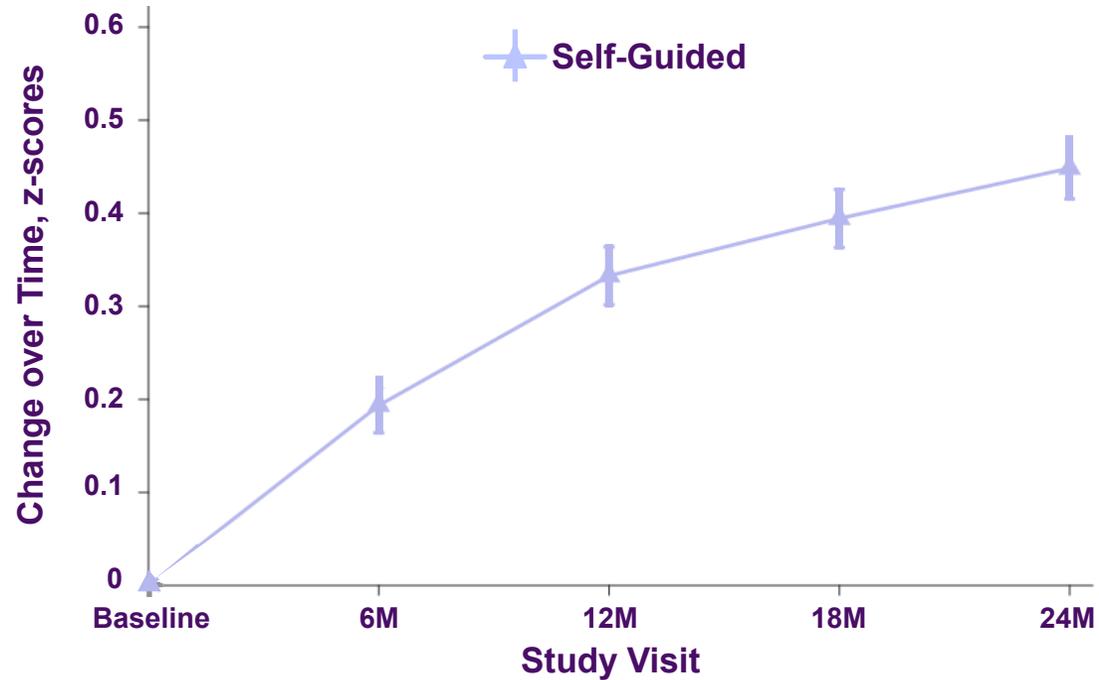


The average MIND diet score was 11 out of 14 points (goal was ≥ 9.5)

3

What we found

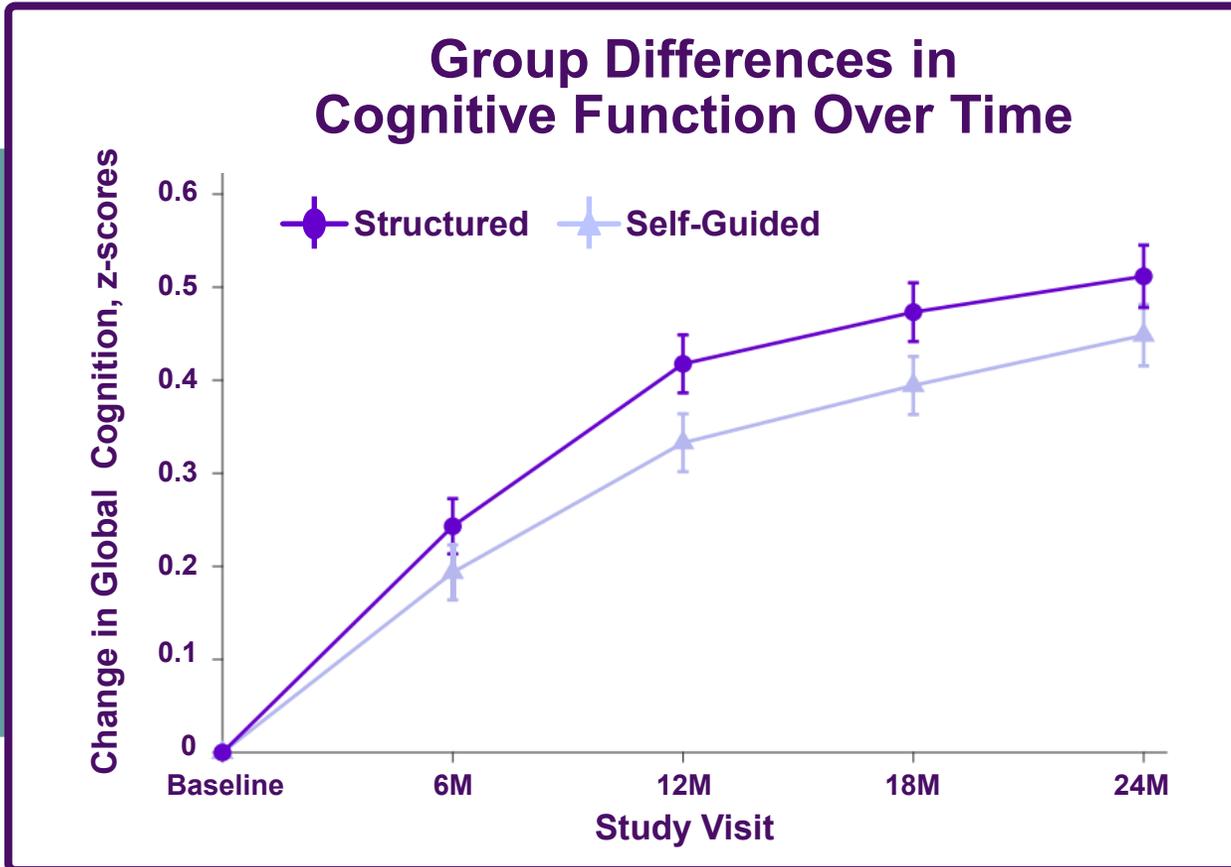
Group Differences in Cognitive Function Over Time



- "Cognitive Function" is represented by a single score for each participant, at every study visit.
- This single score was calculated from the many cognitive tests you took in the clinic.
- The **light purple line** on the left shows the average score at each assessment visit for all participants in the Self-Guided group

3

What we found



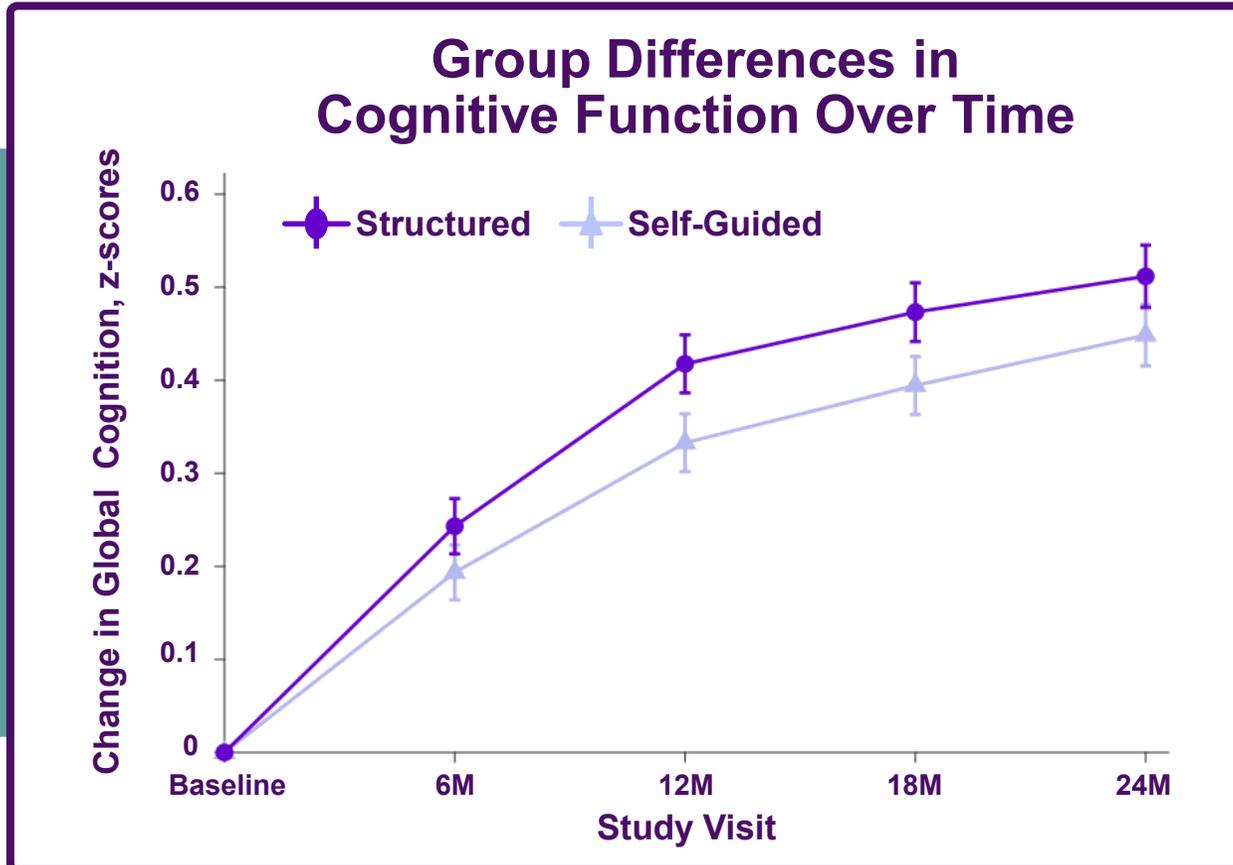
1

Cognitive function improved over time for both groups*

**Some of this improvement is likely due to practice*

3

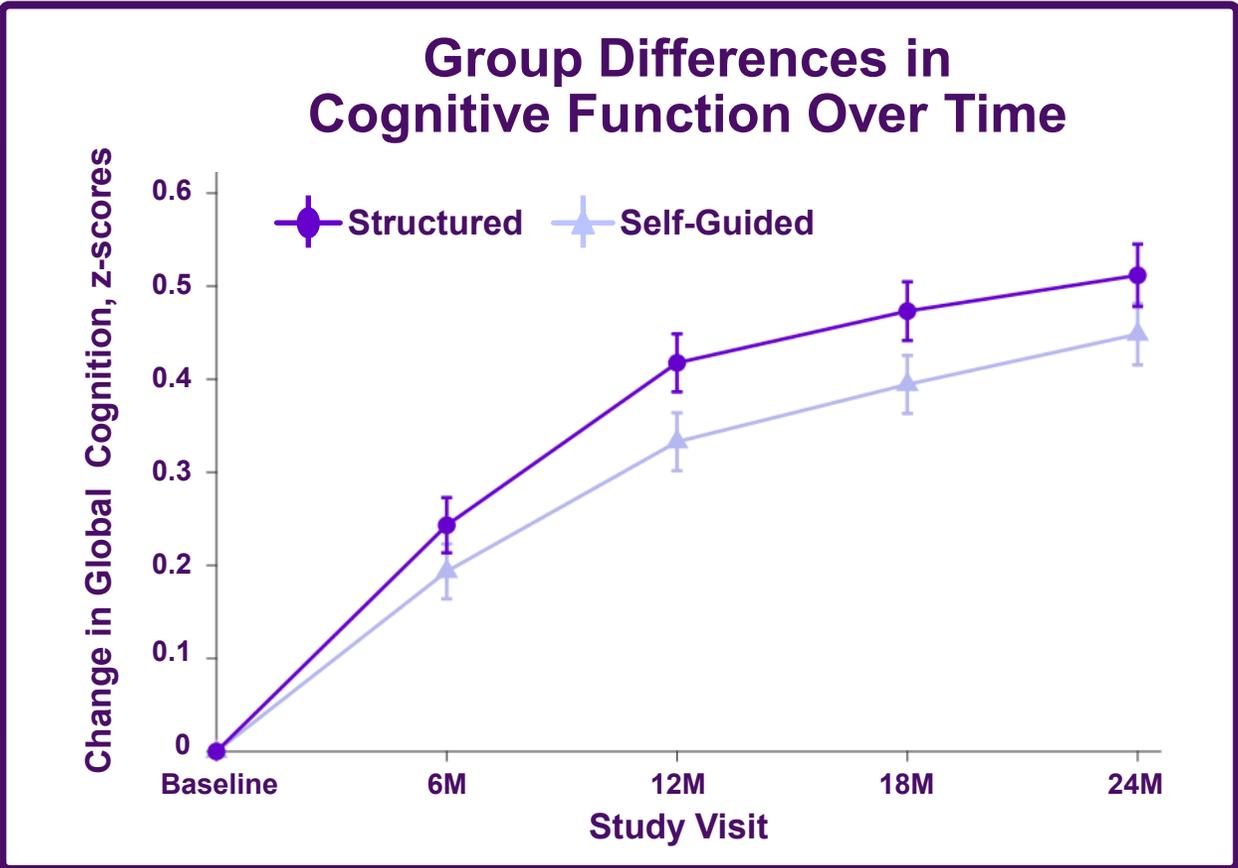
What we found



2 The Structured intervention had a significantly greater benefit on cognitive function

3

What we found



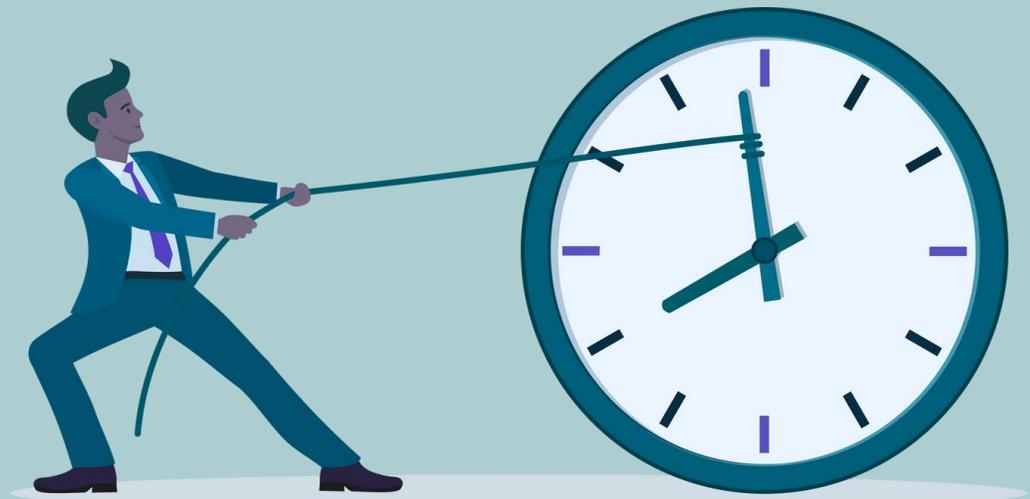
3 This extra benefit was the same regardless of sex, age, ApoE4 genotype, or heart health at the start of the study

4

What this means

Based on information collected in **POINTER** and from other large studies with similar participants...

We estimate that the extra benefit of the 2-year Structured intervention may be that **it slows cognitive aging by 1 to nearly 2 years.**



WHAT THIS JOURNEY HAS MEANT TO OUR PARTICIPANTS

“I learned the importance of self-care. It will always be a part of my life now. I feel better!”

“I have become aware of how important it is to practice balance and stay flexible.”

“I cannot believe how differently I am eating, and my mind feels sharper.”

“This has been a life-changing 2 years... my husband has joined in and is doing the same things I am doing. I can see how much healthier he is, and he can see how much healthier I am... It is such a well ironed out program and my physical, mental, and social health has significantly improved.”



“I’m doing physical exercise again for the first time in years.”

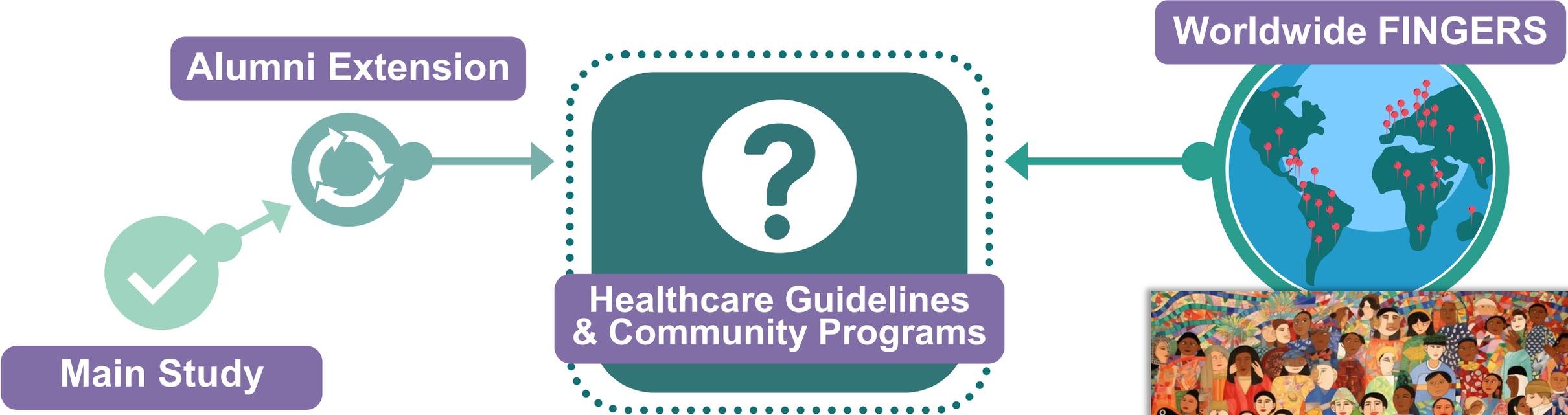
“I feel stronger than most my age.”

“This program has transformed not only my attitudes and behaviors toward brain health but also those of my daughter. Thanks to POINTER, my granddaughter won’t have to make lifestyle changes later in life – the POINTER way will be her way from the beginning.”

5

Where we go from here

CONTINUED COMMITMENT TO BRAIN HEALTH



If we delay onset by 5 years...

DELAYED ONSET

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

would save
\$87 billion in 2050.



5.7
MILLION

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

America would save
\$367 billion in 2050.

alzheimer's  association

THE BRAINS BEHIND SAVING YOURS™

THANK YOU !



<https://health.ucdavis.edu/alzheimers-research/>

QUESTIONS?

