Non-pharmacological Treatment of MCI and Dementia

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UW Project ECHO Dementia May 10th, 2024

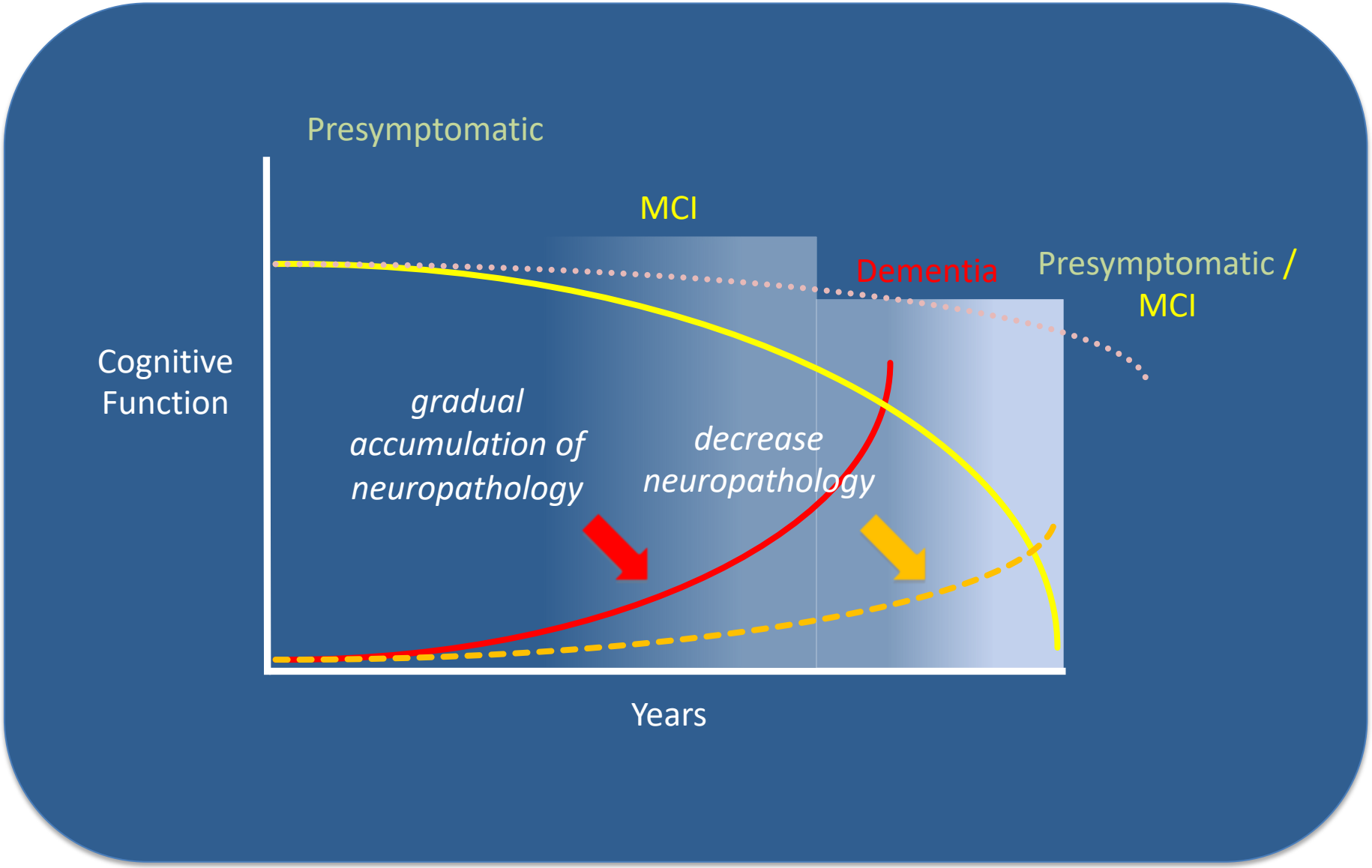
Objectives

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.

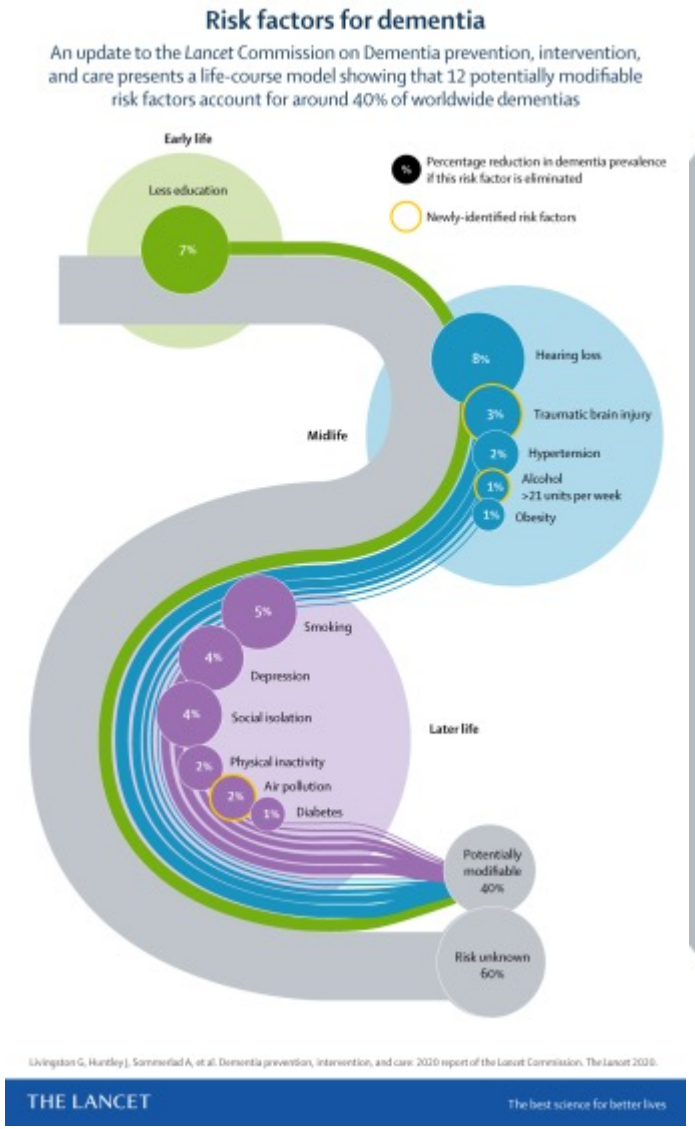
Treatment Targets

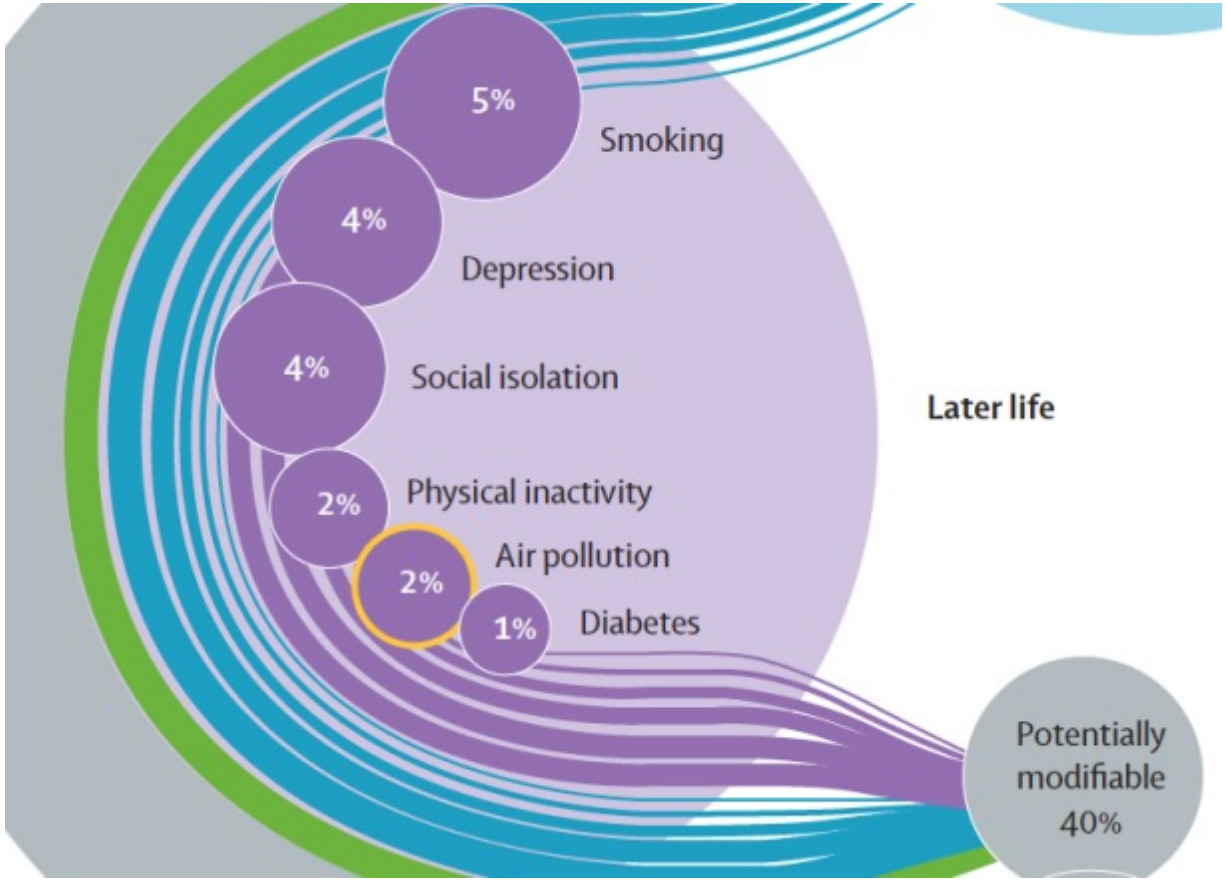


Prevention and Non-Pharmacological Interventions

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

Lancet Commission 2020 Update

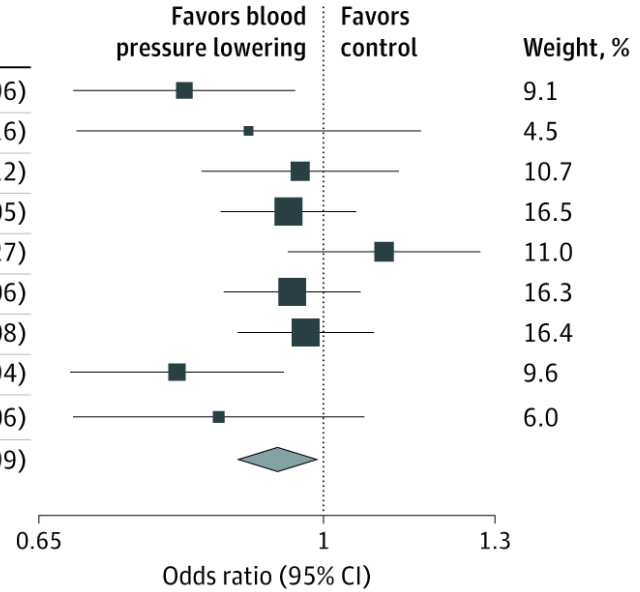




Livingston et al., 2020, Lancet

Midlife Risk Factor Modification - Hypertension

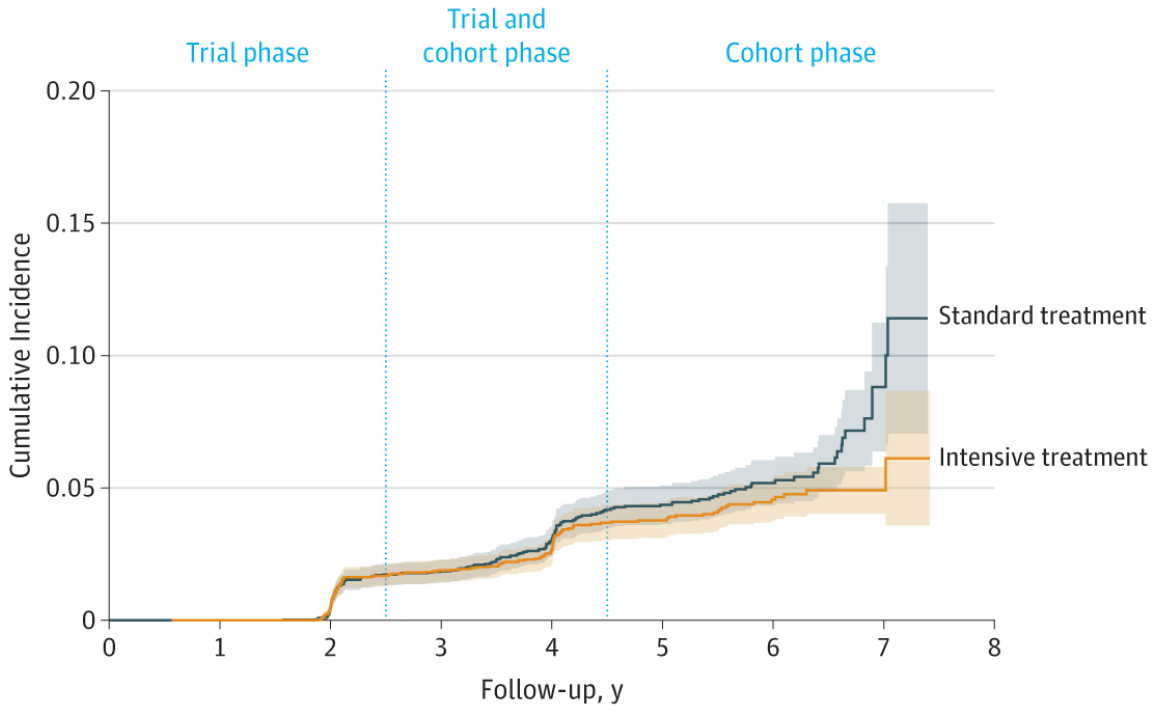
Study	Participants with dementia or cognitive impairment/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)
	Blood pressure lowering group	Control group		
PROGRESS,[23] 2003	276/3051	334/3054	1.89 (0.39 to 3.39)	0.81 (0.68 to 0.96)
SCOPE,[24] 2003	113/2477	125/2460	0.52 (-0.68 to 1.71)	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: $z = -2.28$; $P = .02$ Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 12.60$; $P = .13$; $I^2 = 36.1\%$			0.71 (0.19 to 1.2)	0.93 (0.88 to 0.99)



Hughes, et al. 2020, JAMA

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

SPRINT MIND, JAMA. 2019, 2021

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

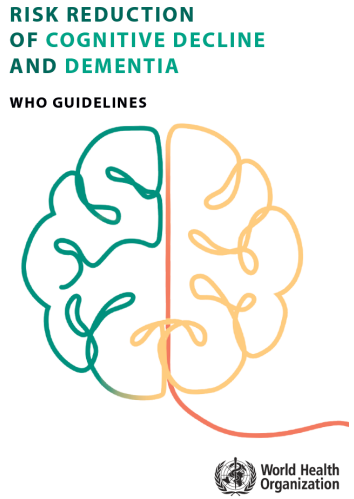
- Pooled effects highest for delaying onset>MCI>dementia
  - Group > individual
  - Across settings, including home-based (de Almeida, 2020, Gerontologist)

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

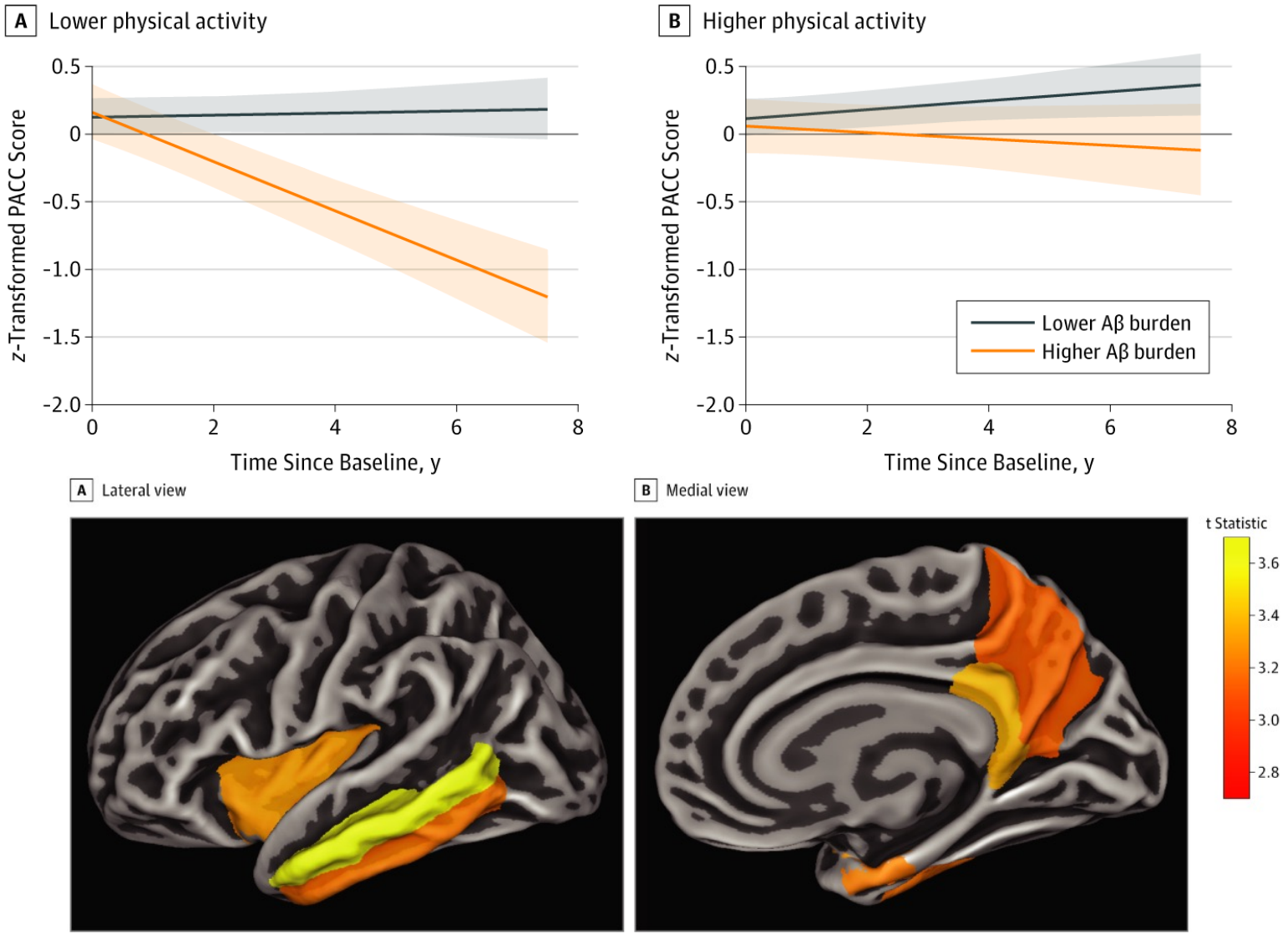
- May be recommended to adults with MCI to reduce the risk of cognitive decline.
  - Quality of evidence: low
  - Strength of the recommendation: conditional

- 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



World Health Organization, 2019

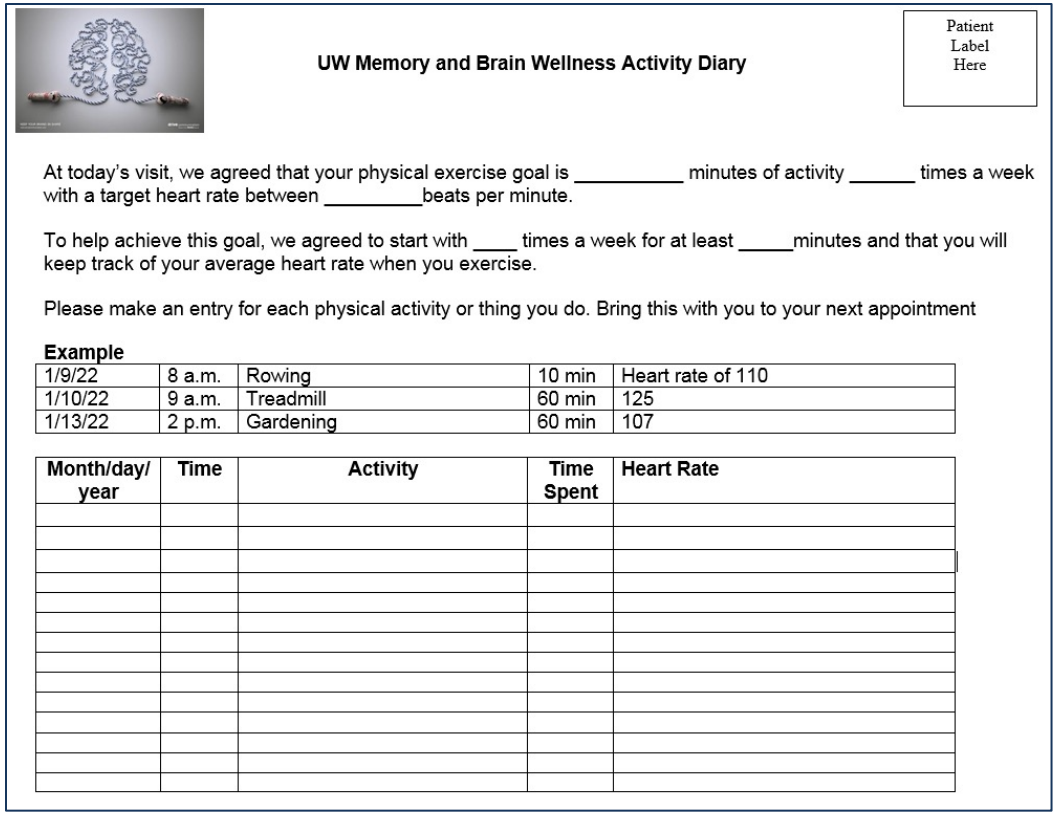
Physical Activity Moderates Aβ Associated Cognitive Decline and Cortical Thinning



Rabin et al., 2019, JAMA Neurol

How to Implement

- Help with scheduling and structure
- Create accountability
  - Classes
  - Exercise partner(s)
  - PT/Trainer
  - Exercise Diaries
  - FitBit/exercise trackers
  - Check in calls
- Program for variability and engagement
- Graduated, well-paced incremental increases
- Motivational interviewing/enhancement



UW Memory and Brain Wellness Activity Diary

Patient Label Here

At today's visit, we agreed that your physical exercise goal is _____ minutes of activity _____ times a week with a target heart rate between _____beats per minute.

To help achieve this goal, we agreed to start with ____ times a week for at least _____minutes and that you will keep track of your average heart rate when you exercise.

Please make an entry for each physical activity or thing you do. Bring this with you to your next appointment

Example

1/9/22	8 a.m.	Rowing	10 min	Heart rate of 110
1/10/22	9 a.m.	Treadmill	60 min	125
1/13/22	2 p.m.	Gardening	60 min	107

Month/day/ year	Time	Activity	Time Spent	Heart Rate

Cognitive Training and Stimulation

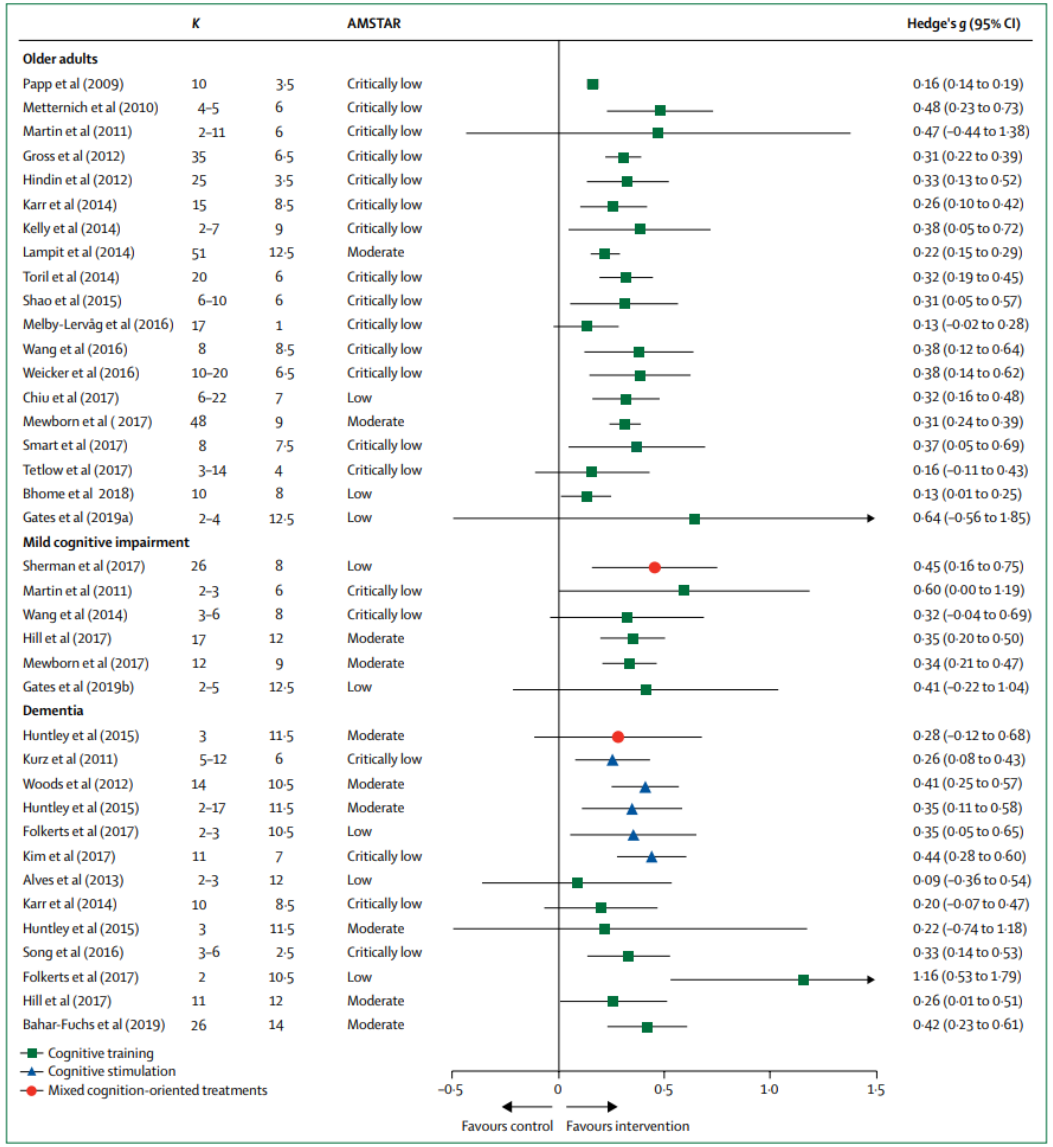


***Figure 3*: Pooled results of meta-analyses investigating objective cognitive outcomes of cognition-oriented treatment in older adults with and without cognitive impairment**
K represents the number of primary trials included in the analysis. If a review reported several effect sizes within each outcome 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,[51] by permission of Springer Nature.

Livingston et al., 2020, Lancet

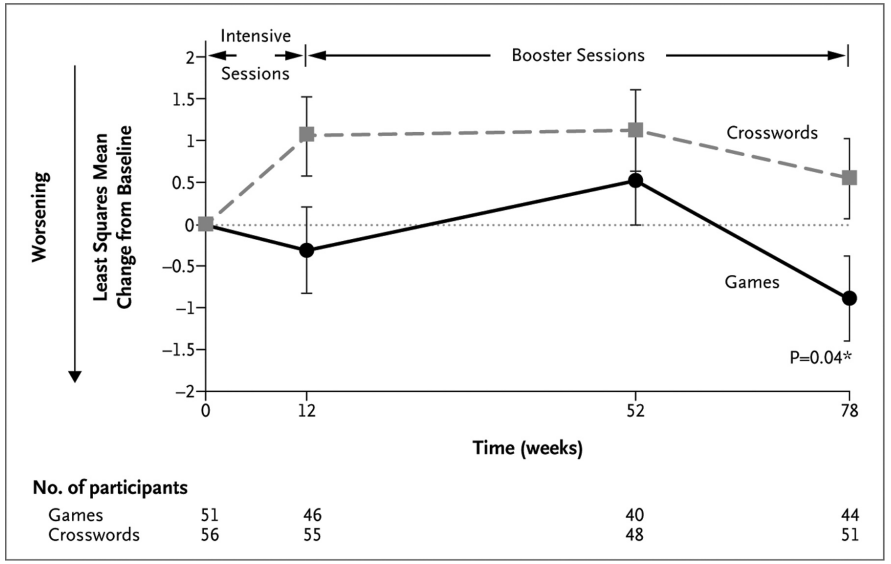
How to Implement

- 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 brain games 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/

Crossword Study

NEJM Evid 2022 Dec;1(12):10

- Participants: 107 participants with MCI
- Intervention: 78 weeks of Lumosity games or crossword puzzles
  - 12 weeks training + 6 booster sessions
- Results:
  - Cognition worsened slightly for games and improved for crosswords at week 78
  - Functional Activities Questionnaire score worsened more with games than crosswords
  - Crossword group had less hippocampal atrophy



Cognitive Rehabilitation

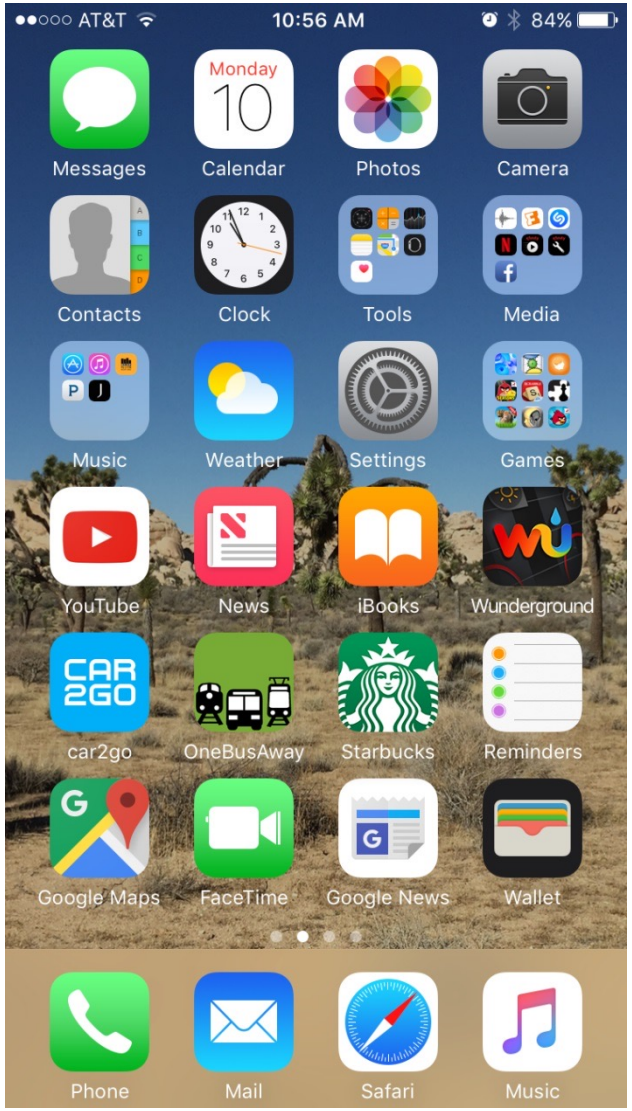
- Restitution vs. Compensation

- Internal vs External Strategies
  - Encoding
    - Mnemonic
    - Chaining (forward/backward)
    - Chunking
    - Errorless learning
  - Storage
    - PQRST
    - 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 / Date	Sunday	Monday	Tuesday	Weds	Thursday	Friday	Saturday
AM Meds (time taken)							
Donepezil 10 mg							
Metformin 20 mg							
Rousvastatin 5 mg							
PM Meds (time taken)							
Melatonin 3 mg							
Gabapentin 300 mg							
Sertraline 50 mg							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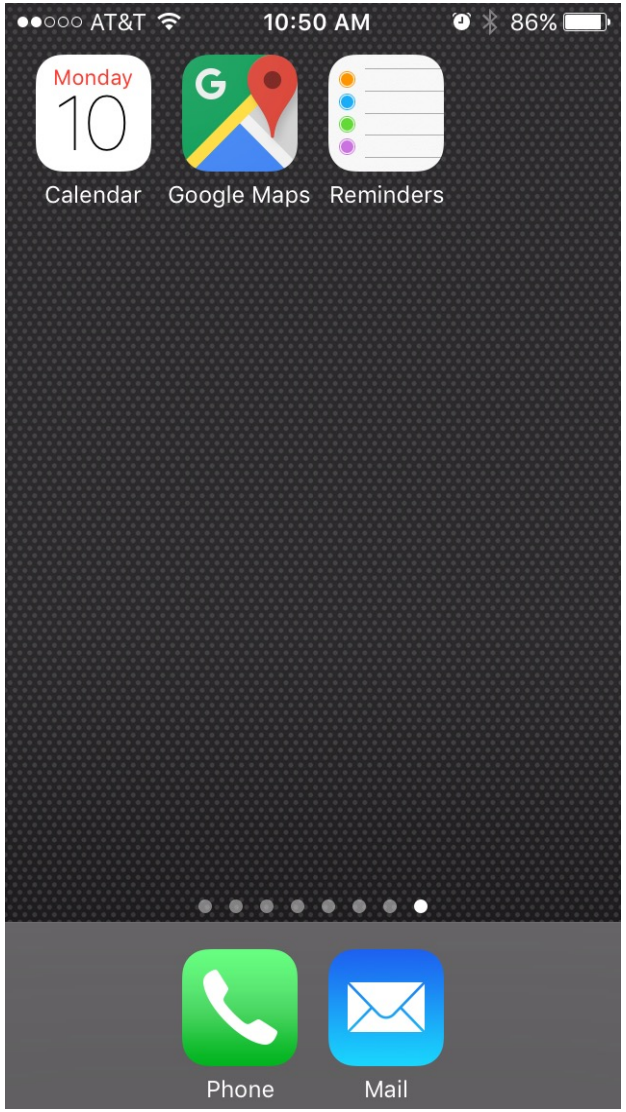
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Meditation and the Brain

Study	Intervention	*n*	Mean age ± SD	Experience with meditation	Loci with increased cortical thickness	Interpretation
Lazar et al. (2005)	Various	20	38.2	9.1 ± 7.1 years, 6.2 ± 4 h per week	Anterior insula, parts of frontal lobe, auditory cortex in temporal lobe	Somato-sensory, auditory, and interceptive processes
Pagnoni and Cekic (2007)	Zen	13	37.2 ± 6.9	>3 years per day	Putamen	Attention
Holzel et al. (2008)	Vipassana	20	34.1 ± 4.7	8.6 years, 2 h daily	Anterior insula, right hippocampus, left inferior temporal gyrus	Anterior insula – awareness of internal experience
Vestergaard-Poulsen et al. (2009)	Tibetan buddhism	10	55 ± 6.2	16.5 ± 5.1 years	Medulla oblongata, anterior cerebellum, superior, and inferior frontal gyrus	Breath control, resistance to stress, attention, calmness
Luders et al. (2009)	Various	22	53 ± 11.5	24 ± 12 years	Orbito-frontal cortex, right talamus, left inferior temporal gyrus	Regulation of emotions and sensory functions
Grant et al. (2010)	Zen	17	37.6 ± 10.9	>1000 h	Anterior cingulate cortex, secondary somato-sensory cortex	Anterior cingulate cortex – adaptive control of behavior
Holzel et al. (2011)	MBSR	16	39 ± 4	0	Left hippocampus, posterior cingulate cortex, temporo-parietal junction, cerebellum	Learning, memory, regulation of emotions, empathy
Luders et al. (2013b)	Various	50	51.4 ± 12.8	20 years	Hippocampus, especially subiculum	Subiculum – regulation of stress
Grant et al. (2013)	Zen	18	37.1 ± 10.9	>1000 h	Cingulo-fronto-parietal network	Attention

n, number of subjects, SD, standard deviation, MBSR, mindfulness-based stress reduction, IBMT, integrative body mind training.

Marciniak et al., 2014

Mindfulness Meditation and MCI

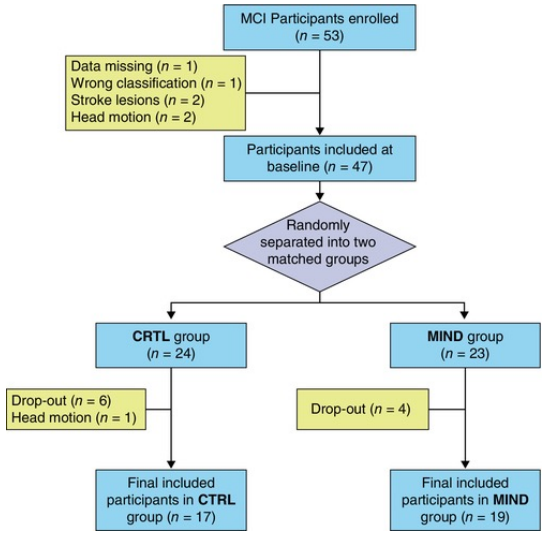
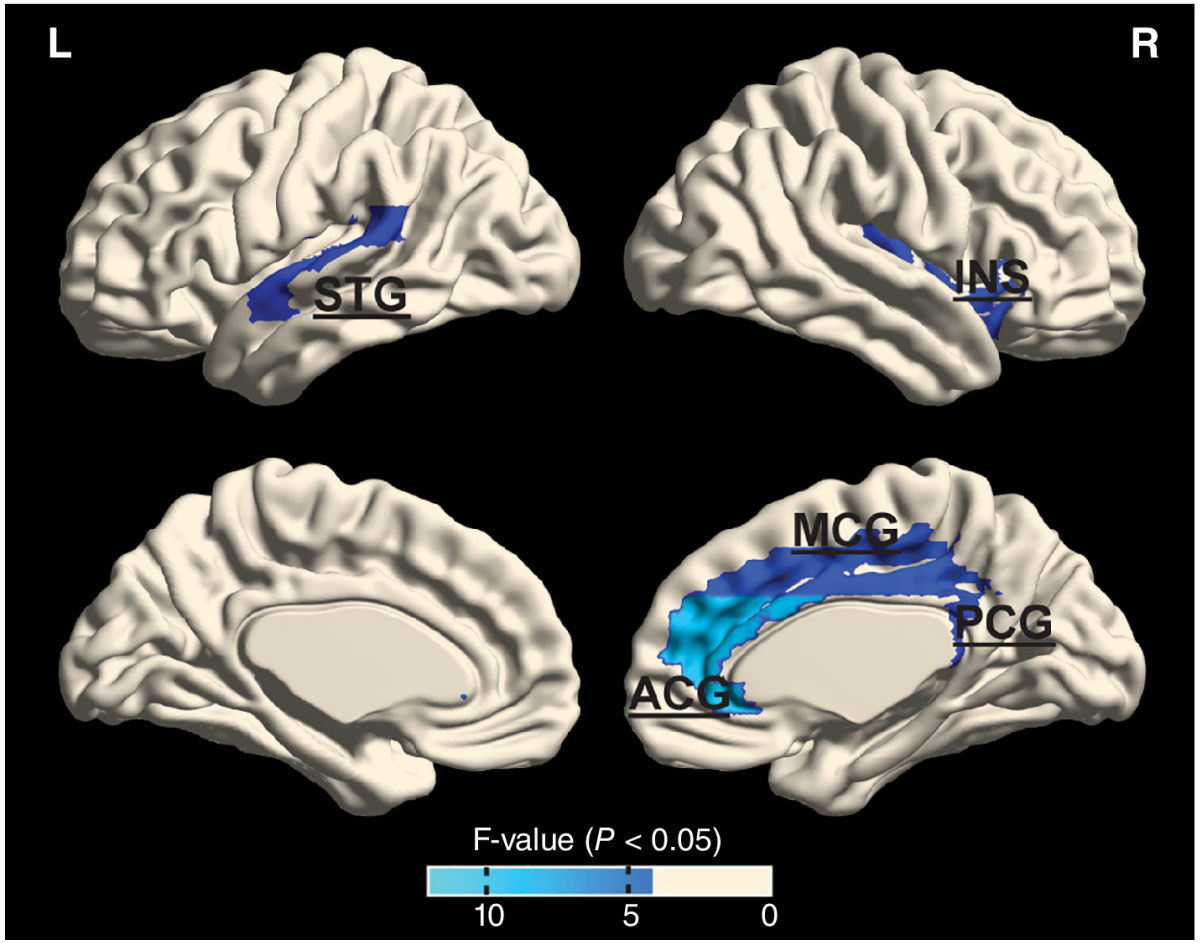


Table 2. Effects of mindfulness practice on the neurocognitive measures and temporal network metrics

	Two-way repeated ANOVA		
Metrics	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 Recognition	0.371 (0.546)	2.387 (0.132)	**4.545 (0.040)**
Block design	2.502 (0.123)	**4.278 (0.046)** ▲	0.807 (0.375)
Temporal network metrics			
E^f_{glb}	3.401 (0.074)	0.001 (0.970)	**6.429 (0.016)**
E^f_{loc}	0.005 (0.953)	**6.405 (0.016)** ▲	0.088 (0.768)

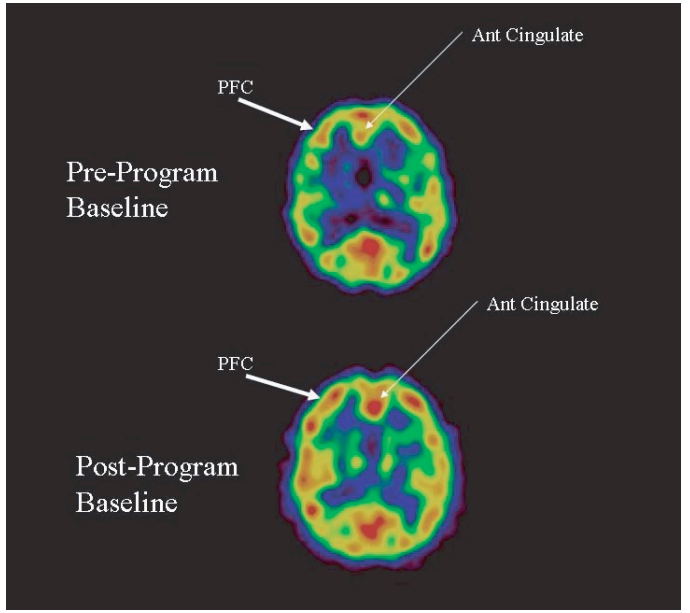
Note: Significant effects ($P < 0.05$) were highlighted by the bold text. ↓ indicates MIND < CTRL; ▲ indicates Pre- < Post-intervention.



Fam, et al, 2020, Psychiatry Clin Neurosci

Meditation and Alzheimer's

- 8 week meditation program
  - Relaxation (music) control
- Sample size = 15
  - Normal control (7)
  - MCI (5)
  - AD (3)



- Improved blood flow to the brain
  - Prefrontal and auditory cortex
- Reduced blood flow to the parietal lobes
- Improved cognition
  - Verbal fluency, divided/working attention, declarative memory

Newberg et al., 2010, J. Alzheimers Dis.

Diet and Dementia Risk

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]

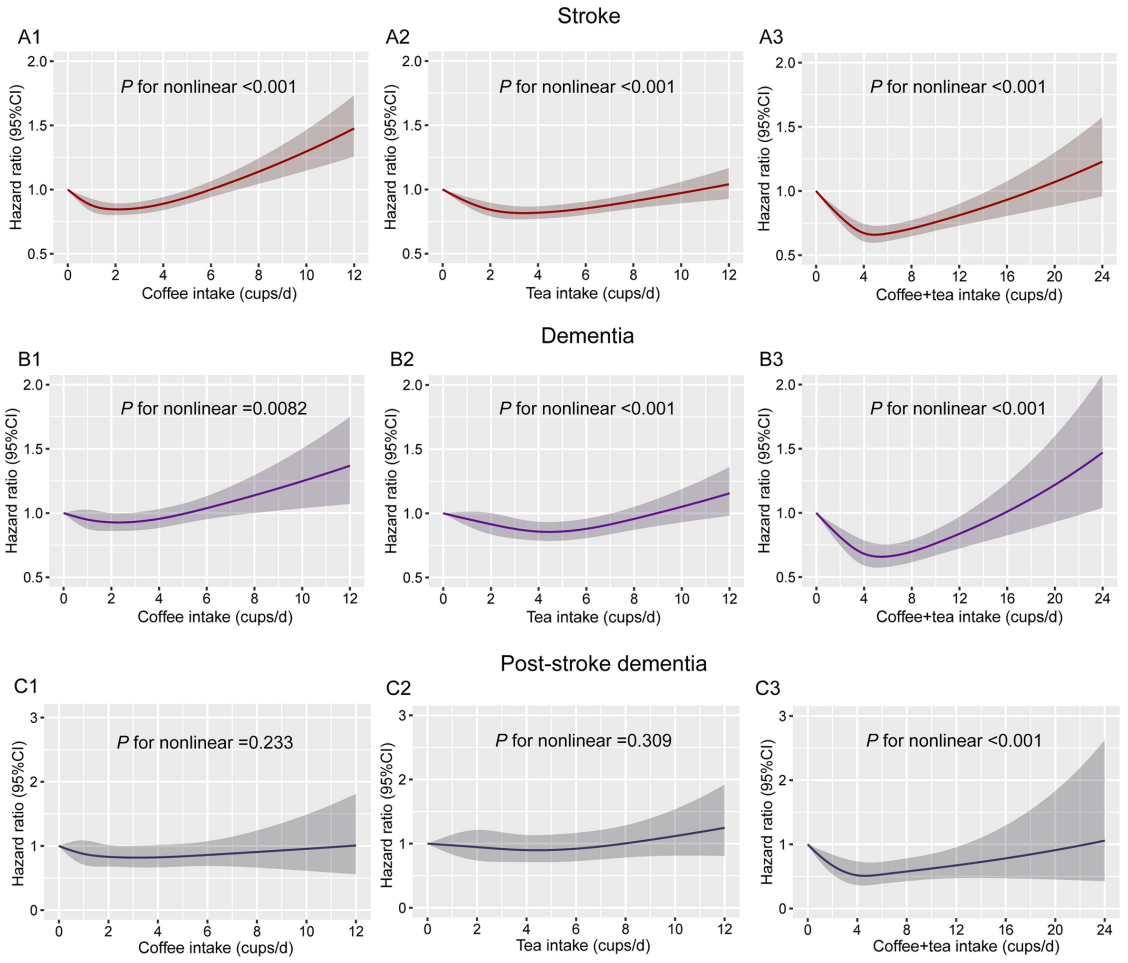
- N = 923
- Age 58-98
- 4.5 years

- DASH + Mediterranean
  - One glass of wine

- 53% reduction in incidence

Lifestyle Interventions

- **Caffeine**
  - Central nervous system stimulant
  - Mid-life use associated with 65% reduced AD risk
    - 3-5 cups?!
    - Suppresses both beta- and gamma –secretase
  - Support in animal models
  - Unknown benefit as a treatment

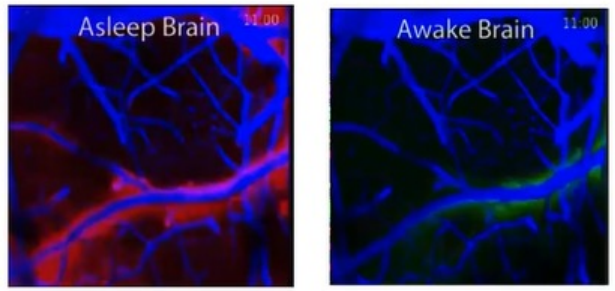


Zhang et al, *PLOS*, 2021

Sleep and Dementia Risk

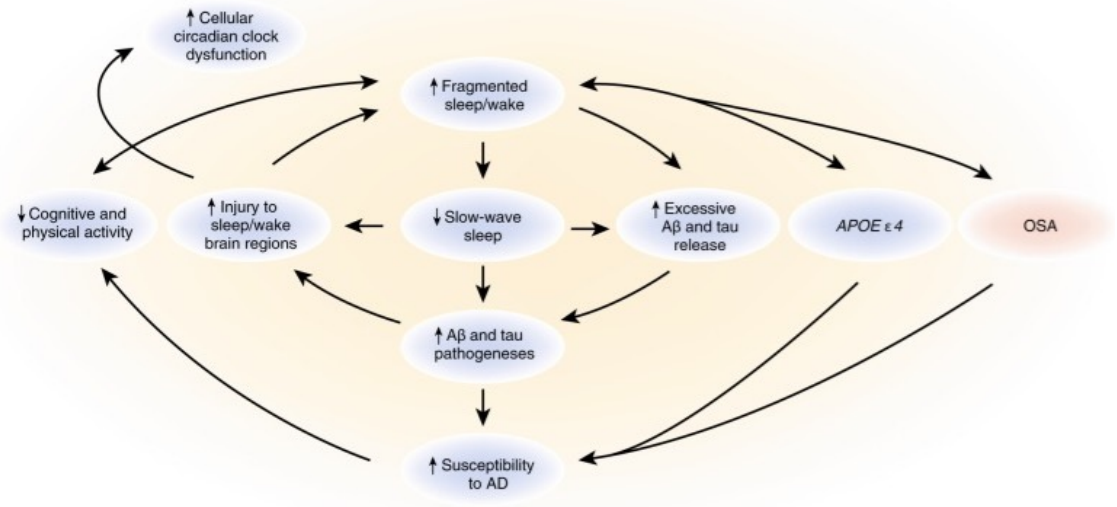
- Bidirectional relationship between sleep and AD

Aβ Clearance Increased During Sleep



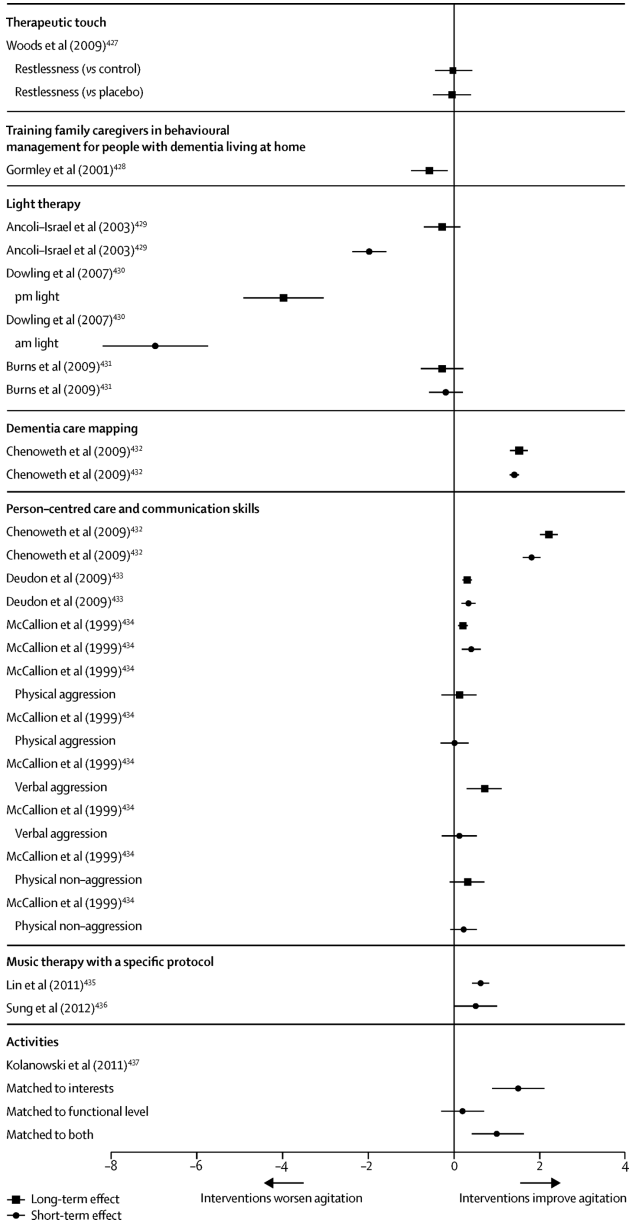
- Cerebrospinal fluid (CSF) flow in asleep (left) and awake (right) brain
- Sleeping mice cleared twice as much Aβ from their brains as conscious mice

Xie et al, *Science,* 2013



Wang & Holtzman, *Neuropsychopharmacology,* 2020

RCTs of effect of psychosocial interventions versus controls for agitation in dementia

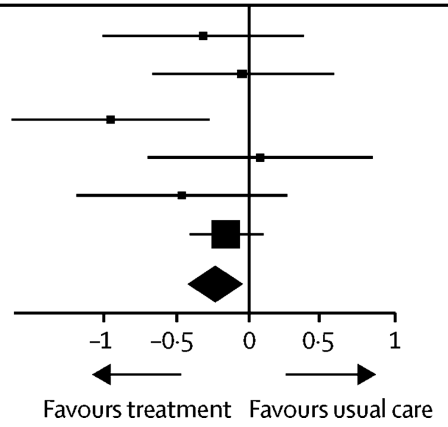


The Lancet DOI: (10.1016/S0140-6736(17)31363-6)

Effect of psychological treatment versus treatment as usual on depression

Study or subgroup	Experimental		Control		Weight %	Mean difference IV, fixed (95% CI)	SMD IV, fixed (95% CI)
	Mean (SD)	N	Mean (SD)	N			
Burgener et al (2008)[474]	3·3 (2·9)	19	4·3 (3·4)	14	7·4		−0·31 (−1·01 to 0·38)
Burns et al (2005)[475]	5·4 (2·6)	20	5·5 (3·1)	20	9·3		−0·03 (−0·65 to 0·59)
Spector et al (2012)[476]	10·38 (5·835)	21	16·72 (7·283)	18	8·0		−0·95 (−1·62 to −0·28)
Stanley et al (2012)[477]	8·2 (2·86)	11	7·8 (5·95)	15	5·9		0·08 (−0·70 to 0·86)
Tappen et al (2009)[478]	15·13 (9·54)	15	19·13 (7·37)	15	6·8		−0·46 (−1·18 to 0·27)
Waldorff et al (2012)[479]	5·05 (4·61)	130	5·77 (5·07)	141	62·7		−0·15 (−0·39 to 0·09)
Total (95% CI)		**216**		**223**	**100·0**		**−0·22 (−0·41 to −0·03)**

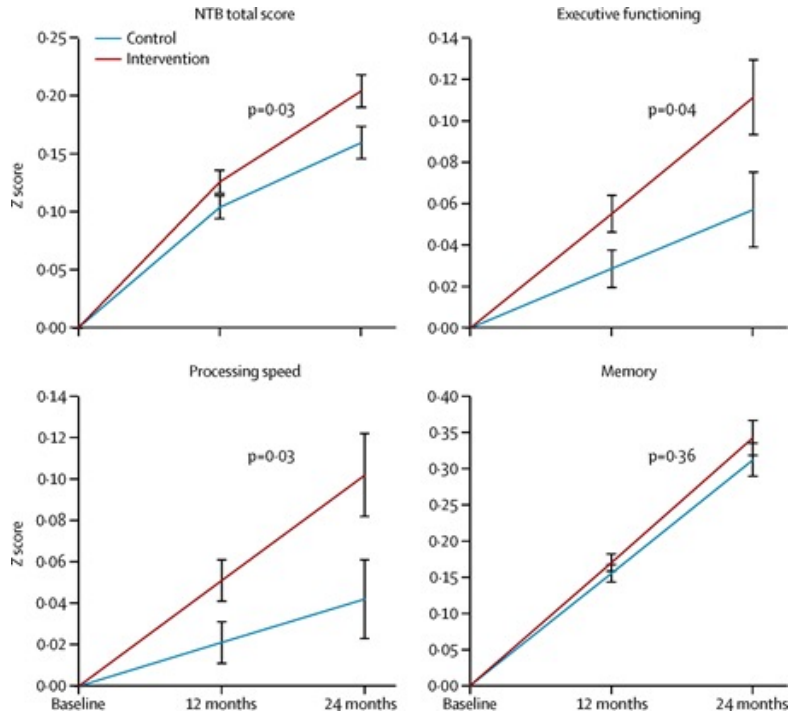
Heterogeneity: $\chi^2 = 6{\cdot}33$, df = 5 (p = 0·28); $I^2 = 21\%$
Test for overall effect: $Z = 2{\cdot}30$ (p = 0·02)



The Lancet DOI: (10.1016/S0140-6736(17)31363-6)

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

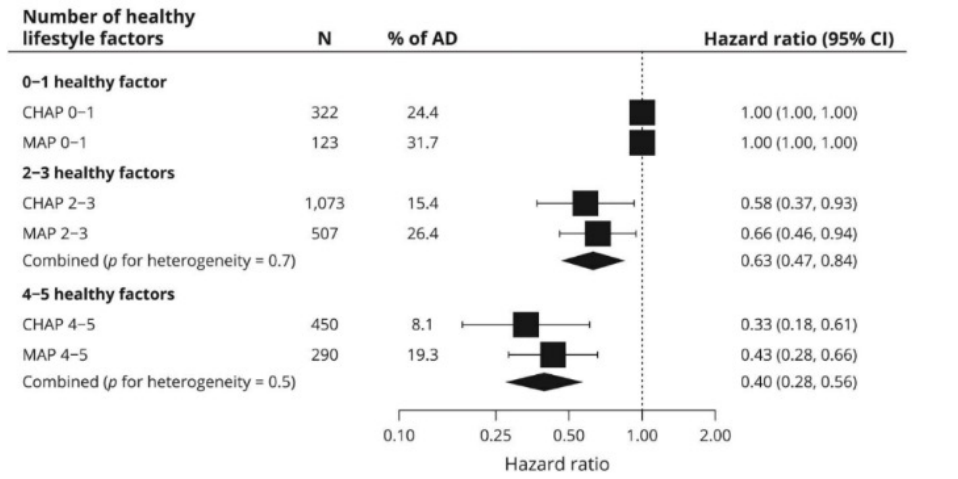
- Results: All 3 cog domains improved over placebo: global, executive function, processing speed ($p < 0.05$)
  - Those >70, or with MMSE <26 improved more

Ngandu, et al., 2015 The Lancet

The Importance of Lifestyle

- 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* 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.

Dhana K, et al., 2020, Neurology

Healthy Action to Benefit

- 10 day brain camp for individuals with MCI, and study partner
  - amnestic MCI (additional cognitive domains okay)
- 5 components
  - physical activity (yoga)
  - brain fitness
  - memory compensation training
  - support group
  - wellness education
- 6 month booster session
- aim: delay or prevent progression to dementia

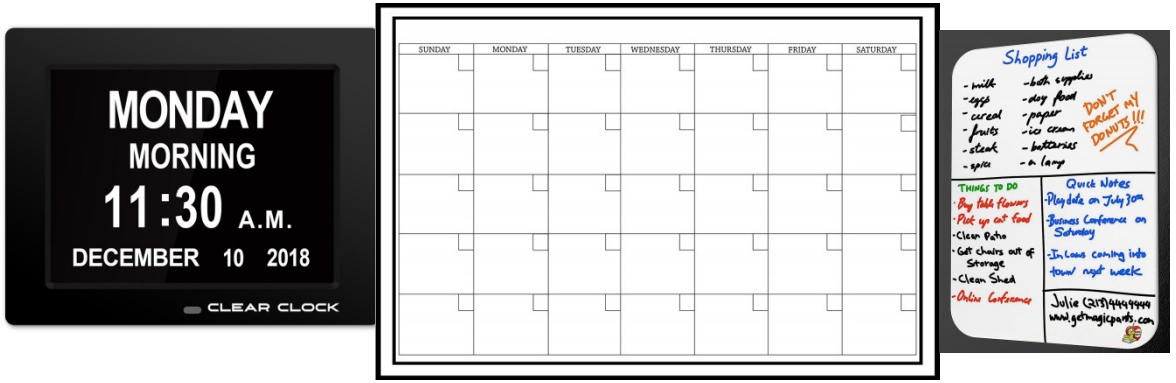
ADAPT Program

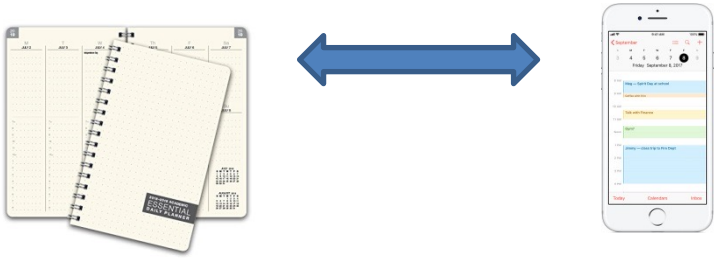
- Applied Daily Activities to Promote Thinking
- Six sessions, taper design
- Multimodal treatment
  - Exercise
  - Meditation
  - Support groups
  - Cognitive rehabilitation
  - Education

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 Engagment

UW Memory and Brain Wellness Center
Memory Hub

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

https://https://thememoryhub.org/

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.momentiaseattle.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
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UW Medicine
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Thank you for your attention!

Questions?

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