Food for Thought: Dietary Factors Promoting Brain Health via Impact on Cognitive Trajectories and Dementia Risk in Aging

Puja Agarwal, PhD
Assistant Professor
Rush Alzheimer's Disease Center
Department of Internal Medicine
Rush University Medical Center, Chicago, IL, USA

37th Annual Southern California Alzheimer's Disease Research Conference, "The Energy Behind Metabolism" **Sept 25th,2026**

Objectives:

Background: Why Diet is important for Brain Health

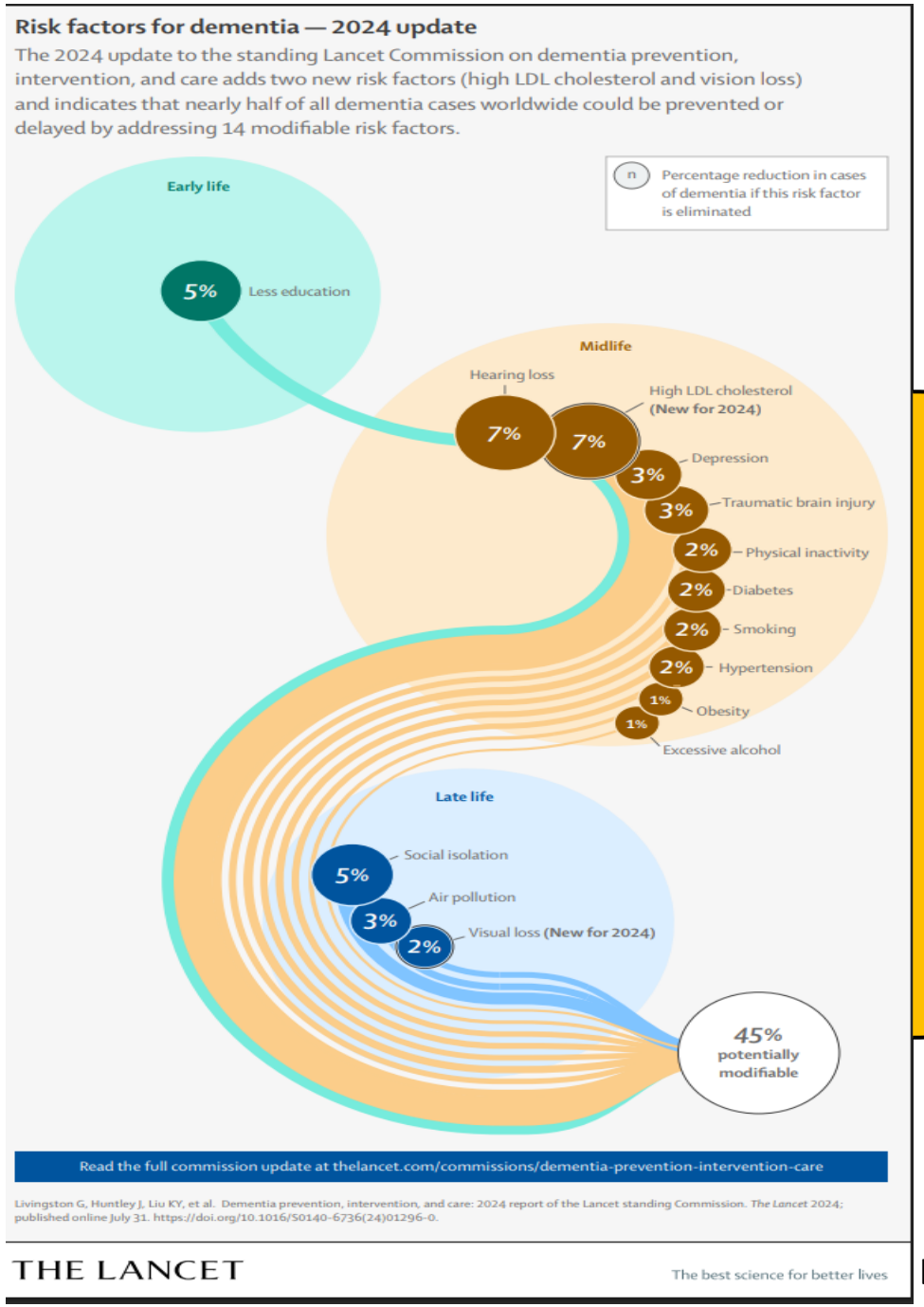
Current scientific evidence of dietary factors for Brain Health

Introduction to different DIETARY PATTERNS for Brain Health

Randomized control trials with dietary intervention

Potential mechanism linking Diet and Brain Health

Modifiable Risk Factors for Dementia

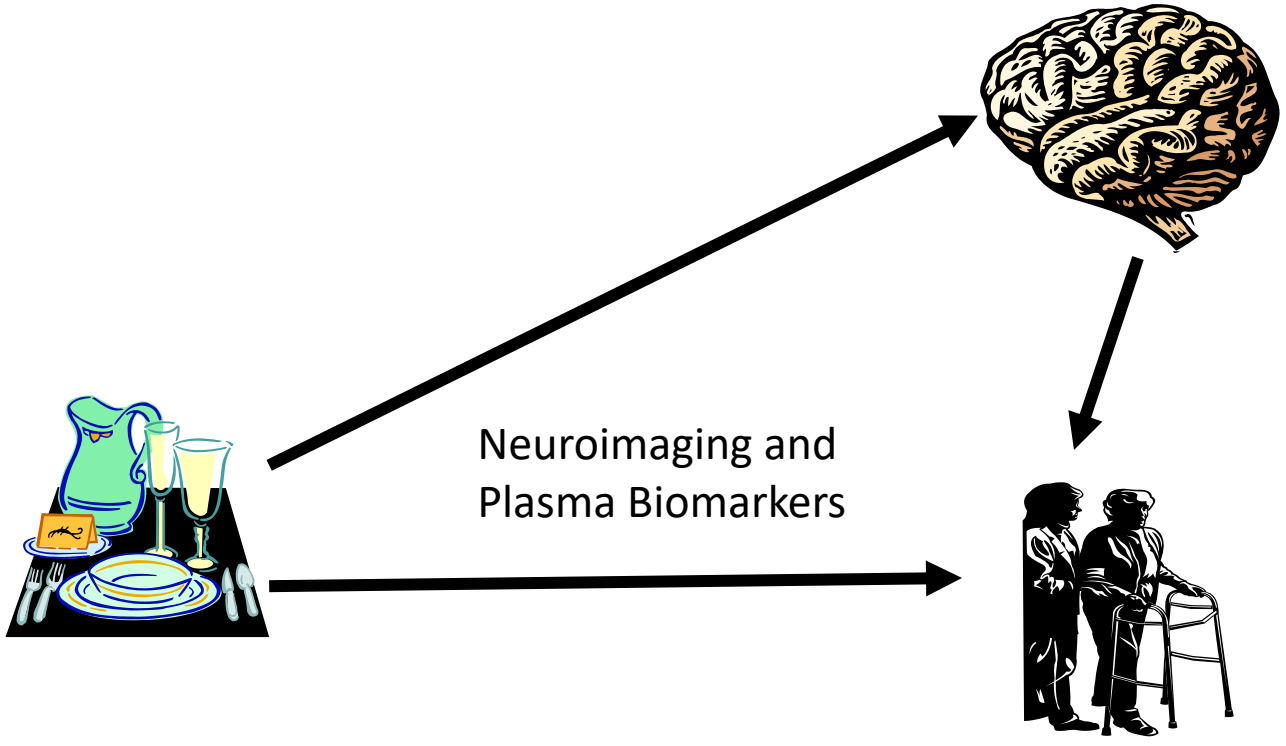


Diet plays a key factor in modifying **LDL Cholesterol**, **Diabetes**, **Hypertension**, **Obesity**
Is important for **vision in late life, depression,** and **modify the effect of air pollution on dementia**

Livingston, The Lancet, 2024


Scientific evidence of nutrients and foods important for brain health

Theoretical Schema of the ongoing Nutrition Studies at Rush Alzheimer's Disease Center



Neural Reserve
Neuropatholgy
Other Vascular pathologies
Structural Brain changes

AD/ ADRD risk,
Cognitive/ Motor decline
Disability Risk, Parkinsonian signs
Depressive symptoms

- **Understanding diet as modifiable risk for various Brain Health outcomes and the potential mechanism using Longitudinal Cohort studies and autopsied brain samples**
- **Randomized clinical trial with dietary intervention**

Micronutrients

MAP: Memory and Aging project
CHAP: Chicago Health and Aging Project
* Unpublished

PROSPECTIVE STUDIES at RUSH (MAP and CHAP)	Exposure	Cognitive decline	Alzheimer's dementia	Parkinsonian signs progression
Morris, 2002; Morris 2015; Agarwal 2020	**Dietary vitamin E** **Brain tocopherol**	↓ ↓	↓ ↓	↓ ↓
Morris, 2002; Agarwal 2020	**Dietary vitamin C**	null	null	↓
Morris, 2002; Morris 2018; Agarwal 2020; Yuan 2020	**Dietary carotenoids** **Lutein/zeaxanthin**	↓ ↓	↓ ↓	↓ ↓
Morris 2018; Holland 2020, 2023; Agarwal 2019	**Dietary flavanols** **Anthocyanidins** **(Pelargonidin)**	↓ ↓	↓ ↓	↓*
Morris, 2005, 2006; Tangney 2009	**Dietary Folate** **Dietary Vit B12** **Serum Vit B12** **Homocysteine**	↓ ↓ ↓ null	null null	
Booth 2022; Shea 2026	**Brain vitamin K (Menaquinone-4)** **Plasma vitamin K (Phylloquinone)**	↓ ↓	↓ - AD pathology ↓	
Dhana 2022; Shea 2023; Shea 2026	**Dietary vitamin D** **Plasma vitamin D** **Brain vitamin D (25 (OH) D3)**	↓ null + Cognition (proximate to death)	↓ ↓	
Morris, 2006; Agarwal 2019; Scott 2021; Agarwal 2021	**Brain mercury** **Brain Bromine** **Dietary Cu + High-fat** **Dietary Cu, Brain Cu** **Brain Fe**	↑ ↓ ↑	null: + AD pathology -AD pathology + AD pathology	↑*

Antioxidants

B-Vitamins

Vitamin D and K

Metals

Macronutrients

PROSPECTIVE STUDIES at RUSH (MAP and CHAP)	Exposure	Cognitive decline	Alzheimer's dementia	Parkinsonian signs progression
Agarwal/ Ford 2023	**Dietary Sugar/** **% calories from sugar** **Fructose** **Sucrose**		↑ ↑ ↑ ↑	
Ongoing analyses	Dietary Protein			↓* Better hand grip strength*
Morris, 2003,2004, 2005; van de Rest 2016	**Dietary Saturated fat** **n-3 Fatty Acids** **MUFA**	↑ ↓ ↓	↓ In APO-ε4 carriers	
Ongoing analyses	**Fiber** **Soluble fiber** **Insoluble fiber** **Carbohydrate-to-fiber Ratio**	**+ cognition**	↓* ↓ - ↑	

MAP: Memory and Aging project
CHAP: Chicago Health and Aging Project

* Unpublished

Sugars

Fats

Fiber

There are other cohorts supporting these findings on the relationship of micro and macro-nutrients with brain health outcomes

Molecular Psychiatry www.nature.com/mp

ARTICLE

Check for updates

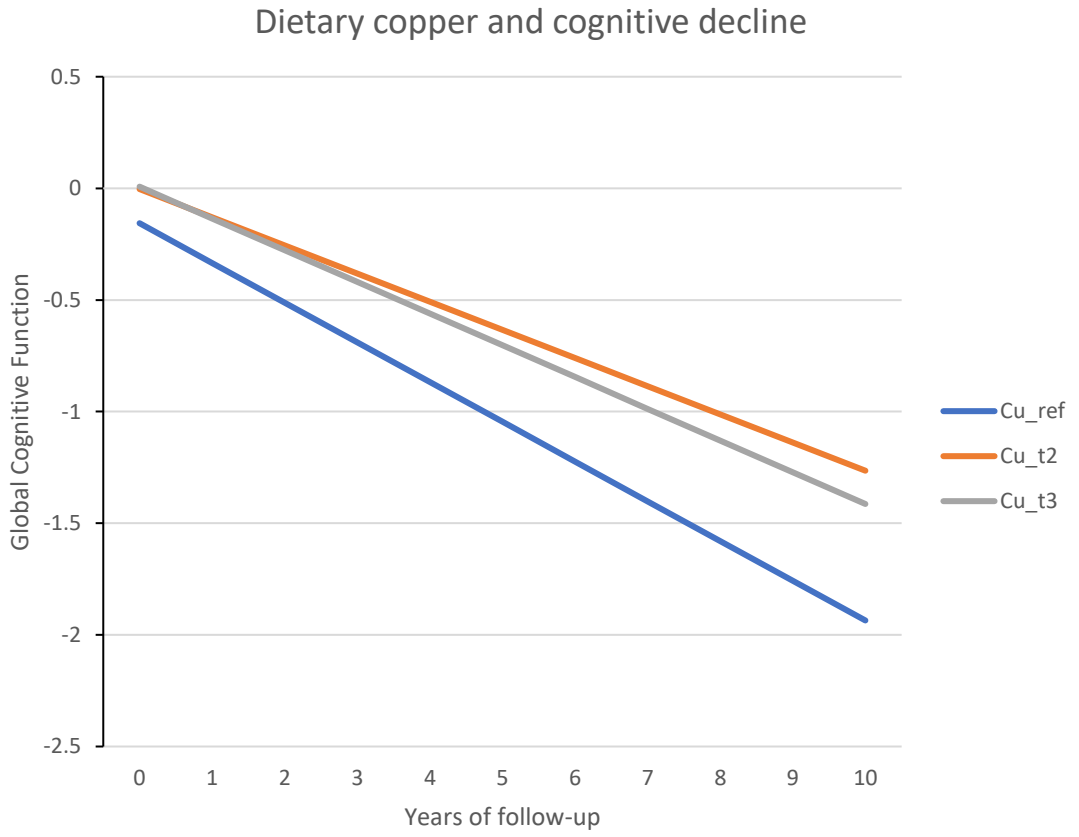
Brain copper may protect from cognitive decline and Alzheimer's disease pathology: a community-based study

Puja Agarwal[1,2,3], Scott Ayton[4], Sonal Agrawal[1,5], Klodian Dhana[2,6], David A. Bennett[1,7], Lisa L. Barnes[1,7], Sue E. Leurgans[1,7], Ashley I. Bush[4] and Julie A. Schneider[1,5,7]

Copper is an essential micronutrient for brain health and dyshomeostasis of copper could have a pathophysiological role in Alzheimer's disease (AD), however, there are limited data from community-based samples. In this study, we investigate the association of brain copper (assessed using ICP-MS in four regions -inferior temporal, mid-frontal, anterior cingulate, and cerebellum) and dietary copper with cognitive decline and AD pathology burden (a quantitative summary of neurofibrillary tangles, diffuse and neuritic plaques in multiple brain regions) at autopsy examination among deceased participants ($N = 657$; age of death: 90.2(±6.2)years, 70% women, 25% *APOE*-ε4 carriers) in the Rush Memory and Aging Project. During annual visits, these participants completed cognitive assessments using a 19-test battery and dietary assessments (using a food frequency questionnaire). Regression, linear mixed-effects, and logistic models adjusted for age at death, sex, education, and *APOE*-ε4 status were used. Higher composite brain copper levels were associated with slower cognitive decline (β(SE) = 0.028(0.01), $p = 0.001$) and less global AD pathology (β(SE) = −0.069(0.02), $p = 0.0004$). Participants in the middle and highest tertile of dietary copper had slower cognitive decline (T2vs.T1: β = 0.038, $p = 0.0008$; T3vs.T1: β = 0.028, $p = 0.01$) than those in the lowest tertile. Dietary copper intake was not associated with brain copper levels or AD pathology. Associations of higher brain copper levels with slower cognitive decline and with less AD pathology support a role for copper dyshomeostasis in AD pathogenesis and suggest that lower brain copper may exacerbate or indicate disease severity. Dietary and brain copper are unrelated but dietary copper is associated with slower cognitive decline via an unknown mechanism.

Molecular Psychiatry; https://doi.org/10.1038/s41380-022-01802-5

Dietary Copper and Cognitive decline



Linear mixed models adjusted for age, sex, education, late life cognitive activity, physical activity, smoking, APOE ε-4 status. *Calorie adjusted dietary copper

Brain Copper, Cognitive decline and AD Pathology

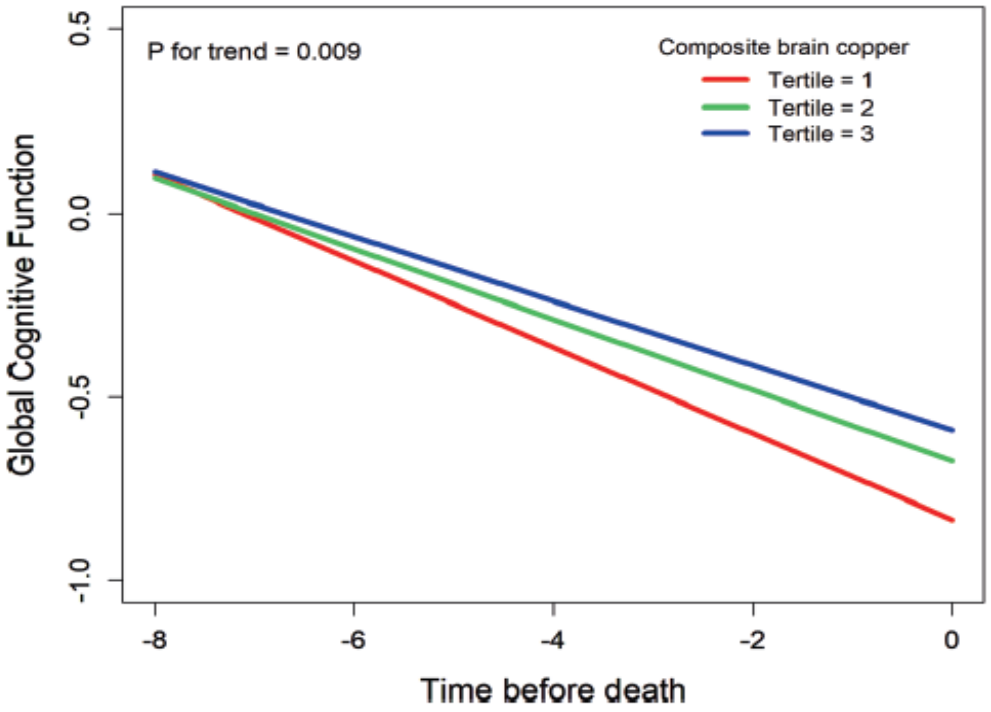
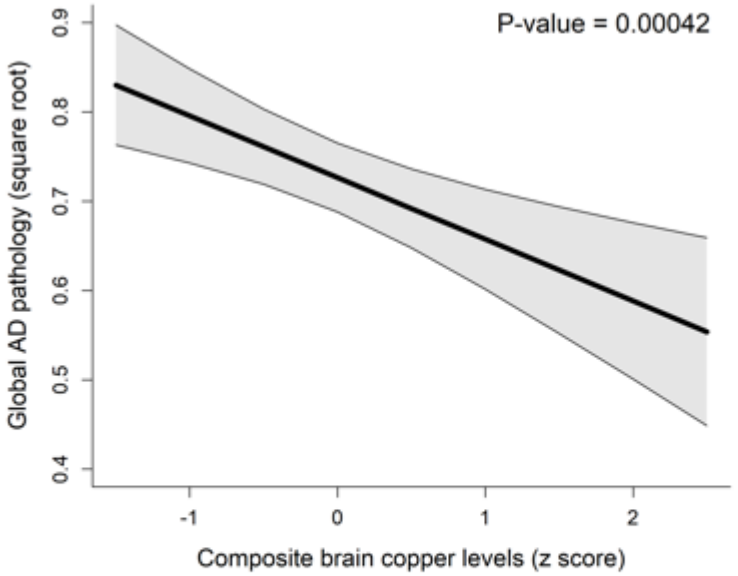


Fig. 1 Brain copper levels and cognitive decline. Association of composite brain copper levels with cognitive decline among 621 autopsied Memory and Aging Project participants. *Composite brain copper levels: Brain copper in all four regions combined (inferior temporal, mid-frontal, anterior cingulate, and cerebellum). Linear mixed-effect model controlled for age at death, sex, education, and APO-ε4 status.



Linear regression models for **Cu and AD pathology** controlled for age at death, sex, education, and APO-ε4 status.

Brain copper assessed in four brain regions- inferior temporal, mid-frontal, anterior cingulate, and cerebellum using inductively coupled plasma-mass spectrophotometry

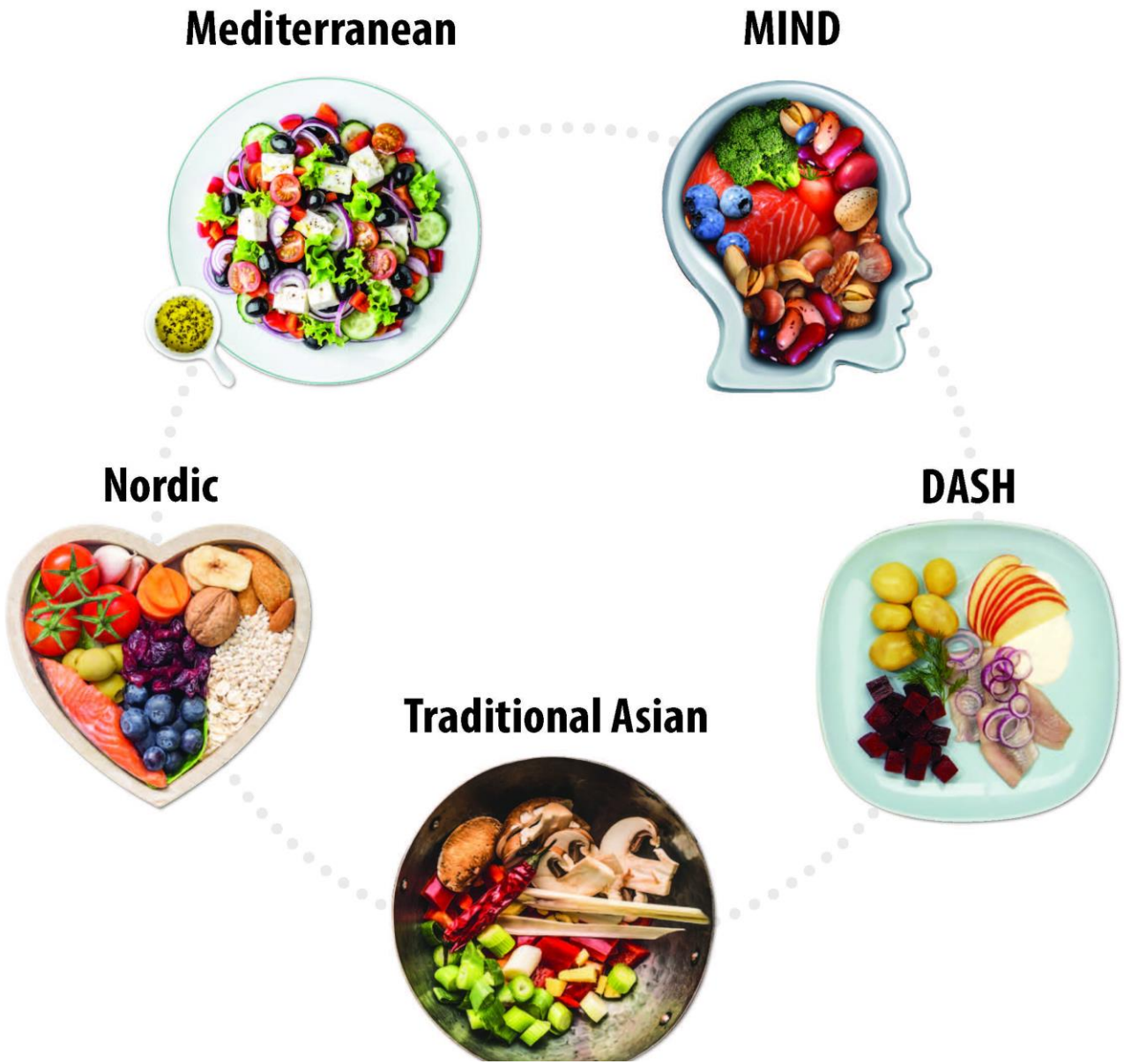
Conclusion

Higher brain Cu levels are associated with slower cognitive decline, thus supports the role of copper homeostasis in maintaining brain health and possibly delaying the disease process.

Brain copper levels are not related to dietary copper intake.

Higher brain Cu levels are associated with fewer AD neuropathology. Brain Cu levels either may reflect the severity of the disease or may indicate its potential beneficial effect on the Alzheimer's pathology.

Dietary copper is negatively associated with cognitive decline.

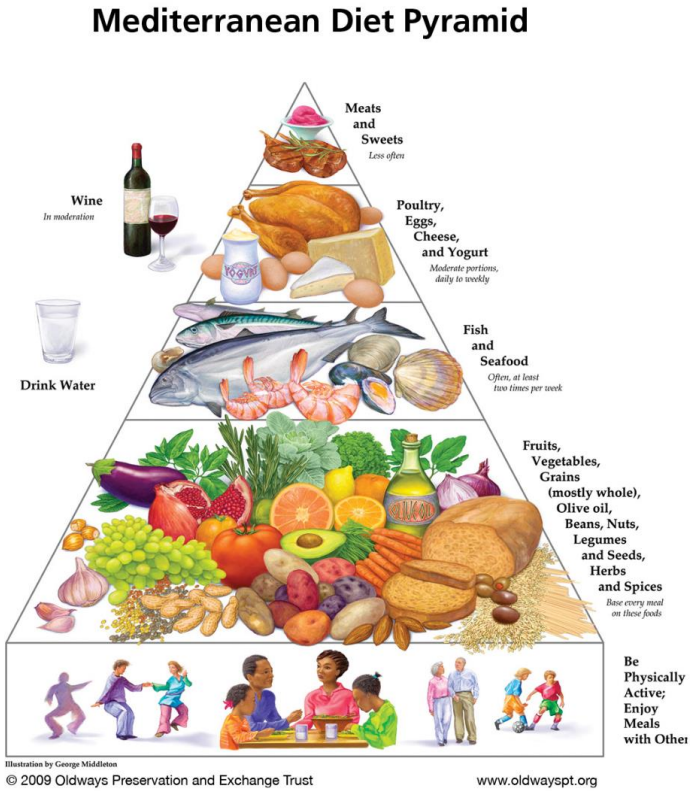


Dietary Patterns for Brain Health

Mediterranean diet

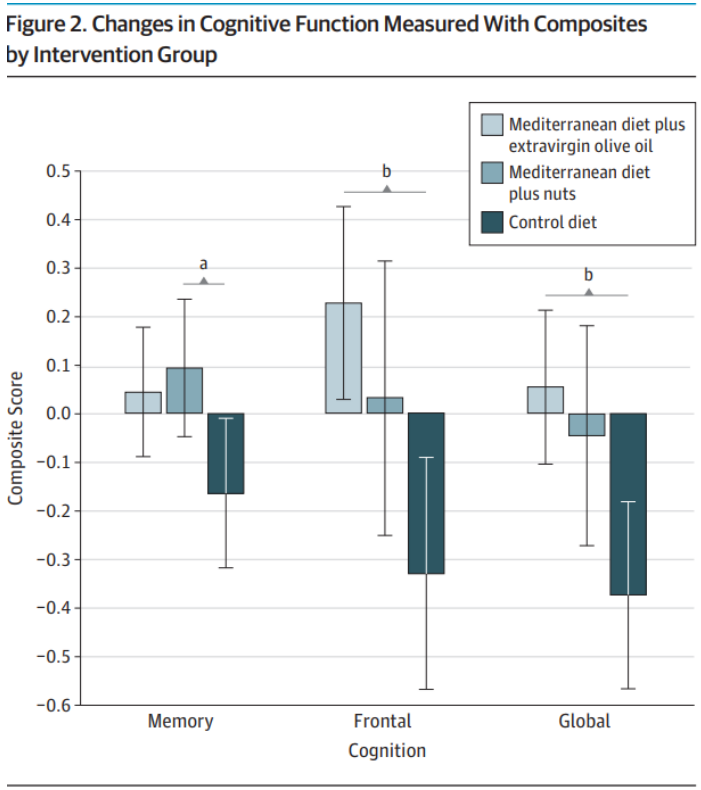
- Includes whole grains, vegetables, legumes, fruits, nuts, seeds, herbs, and spices.
- Olive oil is recommended as the main source of added fat.
- Fish and seafood (rich in omega-3) are emphasized, and dairy and poultry are included in moderation.
- Red meat and sweets are eaten only occasionally.
- Meta-analysis reported Mediterranean diet association with a lower risk of cognitive impairment and AD.

(Fu et al., Front Nutr. 2022)



A randomized controlled trial for Mediterranean diet: PREDIMED

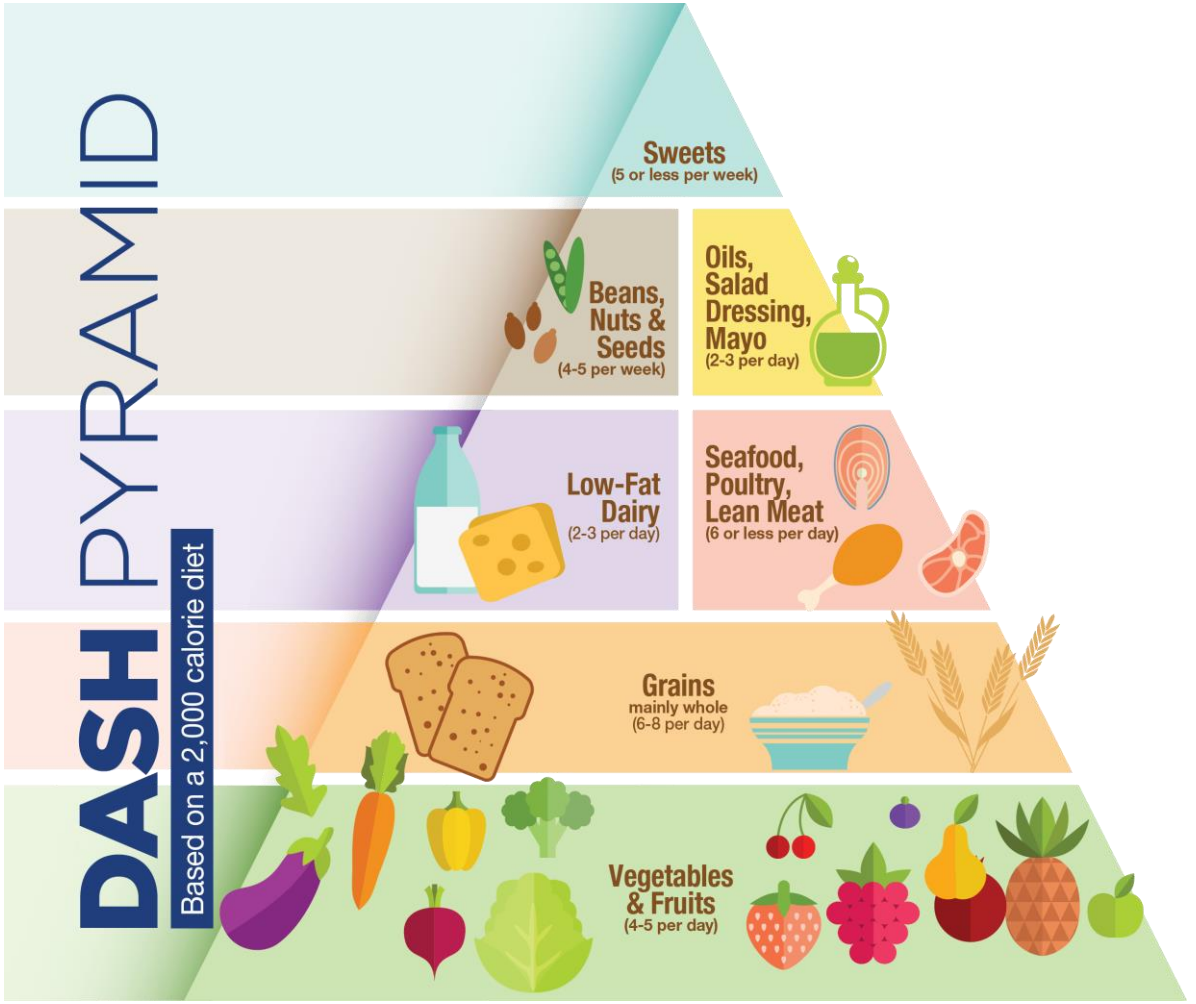
- Mediterranean diet with extra-virgin olive oil or nuts improves cognition compared with control/low-fat diet.



Martínez-Lapiscina 2013; Valls-Pedret 2015

DASH diet

- Dietary Approach to Stop Hypertension
- The DASH diet is associated with a lower risk of cognitive decline in older adults (van den Brink, Adv Nutr. 2019)
- DASH diet in mid-age is associated with better subjective cognitive decline (NHS, HPFS) (Chen et al, 2026)



Recommends limiting sodium intake to 2,300 mg per day

Dr. Martha Clare Morris

ELSEVIER

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

Alzheimer's & Dementia

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]

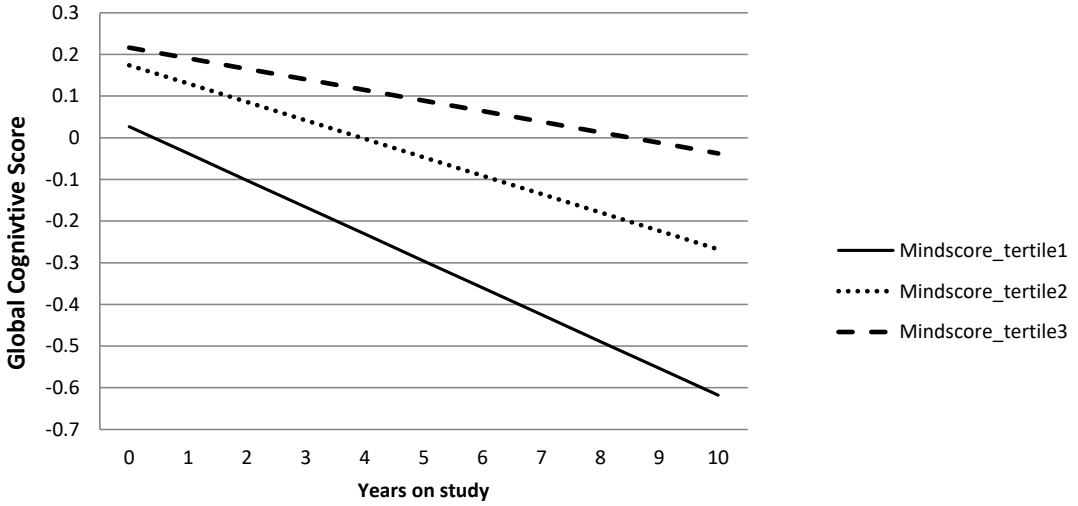
ELSEVIER

Alzheimer's & Dementia 11 (2015) 1015-1022

Alzheimer's & Dementia

MIND diet slows cognitive decline with aging

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



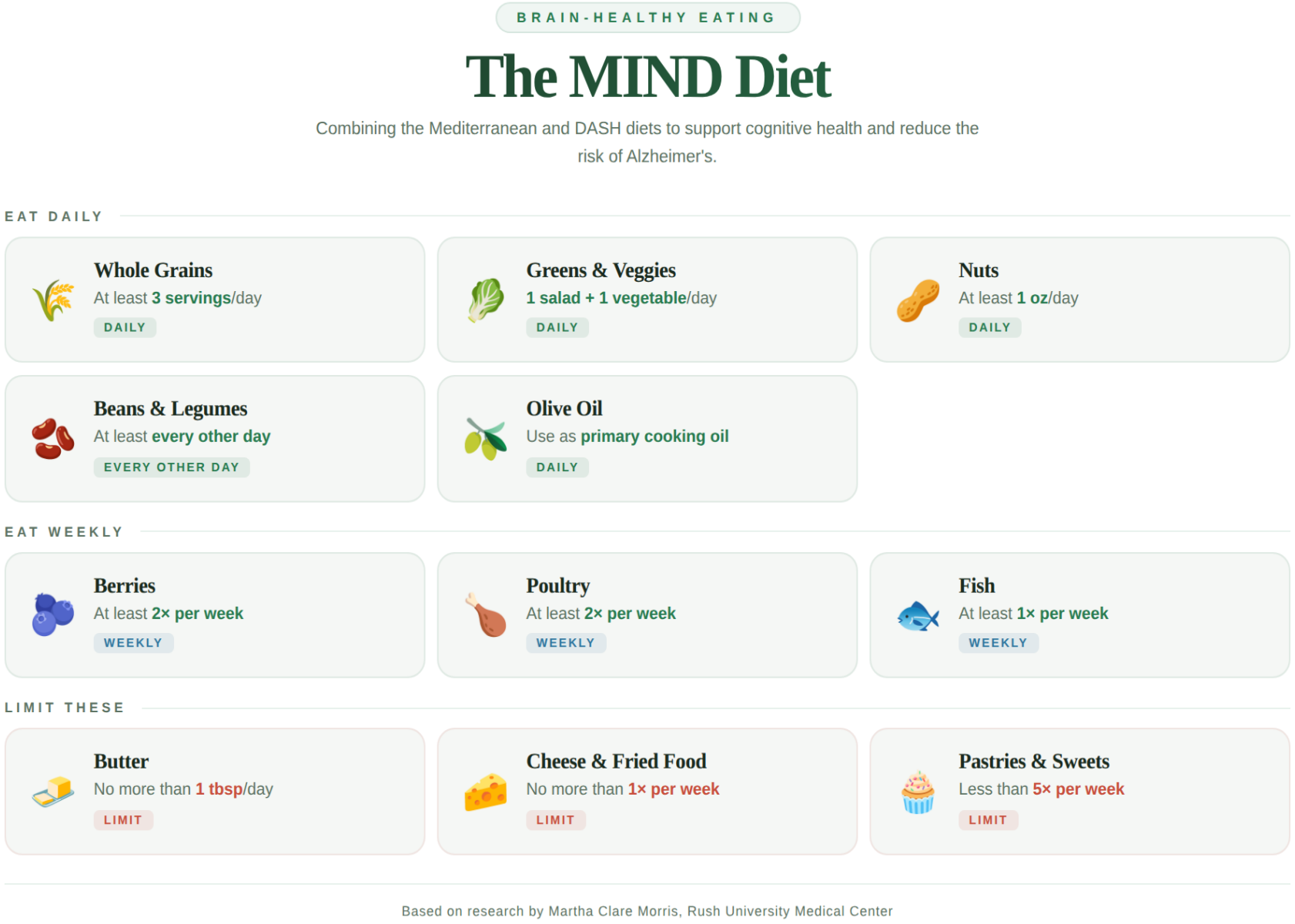
Those who were following the MIND diet had a 35-50% reduced risk of Alzheimer's dementia.

MIND Diet

- **MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet is a hybrid of two established diets.**

- **MIND diet includes foods known to maintain and improve brain health.**

- **MIND diet includes 10 healthy food groups and 5 unhealthy food groups to avoid or limit.**



Differences and Similarities: MIND, Mediterranean & DASH diets

DASH	Mediterranean	MIND
Total Grains 42+/wk	Non-refined Grains 56/wk	Whole Grains >28/wk
Vegetables 28+/wk	Vegetables 42/wk Potatoes 3-5/wk	Green Leafy 7+/wk Other Vegetables 14+/wk
Fruits 28+/wk	Fruits 21/wk	Berries (5+/wk)
Dairy ≥14/wk	Dairy 14/wk	Regular Cheese ≤1/d Butter <1 tsp/d
Nuts, seeds & legumes ≥4/wk	Legumes 3-4/wk	Beans 3+/wk Nuts 1/8 c/d
Lean meat, poultry fish ≤6/wk	Red meat ≤ 1/wk Fish >6/wk Poultry ≤3/wk	Lean Red Meats <4/wk Fish 1+/wk Poultry 2+/wk
Total Fat ≤ 27% of kcal Saturated Fat ≤ 6% of kcal		Fried Foods <1 time/wk
Sweets ≤ 5/wk		Commercial Pastries, sweets <5/wk
Sodium ≤ 2400mg/d	Olive oil 3-4 T/d	Olive Oil>1 T/d or primary oil
	Alcohol < 300mL/d but >0	Alcohol/wine 1/d

MIND Diet Scoring:0-15	0	0.5	1
Healthy Dietary Components/ Recommended Food groups			
Green Leafy Vegetables	≤ 2 servings/wk	> 2 to <7/wk	≥ 7 servings/wk
Other Vegetables	< 5 servings/wk	≥ 5 - < 7/wk	≥ 7 servings/wk
Berries	< 1 serving*/wk	≥1 - < 5/wk	≥ 5 servings*/wk
Nuts	< 1 serving/wk	≥ 1 - < 5/wk	≥ 5 servings/wk
Fish (not fried)	< 1 serving/ mo	1-3 serving/ mo- < 1 serving/ mo	≥ 1 serving/wk
Poultry (not fried, skinless)	< 1 serving/wk	≥ 1 - < 2/wk	≥ 2 servings/wk
Beans & Legumes	< 1 serving/wk	≥ 1- < 3/wk	≥3 servings/wk
Whole Grains	< 7 servings/wk	≥ 7 - < 21/wk	≥ 21 servings/wk
Olive Oil	< 7 T/wk	≥7 - < 14 T/wk	≥ 14 T/wk
Wine	<1 glass/mo- ≥2 glasses/day	>1 glass/mo – 3 glasses /wk	>3 glasses /wk -1 glass/d
Unhealthy Dietary Components/ Foods to limit or avoid			
Butter and stick margarine	≥ 14 pat(tsp)/wk	> 7 - < 14/wk	≤ 7 pat(tsp)/wk
Full-fat Cheese	≥ 7 servings/wk	> 2 – < 7/wk	≤ 2 serving/wk
Red and Processed Meat	≥7 meals/wk	≥4 to <7 meals/wk	<4 meals/wk
Fast and Fried Foods	≥ 4 meal/wk	> 1 - < 4 meal/wk	≤ 1 meal/wk
Pastries & Sweets	≥ 7 servings/wk	≥ 5 - < 7 servings/ wk	< 5 servings/wk
TOTAL SCORE			15

*one serving is considered as ½ cup considering the average intake by older adults in NHANES/ WWEIA data.

Agarwal et al., JAMA Network Open; 2025

MIND diet and cognitive decline in diverse population

RESEARCH ARTICLE

THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Association of MIND diet with cognitive decline among Black and White older adults

AGARWAL ET AL.

Puja Agarwal[1] | Lisa L. Barnes[2] | Klodian Dhana[3] | Xiaoran Liu[3] | Yanyu Zhang[3] | Todd Beck[3] | Marilyn C. Cornelis[4] | Christy Tangney[5] | Kumar B. Rajan[3]

TABLE 2 Association of MIND diet with cognitive decline among 5259 Chicago Health and Aging Participants.

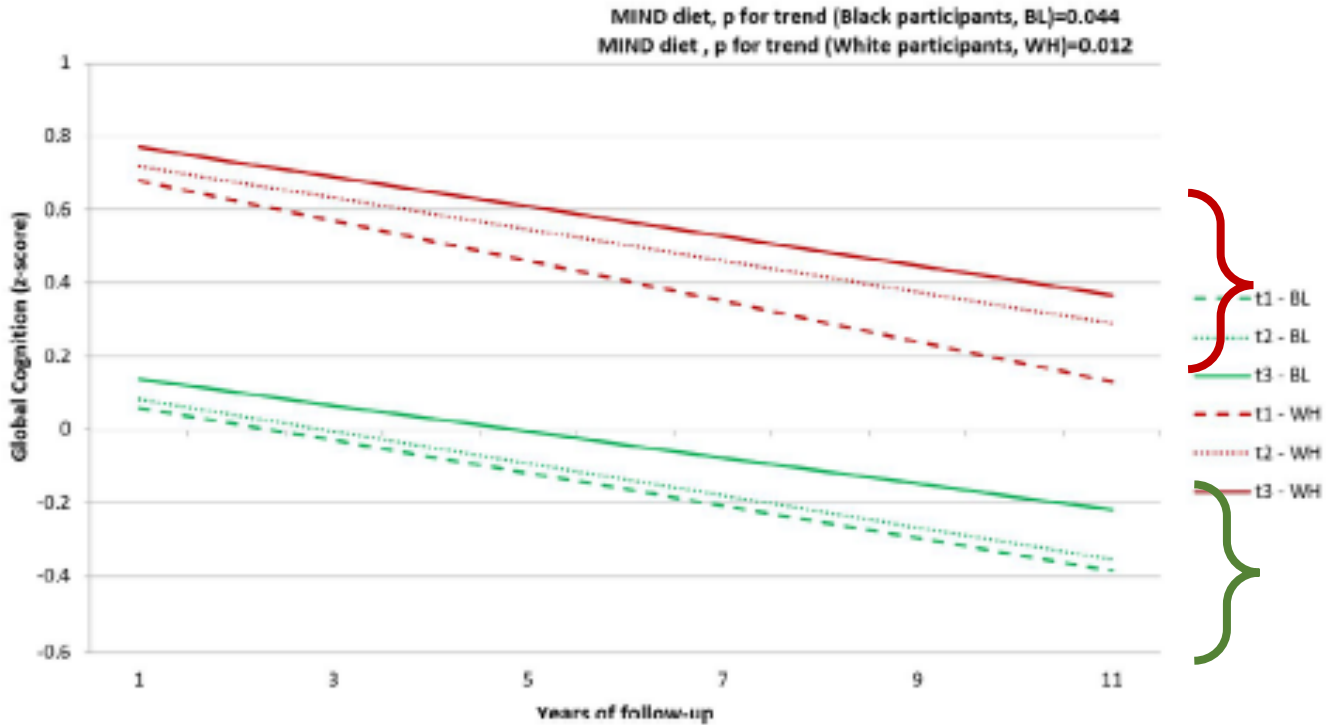
		MIND Diet score (tertiles)			
	Continuous MIND diet score	Tertile 1	Tertile 2	Tertile 3	*p* for trend
		5.5	7.0	8.5	
N	5259	1822	1745	1692	
beta (95% confidence interval)					
Model (A)	0.0024 (0.001, 0.004)	Reference	0.0049 (−0.002,0.011)	0.0104 (0.004,0.017)	0.0025
Model (B)	0.0019 (0.0003,0.004)	Reference	0.0044 (−0.002,0.012)	0.0083 (0.002,0.015)	0.0170

Abbreviation: MIND, Mediterranean–Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay.
Model (A) adjusted for age, sex, socioeconomic status (includes education), race, calories, lag, and lag x each covariate.
Model (B) adjusted for age, sex, socioeconomic status (includes education), race, calories, physical activity, cognitive activity, hypertension, stroke, myocardial infarction diabetes, lag, and lag x each covariate.

Overall Black participants had slightly lower MIND diet score when compared to their White counterparts (6.97 vs. 7.12, $p = 0.010$).

Agarwal et al., Alzheimer's Dement 2024; Chicago Health and Aging Project

MIND diet and Cognitive decline by Race



White participants: Both moderate and high MIND diet scores were associated with slower cognitive decline

Black participants: Only high MIND diet score was associated with slower cognitive decline

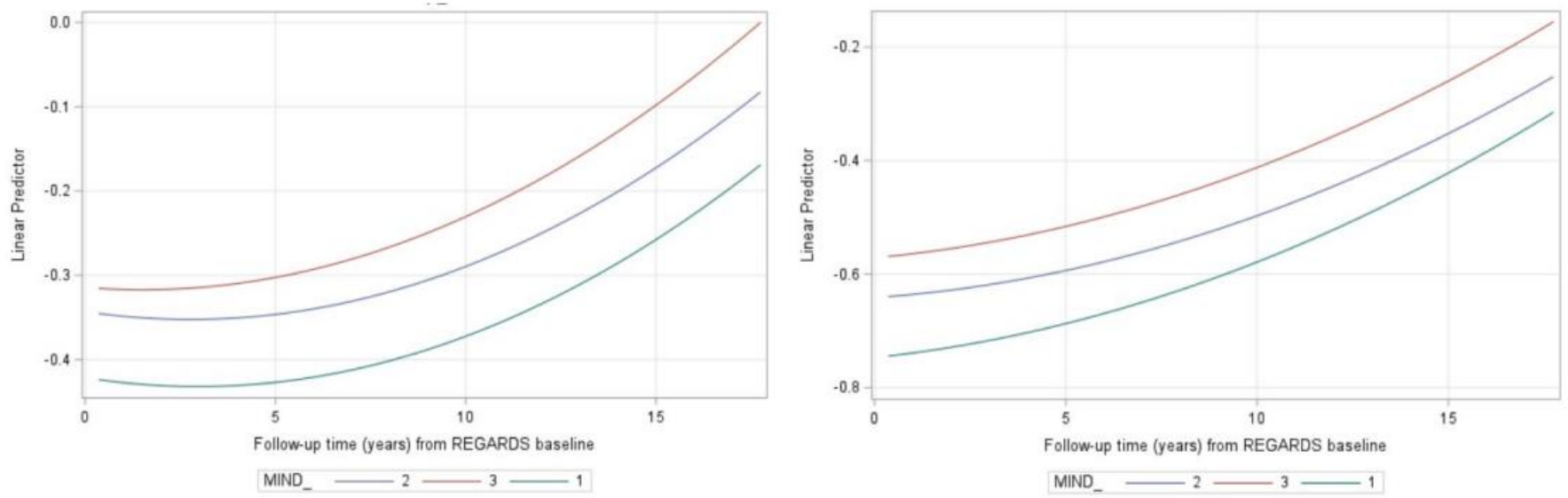
FIGURE 1 MIND diet association with cognitive decline among Black and White participants. Model adjusted for age, sex, socioeconomic status (includes education), calories, lag, and lag x covariates. MIND, Mediterranean–Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay; t1, Tertile 1; t2, Tertile 2; t3, Tertile 3

Agarwal et al., Alzheimer's Dement 2024; Chicago Health and Aging Project

This association was attenuated among Blacks only when further adjusted for other lifestyle and vascular risk factors

Race differences for the association of Diet with Cognitive decline

eFigure 2 White participants on the left and Black participants on the right.



doi: 10.1212/WNL.0000000000209817

Neurology

Sawyer et al., Neurology 2024; REGARDS study

Dietary Patterns

PROSPECTIVE STUDIES at RUSH (MAP and CHAP)	Exposure	Cognitive decline	Alzheimer's dementia	Parkinsonian signs progression	Disability Risk	Depressive symptoms	Alzheimer's and other brain pathologies
Morris 2015; Agarwal 2018,2023, 2024, 2026; Cherian 2021, 2022, 2025	**MIND diet**	**↓ ↓ among those with a history of stroke**	**↓**	**↓**	**↓ IADL ↓ ADL ↓ Mobility disability**	**↓ ↓ among those with a history of stroke**	**Less AD pathology; Amyloid load Less Atherosclerosis among those with vascular risk Less Arteriosclerosis Less Hippocampal Sclerosis and hippocampal neuronal loss**
Morris 2015; Tangney 2014; Agarwal 2018, 2021, 2023, Cherian 2025	**Mediterranean diet**	**↓**	**↓**	**↓**	**↓ IADL ↓ ADL ↓ Mobility disability**	null	**Less AD pathology; Amyloid load Less Atherosclerosis among those with vascular risk**
Morris 2015; Tangney 2014; Agarwal 2018; Cherian 2021, 2022	**DASH diet (Dietary Approach to Stop Hypertension)**	**↓**	**↓**	null	**↓ IADL ↓ Mobility disability**	**↓ ↓ among those with a history of stroke**	Null with AD pathology

Randomized control trial with MIND diet Intervention

What we know so far

Randomized controlled trials with MIND diet interventions and cognitive outcomes

Barnes et al., N Engl J Med. 2023

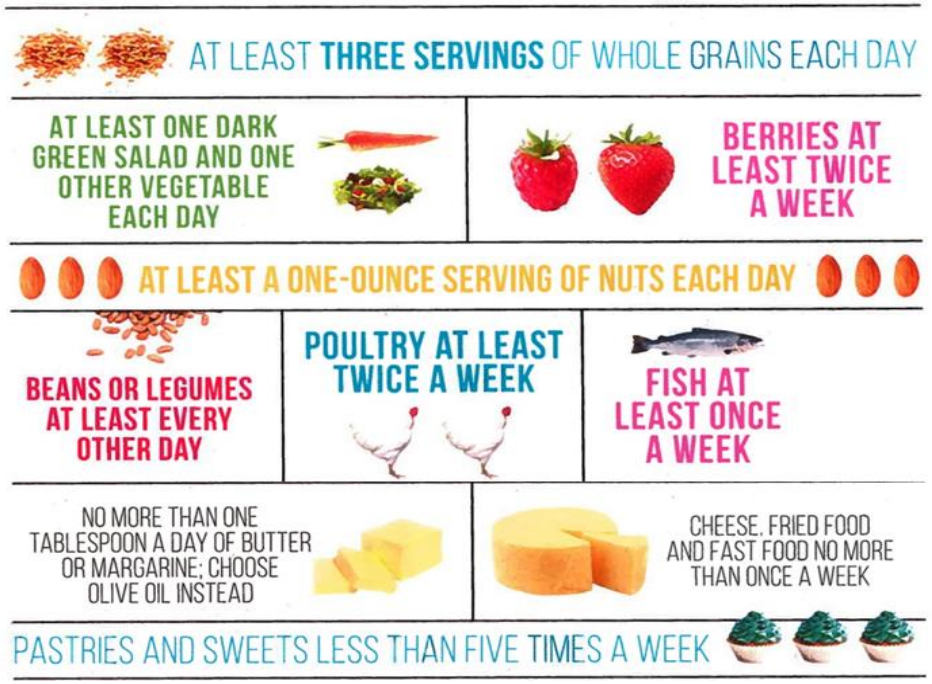
mind

- Chicago and Boston, 3-year period, randomized parallel intervention trial.
- 65- 84 years older adults with family
- history of AD or dementia, BMI≥ 25 and suboptimal diet

Randomization (n=604)

MIND diet + mild weight loss (n=302)

Extra virgin olive oil, blueberries, mixed nuts are provided

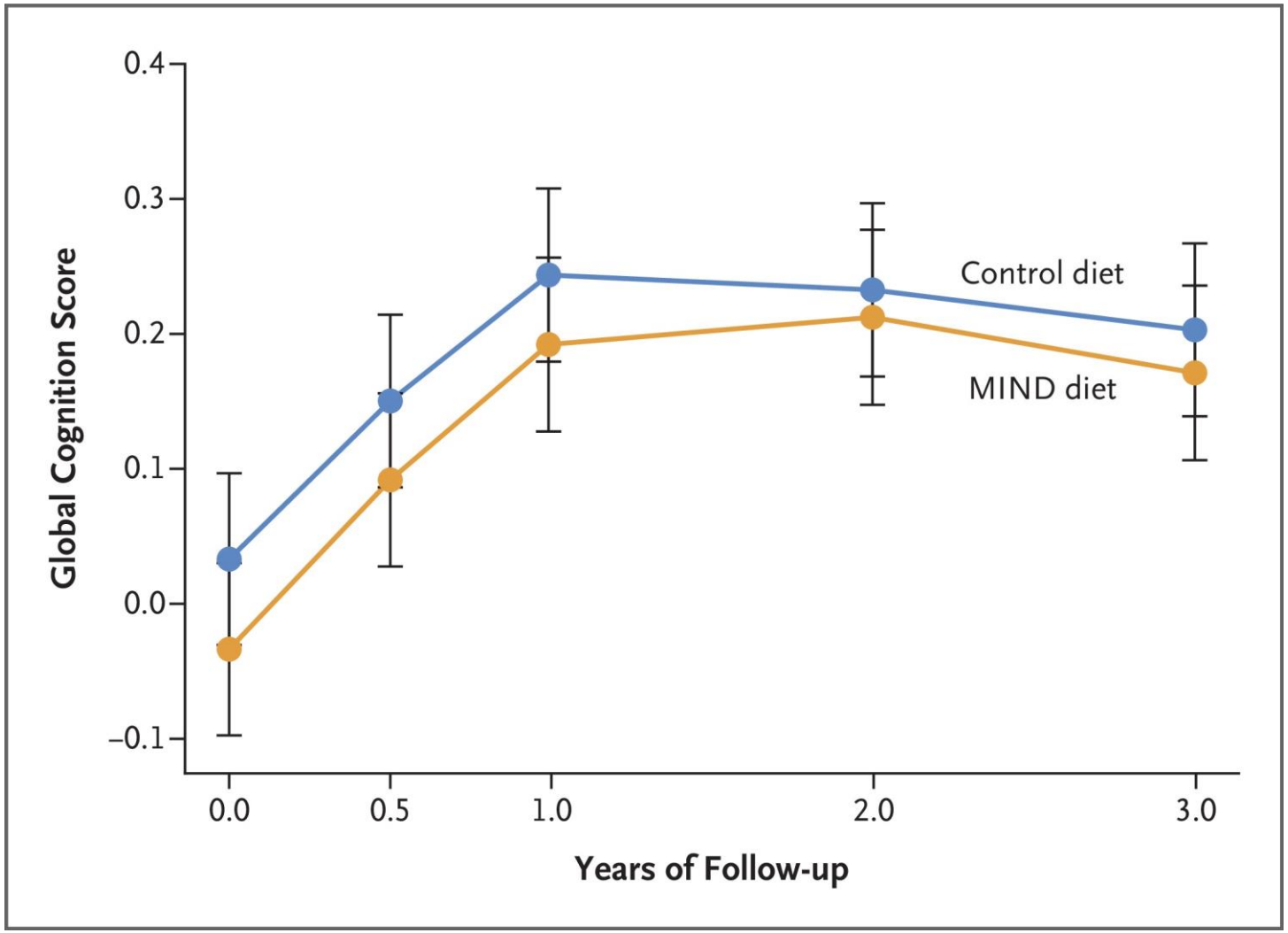


Usual Diet + mild weight loss (n=302)

store vouchers provided

- **Mild calorie restriction (250 kcal deficit/ day)**

mind



Barnes et al., N Engl J Med. 2023

The NEW ENGLAND JOURNAL of MEDICINE

MIND trial Post-hoc Analysis

K. Dhana et al.

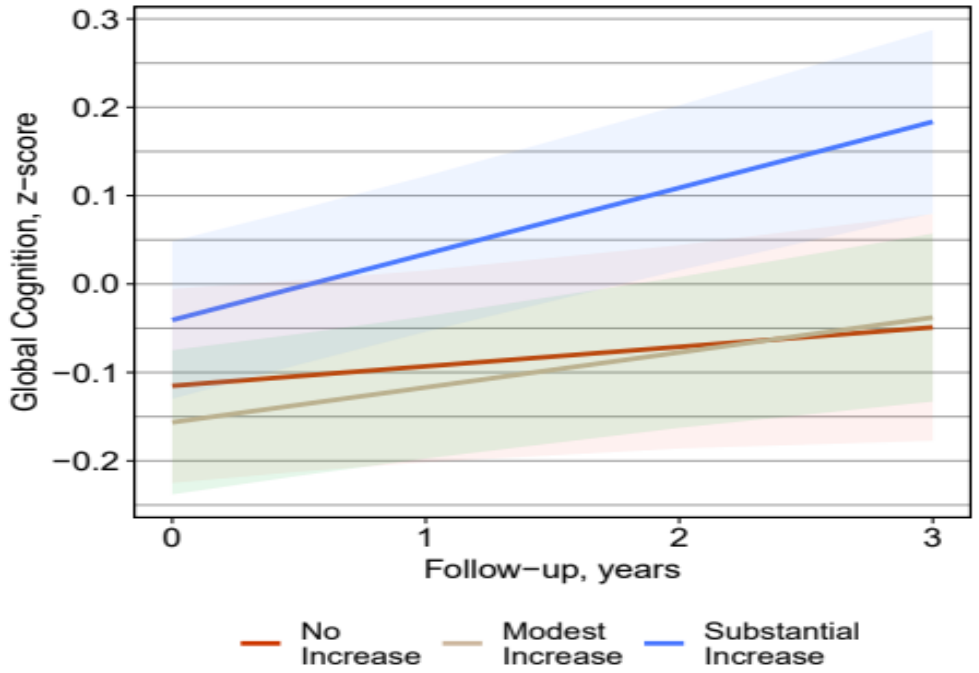
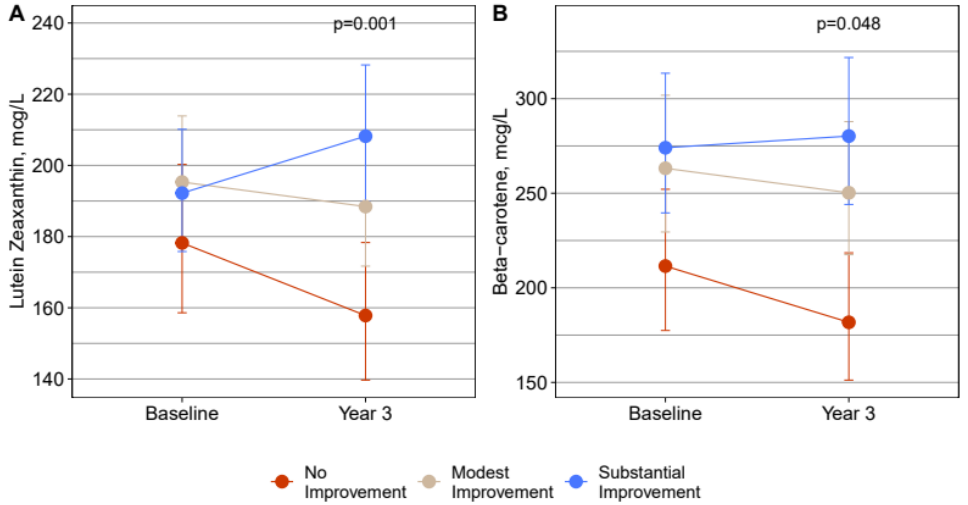


FIGURE 1. Cognitive score trajectories across MIND diet score change–based groups. Models adjusted by age, sex, race, education, APOE ε4, baseline MIND diet score, energy intake, BMI, smoking history, cognitive activity, and physical activity. APOE, apolipoprotein E; MIND, Mediterranean-DASH Intervention for Neurodegenerative Delay.



Modest increase Group: MIND diet score improved by 1 point
Substantial increase Group: MIND diet score improved by 4 points

Dhana et al., Am J Clin Nutr; 2026

U.S. Study to PrOtect brain health through lifestyle INTErvention to Reduce risk (U.S. POINTER)

U.S.POINTER
alzheimer's association

2-year randomized clinical trial with diet and lifestyle interventions. **five** sites (60- 79 years older adults with family history of AD or dementia)

Structured Lifestyle intervention

Nutrition counseling
- MIND diet
- Individualized counselling, meal plans by dieticians.
- Support through peer group meetings and telephone contacts

Physical activity
- Aerobic, resistance, stretching and balance exercise
- Group exercise, primarily at exercise facility (e.g. YMCA)
- Team meetings

Cognitive exercise
- Computer cognitive training at home
- Team meetings to encourage intellectual challenges and social engagement.

Guideline-based Health Coaching
- Appointment with medical advisor to go over blood labs and other health metrics.
- Goal setting

Randomized (N=2,111)

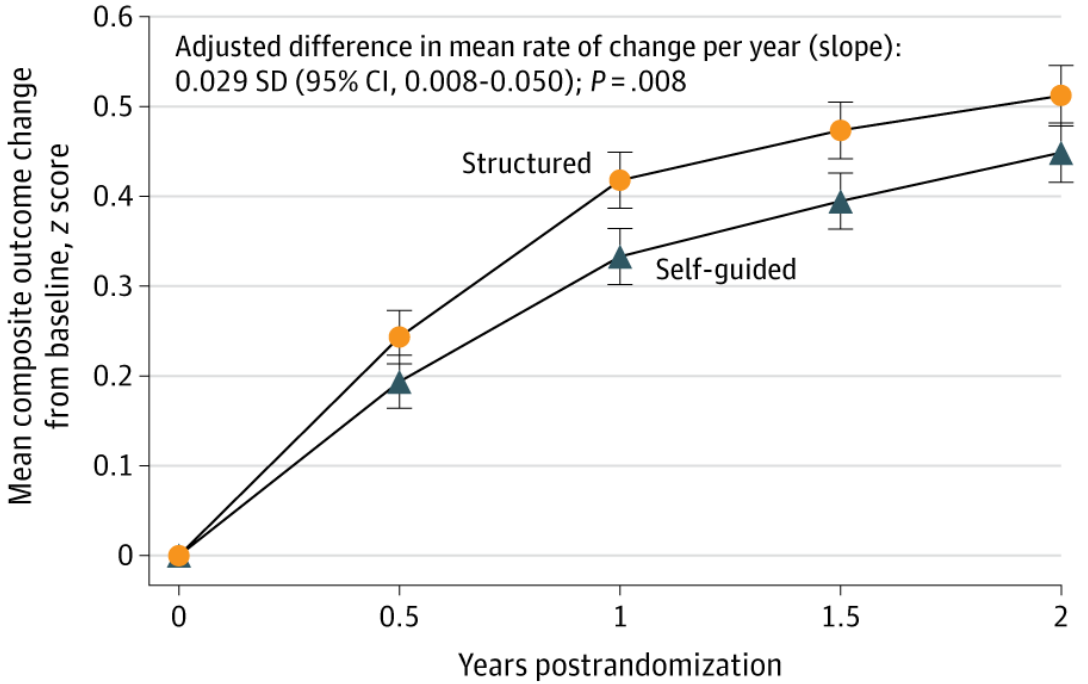
Self-Guided Lifestyle intervention

- Lifestyle Health Education and Support
- Self-guided plans
- Guideline-based health monitoring

JAMA Network™

From: **Structured vs Self-Guided Multidomain Lifestyle Interventions for Global Cognitive Function: The US POINTER Randomized Clinical Trial**

JAMA. 2025;334(8):681-691. doi:10.1001/jama.2025.12923



Total No.					
Structured	1056	965	949	918	923
Self-guided	1055	976	949	929	956

U.S.POINTER alzheimer's association®

Baker et al; JAMA; 2025

A possible mechanistic model for MIND diet and brain

BRAIN-HEALTHY EATING

The MIND Diet

Combining the Mediterranean and DASH diets to support cognitive health and reduce the risk of Alzheimer's.

EAT DAILY

- **Whole Grains** — At least **3 servings**/day — DAILY
- **Greens & Veggies** — **1 salad + 1 vegetable**/day — DAILY
- **Nuts** — At least **1 oz**/day — DAILY
- **Beans & Legumes** — At least **every other day** — EVERY OTHER DAY
- **Olive Oil** — Use as **primary cooking oil** — DAILY

EAT WEEKLY

- **Berries** — At least **2× per week** — WEEKLY
- **Poultry** — At least **2× per week** — WEEKLY
- **Fish** — At least **1× per week** — WEEKLY

LIMIT THESE

- **Butter** — No more than **1 tbsp**/day — LIMIT
- **Cheese & Fried Food** — No more than **1× per week** — LIMIT
- **Pastries & Sweets** — Less than **5× per week** — LIMIT

Based on research by Martha Clare Morris, Rush University Medical Center

DIET AND ALZHEIMER'S DISEASE PATHOLOGY, HIPPOCAMPAL HEALTH, CEREBRAL VASCULAR OUTCOMES

Healthy dietary patterns

Associated with reduced Alzheimer's dementia risk and slower cognitive decline

↑Total brain volume
(Gu 2015-WHICAP; Luciano 2017- Scottish cohort)

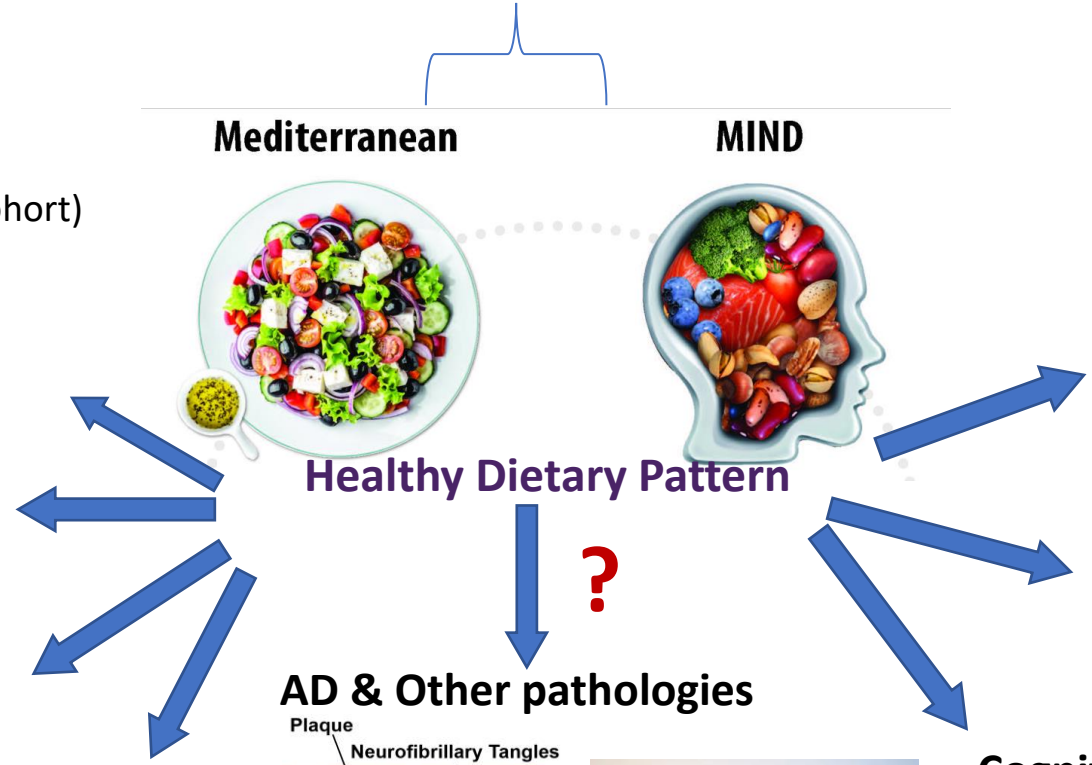
↑ Gray matter volume
(Ballarini 2021- German Longitudinal Study)

↑Cortical thickness
(Mosconi 2014; Staubo 2017- Mayo clinic-study of Aging)

↓White matter hyperintensity
(Gardner 2012- Northern Manhattan Study)

↓Cerebral infarcts
(Scarmeas 2011- WHICAP)

↓PET beta-amyloid load
(Berti 2018- Brain Imaging Study; Rainey-Smith 2018- AIBL; Vassilaki 2018- Mayo clinic-study of Aging)



RADC Neuropathology Lab image

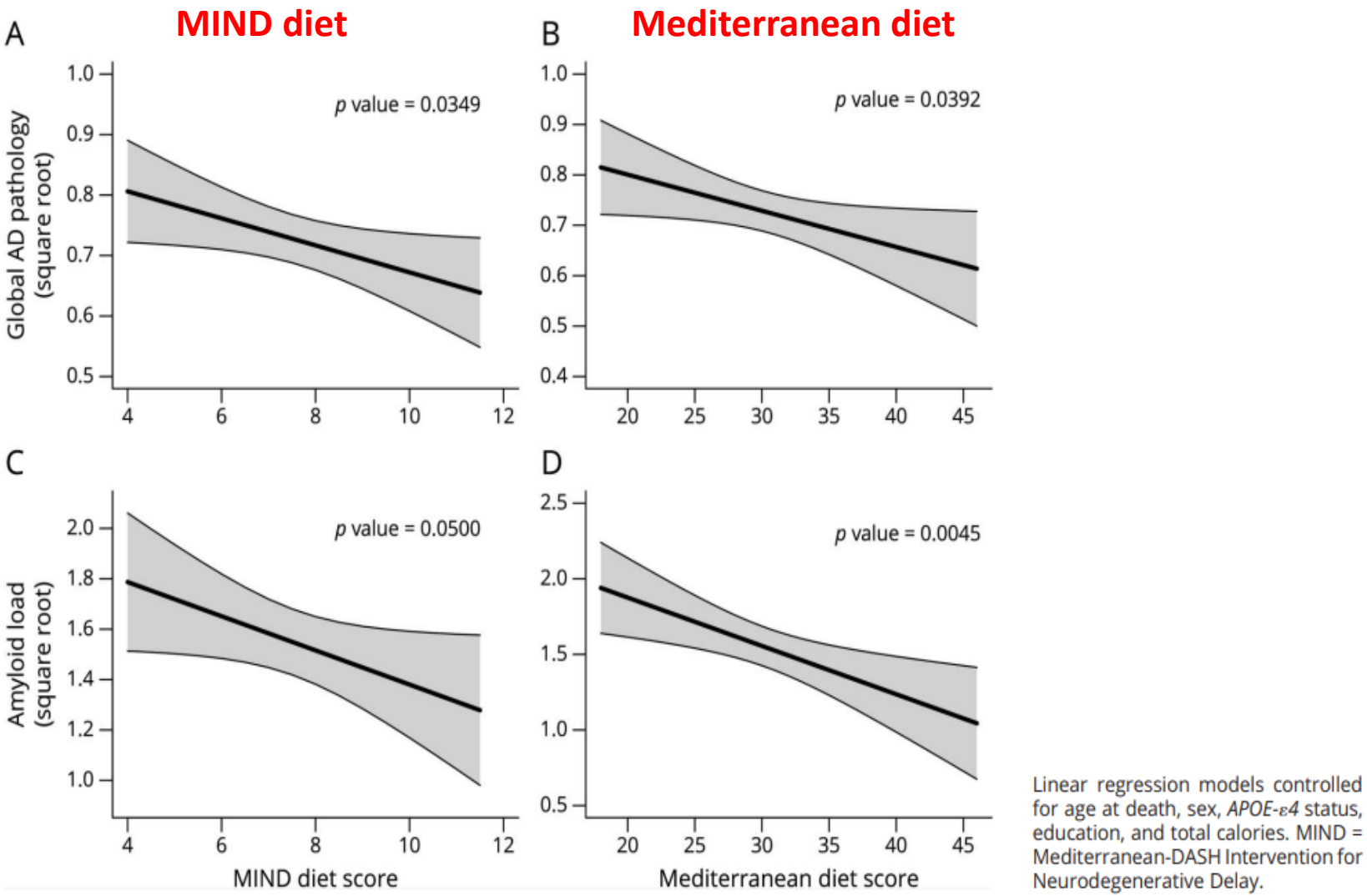
↑Total brain volume
(Melo van Lent 2021- FHS; Chen 2024- UK BioBank; Agarwal 2026)

↓White matter hyperintensity
(Chen 2024-UK Biobank; Agarwal 2026)

Cognitive Resilience (Dhana 2021; Wagner & Agarwal, 2023- MAP)

Diet and AD Pathology

Figure 1 Association Between (A) MIND Diet and Global AD Pathology (B) Mediterranean Diet and Global AD Pathology (C) MIND Diet and Amyloid Load (D) Mediterranean Diet and Amyloid Load

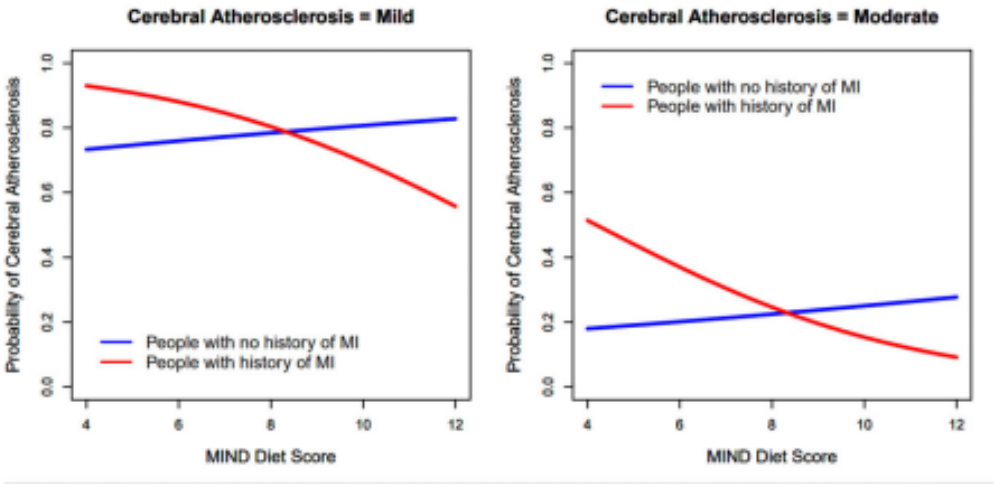


Linear regression models controlled for age at death, sex, *APOE-ε4* status, education, and total calories. MIND = Mediterranean-DASH Intervention for Neurodegenerative Delay.

Agarwal et al., Neurology 2023

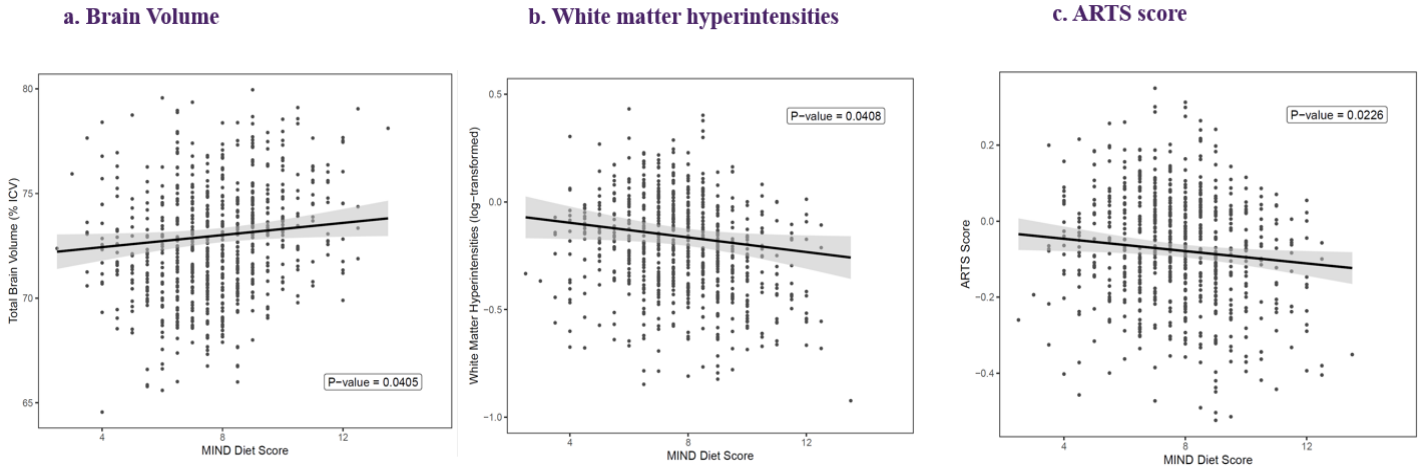
MIND diet and Cerebrovascular Outcomes

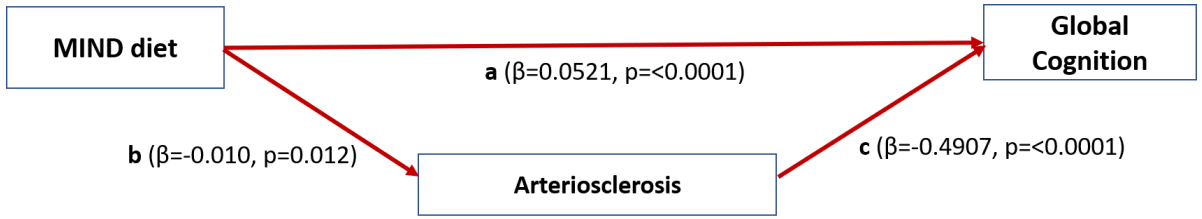
a) MIND diet and ICAD



Cherian et al., Neurology; 2025

b) MIND diet and Neuroimaging Biomarker





About 8.5% of the association between the MIND diet and cognition is through cerebral arteriosclerosis

Agarwal et al., Alzheimer's Dement, 2026

MIND diet and hippocampal sclerosis

JAMA Network Open

Original Investigation | Nutrition, Obesity, and Exercise

MIND Diet and Hippocampal Sclerosis Among Community-Based Older Adults

Puja Agarwal, PhD; Sonal Agrawal, PhD; Maude Wagner, PhD; Laurel J. Cherian, MD; Neelum T. Aggarwal, MD; Bryan D. James, PhD; Thomas M. Holland, MD; David A. Bennett, MD; Lisa L. Barnes, PhD; Sue E. Leurgans, PhD; Julie A. Schneider, MD

Abstract

IMPORTANCE Hippocampal sclerosis (HS), defined as severe neuronal loss and astrogliosis in coronal sections of the midhippocampus cornu ammonis 1 or subiculum, is an important pathology

Key Points

Question Is Mediterranean–Dietary Approaches to Stop Hypertension

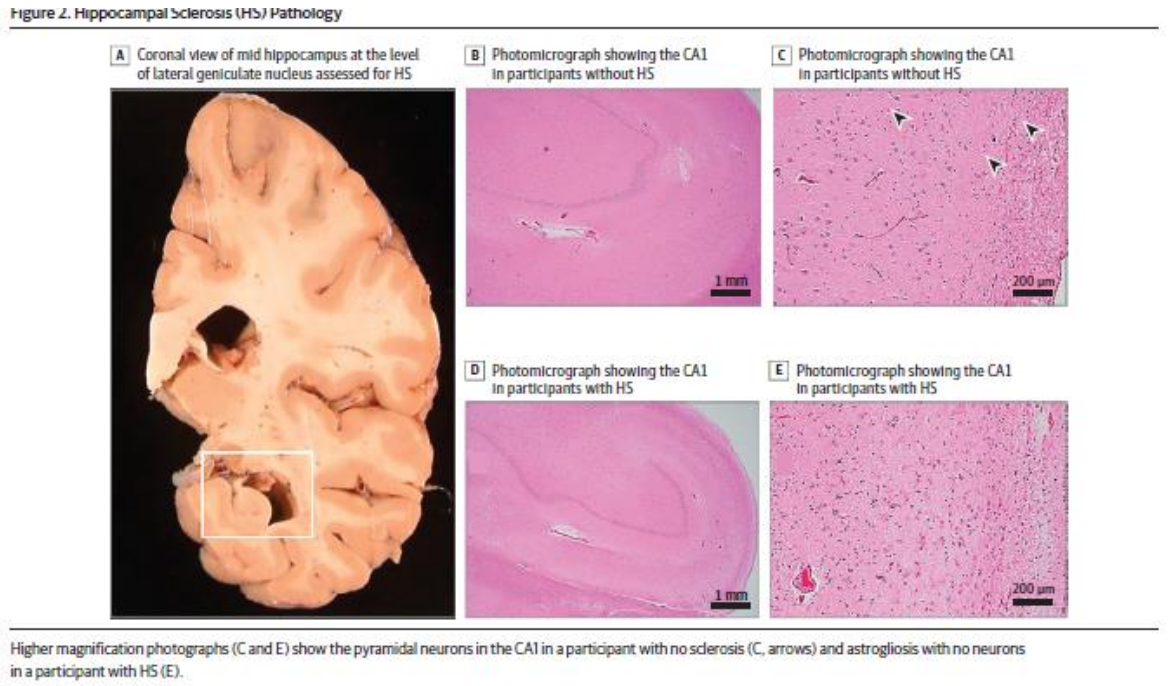


Figure 2. Hippocampal Sclerosis (HS) Pathology

Higher magnification photographs (C and E) show the pyramidal neurons in the CA1 in a participant with no sclerosis (C, arrows) and astrogliosis with no neurons in a participant with HS (E).

- **Sample**: 809 older adults from the Rush Memory and Aging Project; Community-based autopsy cohort study
- Repeated MIND diet assessments over up to 18 years before death
- **Outcomes**: Hippocampal sclerosis, LATE-NC, and neuronal loss in hippocampus.

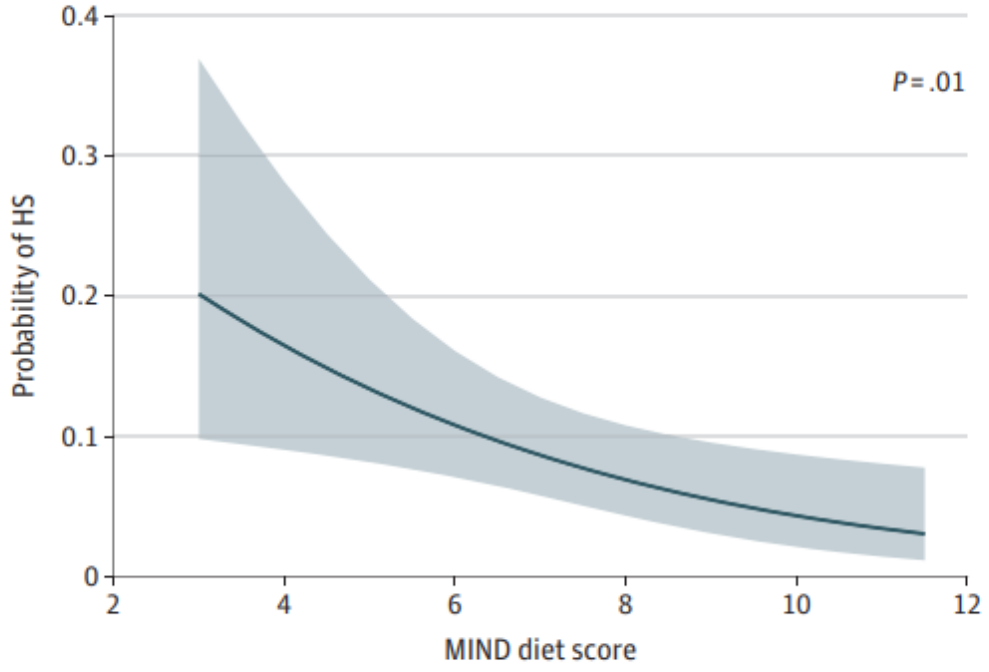
Agarwal et al., JAMA Net Open; 2025

MIND diet and hippocampal sclerosis

- Each 1-point increase in MIND diet was associated with 20% lower odds of hippocampal sclerosis
- HS mediated the relationship between MIND diet score and Alzheimer's Disease

- **Better Diet** during follow-up was also associated with **less Neuronal Loss in the hippocampus.**

Figure 3. Association of Mediterranean-Dietary Approaches to Stop Hypertension (DASH) Intervention for Neurodegenerative Delay (MIND) Diet Score and Risk of Hippocampal Sclerosis (HS)



Model controlled for age at death, sex, education, *APOE-ε4* status, calories, Alzheimer disease, and vascular pathologies.

Agarwal et al., JAMA Net Open; 2025

Mind diet and Transcriptomics

Received: 8 August 2023 | Revised: 1 May 2024 | Accepted: 20 May 2024

DOI: 10.1002/alz.14062

RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

The MIND diet, brain transcriptomic alterations, and dementia

Jun Li[1,2] | Ana W. Capuano[3,4] | Puja Agarwal[3,5] | Zoe Arvanitakis[3,4] | Yanling Wang[3,4] | Philip L. De Jager[6] | Julie A. Schneider[3,4,7] | Shinya Tasaki[3,4] | Katia de Paiva Lopes[3,4] | Frank B. Hu[2,8,9] | David A Bennett[3,4] | Liming Liang[8,10] | Francine Grodstein[3,5]

[1]Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

[2]Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[3]Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, Illinois, USA

[4]Department of Neurological Sciences, Rush University Medical Center, Chicago, Illinois, USA

[5]Department of Internal Medicine, Rush University Medical Center, Chicago, Illinois, USA

[6]Center for Translational & Computational Neuroimmunology, Department of Neurology and the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Irving Medical Center, New York, New York, USA

[7]Department of Pathology, Rush University Medical Center, Chicago, Illinois, USA

[8]Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

[9]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

[10]Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

Correspondence
Jun Li, Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, 900 Commonwealth Ave., Third Floor, Boston, MA 02215, USA.
Email: juli@bwh.harvard.edu

Funding information
National Institute on Aging, Grant/Award

Abstract

INTRODUCTION: Dietary patterns are associated with dementia risk, but the underlying molecular mechanisms are largely unknown.

METHODS: We used RNA sequencing data from *post mortem* prefrontal cortex tissue and annual cognitive evaluations from 1204 participants in the Religious Orders Study and Memory and Aging Project. We identified a transcriptomic profile correlated with

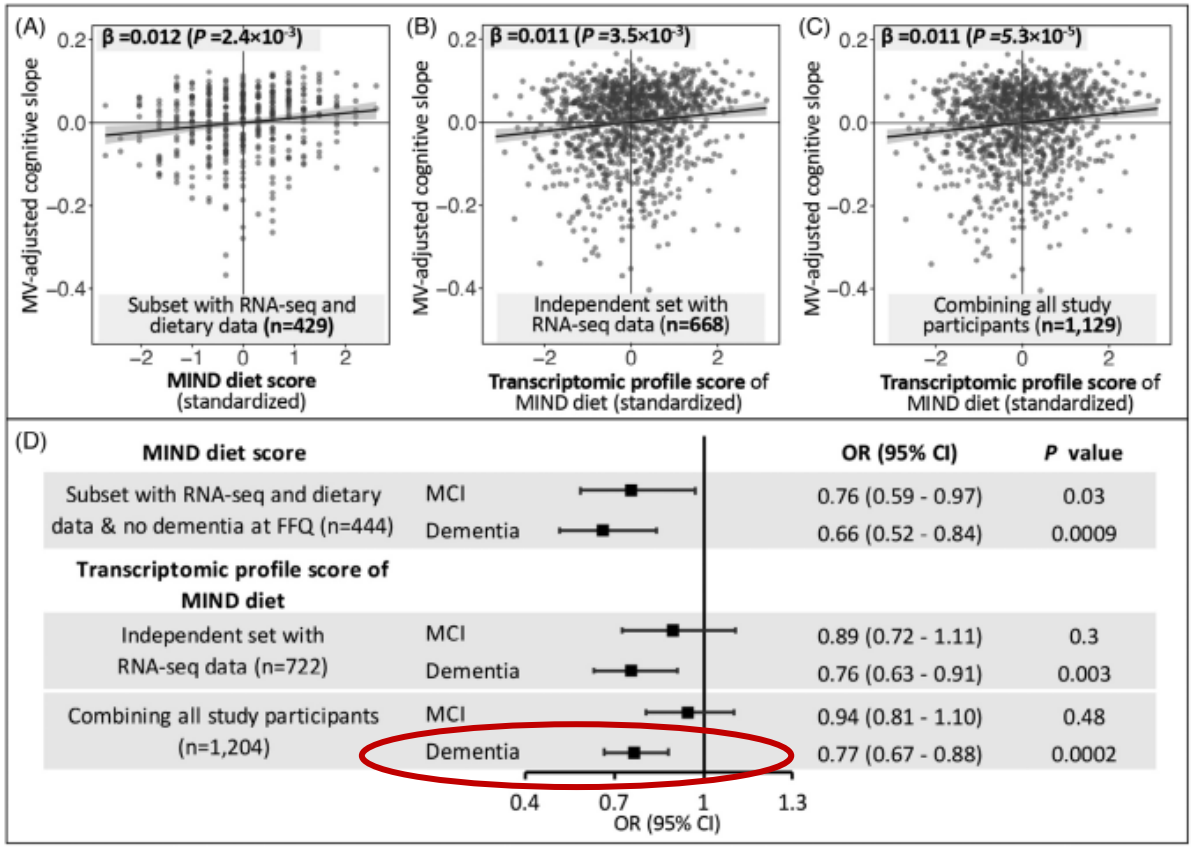
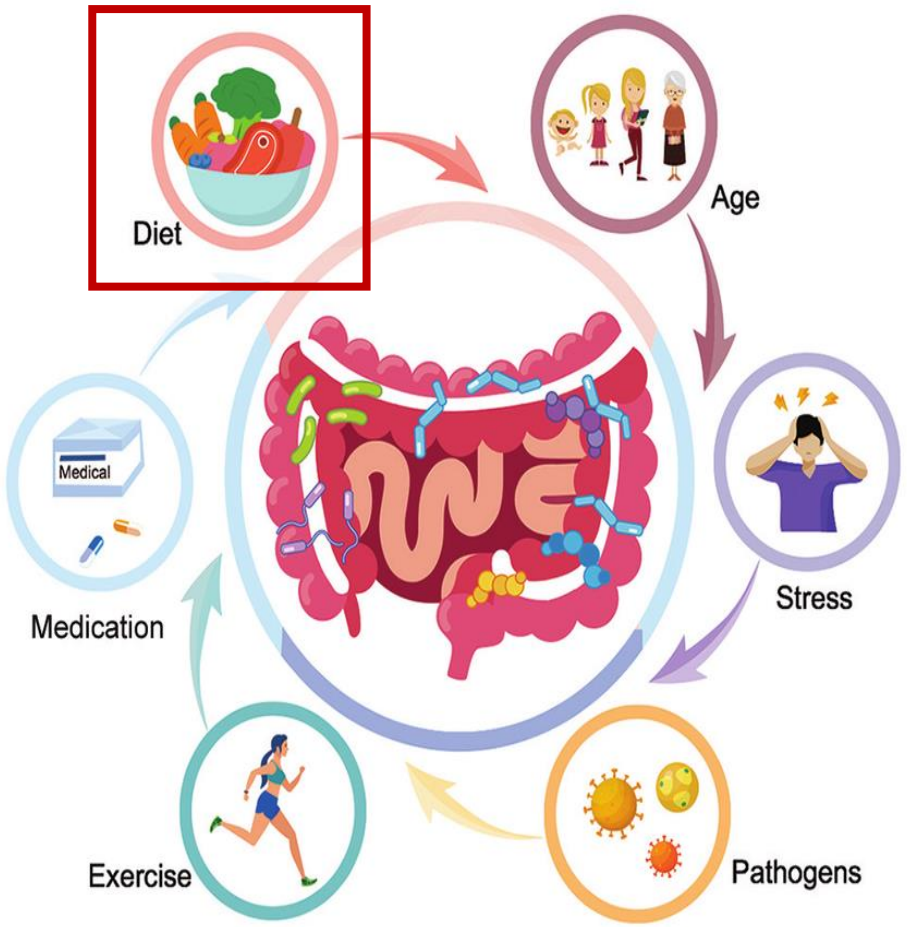


FIGURE 3 Associations of the MIND diet score and its cortical transcriptomic profile score with cognitive trajectory and dementia. The upper panel presents the associations with cognitive decline trajectory, for the MIND diet score (A), and for the transcriptomic profile score of the MIND diet in the independent set (B) and in the combined analysis of all participants (C). In the scatter plots, the solid lines are linear trend, and the gray areas are 95% CI. D, Associations between the MIND diet score and its transcriptomic profile score with dementia and MCI as of death (vs. no cognitive impairment). Black squares and gray lines indicate ORs and 95% CI, respectively. Analyses of the MIND diet score were conducted in participants with dietary data and free of dementia at the time of the FFQ; and were adjusted for age, sex, years of education, BMI, physical activity, smoking, and total energy intake. Associations between the transcriptomic scores were adjusted for age at death, sex, education years, and cohorts. Sample sizes were smaller in the upper panel versus in (D) because some participants had only one cognitive assessment and were thus excluded from cognitive trajectory analysis. BMI, body mass index; CI, confidence interval; FFQ, food frequency questionnaire; MCI, mild cognitive impairment; MIND, Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay; MV, multivariable; OR, odds ratio; RNA-seq, RNA sequencing.

MIND diet and Gut microbiota- Sub-study from the MIND trial



Received: 3 October 2025 | Revised: 17 February 2026 | Accepted: 23 February 2026

DOI: 10.1002/trc2.70239

Translational Research & Clinical Interventions

RESEARCH ARTICLE

Weight loss and metabolic improvements dominate the microbiome response in the MIND diet intervention: a randomized controlled trial

Robin M. Voigt[1,2,3] | Adit Chaudhary[4,5] | Ankur Naqib[1,3,4] | Phillip A. Engen[1] | Darbaz Adnan[1] | Klodian Dhana[2,6] | Stefan J. Green[1,2,5] | Michelle Villanueva[1] | Puja Agarwal[2,7,8] | Lisa L. Barnes[7,9] | Frank Sacks[10] | Ali Keshavarzian[1,2,3,11]

The MIND diet confers a more resilient microbiome response by stabilizing microbial metabolic pathways against the transient stress of caloric restriction, with significantly fewer pathway disruptions compared to the control group.

Voigt et al., Alzheimers Dement (N Y), 2026

There is more to this puzzle…..Diet/ Nutrition & Brain Health

- Understand the **potential mechanism** for this link in human studies.

- Get more data on different populations

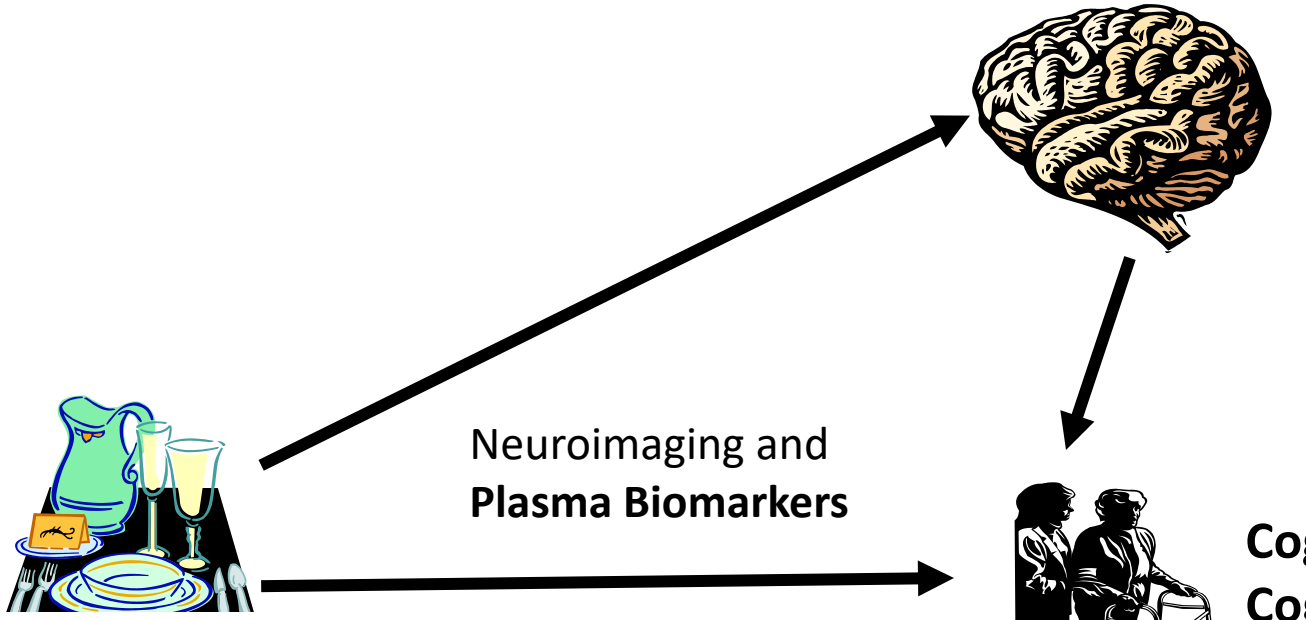
across the globe with culture/ region specific MIND like dietary patterns and brain health outcomes.

- Recognize the role of food environment, food insecurity and food choices.

- Understand the role of **Precision Nutrition** in Neurodegenerative disorders of older adults.

Source: https://www.vecteezy.com/

Future Direction for Nutrition Studies



Neuroimaging and
Plasma Biomarkers

Neuroinflammation, oxidative stress & metabolism – microglia, GFAP, other omics marker

Cognitive resilience
Cognitive decline in diverse populations
Motor function

Dietary data assessments in diverse sample using culturally adaptive tool for Latinos;
Food environment and GIS data

- **Further understanding the potential mechanism using novel blood-based and imaging biomarkers, as well as marker of neuroinflammation, oxidative stress and brain metabolism.**

- **Leveraging completed Randomized clinical trial with dietary intervention to further understand the clinical implications of nutrient parameters for precision nutrition approach.**

Summary

- Antioxidant nutrients **(vitamin E, carotenoids), omega-3,** bioactive (**flavonoids**), **B vitamins**, and metals **(copper)**from dietary sources supports brain health in older adults.

MIND Diet recommends:

- **To eat**: green leafy, other vegetables, berries, fish, nuts, olive oil, legumes, whole grains, and poultry intake.
- **To limit**: unhealthy foods like processed & red meat, full-fat cheese, fried, and sugary foods.

- Recent intervention trials with the **MIND diet** as primary intervention or in combination with other lifestyle intervention establishes the **beneficial effect of MIND diet on cognitive performance**.

- **Different underlying mechanisms** including reduced brain pathologies including AD and vascular, hippocampal neuronal and gut health may explain **Diet-Brain axis**. Further ongoing studies will provide more answers.

Acknowledgment

Rush Alzheimer's Disease Center

Neelum Aggarwal, MD
Sonal Agrawal, PhD
Konstantinos Arfanakis, PhD
Zoe Arvanitakis, MD
Denis Avey, PhD
Lisa Barnes, PhD
David Bennett, MD
Patricia Boyle, PhD
Aron Buchman, MD
Siyi Chen, PhD
Mayra Estrella, PhD
Jose Farfel, MD, PhD
Fran Grodstein, ScD
Bryan James, PhD
Alifiya Kapasi, PhD
Nicola Kearns , PhD
Melissa Lamar, PhD
Brittney Lange-Maia, PhD, MPH
Sue Leurgans, PhD
Katia Lopes, PhD
David X Marquez, PhD *Visiting Appt at Rush
Rupal Mehta, MD
Sukriti Nag, MD, PhD
Bernard Ng, PhD
Shahram Oveisgharan, MD
Victoria Poole, PhD
Julie Schneider, MD
Raj Shah, MD
Ajay Sood, MD, PhD
Shinya Tasaki, PhD
Ricardo Vialle, PhD
Maude Wagner, PhD
Tianhao Wang, PhD
Yanling Wang, PhD
Bob Wilson, PhD
Jishu Xu, MS
Jingyun Yang, PhD
Lei Yu, PhD
Andrea Zammit, PhD
Late Dr. Martha Claire Morris

Department of Clinical Nutrition

Christy Tangney, PhD, FACN, CNS

Department of Neurology

Laurel J Cherian, MD, MS

Study Participants & Study Staff:

Memory and Aging Project (MAP)

Minority Aging Research Study (MARS)

Latino Core and African American Clinical Core

RUSH ADRC

Data Management and Stats Team

Collaborators

Harvard TH Chan School of Public Health, Boston
Tufts University, Boston
Florey Institute of Neuroscience, Australia
Wake Forest University, North Carolina

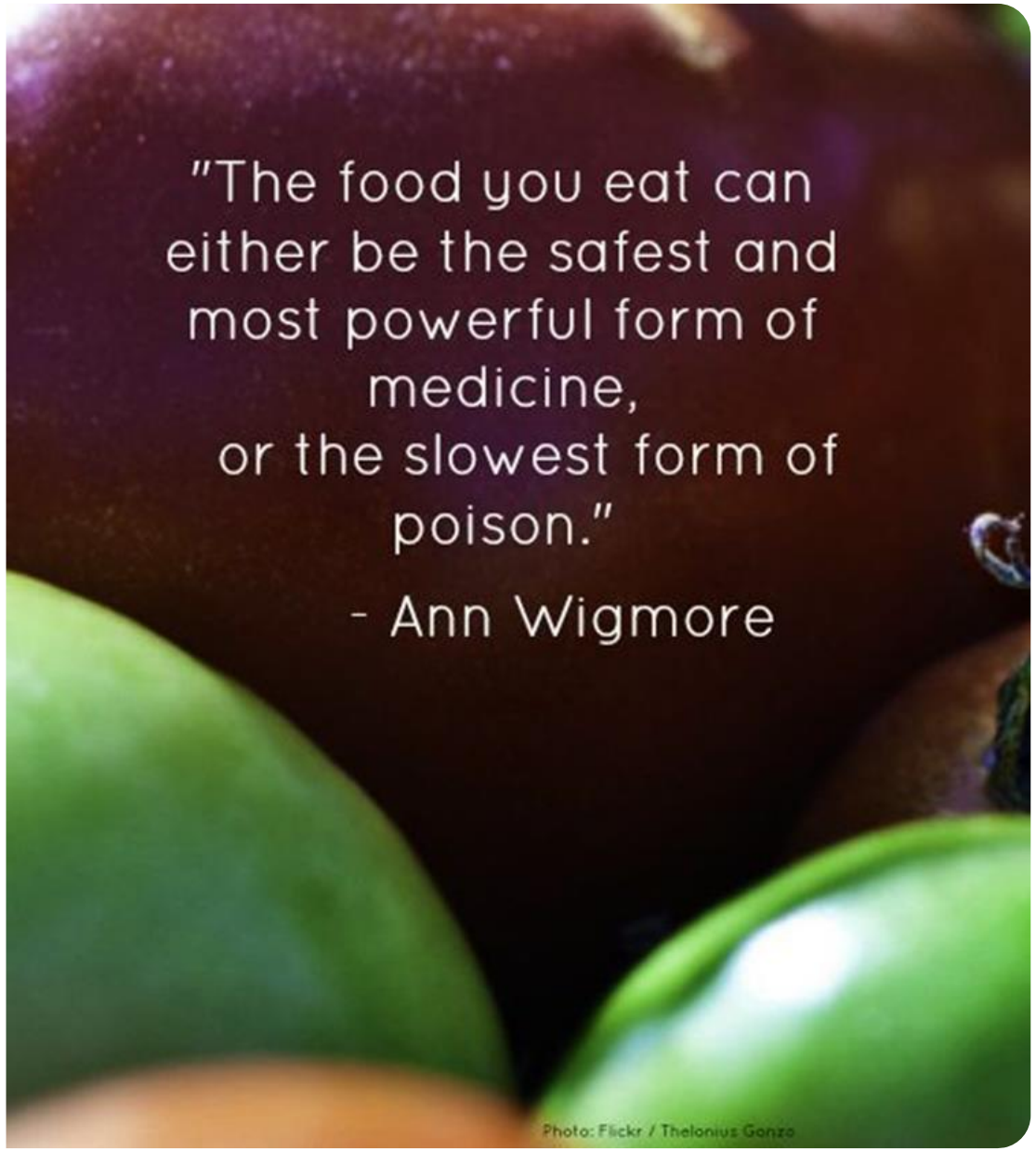
FUNDING SOURCE:

Ongoing grants(NIH/NIA):

R01AG085483 (Agarwal)
R01AG054057 (Schneider/ Bush)
R01AG051641 (Schneider/ Booth)
R01AG022018 (Barnes)
R01AG076143 (Lamar)
R01AG17917 (Bennett)
U01NS100599
P30AG072975; Rush-ADRC Developmental project (Agarwal)

Completed grants:

R01AG054476 (Schneider)
Rush Cohn's Fellowship (Agarwal)
Alzheimer's Association (Agarwal, AARG-21-852512)
Michael J Fox Foundation for Parkinson's Disease (Agarwal, MJFF-16958)
Consolidated Anti-Aging Foundation (Agarwal)



puja_agarwal@rush.edu

@PujaAgarwal1902

Questions?