Dementia Prevention Targeting Modifiable Risks

Nancy Isenberg MD MPH

"Do not complain about growing old. It is a privilege denied to many."

Mark Twain

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Objectives

1. Identify and target 5 modifiable risk factors across lifespan
2. Implement evidence-based approaches to target modifiable risk
3. Implement group visits for dementia prevention

The Problem: Time Lost is Independence Lost

7.2 million people 65+ are projected to have Alzheimer's dementia by **2025**

Annual economic costs >$300M

- Over 80% of PCPs on the front lines of dementia care, over half note they lack the dementia training and tools to adequately address this unmet and growing need.
- Fewer than half of dementia cases are diagnosed in primary care, and too often when diagnosed have progressed to advanced stage where independence has been lost.

Source: https://www.alz.org/media/documents/alzheimers-facts-and-figures.pdf

Providence

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Dementia is a Primary Care disease

People want the connection with their PCP who they know and trust.

Too few neurologists or geriatricians to see all patients with dementia.

PCPs can provide excellent dementia care.

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Age-Friendly Health Systems (AFHS)

Providence's 5 Ms for Age- Friendly Health

WHAT MATTERS

Know your care preferences and set goals for your health. Establish Advance Directives and Trusted Decision Makers.

MEDICATION

Manage your medications and understand how they may impact your mobility and cognition.

MENTATION

Get the emotional and cognitive support you need. Understand, prevent, and seek treatment for dementia, delirium, and depression.

MOBILITY

Keep active and mobile, preventing injuries and falls. Learn how to safely mobilize as you age.

MALNUTRITION

Commit to proper nutrition and assess malnutrition risk regularly.

Progression of Alzheimer's Disease

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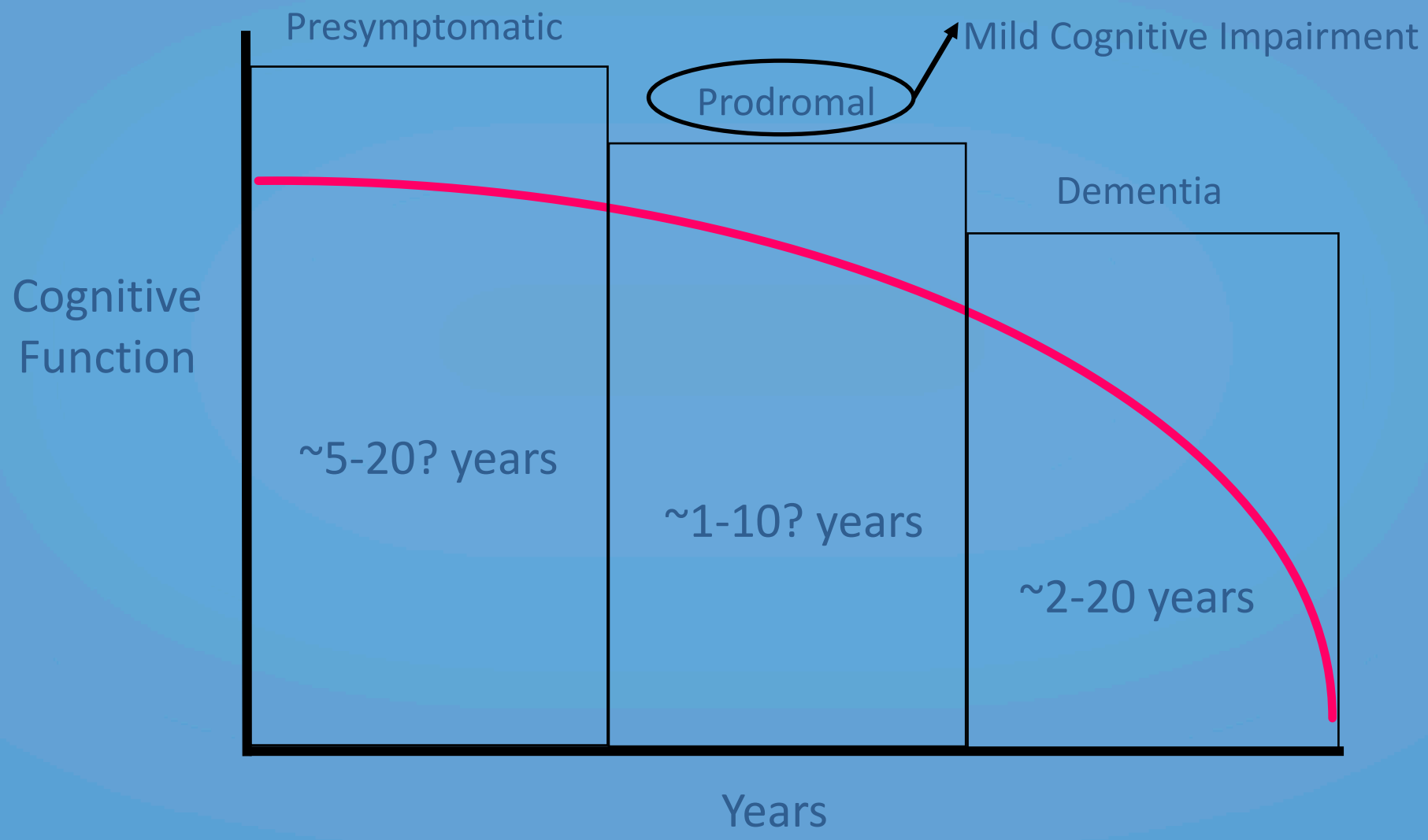
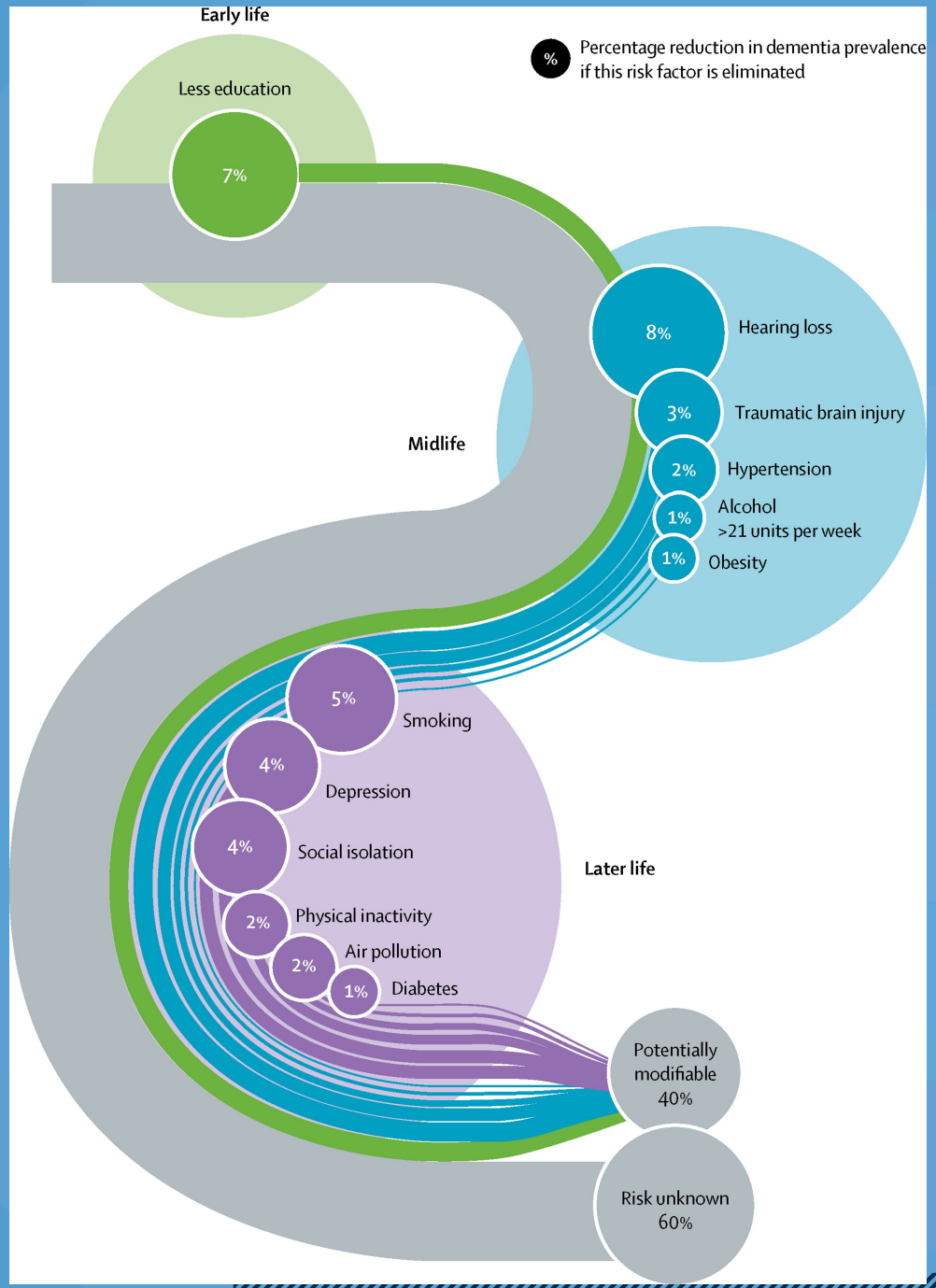


40% of dementia cases are preventable over the lifespan



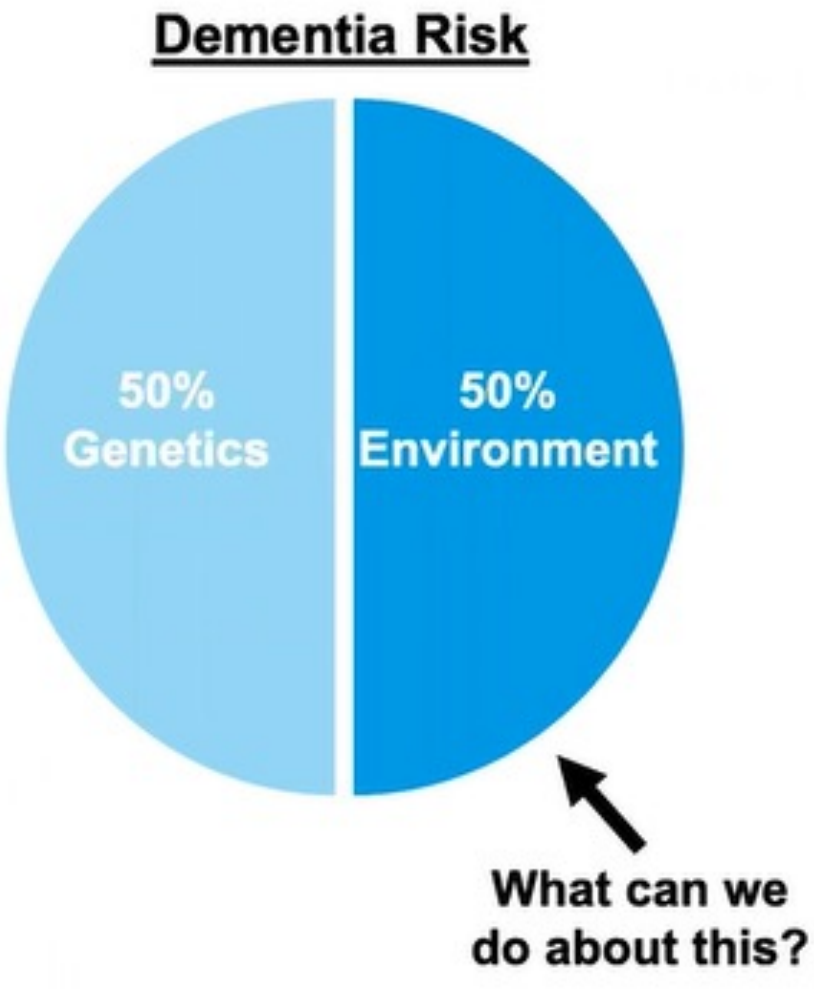
Source: *Livingston et al. A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission*

www.alzint.org

Alzheimer's Disease International
The global voice on dementia

Why Are Modifiable/Behavioral Risk Factors Important for Brain Health

- Identification of modifiable risk factors can help:
  - Understand the mechanisms associated with dementia development
  - Enhance our ability to identify those at highest risk
  - Improve prevention and treatment options
- Modifiable/behavioral factors with the strongest evidence:
  - Cardiovascular factors
  - Physical & cognitive activity
  - Sleep quality & disorders
  - Traumatic brain injury (TBI)
- Biomarker data bolsters this evidence



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Relation of cerebral vessel disease to Alzheimer's disease dementia and cognitive function in elderly people: a cross-sectional study

Zoe Arvanitakis, Ana W Capuano, Sue E Leurgans, David A Bennett, Julie A Schneider

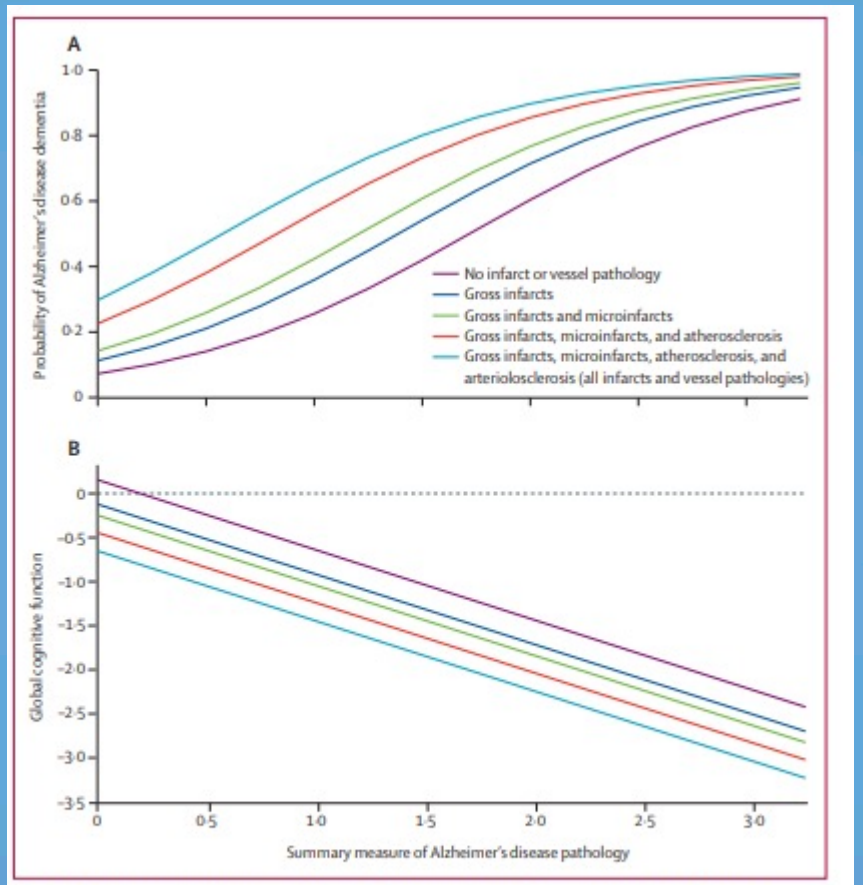

Figure 2: **Relation of cerebral vessel pathologies to Alzheimer's disease dementia and global cognitive function**

(A) The probability of Alzheimer's disease dementia by Alzheimer's disease pathology, showing separate effects of infarcts and cerebral vessel pathologies. (B) The relation of Alzheimer's disease pathology to global cognitive function, showing separate effects of infarcts and cerebral vessel pathologies.

1143 individuals, mean age at death 89. Lancet Neurol. 2016 Aug; 15(9): 934–943.

Review > Ageing Res Rev. 2020 Mar;58:101002. doi: 10.1016/j.arr.2019.101002.
Epub 2019 Dec 30.

A Third of Community-Dwelling Elderly With Intermediate and High Level of Alzheimer's Neuropathologic Changes Are Not Demented: A Meta-Analysis

Mahmoud Reza Azarpazhooh [1], Abolfazl Avan [2], Lauren E Cipriano [3], David G Munoz [4], Mahdiyeh Erfanian [5], Amin Amiri [6], Saverio Stranges [7], Vladimir Hachinski [8]

Viewpoint

ONLINE FIRST

April 27, 2020

White Matter Degeneration—A Treatable Target?

Austyn Roseborough, MSc[1]; Vladimir Hachinski, MD, DSc[2]; Shawn Whitehead, PhD[1]

» Author Affiliations | Article Information

JAMA Neurol. Published online April 27, 2020. doi:10.1001/jamaneurol.2020.0814

Healthy lifestyle and the risk of Alzheimer dementia

Findings from 2 longitudinal studies

Klodian Dhana, MD, PhD, Denis A. Evans, MD, Kumar B. Rajan, PhD, David A. Bennett, MD, and Martha C. Morris, ScD

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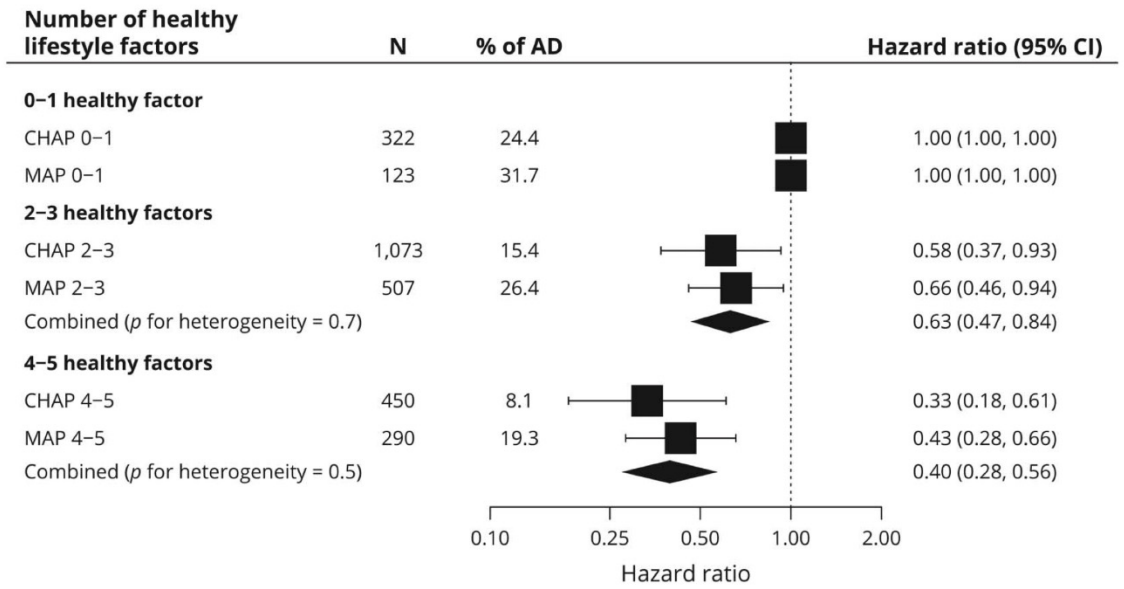
Neurology® 2020;95:1-10. doi:10.1212/WNL.0000000000009816

Figure HRs of AD according to the combination of healthy lifestyle factors in the prospective cohort studies



Model adjusted for age, sex, race, education, *APOE* ε4, and prevalence of cardiovascular disease (including heart disease or stroke). A random-effects meta-analysis was used to combine cohort-specific results. AD = Alzheimer dementia; CHAP = Chicago Health and Aging Project; CI = confidence interval; HR = hazard ratio; MAP = Rush Memory and Aging Project; N = number of participants in each group.

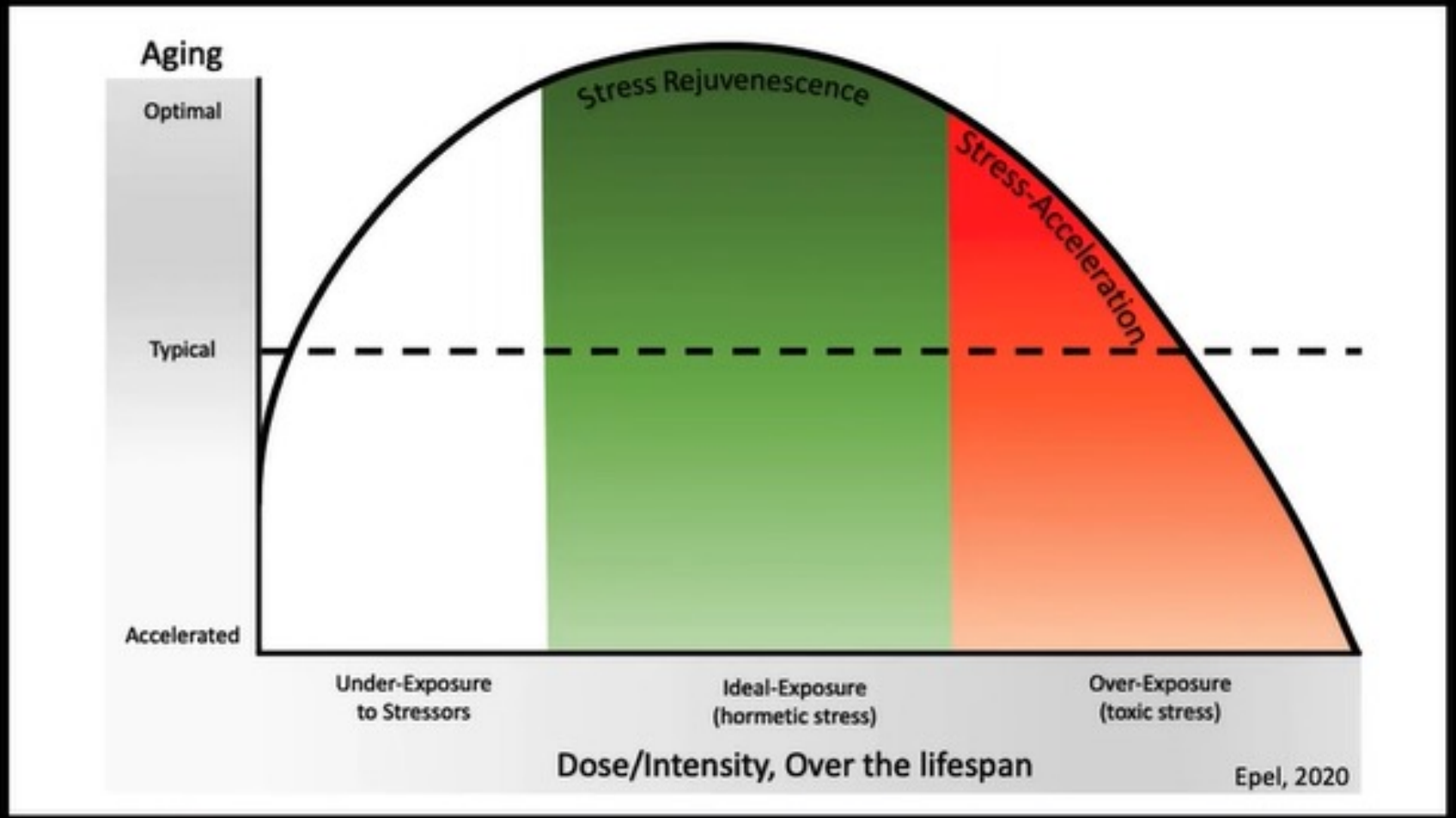
Nonsmoking, ≥150 min/wk moderate/vigorous-intensity physical activity, light to moderate alcohol consumption, high-quality Mediterranean-DASH Diet Intervention for Neurodegenerative Delay diet (upper 40%), and engagement in late-life cognitive activities (upper 40%)

Talking Prognosis of MCI

- "There's a ~50% chance that 3 years from now you could remain independent as you are now."
- "…there is also the chance that this could be the first sign of Alzheimer's Disease."
- "Either way, I'll be here with you. It's so good we are talking about **what you can do, what matters to you** and that you have your family here to help. We're hoping for the best. I'm here to help if things get worse."

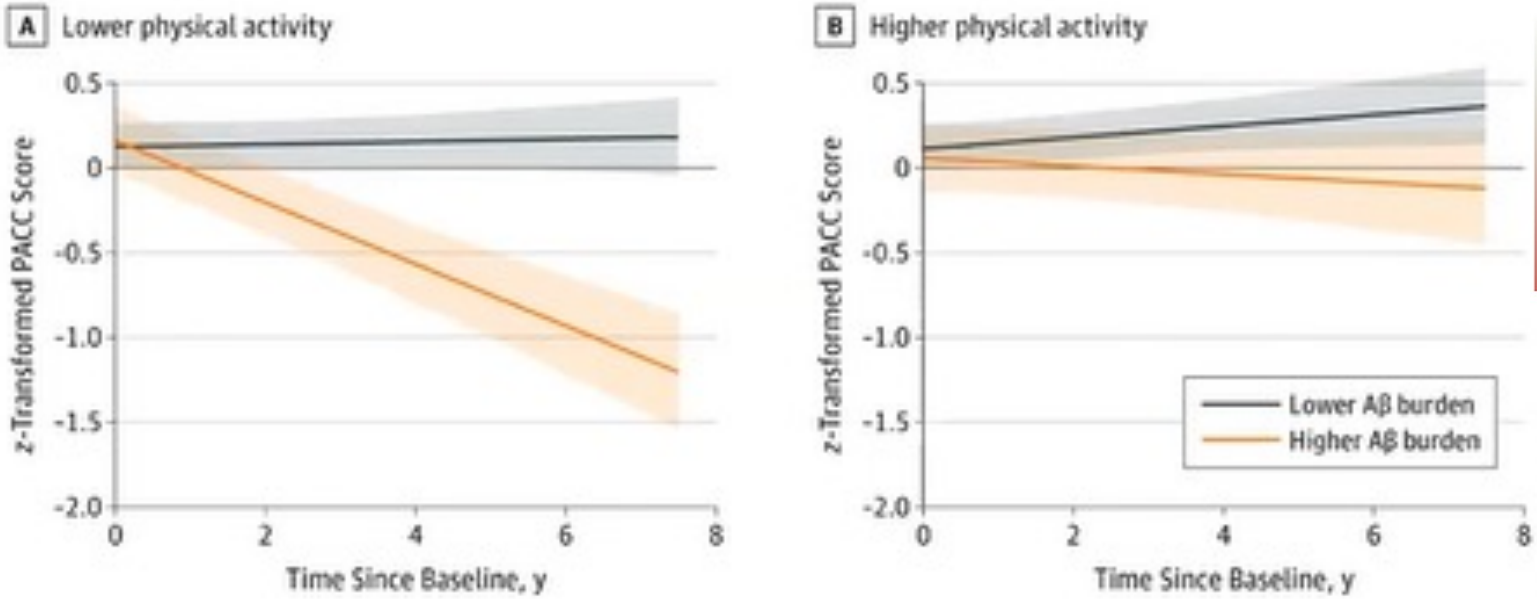
Angevaare et al, *Neurology,* 2022, (accepted)

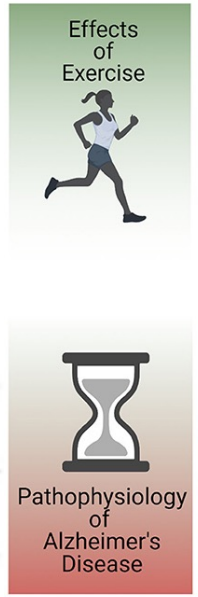
Toxic vs Hormetic Stress & Aging

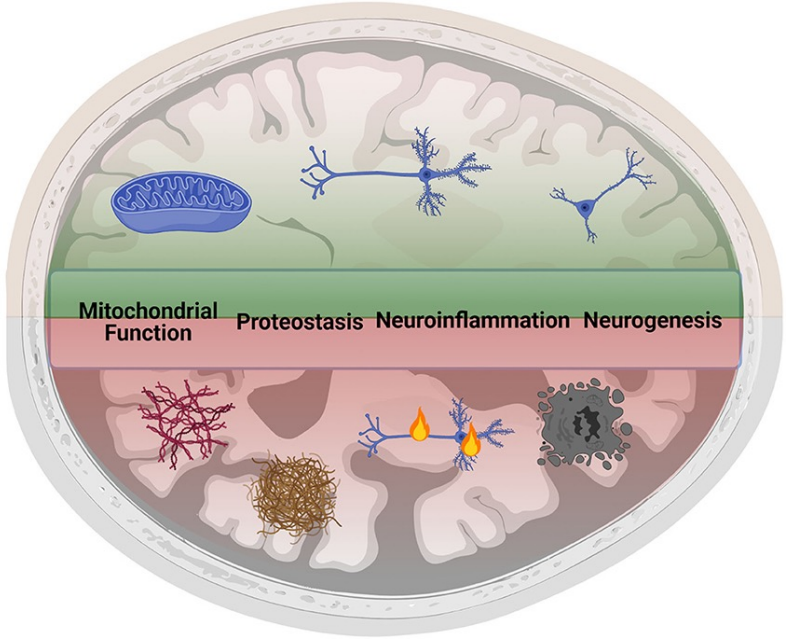


Have we become too comfortable?

Physical Activity Moderates the Association of Amyloid β with Cognitive Decline







Gupta et al, *Front. Neurol,* 2021

Rabin et al, *JAMA Neurol, 2019.*

Late-life physical activity relates to brain tissue synaptic integrity markers in older adults

Kaitlin Casaletto PhD, Alfredo Ramos-Miguel PhD, Anna VandeBunte BA, Molly Memel PhD, Aron Buchman MD, David Bennett MD, William Honer MD

First published: 07 January 2022 | https://doi.org/10.1002/alz.12530

ELSEVIER

Alzheimer's & Dementia 11 (2015) 1007-1014

Featured Articles

MIND diet associated with reduced incidence of Alzheimer's disease

Martha Clare Morris[a,*], Christy C. Tangney[b], Yamin Wang[a], Frank M. Sacks[c], David A. Bennett[d,e], Neelum T. Aggarwal[d,e]

MIND diet, common brain pathologies, and cognition in community-dwelling older adults

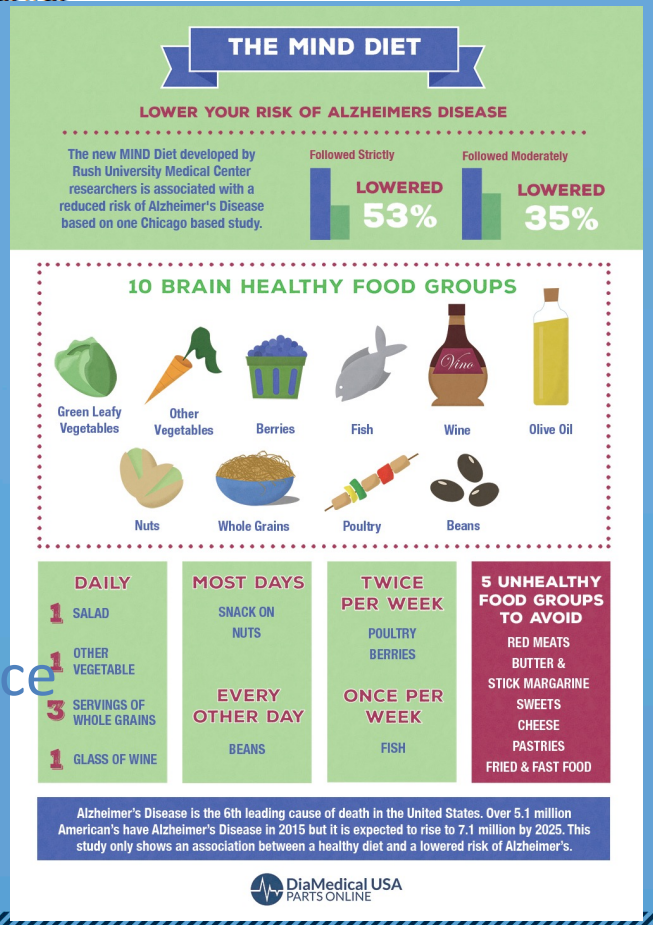
Klodian Dhana, MD, PhD,[a,b] Bryan D. James, PhD,[b,c] Puja Agarwal, PhD,[a,b] Neelum T. Aggarwal, MD,[c,d] Laurel J Cherian, MD, MS,[d] Sue E. Leurgans, PhD,[c,d] Lisa L. Barnes, PhD,[c,d] David A. Bennett, MD,[c,d] and Julie A. Schneider, MD, MS[c,d,e]

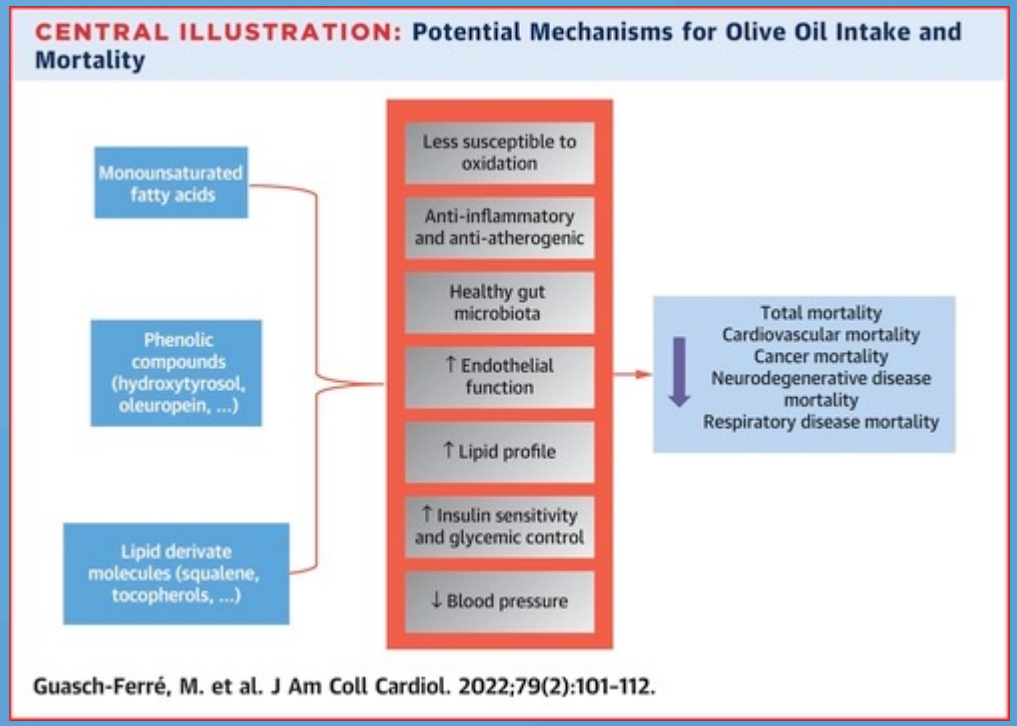
J Alzheimers Dis. 2021; 83(2): 683–692.

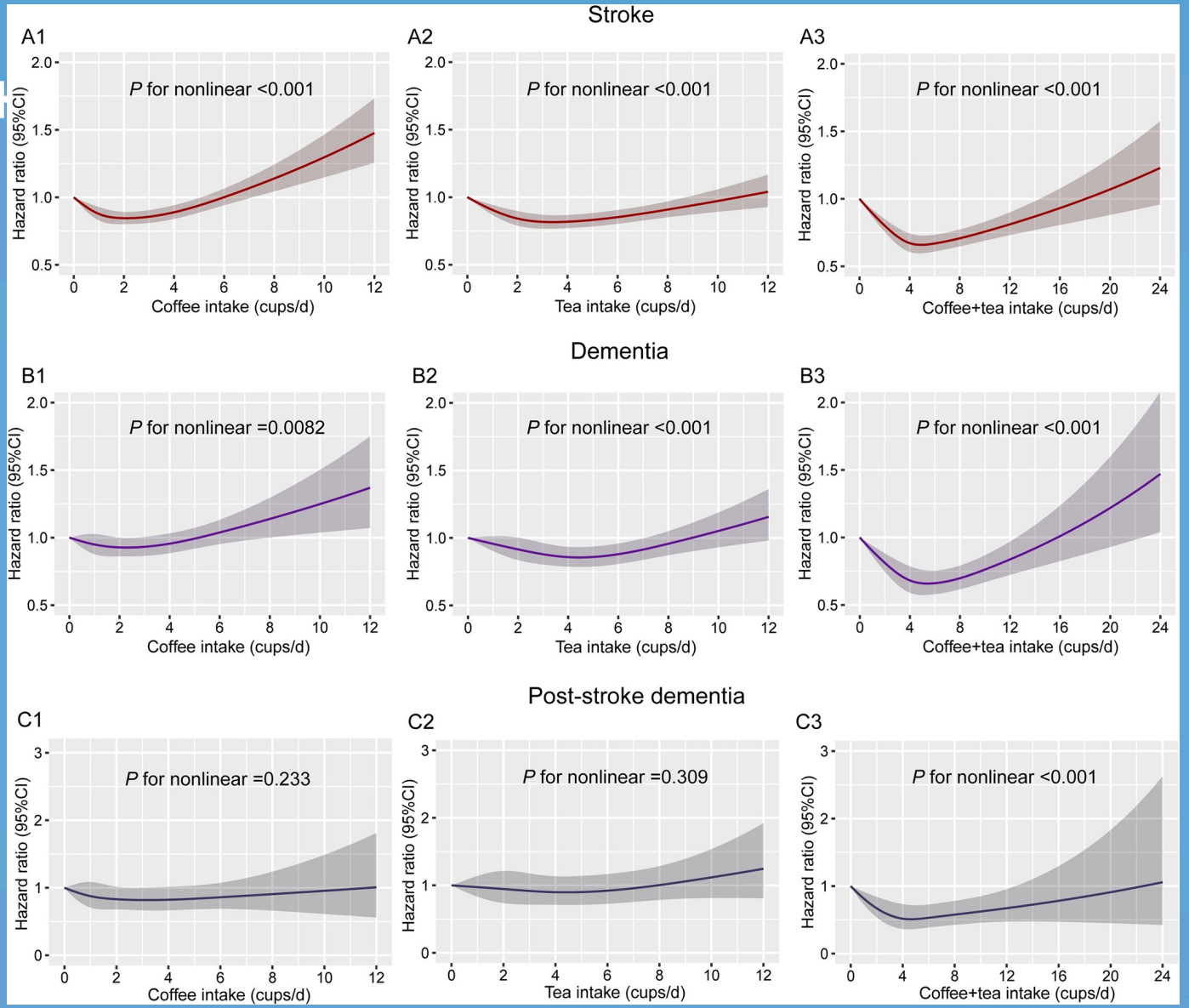
- N = 923
- Age 58-98
- 4.5 years

- DASH + Mediterranean
  - One glass of wine

- 53% reduction in incidence



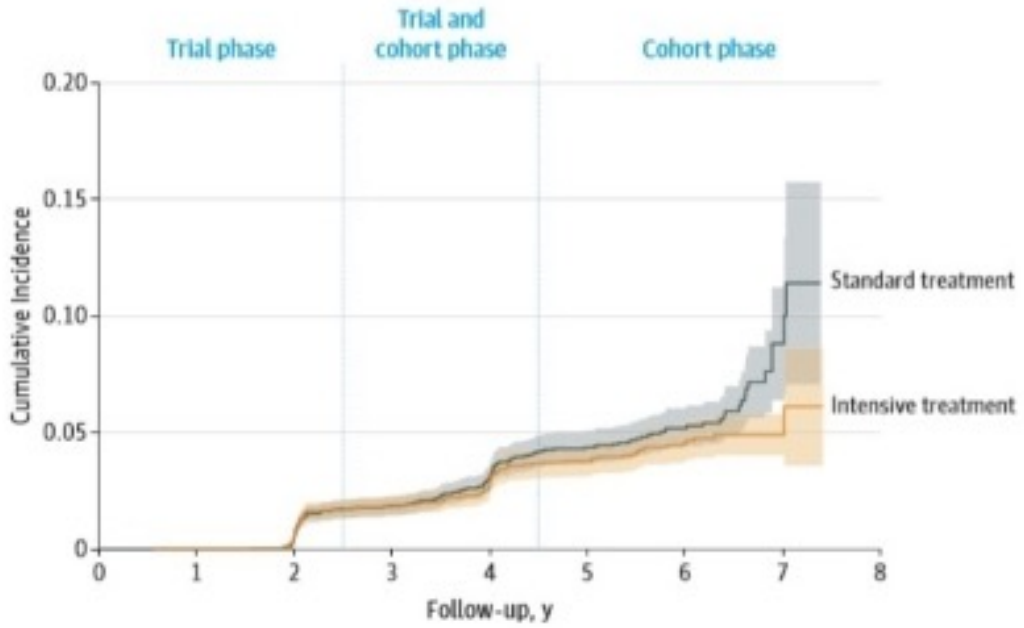




Zhang et al, *PLOS,* 2021

Fig 1. Restricted cubic spline models for the relationship between coffee, tea, and their combination with stroke, dementia, and poststroke dementia.(A1) Coffee and stroke. **(A2)** Tea and stroke. **(A3)** Combination of coffee and tea on stroke. **(B1)** Coffee and dementia. **(B2)** Tea and dementia. **(B3)** Combination of coffee and tea on dementia. **(C1)** Coffee and poststroke dementia. **(C2)** Tea and poststroke dementia. **(C3)** Combination of coffee and tea on poststroke dementia. The 95% CIs of the adjusted HRs are represented by the shaded area. Restricted cubic spline model is adjusted for sex, age, ethnicity, qualification, income, BMI, smoking status, alcohol status, physical activity, diet pattern, consumption of sugar-sweetened beverages, HDL, LDL, cancer, diabetes, CAD, and hypertension, and we adjusted for coffee in tea analysis or for tea in coffee analysis. BMI, body mass index; CAD, cardiovascular arterial disease; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein. **365,682 participants from UK Biobank– 4-6 cups daily assc. lowest risk**

Figure 2. Probable Dementia by Treatment Group



No. at risk									
Standard treatment	4285	4282	4168	3886	2829	2107	989	87	0
Intensive treatment	4278	4277	4171	3917	2893	2189	1027	93	0

Shaded regions indicate 95% confidence intervals. Median follow-up time was 5.14 years (interquartile range, 3.91-6.00) for the intensive treatment group and 5.07 years (interquartile range, 3.87-5.98) for the standard treatment group. For group comparison of incidence, hazard ratio, 0.83; 95% CI, 0.67-1.04; *P*=.10.

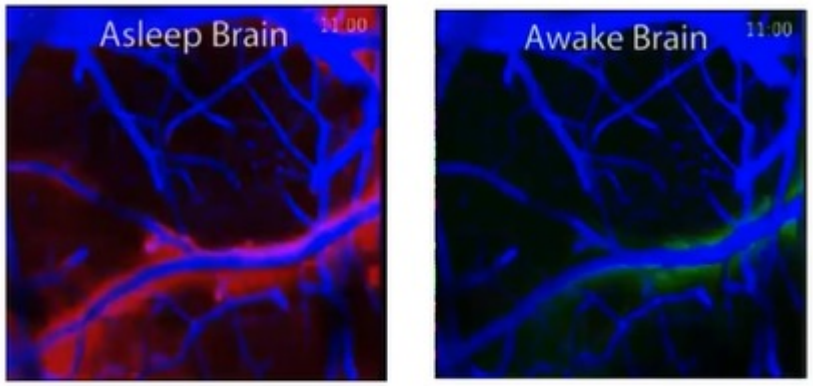
SPRINT-MIND JAMA 2019

SBP<120 assc with decreased risk MCI, fewer white matter lesions, total brain volume and no difference in stroke types based on treatment in subsequent analysis in 2021

SLEEP LINKED TO AMYLOID AND TAU

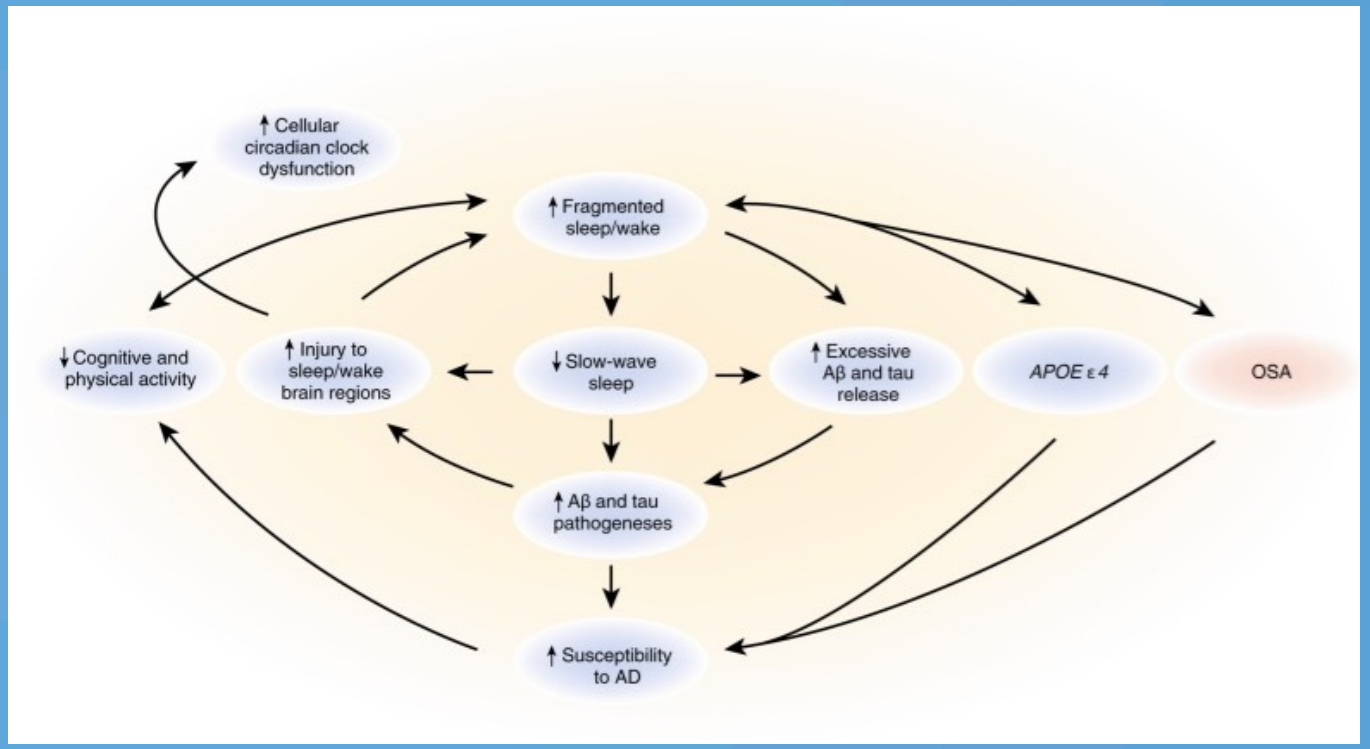
Bidirectional relationship between sleep and AD

Aβ Clearance Increased During Sleep



- Cerebrospinal fluid (CSF) flow in asleep (left) and awake (right) brain
- Sleeping mice cleared twice as much Aβ from their brains as conscious mice

Xie et al, *Science,* 2013



Wang & Holtzman, *Neuropsychopharmacology,* 2020

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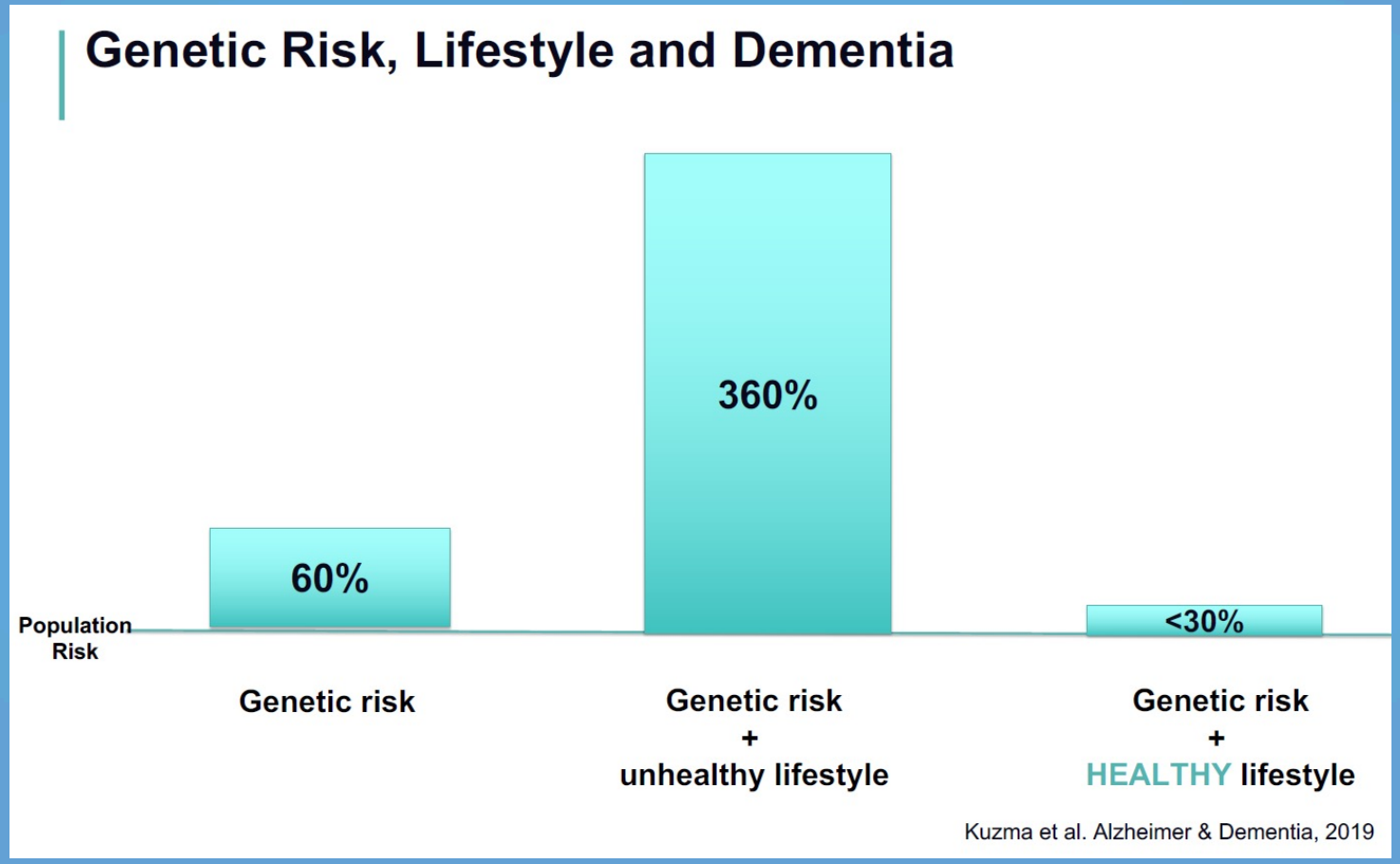
Epigenetics

Adherence to a healthy lifestyle can offset genetic risk



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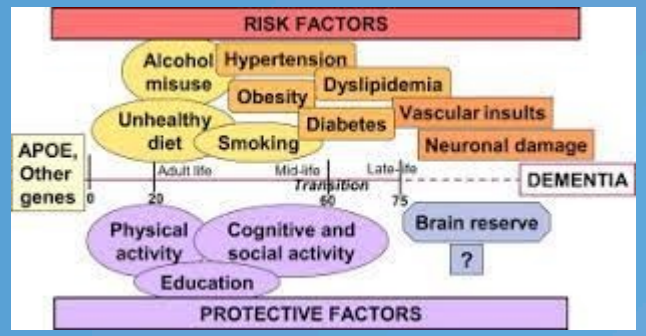
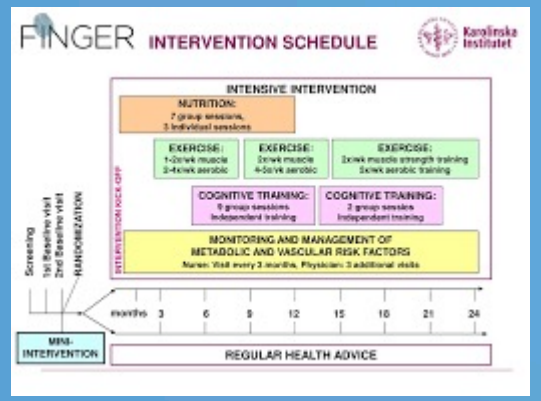
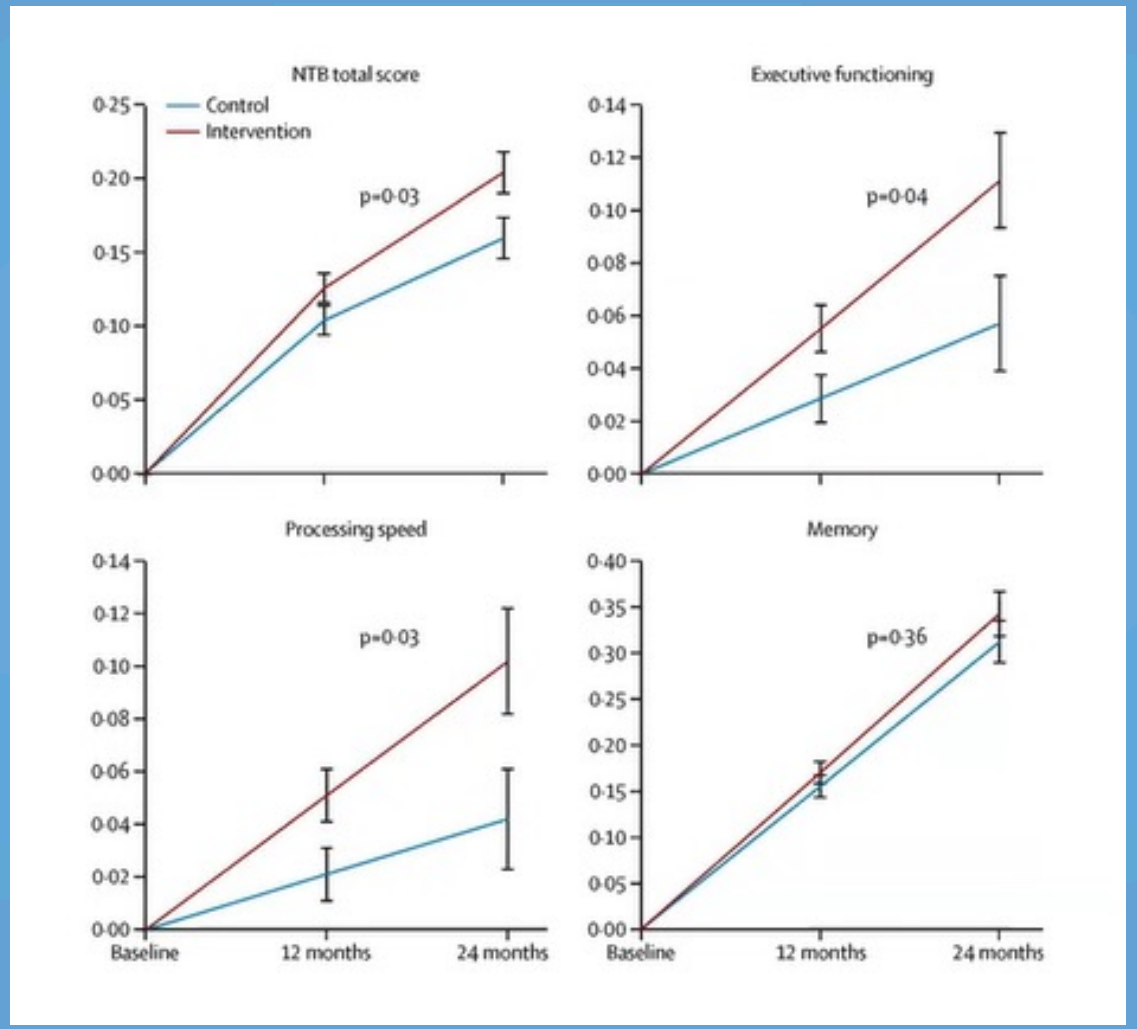
Cognitive Checklist/Plan

- ❑ **Labs**: B12 + TSH, routine studies
- ❑ **Screen questions**: EtOH + depression
- ❑ **Meds**: Benzos, Ambien, oxybutynin, benadryl
- ❑ **Other**: Sleep apnea + hearing loss/cataracts/sensory challenges
- ❑ **Imaging:** MRI with hippocampal volumes **(dx MCI)**

Multidomain Interventions FINGER study



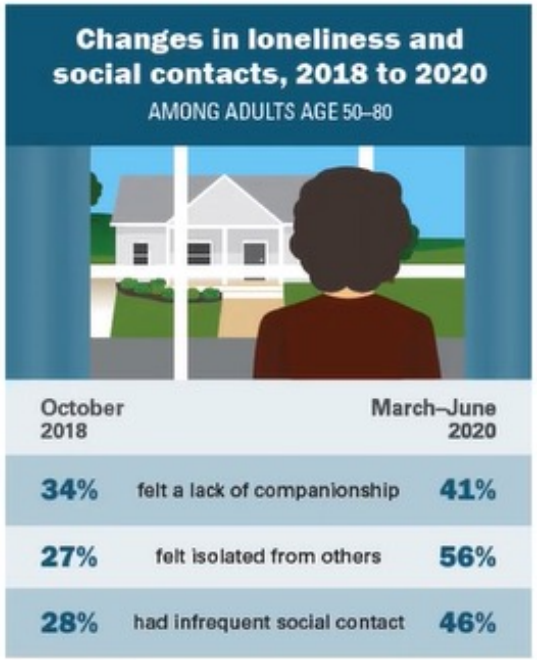




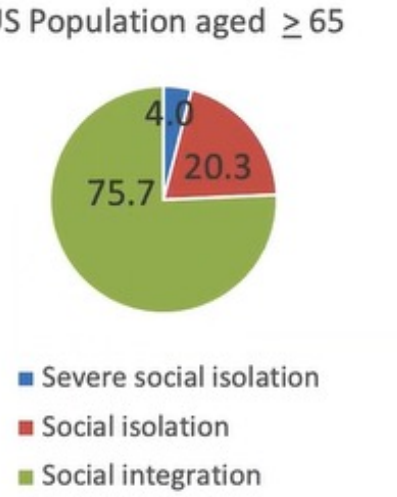
A combination of lifestyle interventions prevents or slows down cognitive decline

Ngandu et al, *Lancet,* 2015

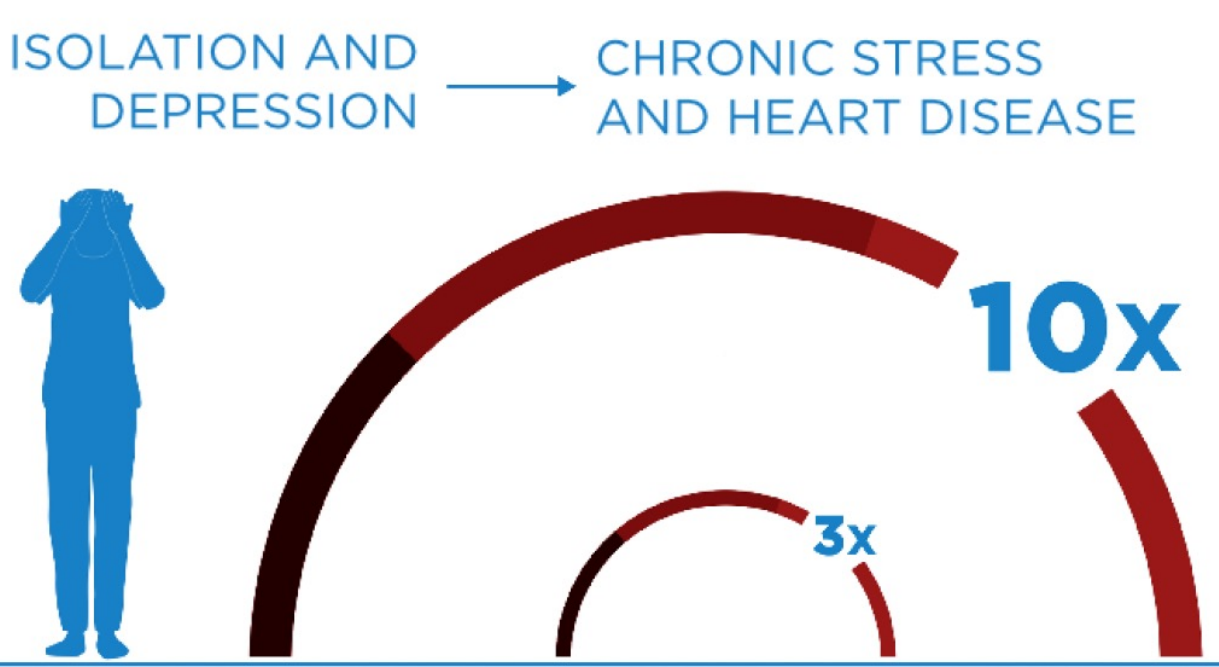
University of Michigan National Poll on Healthy Aging



≤ 1/week with family, friends or neighbors



The Epidemiology of Social Isolation. Cudjoe et al JGSS 2020



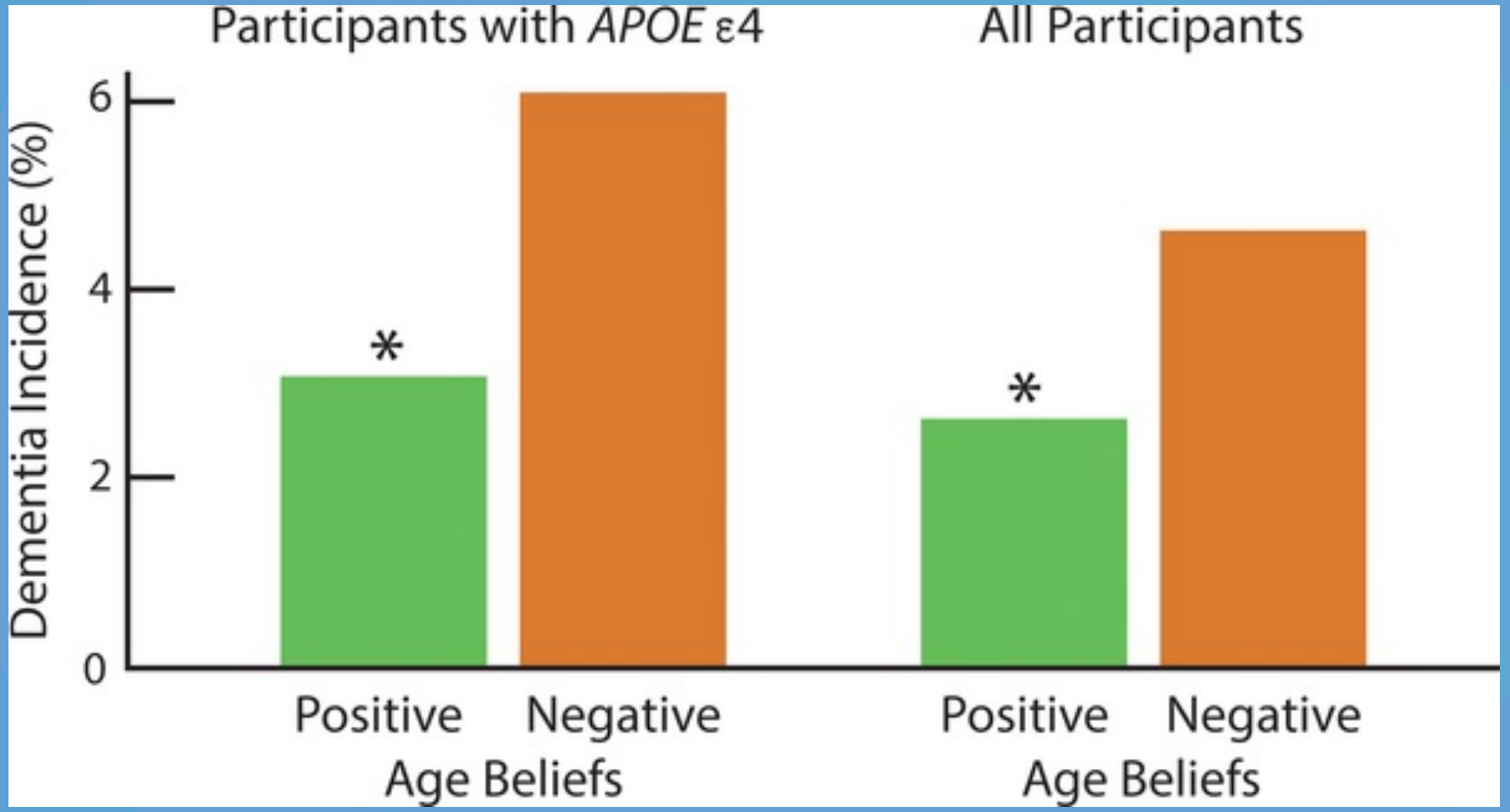


Fig 1. Positive age beliefs associated with reduced dementia among participants with APOE ε4 and all participants.

Levy BR, Slade MD, Pietrzak RH, Ferrucci L (2018) Positive age beliefs protect against dementia even among elders with high-risk gene. PLOS ONE 13(2): e0191004. https://doi.org/10.1371/journal.pone.0191004
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0191004
N>4000 subjects over > 4 years, ¼ population apoe4

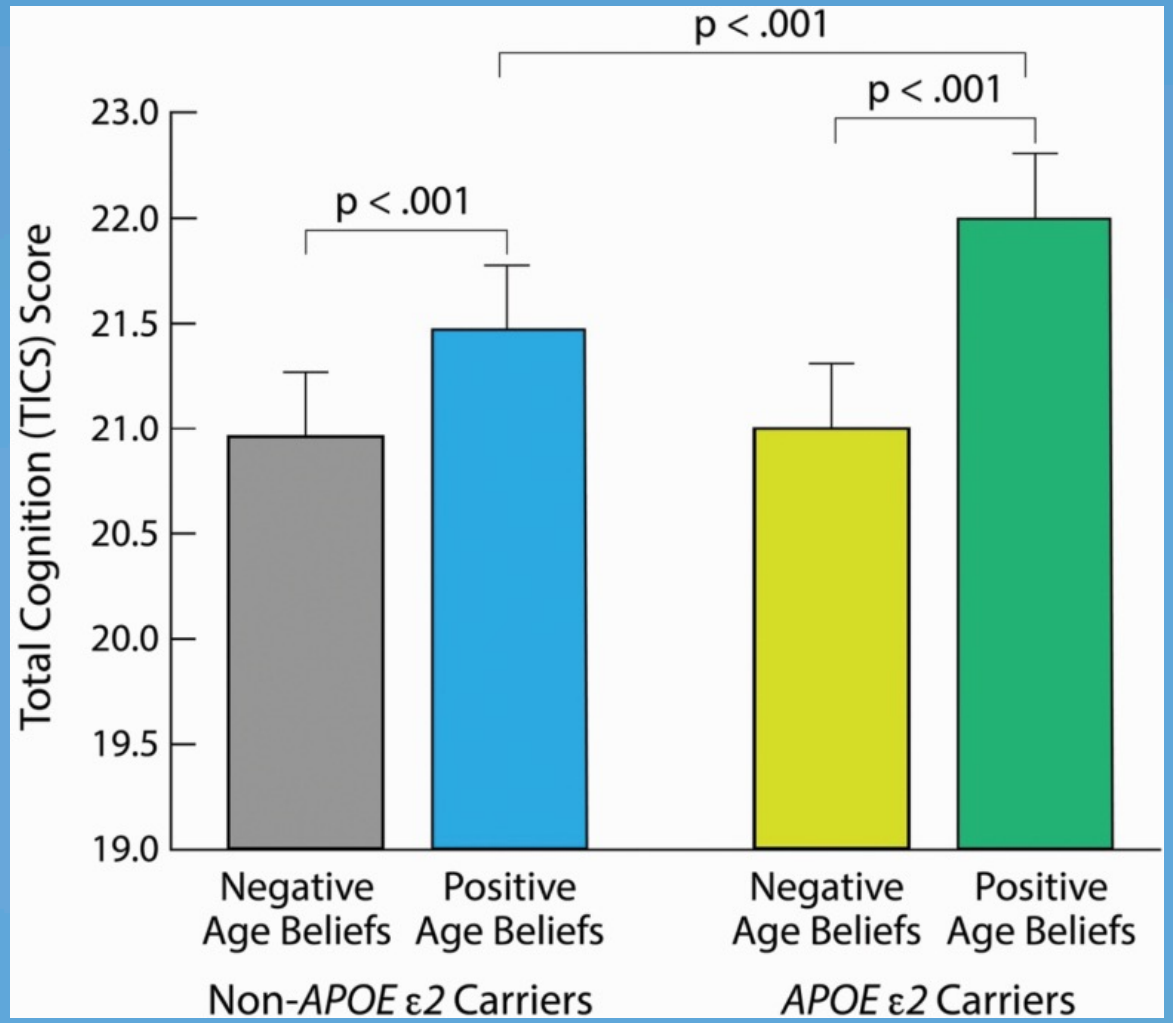


Figure 1. Positive age beliefs' amplification of *APOE* ε2 benefit on cognition. Note: Age-belief groups were split into those below and those equal to or above the mean of 15. The total cognition scores were adjusted for all covariates, including baseline cognition, using the mean for continuous variables and the mode for categorical values.

Levy BR, Slade MD, Pietrzak RH, Ferrucci L. When Culture Influences Genes: Positive Age Beliefs Amplify the Cognitive-Aging Benefit of APOE ε2. J Gerontol B Psychol Sci Soc Sci. 2020 Sep 14;75(8):e198-e203. doi: 10.1093/geronb/gbaa126. PMID: 32835364; PMCID: PMC7489069.
HEALTH AND RETIREMENT STUDY
3,895 subject 60 and older, five cognitive assessments over 8 years

MBI's and Gene Expression

- MBIs --Mindfulness, Yoga, Tai Chi, Qigong, relaxation response, and breath regulation
- Reduced signalling of **NF-kb** – key transcription factor that leads to stress related gene expression for inflammation

Bower & Irwin, 2016, N = 26 trials)

Buric et al, 2017, N = 18 trials

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Brain Health Rx

- **Alcohol (and drugs)**: Limiting 0-1 drinks
- **Medications**: deprescribe/avoid sedating and anticholinergic
- **Contributing Conditions**: Sleep apnea, hearing loss.
- **Exercise**: >150 min/week aerobic & strength training.
- **Cognitive Stimulation/Mindfulness**
- Socialization (generally more useful than puzzles) try HealthyMinds

https://hminnovations.org/meditation-app

- **Nutrition** Mediterranean/ MIND/ WFPD
- **SBP <120 as tolerated**
- **LDL <70 if prior TIA or stroke**

Shared Medical Appointment Benefits

Patients

- Access, quality
- Additional resources
- Education
- Health management skills
- Patient satisfaction

Providers

- Provider/team satisfaction
- Improve access
- Leverage resources
- High quality of care

Enterprise

- Cost-effective, high quality
- Decrease cost/episode
- Decrease hospital readmissions
- Resource integration

LIFESTYLE MEDICINE

Lifestyle medicine is an evidence-based approach to preventing, treating and even reversing diseases by replacing unhealthy behaviors with positive ones – such as eating healthfully, being physically active, managing stress, avoiding risky substance abuse, adequate sleep and having a strong support system.

LM2021

Patient Centered. Value Based. Outcome Driven.

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Virtual Group Visits (VGVs)

- 4-10 patients in a Zoom room
- 1 physician facilitator + 1 medical assistant
- 60-minute visit

Physician Quote

"[Patients] tell me they are learning both very helpful content & picking up practical tips ([especially] from other patients)… I love the opportunity to get into these topics in more detail, it really helps solve a big gap in primary care."

- Behavior change and healthy lifestyles
- Target patient populations to reduce disparities
- Private and secure
- Billed as medical visit (incremental revenue)

Patient Quote

"I always enjoy your group visits because it helps me feel less isolated from you and my health care."

Patient Quote

"These types of sessions as part of patients' regular health regimen would be very beneficial in changing lifestyles and lead to much better health."

Mirsky & Thorndike, *American Journal of Health Promotion,* 2021

Take-Aways for Dementia Capable Care

- Growing evidence regarding the importance of timely detection and accurate diagnosis
- Cardiometabolic risk reduction/improving management of comorbid conditions/reducing polypharmacy/iatrogenic harm
- Connecting with community resources, programs/services
- Reducing preventable hospitalizations, inappropriate surgeries, delirium, PHCD/POCD and emergency room visits
- planning for future/POA/Identifying goals around **what matters**, end-of-life care and improving advance care planning

More Information:

https://www.swedish.org/locations/center-for-healthy-aging

http://depts.washington.edu/mbwc/resources/echo

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Resources/references:

NIA Go4Life exercise videos

https://www.nia.nih.gov/health/exercise-physical-activity

https://www.youtube.com/playlist?list=PLmk21KJuZUM4HTrJ7hrJ8yxhToKkJT8a8

https://www.thelancet.com/article/S0140-6736(20)30367-6/fulltext

https://n.neurology.org/content/95/4/e374

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8. Noya CE, Chesla C, Waters C, Alkon A. Shared Medical Appointments: An Innovative Model to Reduce Health Disparities Among Latinxs With Type-2 Diabetes. *West J Nurs Res*. 2020;42(2):117-124. doi:10.1177/0193945919845677

9. Kahkoska AR, Brazeau NF, Lynch KA, et al. Implementation and Evaluation of Shared Medical Appointments for Type 2 Diabetes at a Free, Student-Run Clinic in Alamance County, North Carolina. *J Med Educ Train*. 2018;2(1). https://www.ncbi.nlm.nih.gov/pubmed/30035272

10. Tkachenko E, Refat MA, Balzano T, Maloney ME, Harris JE. Patient satisfaction and physician productivity in shared medical appointments for vitiligo. *J Am Acad Dermatol*. 2019;81(5):1150-1156. doi:10.1016/j.jaad.2019.03.044

11. Schneeberger D, Golubíc M, Moore HCF, et al. Lifestyle Medicine-Focused Shared Medical Appointments to Improve Risk Factors for Chronic Diseases and Quality of Life in Breast Cancer Survivors. *J Altern Complement Med*. 2019;25(1):40-47. doi:10.1089/acm.2018.0154

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Thank you for your attention!

Questions?

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