

Non-pharmacological Treatment of MCI and Dementia



Kristoffer Rhoads, PhD

Clinical Neuropsychologist

Associate Professor, Department of Neurology

Memory and Brain Wellness Center

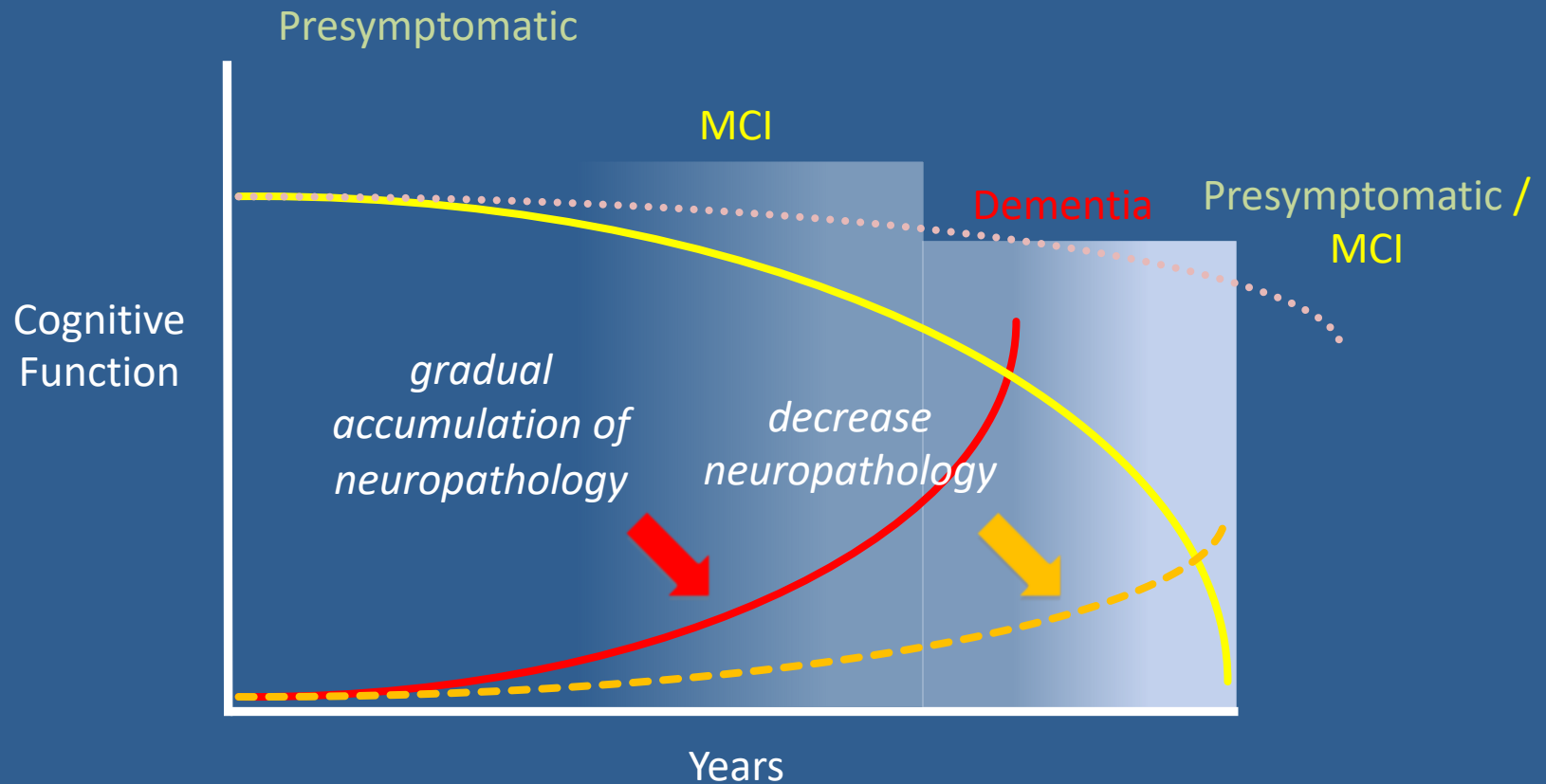
Harborview Medical Center/University of Washington School of Medicine

UW Project ECHO Dementia March 10th, 2022

Objectives

- 1) Increase awareness of risk factors for cognitive impairment and dementia and risk reduction through improved management.
- 2) Identify lifestyle interventions (i.e., exercise, diet, cognitive stimulation) that have impact on cognition and neurological disease processes, from prodromal phases to early dementia.
- 3) Identify local, state, regional and national programs and services to improve the quality of life for individuals and families living with dementia.

Treatment Targets



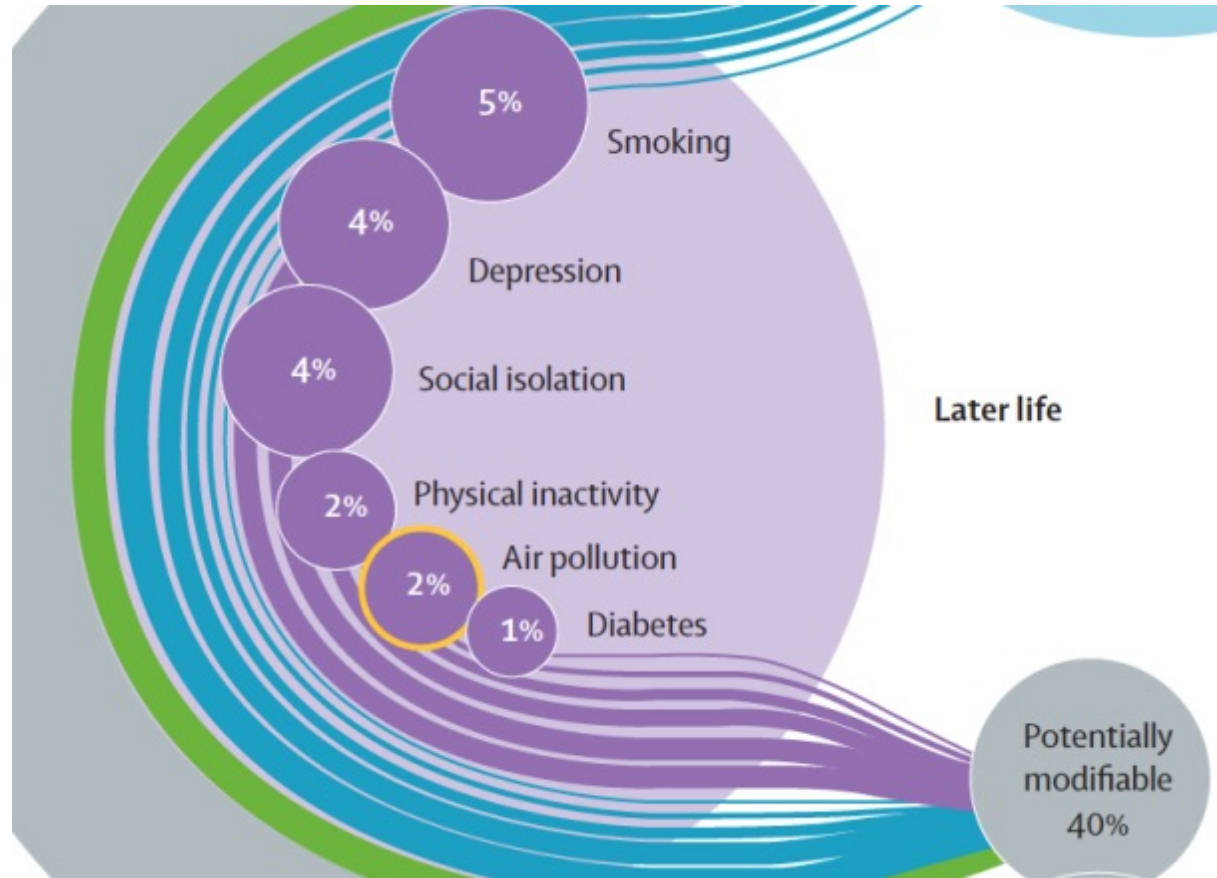
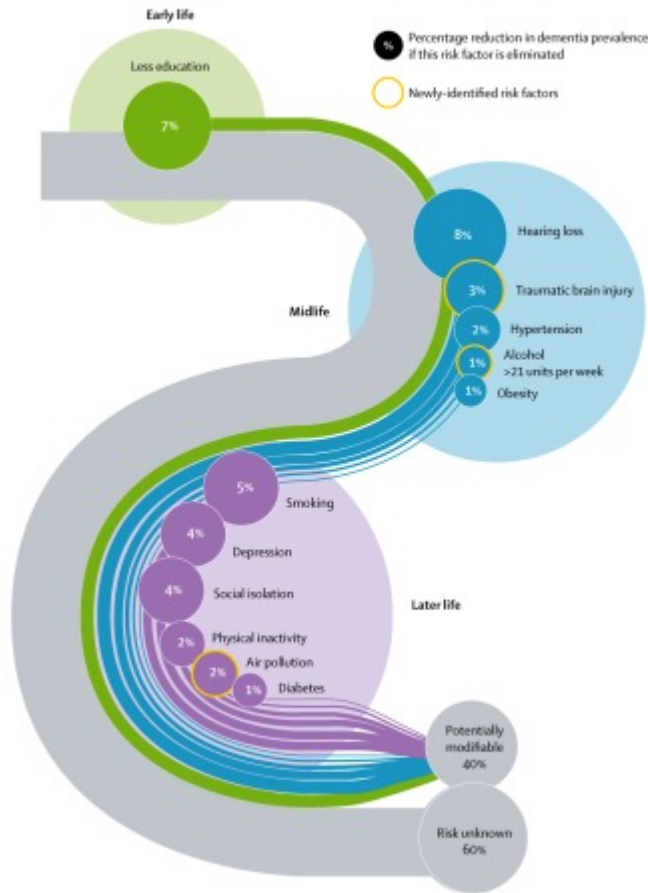
Prevention and Non-Pharmacological Interventions

- Treatment of Modifiable Risk Factors
- Cardiovascular Exercise
- Cognitive Activation and Rehabilitation
- Dietary Interventions
- Optimizing Sleep
- Stress / Distress Management
- Community Engagement / Socialization

Lancet Commission 2020 Update

Risk factors for dementia

An update to the Lancet Commission on Dementia prevention, intervention, and care presents a life-course model showing that 12 potentially modifiable risk factors account for around 40% of worldwide dementias

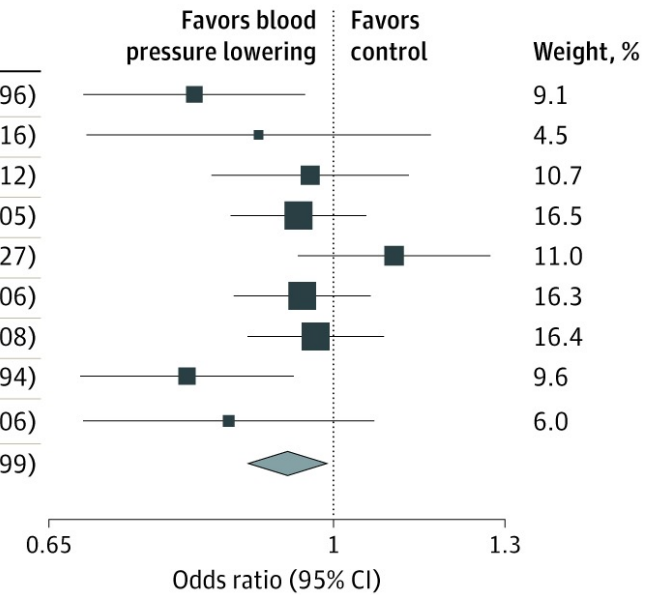


Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. The Lancet 2020.

Midlife Risk Factor Modification - Hypertension

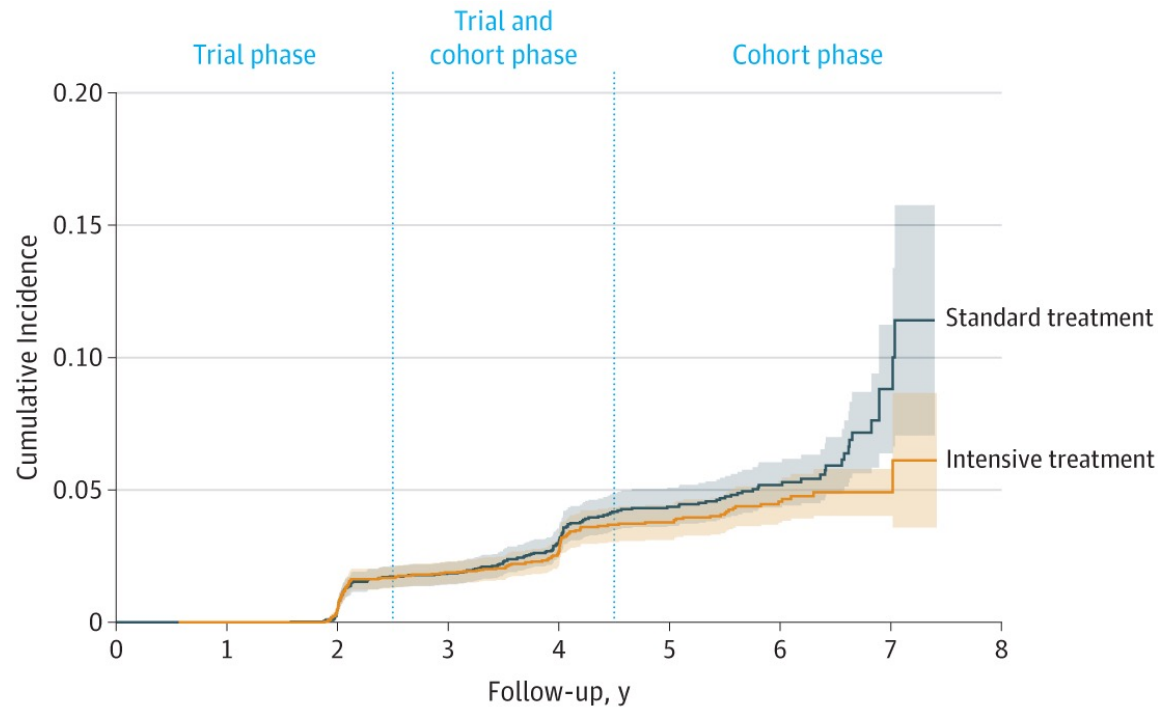
Study	Participants with dementia or cognitive impairment/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)
	Blood pressure lowering group	Control group		
PROGRESS, ²³ 2003	276/3051	334/3054	1.89 (0.39 to 3.39)	0.81 (0.68 to 0.96)
SCOPE, ²⁴ 2003	113/2477	125/2460	0.52 (-0.68 to 1.71)	0.89 (0.69 to 1.16)
HYVET-COG, ⁶ 2008	485/1687	486/1649	0.72 (-2.36 to 3.81)	0.97 (0.83 to 1.12)
PRoFESS, ²⁶ 2008	795/7531	832/7518	0.51 (-0.48 to 1.50)	0.95 (0.86 to 1.05)
TRANSCEND, ⁷ 2011 ^a	454/2642	412/2589	-1.27 (-3.28 to 0.74)	1.10 (0.95 to 1.27)
ON TARGET (Dual), ⁷ 2011	1240/7461	657/3801	0.67 (-0.80 to 2.13)	0.95 (0.86 to 1.06)
ON TARGET (ARB), ⁷ 2011	1279/7566	657/3801	0.38 (-1.09 to 1.85)	0.97 (0.88 to 1.08)
SPRINT MIND, ¹² 2019	287/4278	353/4285	1.53 (0.42 to 2.64)	0.80 (0.68 to 0.94)
HOPE-3, ¹³ 2019	584/811	612/815	3.08 (-1.20 to 7.37)	0.85 (0.68 to 1.06)
Test for overall effect: $z = -2.28$; $P = .02$			0.71 (0.19 to 1.2)	0.93 (0.88 to 0.99)

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 12.60$; $P = .13$; $I^2 = 36.1\%$



SPRINT-MIND

- Aggressive treatment of blood pressure (SBP<120)
 - Decreased risk MCI
 - Fewer white matter lesions
 - Total brain volume and
 - No difference in stroke types (2021)



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

Exercise and Physical Activity and Dementia

- Over 90 meta-analyses in the last 5 years
- Highest quality/most consistent evidence
- Likely multiple mechanisms of action (Wilckens et al., 2021, Hippocampus)
- Likely beneficial in multiple domains
 - Cognition (processing speed, EF>memory) (Wang et al., 2020, Aging)
 - Physical function/mobility/falls (Lai et al., 2019, AM J Phys Med Rehabil)
 - Sleep (O'Caoimh et al., 2019)
 - Neuropsychiatric symptoms (Watt, et al, 2021, BMJ)
- Likely most beneficial in combination with other NPTs
- Pooled effects highest for delaying onset>MCI>dementia
 - Group > individual
 - Across settings, including home-based (de Almeida, 2020, Gerontologist)

Exercise and Physical Activity

- Should be recommended to adults with normal cognition to reduce the risk of cognitive decline.
 - Quality of evidence: moderate
 - Strength of the recommendation: strong
- May be recommended to adults with MCI to reduce the risk of cognitive decline.
 - Quality of evidence: low
 - Strength of the recommendation: conditional
- 150 min of moderate-intensity or 75 min vigorous-intensity /week
 - Double for additional health benefits
- Aerobic activity = 10+ minutes' duration
- Poor mobility = balance and fall prevention on 3+ days/week
- Muscle-strengthening = major muscle groups on 2+ days/week
- Limitations = as physically active as abilities and conditions allow

RISK REDUCTION
OF COGNITIVE DECLINE
AND DEMENTIA

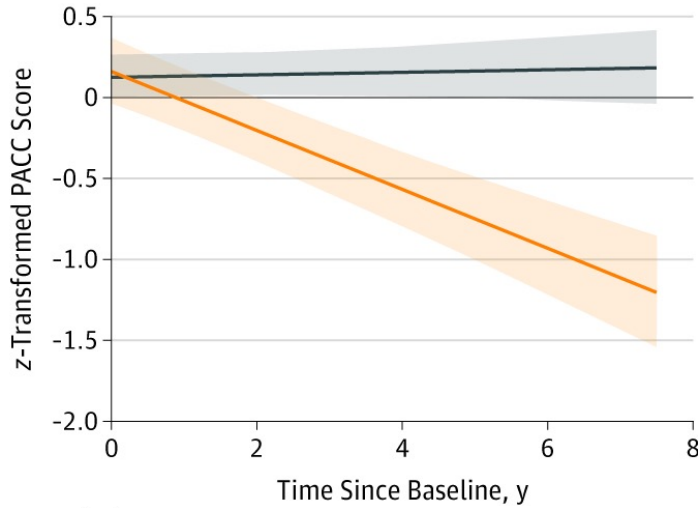
WHO GUIDELINES



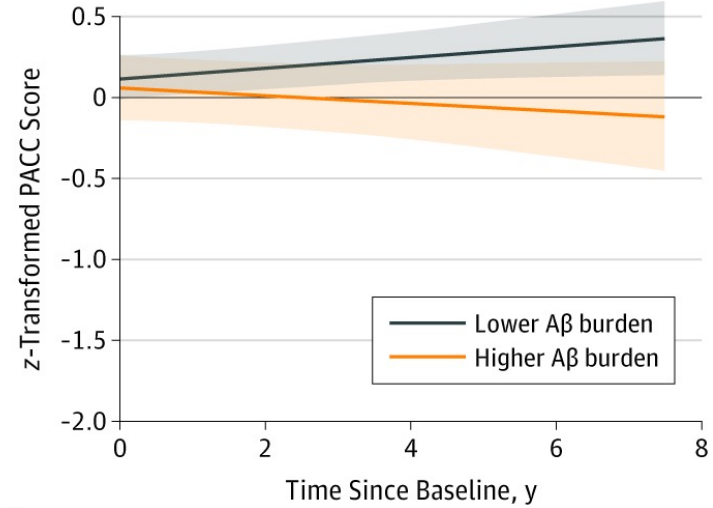
World Health
Organization

Physical Activity Moderates A β Associated Cognitive Decline and Cortical Thinning

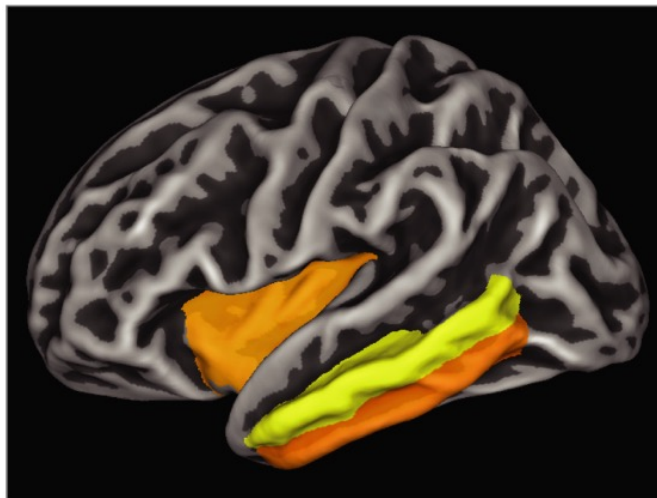
A Lower physical activity



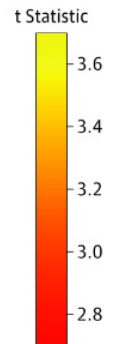
B Higher physical activity



A Lateral view



B Medial view



o Imple

- [illegible]

Cognitive Training and Stimulation

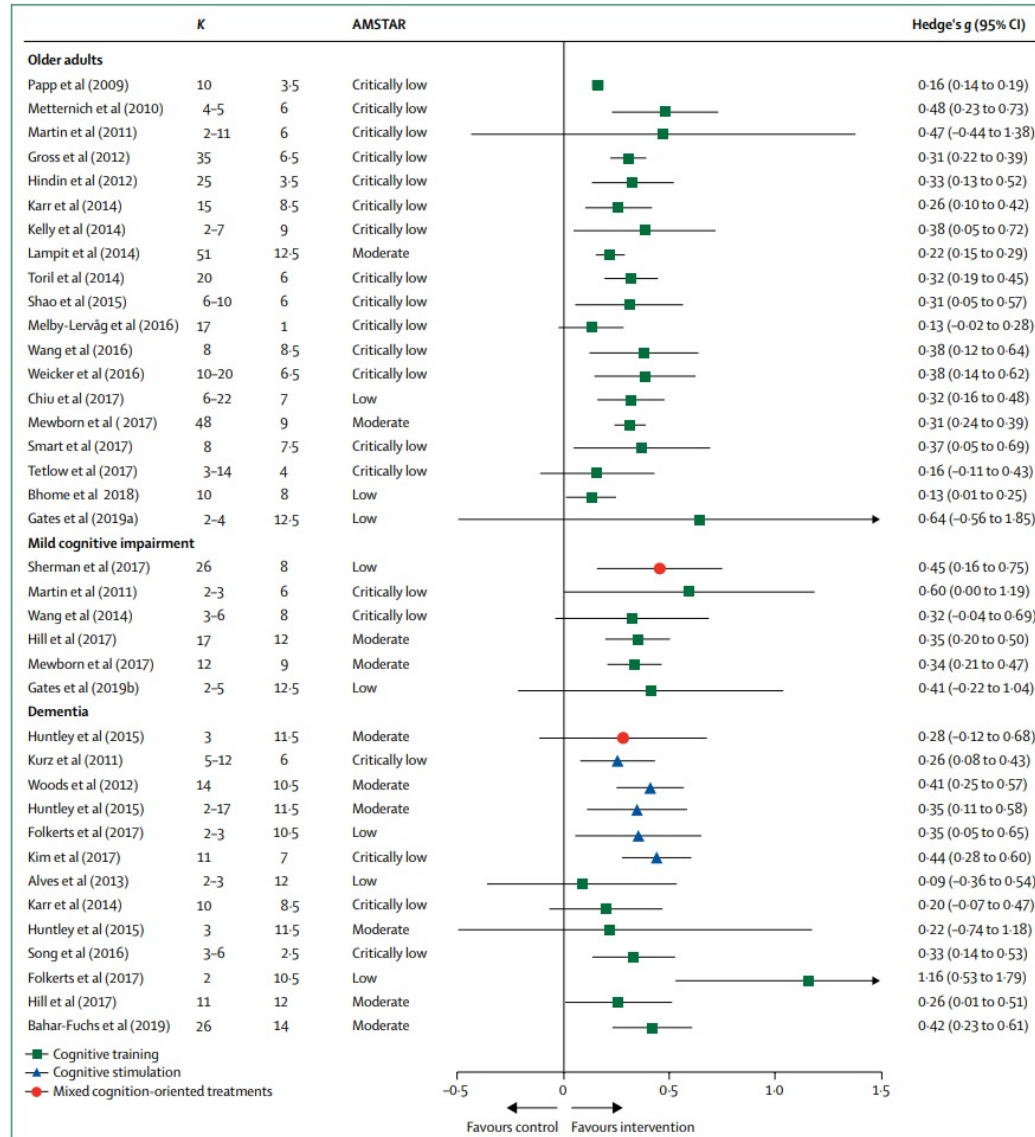


Figure 3: Pooled results of meta-analyses investigating objective cognitive outcomes of cognition-oriented treatment in older adults with and without cognitive impairment

K represents the number of primary trials included in the analysis. If a review reported several effect sizes within each outcome domain, a composite was created and k denotes the range of the number of primary trials that contributed to the effect estimate.

AMSTAR=A MeaSurement Tool to Assess systematic Reviews (max score 16).

Adapted from Gavelin et al.¹⁰ by permission of Springer Nature.

How to Implement

- Engaging in a variety of activities that challenge memory, language, spatial reasoning, attention, etc.
 - Tasks emphasizing processing speed may most helpful (Rebok et al, 2014, JAGS)
- The difficulty should be adjustable to gently but consistently push your skills (without being too frustrating or discouraging)
- Activities done as a group or with a partner
- Activities that involve new learning (i.e., a new card game, language, instrument, lecture series)
- At least a hour a day of things that keep your mind active, like reading, socializing, games
- Some pre-packaged, computerized programs include:
 - Posit Science / Brain HQ - <https://www.brainhq.com/>
 - Lumosity - <https://www.lumosity.com/>
 - AARP Brain Games - <https://stayingsharp.aarp.org/about/brain-health/games/>

Cognitive Rehabilitation

- Restitution vs. Compensation
- Internal vs External Strategies
 - Encoding
 - Mnemonic
 - Chaining (forward/backward)
 - Chunking
 - Errorless learning
 - Storage
 - PQIRST
 - Spaced retrieval
 - Retrieval
 - Cues/prompts
 - Recognition strategies



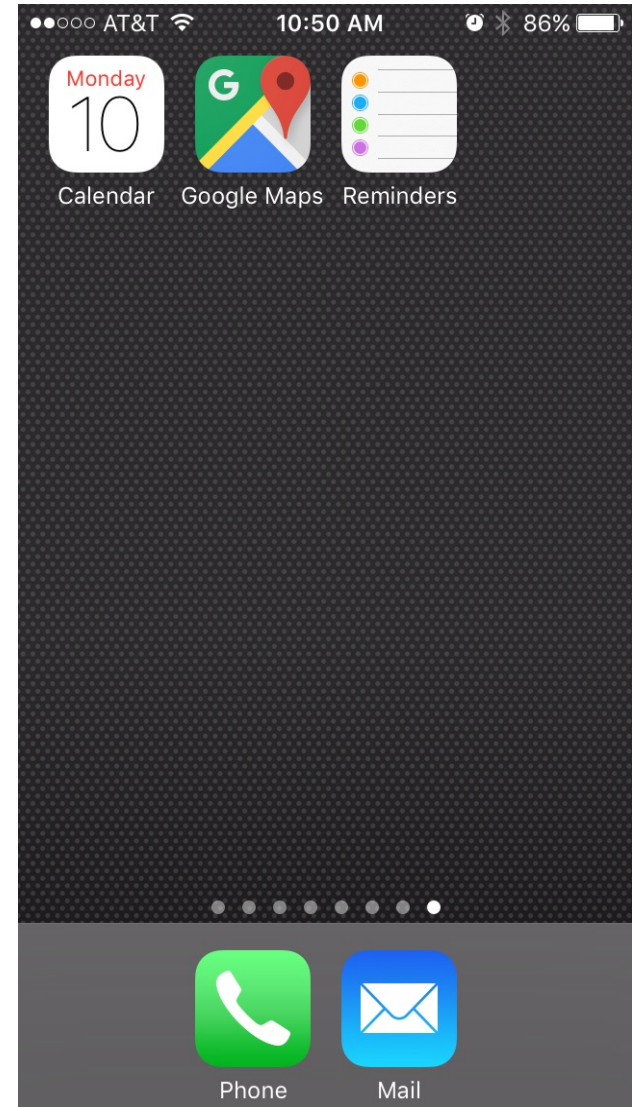
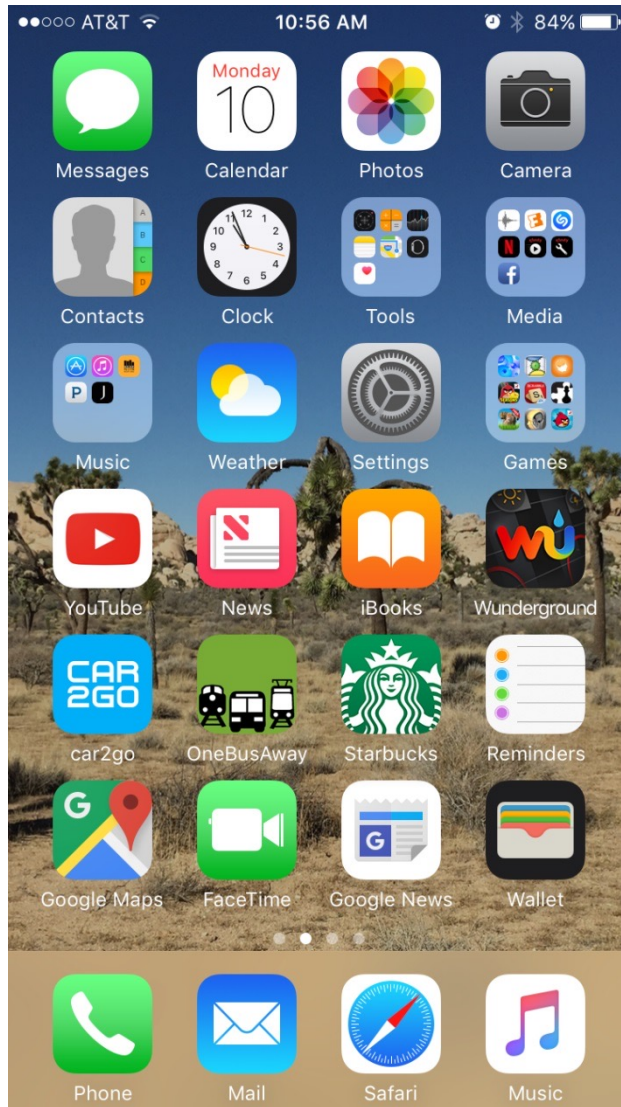
Memory Rehabilitation - Combined

— Compensatory System

- Mediset
- Pill reminders/alarms
- Tracking Sheet
- Incorporate other tools/techniques
 - Calendar
 - Errorless learning
 - Location of practice



Day of the Week	Sunday	Monday	Tuesday	Weds	Thursday	Friday	Saturday
Date							
AM Meds (time taken)							
Donepezil 10 mg							
Metformin 20 mg							
Rosuvastatin 5 mg							
PM Meds (time taken)							
Melatonin 3 mg							
Gabapentin 300 mg							
Sertraline 50 mg							



How to Implement

- Referral to SLP/cognitive rehabilitation/OT/therapist
- Critical importance of a care partner
 - Follow through
 - Carryover
 - Generalization/adaptation
- Capitalizing on previously used tools
- Shopping for the right version of the tool
- Recruit the family or friend tech support person
- Pick one area/intervention at a time
- Stress the importance of practice and need for time

Diet and Dementia Risk

Table 1. Medi/DASH/MIND dietary components and potential neuroprotective benefits.

Dietary Component	Vascular Protection	Anti-Inflammatory Protection	Antioxidant Protection	Neural Protection
Whole Grains [2,13,29,41–46]	X	X	X	X
Vegetables (MIND diet emphasizes leafy greens in addition to other vegetables) [2,29,39,41–47]	X	X	X	
Fruits (MIND diet emphasizes berries over other fruits) [2,29,39,41–47]	X	X	X	
Fatty Fish (e.g., salmon, tuna, sardines) [2,13,14,31,41,42]	X	X	X	X
Legumes/Beans [2,41,45,48]	X	X	X	X
Nuts [2,29,41,46,47]	X	X	X	X
Olive Oil (Medi, MIND diets) [33,49,50]		X	X	
Red Wine (Medi, MIND diets) [29,46,49,51–53]		X	X	

“X” indicates association with the neuroprotective benefit listed.

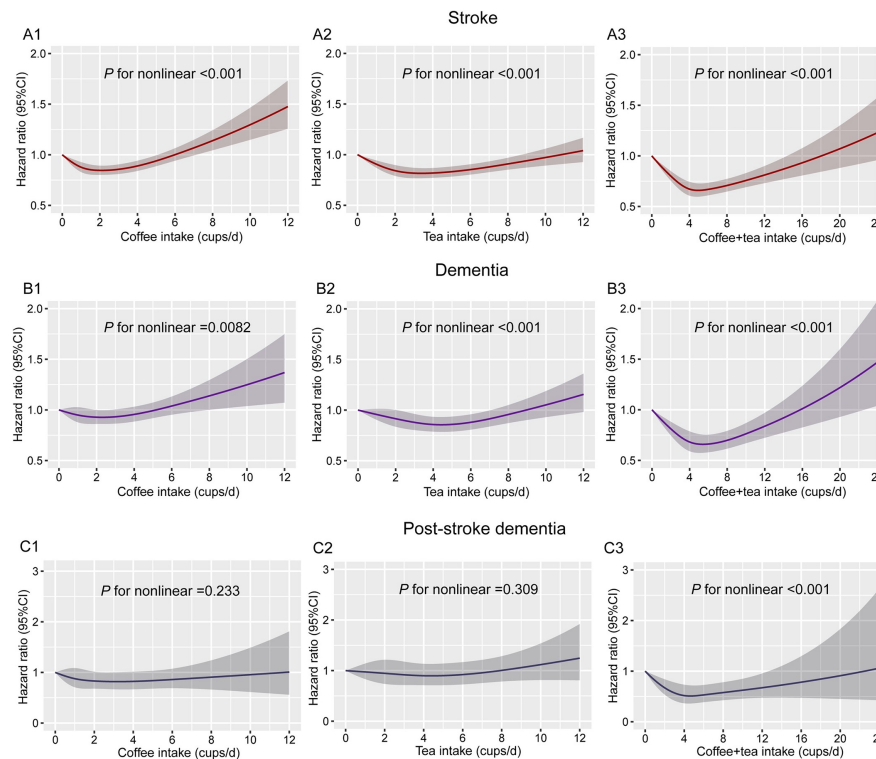
Diet and Dementia Risk

Table 2. Comparison of Mediterranean, DASH, and MIND dietary components. The components in bold are common across all three dietary patterns.

	Mediterranean [17,54,55]	DASH [56,57]	MIND [17]
HIGH AMOUNTS	Olive Oil (exclusive) Fish Grains (non-refined) Fruits Vegetables - Potatoes Legumes Beans Nuts Seeds -	- - Grains Fruits Vegetables - - Legumes - Nuts Seeds Low-fat dairy	- - Grains (whole) Berries Green leafy vegetables Other vegetables - - Beans Nuts - -
MODERATE AMOUNTS	Poultry - Alcohol - Full-fat dairy	Poultry Fish - - -	Poultry Fish Alcohol Olive oil (primary) -
SMALL AMOUNTS	Red meat Processed meat Sweets - -	Red meat - Sweets Saturated fat as a % of total fat Sodium <2400 mg/d	Red meat - Sweets/pastries - -
RESTRICTED	- - -	- - -	Cheese Butter/margarine Fast/fried foods

Caffeine Intake and Dementia Risk

- Prospective cohort study (N= 365,682) from the UK Biobank
- 50 to 74 years old
- Median follow-up of 11.4 years (5,079 w/dementia & 10,053 w/stroke)
- 2 to 3 cups
 - 32% lower risk of stroke (HR, 0.68, 95% CI, 0.59 to 0.79; $P < 0.001$)
 - 28% lower risk of dementia (HR, 0.72, 95% CI, 0.59 to 0.89; $P = 0.002$)
- 3 to 6 cups
 - lowest risk of poststroke dementia (HR, 0.52, 95% CI, 0.32 to 0.83; $P = 0.007$)

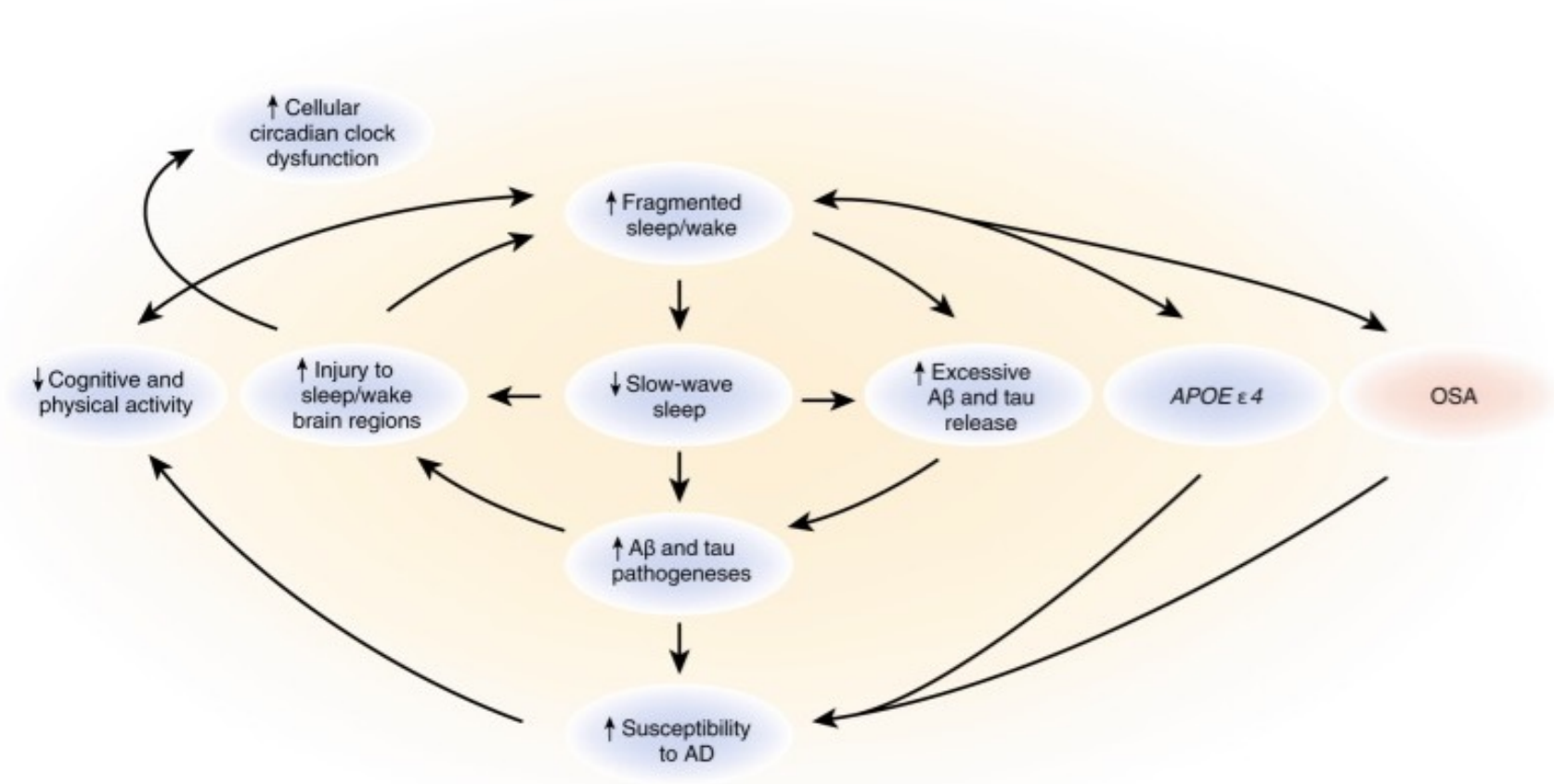


How to Implement

- Assess needs/preferences/willingness of others
 - Especially the grocery shopper
- Referral to dietician/nutritionist
- Consider incremental changes
- Harm reduction model
- Pre-packaged meals
- Consider different textures, spices, plate to food contrast
- Importance of routines, consistent table settings
- Consider involving company or family
- Offering limited choices
 - “Do you want broccoli or spinach?”

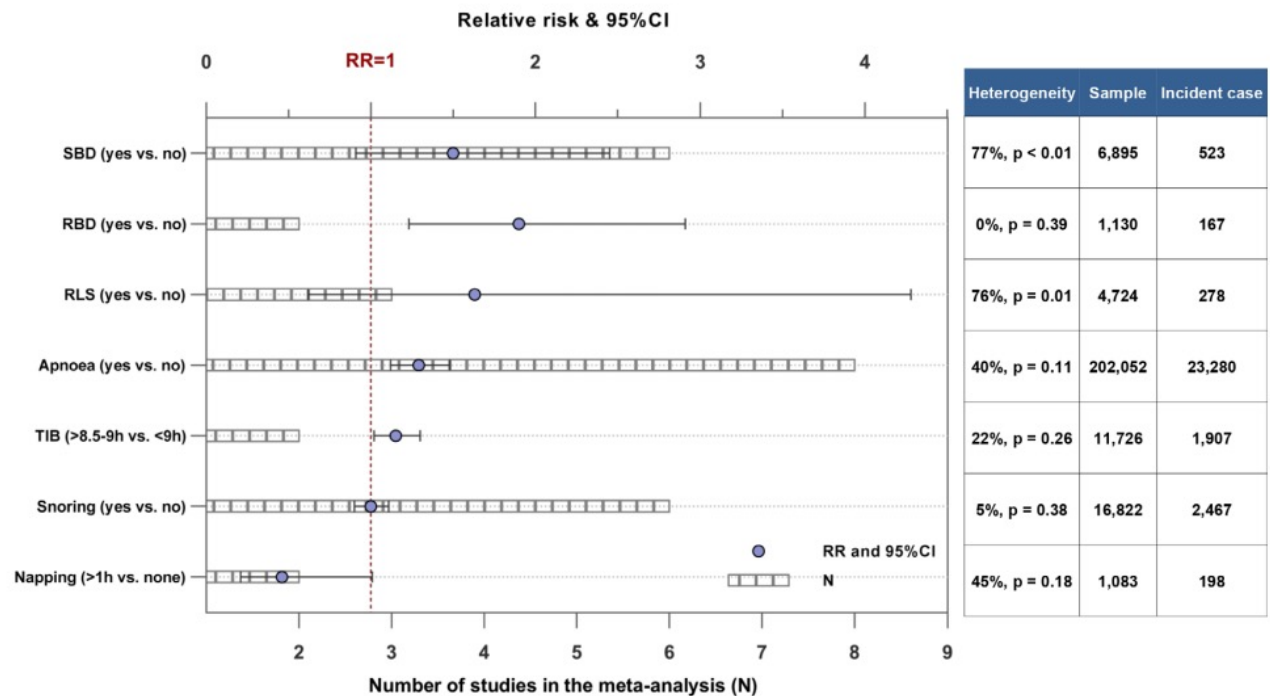
Sleep and Dementia Risk

- Bidirectional relationship between sleep and AD



Sleep and Dementia Risk

- Association between sleep-related problems and cognitive disorders
 - REM behavioral disorder
 - Sleep apnea
 - Longer time in bed
 - Habitual napping

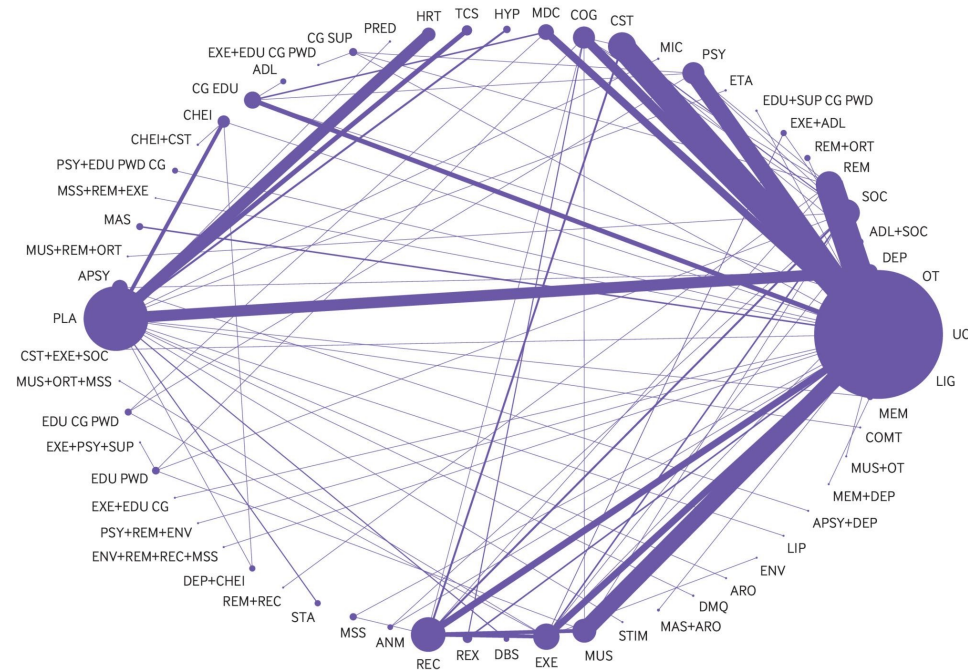


How to Implement

- Sleep hygiene/habits
 - Establish consistent sleep and wake times
 - Importance of a wind-down routine
 - Avoiding screens (30-45 min before bed)
 - Avoid caffeine and alcohol (4-6 hours before bed)
 - Exercise (earlier in the day)
 - Quiet, cool, dark room
 - Bedroom is for sleeping and sex only
 - Avoid or program naps
 - Avoid pets in the bed
 - Sleep restriction
- Referral for CBT-I
 - Associations with anxiety, depression, QOL
 - Effective in MCI, early stage dementia (Blackman et al., 2021; Jin et al., 2021)

Non-pharm Treatment of Depression in Dementia

- 61 interventions across 213 studies (N = 25,177)
- Mild to moderate dementia with and without MDD
- 10 interventions with high probability of a meaningful change
 - Exercise combined with social interaction and cognitive stimulation
 - Psychotherapy combined with reminiscence therapy and environmental modification
 - Cognitive stimulation and a cholinesterase inhibitor
 - Cognitive stimulation
 - Animal therapy
 - Reminiscence therapy
 - Exercise
 - Massage and touch therapy
 - Multidisciplinary care
 - Occupational therapy



Mindfulness Meditation and MCI

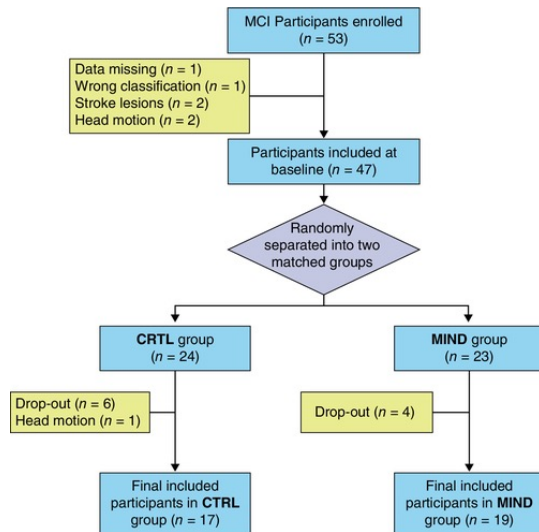
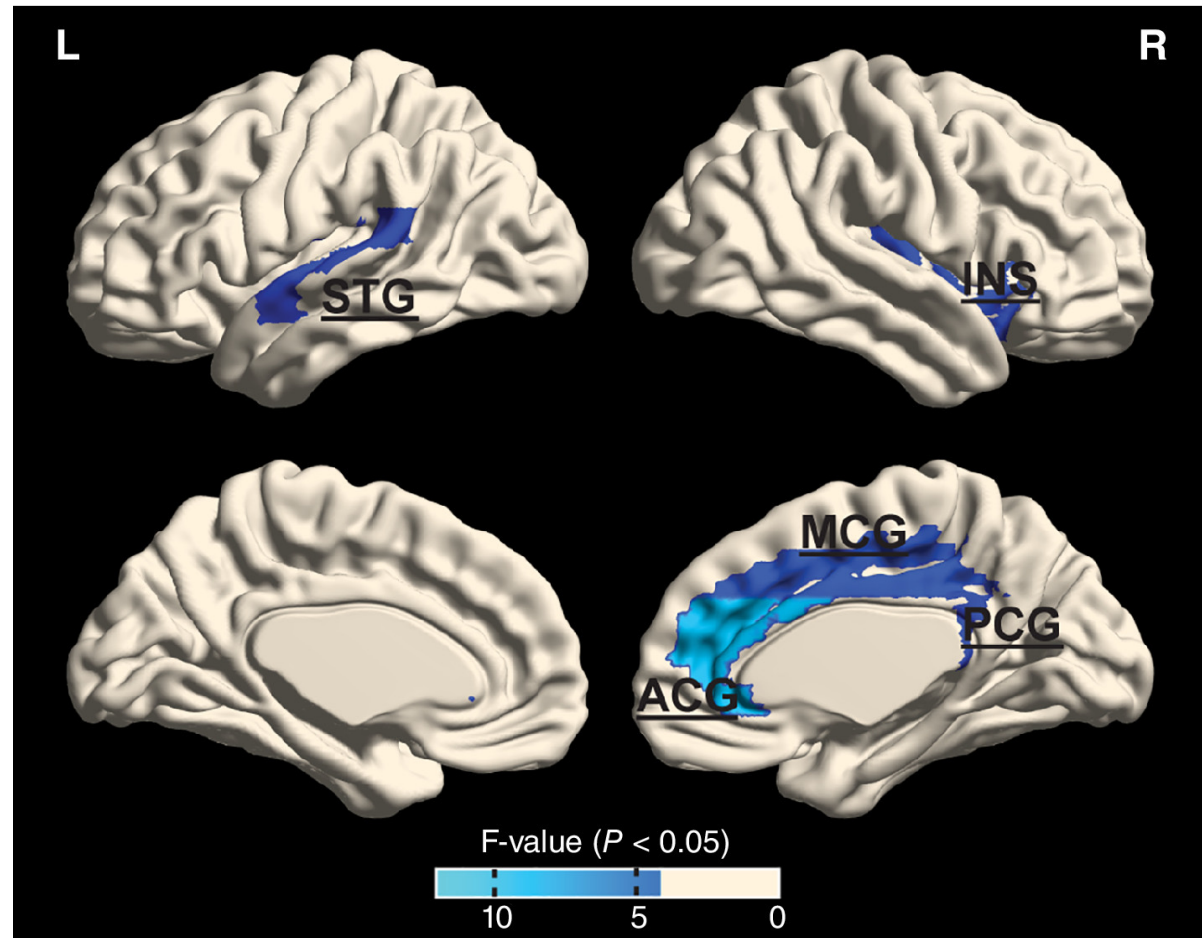


Table 2. Effects of mindfulness practice on the neurocognitive measures and temporal network metrics

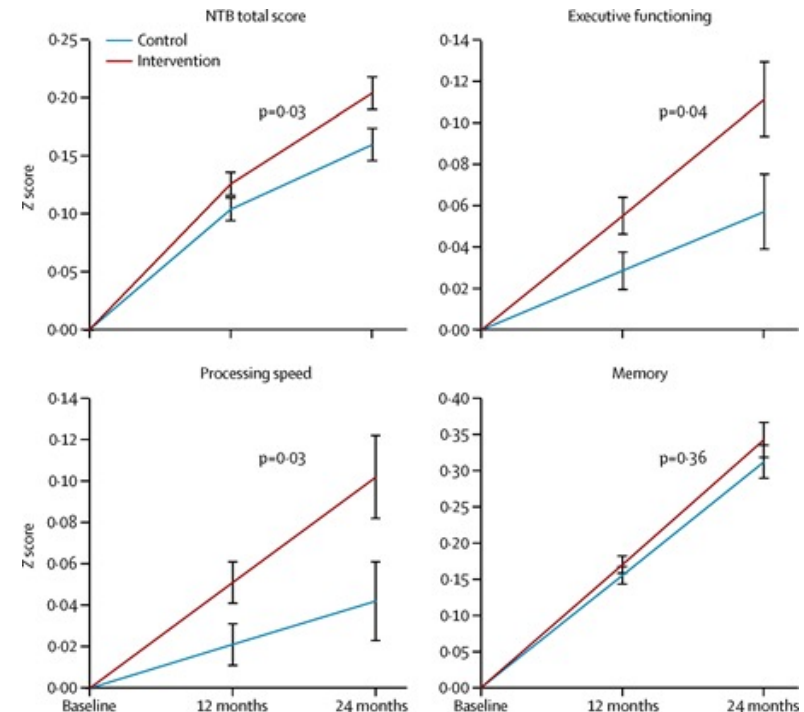
Metrics	Two-way repeated ANOVA		
	Group effect $F_{1, 34}$ (P -value)	Time effect $F_{1, 34}$ (P -value)	Interaction $F_{1, 34}$ (P -value)
Neurocognitive measures			
MMSE	0.925 (0.343)	0.006 (0.940)	0.090 (0.766)
RAVLT	5.938 (0.020) [‡]	17.092 (<0.001) [▲]	1.239 (0.273)
Delayed recall			
RAVLT	0.371 (0.546)	2.387 (0.132)	4.545 (0.040)
Recognition			
Block design	2.502 (0.123)	4.278 (0.046) [▲]	0.807 (0.375)
Temporal network metrics			
E_{gib}^T	3.401 (0.074)	0.001 (0.970)	6.429 (0.016)
E_{loc}^T	0.005 (0.953)	6.405 (0.016) [▲]	0.088 (0.768)

Note: Significant effects ($P < 0.05$) were highlighted by the bold text.
[‡] indicates MIND < CTRL; [▲] indicates Pre- < Post-intervention.



Multimodal Interventions

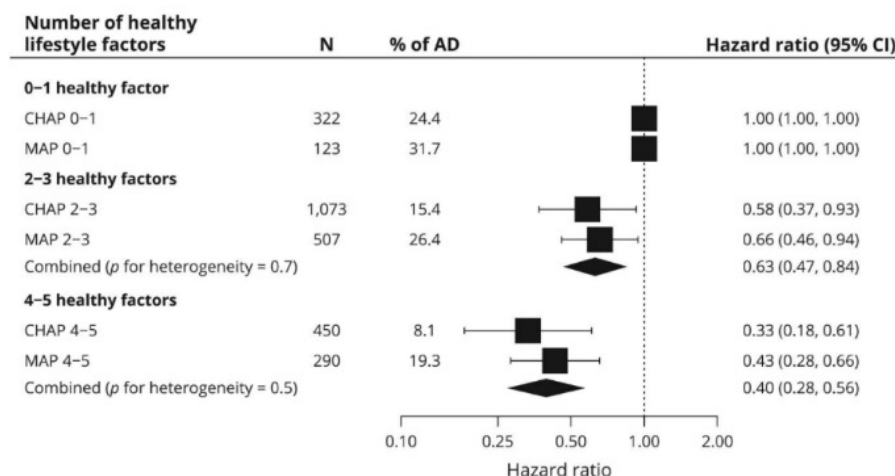
- FINGER
- 1260 people for 2 years
 - Nutritional guidance, exercise
 - Cognitive training/social activities
 - Improvement of metabolic/vascular RF
 - Control group: 13 pep talks
- Adherence: 12% dropout rate
- Results: All 3 cog domains improved over placebo: global, executive function, processing speed ($p < 0.05$)
 - Those >70 , or with MMSE <26 improved more



Multimodal Interventions

- Combining multiple healthy lifestyle factors may be more impactful for reducing dementia risk
 - Healthy diet
 - Moderate to vigorous physical activity
 - Light to moderate alcohol intake
 - Smoking
 - Cognitive stimulation
- 4 or 5 = 59% lower risk
- 2 or 3 = 39% lower risk
- May offset genetic risk

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* ϵ 4, 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.

Healthy Action to Benefit Independence and Thinking HABIT (Mayo Clinic)

- 10 day brain camp for individuals with MCI, and study partner
 - amnesic MCI (additional cognitive domains okay)
 - 272 dyads
 - Age: M=75, SD = 8
 - Male 58.8%
- 5 components (suppression design)
 - physical activity (yoga)
 - brain fitness
 - memory compensation training
 - support group
 - wellness education
- 6 month booster session
- Aim: delay or prevent progression to dementia

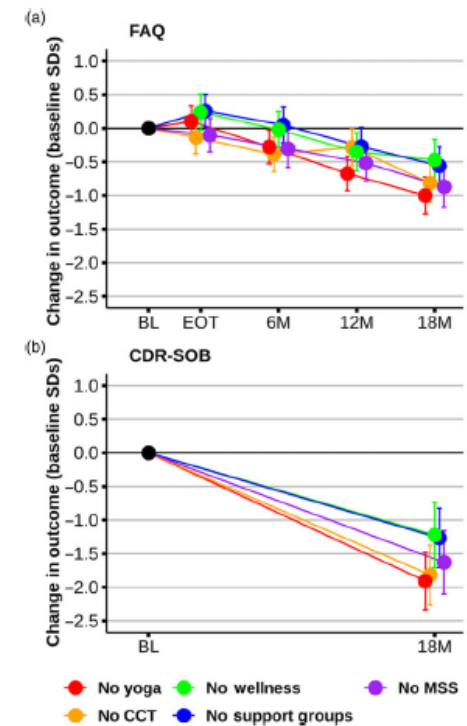


Figure 1. Effect sizes by study arm.

ADAPT Program

- Applied Daily Activities to Promote Thinking
- Six sessions, taper design
- Multimodal treatment
 - Exercise
 - Meditation
 - Support groups
 - Cognitive rehabilitation
 - Education

Time	Activity
8:45 – 9 AM	Arrival, Check-In
9 – 9:15 AM	Welcome Mindfulness Meditation
9:15 – 10:15 AM	Staying in Motion
10:15 – 11:15 AM	Calendar Training
11:15 - 12:15 AM	Support Groups
12:15 – 12:30 PM	Mindfulness Meditation Closing

ADAPT Calendar Training

Home System



Personal System (Pencil and Paper or Electronic)

Programs and Services

- Support groups/educational events
- Dementia Friendly Communities
- Momentia
 - Zoo/Garden walks
 - Alzheimer's cafes
 - Arts events
- Dementia Friends
- Intergenerational programs



Socialization and Community Engagement



UW Memory and Brain Wellness Center Memory Hub

- Outreach center in partnership with Frye Art Museum
 - Dementia-Friendly Community, Collaboration, and Statewide Impact



Resources

- WHO Dementia Risk Reduction Guidelines
 - <https://www.who.int/publications/i/item/9789241550543>
- Alzheimer's Association
 - Taking Action workbook:
http://www.alz.org/mnnd/documents/15_ALZ_Taking_Action_Workbook.pdf
 - Living Well workbook:
http://www.alz.org/mnnd/documents/15_ALZ_Living_Well_Workbook_Web.pdf
- Mindfulness Northwest
 - <http://www.mindfulnessnorthwest.com/>
- Momentia Seattle
 - www.momentiasseattle.org
- UW Memory Hub
 - <https://https://thememoryhub.org/>

Contact Information

Memory and Brain Wellness Center

<https://depts.washington.edu/mbwc/>

Harborview Medical Center

325 9th Ave., 3rd Floor West Clinic

Seattle, WA 98104

Phone 206-744-3045

Fax 206-744-5030

krhoads@uw.edu

UW Medicine

HARBORVIEW
MEDICAL CENTER





Thank you for your attention!



Questions?

References/Resources

- Blackman J, Swirski M, Clynes J, Harding S, Leng Y, Coulthard E. Pharmacological and non-pharmacological interventions to enhance sleep in mild cognitive impairment and mild Alzheimer's disease: A systematic review. *J Sleep Res.* 2021 Aug;30(4):e13229. doi: 10.1111/jsr.13229. Epub 2020 Dec 2. PMID: 33289311; PMCID: PMC8365694.
- de Almeida SIL, Gomes da Silva M, Marques ASPD. Home-Based Physical Activity Programs for People With Dementia: Systematic Review and Meta-Analysis. *Gerontologist.* 2020 Nov 23;60(8):600-608.
- Dhana K, Evans DA, Rajan KB, Bennett DA, Morris MC. Healthy lifestyle and the risk of Alzheimer dementia: Findings from 2 longitudinal studies. *Neurology.* 2020 Jul 28;95(4):e374-e383.
- Duplantier SC, Gardner CD. A Critical Review of the Study of Neuroprotective Diets to Reduce Cognitive Decline. *Nutrients.* 2021 Jun 30;13(7):2264.
- Fam J, Sun Y, Qi P, Lau RC, Feng L, Kua EH, Mahendran R. Mindfulness practice alters brain connectivity in community-living elders with mild cognitive impairment. *Psychiatry Clin Neurosci.* 2020 Apr;74(4):257-262.
- Hughes D, Judge C, Murphy R, et al. Association of Blood Pressure Lowering With Incident Dementia or Cognitive Impairment: A Systematic Review and Meta-analysis. *JAMA.* 2020;323(19):1934–1944.
- Jin JW, Nowakowski S, Taylor A, Medina LD, Kunik ME. Cognitive Behavioral Therapy for Mood and Insomnia in Persons With Dementia: A Systematic Review. *Alzheimer Dis Assoc Disord.* 2021 Oct-Dec 01;35(4):366-373.
- Lai CH, Chen HC, Liou TH, Li W, Chen SC. Exercise Interventions for Individuals With Neurological Disorders: A Systematic Review of Systematic Reviews. *Am J Phys Med Rehabil.* 2019 Oct;98(10):921-930.
- Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C, Burns A, Cohen-Mansfield J, Cooper C, Costafreda SG, Dias A, Fox N, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Ogunniyi A, Orgeta V, Ritchie K, Rockwood K, Sampson EL, Samus Q, Schneider LS, Selbæk G, Teri L, Mukadam N. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet.* 2020 Aug 8;396(10248):413-446.
- Marciniak, R., Sheardova, K., Cermáková, P., Hudeček, D., Sumec, R., & Hort, J. (2014). Effect of meditation on cognitive functions in context of aging and neurodegenerative diseases. *Frontiers in behavioral neuroscience*, 8, 17.
- Newberg et al., (2010). Meditation effects on cognitive function and cerebral blood flow in subjects with memory loss: a preliminary study. *J. Alzheimers Dis.* 2010. 20, 517–526.
- Ngandu T, Lehtisalo J, Solomon A, Levälahti E, Ahtiluoto S, Antikainen R, Bäckman L, Hänninen T, Jula A, Laatikainen T, Lindström J, Mangialasche F, Pajananen T, Pajala S, Peltonen M, Rauramaa R, Stigsdotter-Neely A, Strandberg T, Tuomilehto J, Soininen H, Kivipelto M. 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. *Lancet.* 2015 Jun 6;385(9984):2255-63.

References/Resources

- O'Caoimh R, Mannion H, Sezgin D, O'Donovan MR, Liew A, Molloy DW. Non-pharmacological treatments for sleep disturbance in mild cognitive impairment and dementia: A systematic review and meta-analysis. *Maturitas*. 2019 Sep;127:82-94.
- SPRINT MIND Investigators for the SPRINT Research Group, Williamson JD, Pajewski NM, Auchus AP, Bryan RN, Chelune G, Cheung AK, Cleveland ML, Coker LH, Crowe MG, Cushman WC, Cutler JA, Davatzikos C, Desiderio L, Erus G, Fine LJ, Gaussoin SA, Harris D, Hsieh MK, Johnson KC, Kimmel PL, Tamura MK, Launer LJ, Lerner AJ, Lewis CE, Martindale-Adams J, Moy CS, Nasrallah IM, Nichols LO, Oparil S, Ogrocki PK, Rahman M, Rapp SR, Reboussin DM, Rocco MV, Sachs BC, Sink KM, Still CH, Supiano MA, Snyder JK, Wadley VG, Walker J, Weiner DE, Whelton PK, Wilson VM, Woolard N, Wright JT Jr, Wright CB. Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial. *JAMA*. 2019 Feb 12;321(6):553-561.
- Wang, X., Wang, H., Ye, Z., Ding, G., Li, F., Ma, J., & Hua, W. (2020). The neurocognitive and BDNF changes of multicomponent exercise for community-dwelling older adults with mild cognitive impairment or dementia: a systematic review and meta-analysis. *Aging*, 12(6), 4907–4917.
- Watt JA, Goodarzi Z, Veroniki AA, Nincic V, Khan PA, Ghassemi M, Lai Y, Treister V, Thompson Y, Schneider R, Tricco AC, Straus SE. Comparative efficacy of interventions for reducing symptoms of depression in people with dementia: systematic review and network meta-analysis. *BMJ*. 2021 Mar 24;372:n532.
- WHO. Risk reduction of cognitive decline and dementia: WHO guidelines. Geneva: World Health Organization, 2019
- Wilckens KA, Stillman CM, Waiwood AM, Kang C, Leckie RL, Peven JC, Foust JE, Fraundorf SH, Erickson KI. Exercise interventions preserve hippocampal volume: A meta-analysis. *Hippocampus*. 2021 Mar;31(3):335-347.
- Xu W, Tan CC, Zou JJ, Cao XP, Tan L. Sleep problems and risk of all-cause cognitive decline or dementia: an updated systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2020 Mar;91(3):236-244.
- Zhang Y, Yang H, Li S, Li WD, Wang Y. Consumption of coffee and tea and risk of developing stroke, dementia, and poststroke dementia: A cohort study in the UK Biobank. *PLoS Med*. 2021 Nov 16;18(11):e1003830.