



38TH ANNUAL CONFERENCE
OCTOBER 17-20, 2018

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Multi-dimensional behavioral interventions to prevent or delay dementia in patients with MCI and in older adults at increased risk

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Honoraria from: N/A

Outline

- HABIT program for MCI (Dr. Locke)
 - Background & description
 - Current evidence
 - Future directions
- Break
- Brain Boosters program for at risk older adults (Dr. Farias)
 - Background & description
 - Current evidence
 - Future directions

Multidimensional behavioral interventions Part I: Targeting patients diagnosed with MCI

Dona Locke, Ph.D., ABPP-CN
Mayo Clinic Arizona



HABIT Healthy Action To Benefit Independence & Thinking

- 50 hour, group-based, treatment and wellness program for patients with amnesic MCI
- Program partner required
- 5 components
 - Cognitive rehabilitation
 - Support group
 - Cognitive exercise
 - Physical exercise
 - Wellness health behavior change classes

How we began....Cognitive Interventions

- Restitution
 - Aiming to improve back to baseline
 - Rebuilding the circuits in the brain
 - Strengthening a cognitive ability
- Compensating
 - Adapting to an existing deficit
 - Learning ways to “work around” a deficit in daily life
 - External (memory notebook) vs. Internal (mnemonics)
 - External compensatory strategies are recommended
Practice Standing in ABI for more severe memory deficits.

Memory Support System (MSS)

17 SUNDAY January 2010

APPOINTMENTS & SCHEDULED EVENTS

7 1000
8 0800 May 10 - See Shemie on 11th floor ✓
9 0900
10 1000
11 1100
12 1200 Lunch w/ Stephanie @ Candace's house ✓
1 1300
2 1400
3 1500
4 1600
5 1700
6 1800 Bridge @ Jeans ✓
7 1900
8 2000

17 SUNDAY January 2010 17

TO BE DONE TODAY

- Shovel the sidewalk ✓
- buy snacks for bridge ✓
- Schedule hair appt. ✓

Medications
am - Prozac ✓
Multi Vitamin ✓
pm - Lascol ✓
trazodone ✓

THINGS I WANT TO REMEMBER

- Had lunch w/ Stephanie. She says Emma is doing well. She will get out of the hospital next Friday. Remember to wash a batch of clothes and visit her.
- George called about the grill - I will check the prices and call back.

- Individualized instruction
- Structured/manualized curriculum
 - Acquisition
 - Application
 - Adaptation
- Procedural memory/“HABIT” building
- Program partner crucial

Initial Questions about the MSS

- Can patients with MCI learn this procedure?
- Are training sessions required to do so?
- Does the technique impact outcomes?

Proof of Concept: Can patients with MCI learn this procedure?

A behavioral rehabilitation intervention for amnesic Mild Cognitive Impairment

Melanie C. Greenaway, Ph.D.¹, Sherrie M. Hanna, M.A.², Susan W. Lepore, B.S.², and Glenn E. Smith, Ph.D.²

¹ Emory University School of Medicine, Atlanta, Georgia

² Mayo Clinic, Rochester, Minnesota

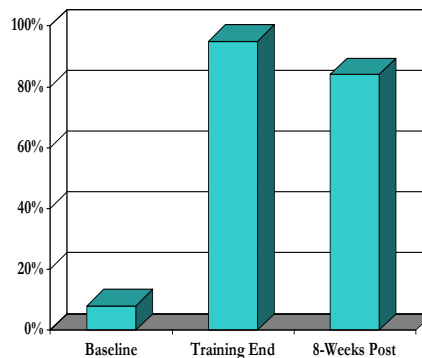
Abstract

Individuals with amnesic Mild Cognitive Impairment (MCI) currently have few treatment options for combating their memory loss. The Memory Support System (MSS) is a calendar and organization system with accompanying 6-week curriculum designed for individuals with progressive memory impairment. Ability to learn the MSS and its utility were assessed in 20 participants. Participants were significantly more likely to successfully use the calendar system after training. Ninety-five percent were compliant with the MSS at training completion, and 89% continued to be compliant at follow-up. Outcome measures revealed a medium effect size for improvement in functional ability. Subjects further reported improved independence, self-confidence, and mood. This initial examination of the MSS suggests that with appropriate training, individuals with amnesic MCI can and will use a memory notebook system to help compensate for memory loss. These results are encouraging that the MSS may help with the symptoms of memory decline in MCI.

Mayo Funded; PIs Smith and Greenaway (now Chandler)

Memory Support System Adherence

% of MCI patients adherent to MSS use



$n = 20, p < .001$

Greenaway, Hanna, Lepore, Smith. American Journal of Alzheimer's Disease & Other Dementias. 2008, 23(5) 451-461.

Is training necessary? **Study #1**

Comparison Group: No treatment controls

RESEARCH ARTICLE

International Journal of
Geriatric Psychiatry

The memory support system for mild cognitive impairment: randomized trial of a cognitive rehabilitation intervention

M. C. Greenaway¹, N. L. Duncan¹ and G. E. Smith²

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²Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA

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Funding Sources: Alzheimer's Associations, NIRG-07-58843
Emory ADRC (AG025688), Pilot Award PI: Greenaway (now Chandler)


Is training necessary? **Study #2**

Comparison Group: Active Control



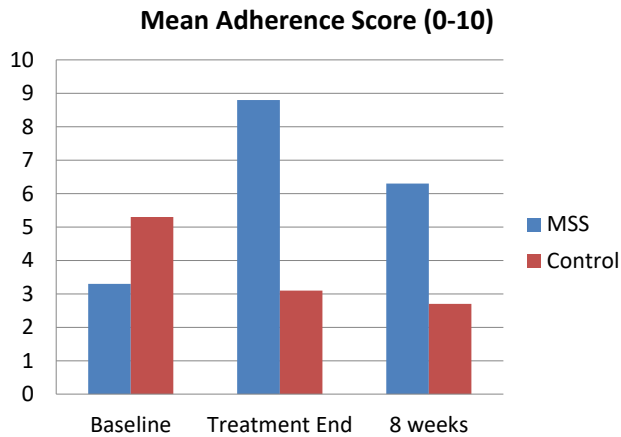
Article

Computer versus Compensatory Calendar Training in Individuals with Mild Cognitive Impairment: Functional Impact in a Pilot Study

Melanie J. Chandler^{1*}, Dona E. C. Locke², Noah L. Duncan³, Sherrie M. Hanna⁴,
Andrea V. Cuc² , Julie A. Fields⁴, Charlene R. Hoffman Snyder², Angela M. Lunde⁴ and
Glenn E. Smith⁵

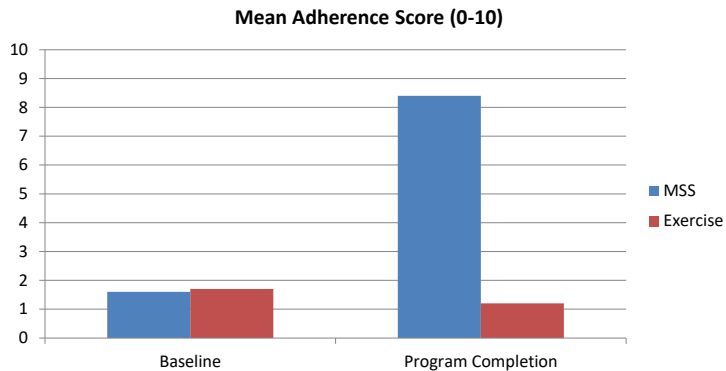
Funding Source: NIH NINR (R01 NR012419) Co-PIs: Locke and
Chandler

Is training necessary? Study #1 = Yes



Greenaway, Duncan, Smith. *Int J Geriatr Psychiatry*. 2012, 28(4), 402-409.

Is training necessary? Yes Study #2: MSS vs. Brain Exercise group



Chandler, Locke, Duncan, Hanna, Cuc, et al. *Brain Sciences*. 2017. 7, 112-122.
Locke, Chandler Greenaway, Duncan, Fields, Cuc et al. *Journal of Prevention of Alzheimer's Disease* 1 (3), 143-150.

Does the technique impact outcomes? Patient ADL Outcomes: Effect sizes favor MSS

- Improved Memory ADLs vs. no treatment controls
 - $d=1.0$ at training end
 - $d=.89$ at 8 weeks
 - $d=.30$ in adherent users at 6 months
- Improved Memory ADLs vs. Active cognitive exercise controls
 - $d=.39$ at training end
 - ns at 6 month follow-up

Greenaway, Duncan, Smith. *Int J Geriatr Psychiatry*. 2012, 28(4), 402-409.
Chandler, Locke, Duncan, Hanna, Cuc, et al. *Brain Sciences*. 2017. 7, 112-122.

Patient Outcomes: Self-efficacy

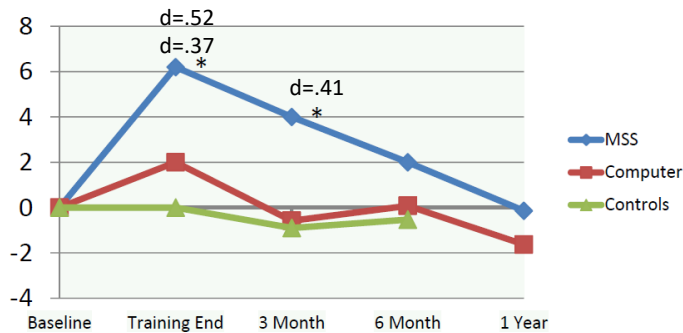


Figure 2. Change in Self Efficacy Over Time. * $p < 0.05$ within-subject change.

Greenaway, Duncan, Smith. *Int J Geriatr Psychiatry*. 2012, 28(4), 402-409.
Chandler, Locke, Duncan, Hanna, Cuc, et al. *Brain Sciences*. 2017. 7, 112-122.

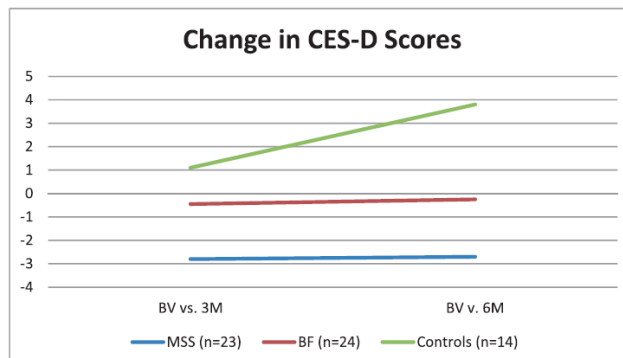
Impact on partners: Most effect sizes favor MSS

- Stable Mood vs. no treatment controls
 - $d=1.45$ at 6 months
- Stable Mood vs. active controls
 - $d=.52$ at 6 months
- Improved QOL vs. active controls
 - $d=.35$ at 6 months
- Stable Burden vs no treatment controls
 - $d=.63$ at 6 months
- Stable Burden vs. active controls
 - $d=.32$ at 6 months

Cuc, Locke, Duncan, Fields, et al. Int J of Geriatr Psychiat, 32, e180-e187

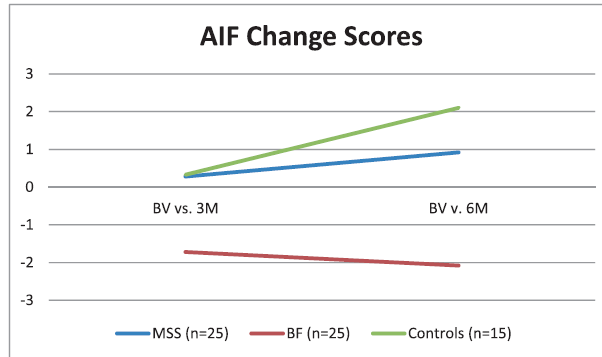
Interesting partner pattern:

Stability in treatment partners; Increasing distress in controls



Note: BV = baseline visit; 3M = 3 month visit; 6M = 6 month visit; MSS = memory support system; BF = brain fitness; Positive scores indicate increasing depression; Negative scores indicate decreasing depression

Impacts on partners: Effect favoring computer exercise



Note: BV = baseline visit; 3M = 3 month visit; 6M = 6 month visit; MSS = memory support system; BF = brain fitness; Positive scores indicate increasing anxiety; Negative scores indicate decreasing anxiety



**THAT'S HOW WE
BEGAN.**

Now how did we evolve?

HABIT Evolution 2005-2008: From Cognitive Rehab to Multicomponent Intervention

- Ongoing research happening with other interventions:
 - Cognitive exercise trials (e.g., ACTIVE trial, IMPACT trial by HABIT co-founder Dr. Glenn Smith, MCI IMPACT trial by Dr. Deborah Barnes) = Evolution of HABIT to include cognitive exercise class.
 - Physical exercise trials (Nurses Health Study; Lautenschlager et al JAMA 2008; Smith PJ et al meta-analysis Psychosomatic Medicine 2010) = Evolution of HABIT to include mindful movement class
- Other programs in existence or being developed at Mayo Clinic or in the area at the time
 - Long standing support groups through the Mayo Rochester ADRC = Evolution of HABIT to include support groups
 - Development of caregiver wellness education classes at Mayo and other organizations such as the Alzheimer's Association = Evolution of HABIT to include wellness education/health behavior change classes.

2014 JAMA Treatment guidelines for MCI

- No drug has proven effective in treatment of MCI
- Control vascular risk factors
- Beneficial Behaviors
- Social needs
- Prognosis and follow-up

Langa & Levine. JAMA 2014, 312(23): 2551-2561

Box 3

Treating and Counseling Patients with MCI

Control of vascular risk factors, and prevention of stroke and subclinical brain injury
Hypertension present: control blood pressure and avoid hypotension
Diabetes present: control severe hyperglycemia and avoid severe hypoglycemia
Statin if indicated for primary or secondary stroke prevention
Atrial fibrillation present: initiate anti-coagulant or anti-thrombotic therapy if no contraindications
Beneficial behaviors
Abstain from heavy alcohol or illicit drug use
Engage in mental activity
Engage in physical activity
Stop smoking
Social Needs
Encourage and facilitate social interactions
Discuss living will, durable power of attorney, financial and long-term care plans
Provide community resources for patient and caregivers
Discuss driving safety
Discuss home safety, including kitchen safety, firearms, poisons, and potential fall risks
Prognosis and Follow-up
Discuss current evidence and uncertainty regarding MCI prognosis with patient and family
Arrange follow-up approximately every 6 months to assess changes in cognitive function and potential evolving needs for social support

HABIT Healthy Action To Benefit Independence & Thinking

- 50 hour, group-based, treatment and wellness program for patients with amnesic MCI
- Program partner required
- 5 components
 - Cognitive rehabilitation
 - Support group
 - Cognitive exercise
 - Yoga class
 - Wellness health behavior change classes

HABIT Evolution continued

- Launched as a clinical service at Mayo Minnesota 2008
- Launched as a clinical service at both Mayo AZ and Mayo FL in 2013
- 150 couples per year across the institution

HABIT vs. no treatment controls

(Non-randomized, Dr. Julie Fields K-award)

Patient results

- Compared to own baseline at 3 months:
- HABIT MCI participants:
 - Less depression ($p=.002$)
 - Less anxiety ($p<.01$)
 - Better QOL ($p<.0001$)
- Control MCI patients
 - No change

Fields JA, et al. (2013). INS. July 10-13, 2013.

HABIT vs. no treatment controls Partner results

- Compared to own baseline at 3 months:
- HABIT partner
 - Less depression ($p < .01$)
 - Less anxiety ($p < .0001$)
 - Less distress ($p < .02$)
- Control partner
 - No change
- Long term follow-up analyses coming soon.

Fields JA, et al. (2013). INS, July 10-13, 2013.

Are all 5 components necessary?

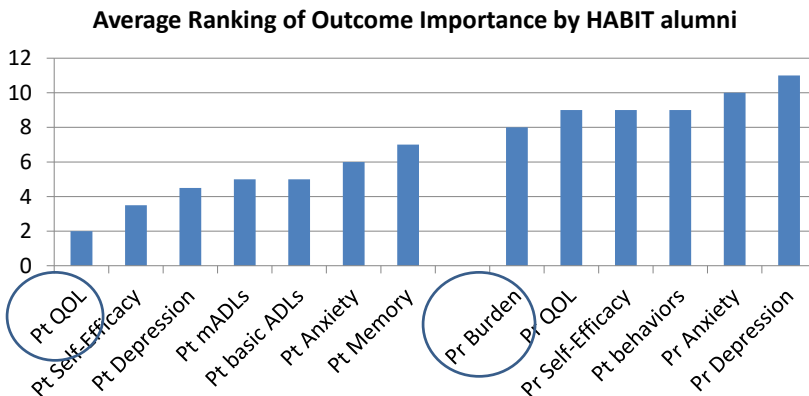
- PCORI Comparative Effectiveness Trial
 - Compare effect of the 5 HABIT interventions
 - Focus groups with advocates in the field (e.g., Alzheimer's association professionals) and HABIT alumni groups
 - Study design
 - Primary outcome

Major Impacts of that Design?

- Patients wanted us to give as much treatment as possible = study design to randomly suppress 1 intervention (couples received 4/5 of the behavioral treatments).
- Of 13 possible outcomes related to cognitive function patient quality of life (QOL) was rated as most important.
- Of the partner outcomes, burden was rated most important, but rated of lower rank than essentially all patient outcomes.

Smith, Chandler, Fields, Aakra, Locke. J Alzheimers Dis, 2018. 63(4): p. 1459-1468.
Smith, Chandler, Locke, Fields, Phatak, et al. JMIF Res Protoc, 2017. 6(11), e223.

Survey Results: Ranking outcome importance



Pt = patient; Pr = partners; Rank ordering on a scale of 1= most important to 12= least important

Smith, G.E., et al., J Alzheimers Dis, 2018. 63(4): p. 1459-1468.

PCORI Sample

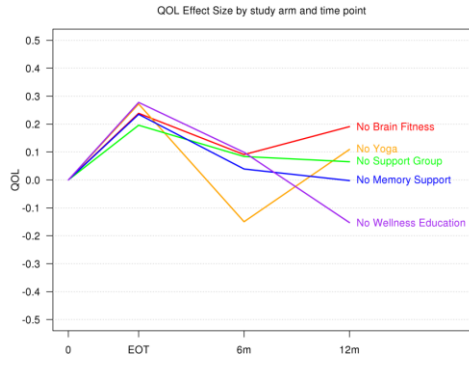
- 272 patient and partner dyads
- 4 centers: Mayo MN, FL, and AZ; U of Washington
- Block randomization per group not per patient (i.e., all attendees to a particular group session had the same suppression paradigm)
- Two week session with follow-ups and boosters at 6m and 12m
- Final measurement at 18 m

Smith, G.E., et al., *Behavioral interventions to prevent or delay dementia: Protocol for a randomized comparative effectiveness study*. JMIR Research Protocols, 2017. 6 (11): p. e223.

Sample Description

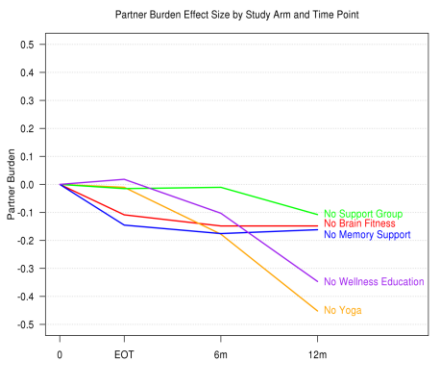
	No BF (n=54)	No MSS (n=57)	No Group (n=53)	No Wellness (n=52)	No Yoga (n=56)
Patient Age	75 (8)	74 (8)	75 (7)	77 (7)	74 (7)
Patient Gender (%M)	61%	54%	60%	58%	61%
Patient Education	16 (2.7)	15.8 (3.0)	16.1 (3.0)	15.8 (2.6)	16.6 (2.8)
Patient Race (%white)	98%	91%	96%	98%	95%
DRS Total	128 (9)	130 (9)	131 (8)	128 (8)	128 (9)
Type of Partner (% spouse)	821	78	91	84	93
Partner Median Age	72	70	73	72	73
Partner Gender (%M)	28%	29%	34%	35%	32%
Partner Median Education	16	16	16	16	16
Lives with patient	81%	83%	92%	86%	96%

Primary Outcome: Patient QOL



- All groups improved by end of treatment ($p < .05$)
- Wellness education was significantly more important to patient QOL than BF at 12 months ($p = .02$, Effect Size = .34)

Primary Partner Outcome: Burden



- Wellness education and yoga were significantly more important to caregiver burden than support group at 12 months ($P < .01$ & $< .001$; Effect Size = .35 & .45)

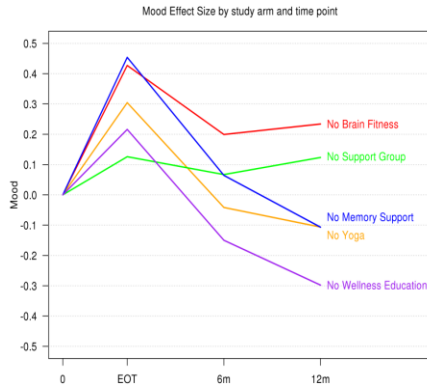
Secondary outcomes

Patient self-efficacy



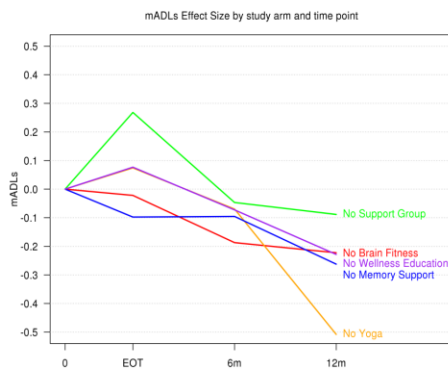
- Support group was significantly more important to patient self-efficacy than BF at 12 months ($p = .04$, Effect Size = .31)

Patient depression



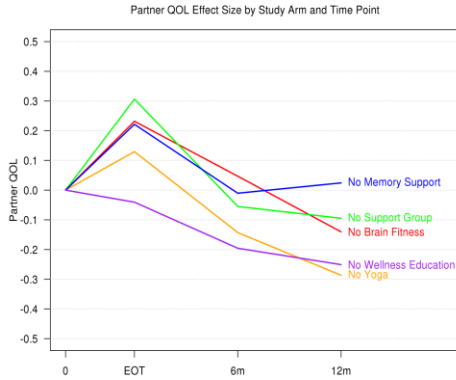
- Wellness education ($p=.001$, effect size = .53) , yoga and MSS calendar training (both $p=.04$, effect size = .34) were significantly more important to patient mood than BF at 12 months.
- Conversely: Best outcome with support group, MSS, yoga, wellness

Patient mADLs



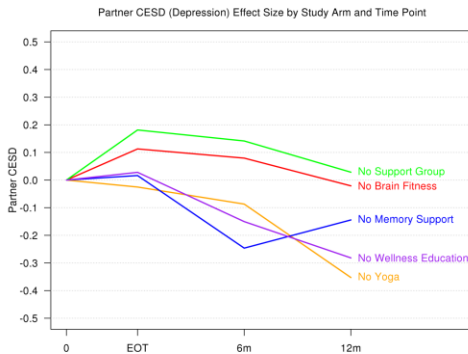
- Yoga significantly more important to patient mADLs than support group at 12 months.
- Conversely, best outcomes for mADLs with BF, Wellness, MSS, Yoga

Partner QOL



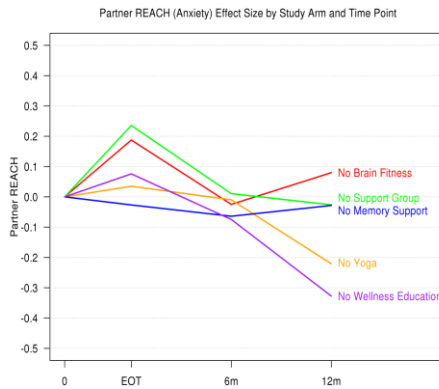
- Wellness education ($p=.05$, effect size = .25) and yoga ($p=.01$, effect size = .29) were significantly more important to partner QOL than MSS calendar training at 12 months.

Partner depression



- Wellness education ($p=.05$, effect size = .28) and yoga ($p=.01$, effect size = .35) were significantly more important to partner depression than support group at 12 months.

Partner anxiety




- Wellness education ($p=.05$, effect size = .29) was significantly more important to partner anxiety than brain fitness at 12 months.

Developing a Menu of Interventions to Suit the Patient

- For participants (like our patient advisors) who prioritize patient QOL, self-efficacy, mood, and daily functioning, the most benefit may come longer term from participating in a program of **wellness education, yoga, MSS calendar training, and support group**.
- However, the future goal is to tailor interventions to the desires of the individual.
- More comparative intervention studies like this are needed towards that goal.
- For partners, **wellness education** and **yoga** appear to be most impactful to their highest rated outcomes of QOL and burden in addition to depression and anxiety.

Future directions

- Cognitive and physical outcome analyses are planned for this study as are 18 month outcomes to include CDR and FAQ data.
- Loss of brain exercise did not impact the outcomes most important to patients, but we have yet to analyze other outcomes including actual cognitive functioning.
- We have adherence measurements and we plan to evaluate overall adherence rates and the impact of adherence on outcomes.
- Comparison to the full 5 component HABIT and no treatment controls from my colleague Dr. Field's K-award.
- How to incorporate more ongoing support/booster classes for patients to help sustain behaviors.
- Translation of the program for Spanish-speakers (linguistically and culturally)
- Helping centers interested in starting HABIT implement in their settings.



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HABIT Informational Resources:

Mayo Clinic Connect: Living with Mild Cognitive Impairment

- Program Overview:
<https://connect.mayoclinic.org/page/living-with-mild-cognitive-impairment-mci/tab/resource-5394/>
- Informational video for patients:
<https://www.youtube.com/watch?v=0trSH5Jnmlw>



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Thank you to the **HABIT** Team!

Mayo Clinic, Arizona

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QUESTIONS? AND BREAK



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Multidimensional behavioral interventions

Part II: Targeting 'at risk' older adults

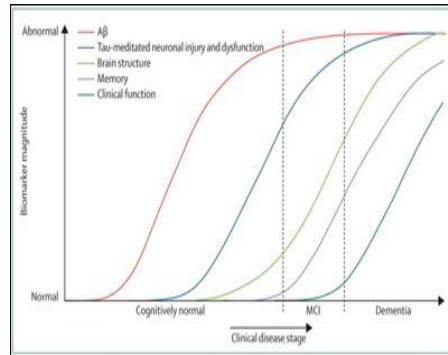
Sarah Parias, Ph.D., ABPP-CN
University of California, Davis

Outline

- The importance of early intervention
- Modifiable risks and target populations
- Two examples of multimodal behavioral interventions to promote cognitive health among normal 'at risk' older adults
 - UC Davis 'Brain Boosters' Program: Compensation training and lifestyle modification
 - FINGER and U.S. POINTER Studies: intensive multidimensional lifestyle modifications

Moving towards prevention/delaying onset of symptoms

- 5.7 million individuals with AD in the U.S. currently
- The prevalence is projected to triple in the next 30 yrs
- Direct costs in 2016 in the U.S. = \$236 billion
- Pathological brain changes associated with AD likely start a decade before sx development
- Tx for AD and related disorders needs to start early, ideally before significant symptoms develop
- Delaying onset of dementia symptoms by 5 years would cut the prevalence and cost of AD by 50%
- Delay by 2 years would cut prevalence in the U.S. by 2 million



Jack et al., 2010

Dementia is often multifactorial

- Mixed pathology is more common than a single pathology
 - AD pathology rarely occurs in isolation
 - 2/3 of people have two neuropathological processes present; 1/2 have 3 or more (Boyle et al., 2018)
- Because there are multiple pathways leading to dementia, multimodal interventions may be most effect

Modifiable risks

- A recent Lancet review concluded that up to 1/3 of dementia is attributable to 7 potentially modifiable risk factors: “Dementia prevention, intervention, and Care” Lancet 390, 2017, pg 2673
 - Physical inactivity
 - Smoking
 - Midlife hypertension
 - Midlife obesity
 - Diabetes
 - Depression
 - Low educational attainment
- More conservative in its conclusions, a recent report commissioned by the NIH noted encouraging evidence for particular modifiable risks and intervention approaches: “Preventing Cognitive Decline and Dementia: A way forward” (<http://nap.edu/24782>)
 - Cognitive training
 - Management of hypertension
 - Physical exercise

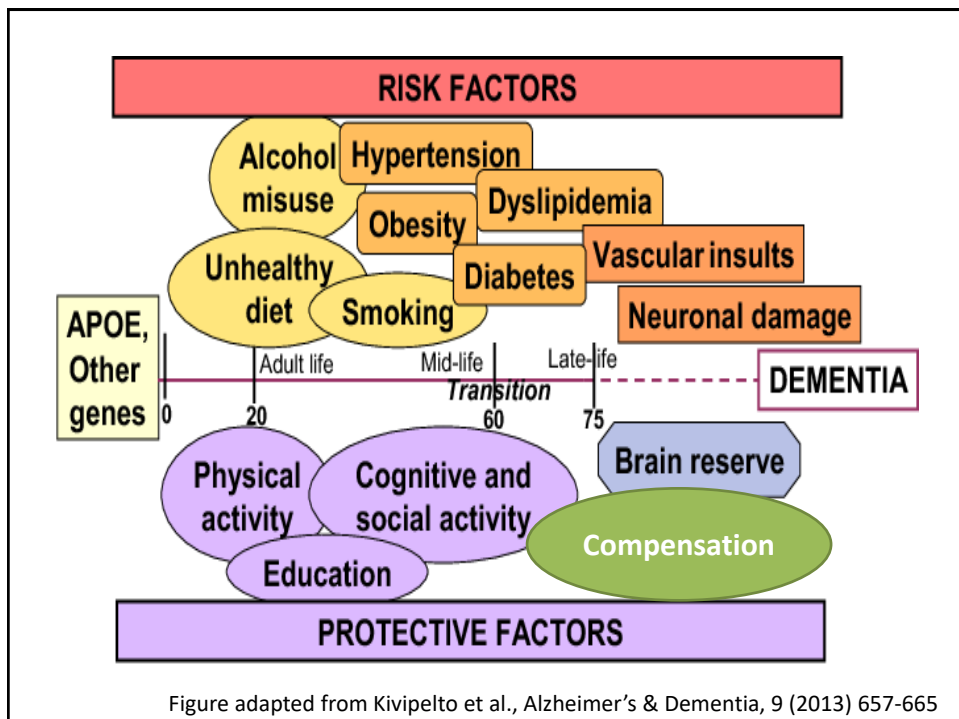


Figure adapted from Kivipelto et al., Alzheimer's & Dementia, 9 (2013) 657-665

Approaches to identifying an 'at risk' population

- Biomarkers
- Genetic risk factors
- Family history of dementia
- Subjective cognitive or functional complaints
- Low normal cognitive performance
- Comorbidities (risks for cerebrovascular disease)
- Lifestyle risk factors (sedentary, poor diet, low cognitive stimulation, isolation)

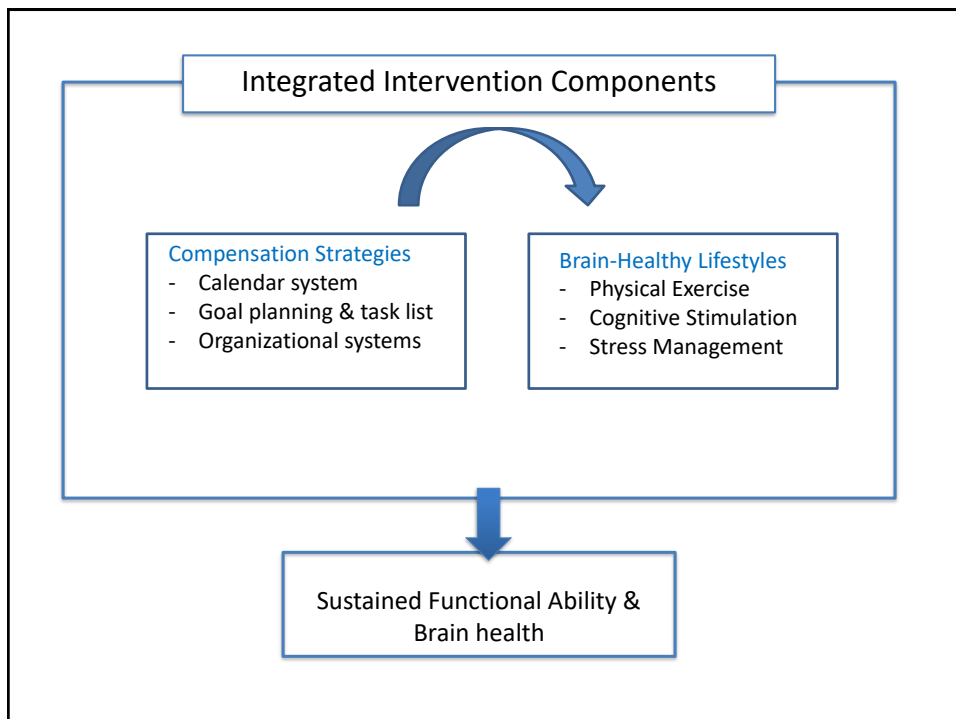
Examples of Multidimensional Interventions with 'at risk' older adults



Brain Boosters: Rational



- Subtle changes in everyday function predate clear evidence cognitive impairment (Farias et al., 2013; 2018)
- Greater use of compensatory strategies in daily life is associated with better functional abilities and slower decline in functional abilities (Farias et al, in preparation)
- Window for opportunity to intervene and **directly target functional abilities through enhanced compensation**
- Literature both on the types of early functional changes as well as the cognitive impairments most closely linked with everyday function suggest we need to target **supporting BOTH memory and executive abilities in everyday life**
- Most previous compensatory training approaches for older adults have focused on memory supports
- Rehabilitation in other populations (TBI and ADHD) have focused on supporting executive abilities



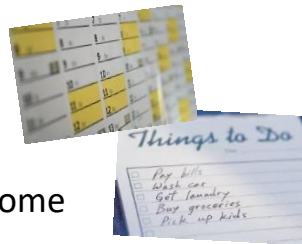
Brain Boosters Format

- Group sessions
 - 10 two-hour weekly sessions
 - 1 introduction session
 - 6 content sessions
 - 3 review sessions
 - Interactive sessions and homework assignments

Sample Class Schedule	
Time Period	Activity
20 minutes	Review homework
20 minutes	Present new material
10 minutes	Break and time to check homework
50 minutes	In class exercise and small and/or large group discussion
20 minutes	New homework assignment and wrap up discussion

Intervention components

- Compensatory strategies
 - Calendar use system
 - Goal Planning and Task lists
 - Organizational strategies for the home
- Brain-Healthy Lifestyle Activities
 - Physical exercise
 - Cognitively stimulating activities
 - Stress management (focus on meditation)



Calendar System

- Flexible approach: Allowed paper or electronic calendar
- Emphasize habitual use
 - routinely putting all re-occurring and non-reoccurring events into calendar
 - checking the calendar \geq twice daily
- Essential components:
 - A single calendar
 - Easy to use
 - Portable – always available
 - Ample space for to do lists*



Goal setting and task list

- Identifying long-term goals (e.g., 3-6 month)
- Planning and prioritizing steps to accomplish goals
- Breaking goals into smaller and manageable steps
- Transferring smaller steps to a weekly task list to help promote accomplishment of goals and other daily activities
 - Counteracts inertia and promotes staying on track
 - Increasing sense of purpose and accomplishment
 - Increase productivity and meet long-term goals



Organizational strategies

- Identification of 'functional zones' in the home or environment (home office, garage/tool box, kitchen pantry, purse or gym bag)
- A place for everything... and everything in its place!
- Basic properties of 'functional zones':
 - Easily identifiable
 - Easily accessible
 - Neat in appearance
- Benefits of being organized:
 - Find things more easily
 - Spend less time looking for things –more efficient
 - Reduce stress
 - Surroundings look more neat, attractive
 - Provides environmental cueing



Cognitive stimulation

- Psychoeducation on benefits (evidence based)
- Emphasizes engagement in 'productive' activities that require novelty, challenge, and sustained processing rather than highly familiar or low challenge activities
 - Activities should be challenging, but still fun and energizing
- Target behavior frequency: 4x/week for ≥ 30 minutes



Examples of mentally stimulating activities

- Learning to speak a new language
- Reading a book
- Playing guitar
- Playing a board/card game
- Watching a TED talk
- Going to a play or movie
- Cooking a new recipe
- Doing a crossword puzzle
- Helping your children/grandchildren with homework
- Playing music
- Engaging in artistic activity (e.g., painting)
- Going to a museum
- Reading a newspaper
- Volunteer work
- Taking a class

Physical exercise

- Psychoeducation on the benefits of regular aerobic exercise to brain health
- Participants are taught how to monitor heart rate
- No specific exercise regime is provided, participants chose their activities (e.g., brisk walking, biking, swimming)
- Target behavior: engage in physical activity resulting in increasing heart rate to 50-70% (or moderate activity) of one's maximum heart rate 4x/week for ≥ 30 minutes



Stress management

- Provides psychoeducation on the contribution of depression, anxiety, and ill effects of stress on cognitive/brain health
- Intervention focused on mediation
 - Taught sitting meditation and body scanning
- Target behavior: meditate 4x/week ≥ 15 minutes at a time



Goals of the study

1. Assess the feasibility: a) class attendance rates, b) weekly homework completion
2. Assess participant acceptability: a) satisfaction on quantitative and qualitative ratings
3. Obtain initial evidence of intervention efficacy
 - *Primary outcomes*: self-reported change in compensation use, engagement in physical activity, cognitive activity, and meditation
 - *Secondary outcomes*: everyday function, depression, anxiety, cognition
 - *Durability of primary and secondary outcomes at 3 & 6 months*

alzheimer's
association

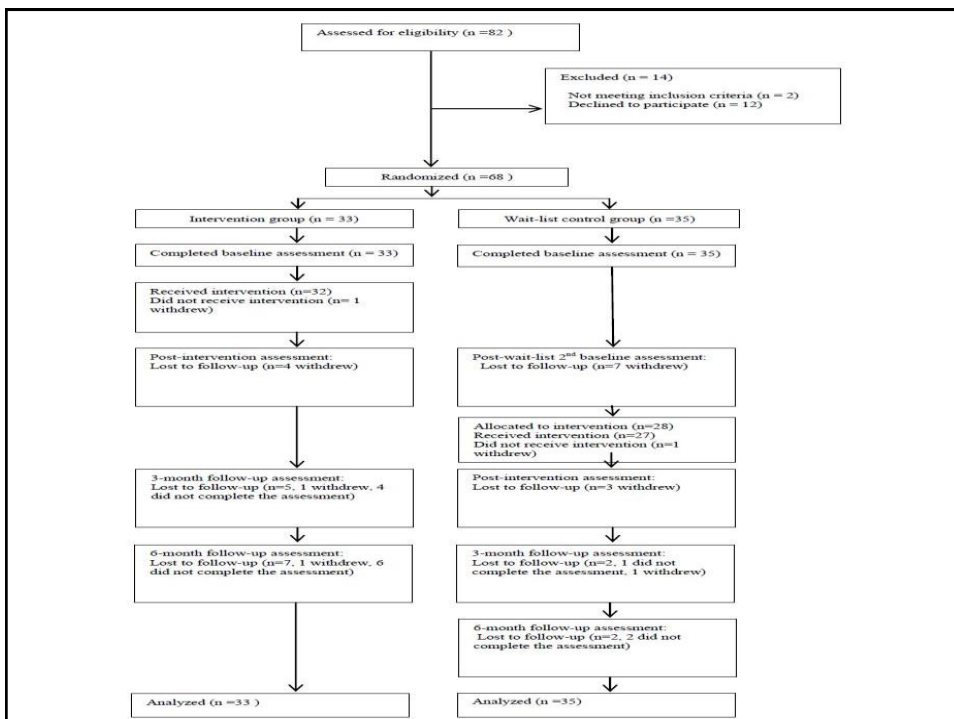
Study supported by a new investigator grant from the Alzheimer's Association (PI, Katherine Denny, Ph.D.)



Study Design



- Random assignment; wait-listed control vs intervention group
- Inclusion/exclusion:
 - 65 years and older
 - Risk: Positive for subjective memory complaint
 - Normal cognitive function on MMSE
 - No known diagnosis of MCI/dementia
 - Independent in IADLs



Study Sample Characteristics

	Total (n=68)	Intervention (n=33)	Waitlist control (n=35)	p-value
Age	74.7 (6.3)	75.8 (6.0)	73.6 (6.4)	.15
Education	16.5 (2.1)	16.6 (2.1)	16.4 (2.2)	.6
Female (%)	73%	65.6	82.9	.1
Caucasian (%)	74%	80.6	71.4	.6
MMSE	28.8 (1.2)	28.6 (1.5)	29.0 (0.9)	.2

Findings: Feasibility

- **Class attendance** was high (80% attendance across the 10 classes)
- **Homework adherence** was at least moderately high 68% overall, but was higher for many program components

Criteria	Points
Brought calendar to Session	1 point
Participant has at least one course related entry for today's date	1 point
Participant has entries for 50% of required brain health activity	2 points
Participant has at least one entry for a personal event for today's date	2 points
Called researcher at designated time	4 points
Total	/10
Percent of activities completed	%

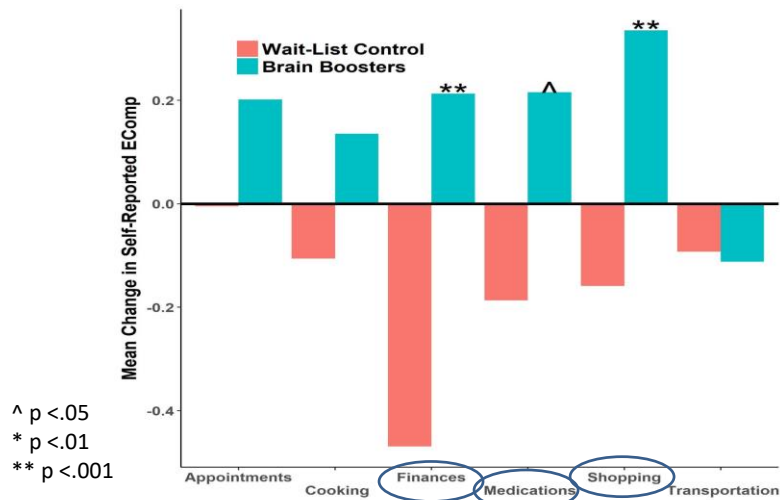
	Percent of homework completed over 10 weeks
Total Adherence	68%
Adherence by training component	
Calendar	75%
Task List	62%
Home Organization	42%
Exercise	75%
Cognitive Activities	78%
Meditation	62%

Findings: Acceptability/Satisfaction

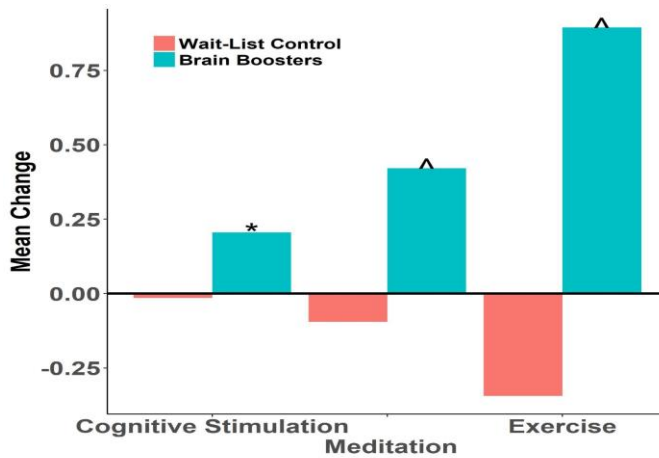
- Participants rated each intervention component:
 - How useful each session was (e.g., 1=not at all useful, 2=mildly useful, 3=somewhat useful, 4=quite useful, 5=very useful)
 - How easy it was to implement
 - How enjoyable it

Mean Satisfaction Ratings			
	Informative/usefulness	Ease of implementation	Enjoyable
Calendar system	4.51	4.03	3.81
Task list	4.51	4.09	3.71
Organizational strategies	4.29	3.85	3.75
Exercise	4.44	4.12	4.32
Cognitive Activities	4.55	4.45	4.45
Meditation	4.13	3.90	3.93

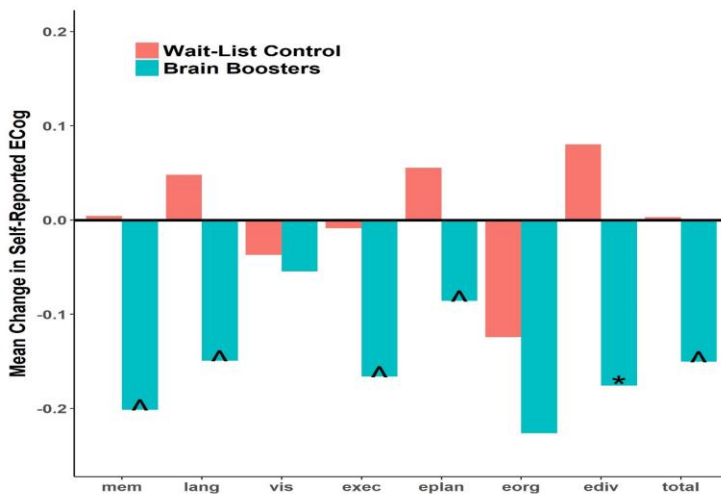
Efficacy: Change in compensation use in IADL domains



Efficacy: Behavioral/lifestyle changes



Efficacy: Everyday function



Findings: Efficacy

Mood

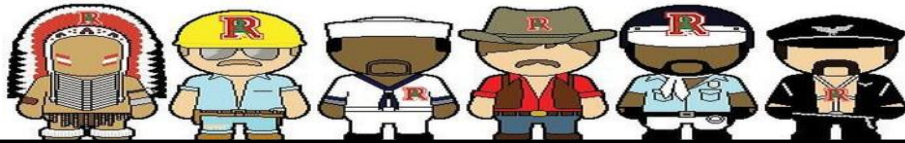
- No differences in change in depression (BDI) or anxiety (BAI)

Durability of findings: 3 and 6 month follow-up results

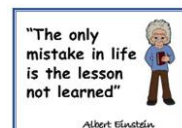
- Compensation within IADL domains
 - Appointments: maintained at 3 & 6 months
 - Shopping: maintained at 3 & 6 months
 - Cooking: maintained at 3 months
 - Financial Management: maintained at 3 & 6 months
 - Medication Management: maintained at 3 & 6 months
- Brain-Healthy Lifestyle Activities
 - Cognitive activity: maintained at 3 months
 - Meditation: maintained at 3 months
 - Exercise: not sustained
- Everyday function
 - Everyday Memory: maintained at 3 & 6 months
 - Everyday Language: maintained at 3 & 6 months
 - Everyday Planning: maintained at 3 months
 - Everyday Divided Attention: maintained at 3 & 6 months

Brain Boosters Study Team (It takes a village)

- Katherine Denny, Ph.D.
- Sarah Farias, Ph.D.
- Michelle Chan, Ph.D.
- Jason Gravano, Ph.D.
- Danielle Harvey, Ph.D.
- Rebekha Alfaro
- Olivia Huss
- Alexa Morales Arana
- Madeleine Marroquin
- Kim Carter



- The adoption of various supportive/compensation skills in the context of daily activities appears achievable
- Behavioral change related to increasing engagement in cognitively stimulating activities and meditation are readily achievable
- Durability of effects – the maintenance of engagement in the brain-healthy lifestyles booster sessions of some kind are needed (especially for physical exercise)



Future Directions

- Use of the MSS as the calendar and goal setting/task list tool
- Incorporation of a more structured exercise program (that is sustainable after the intervention is over)
- Booster/Alumni club (monthly)
- Implementation of objective measures of compensation, activity levels, and daily function



The FINGER Study and extension to
the U.S. POINTER Trial:
Intensive, multidomain behavioral
interventions to reduce risk of
cognitive impairment and Alzheimer's
disease

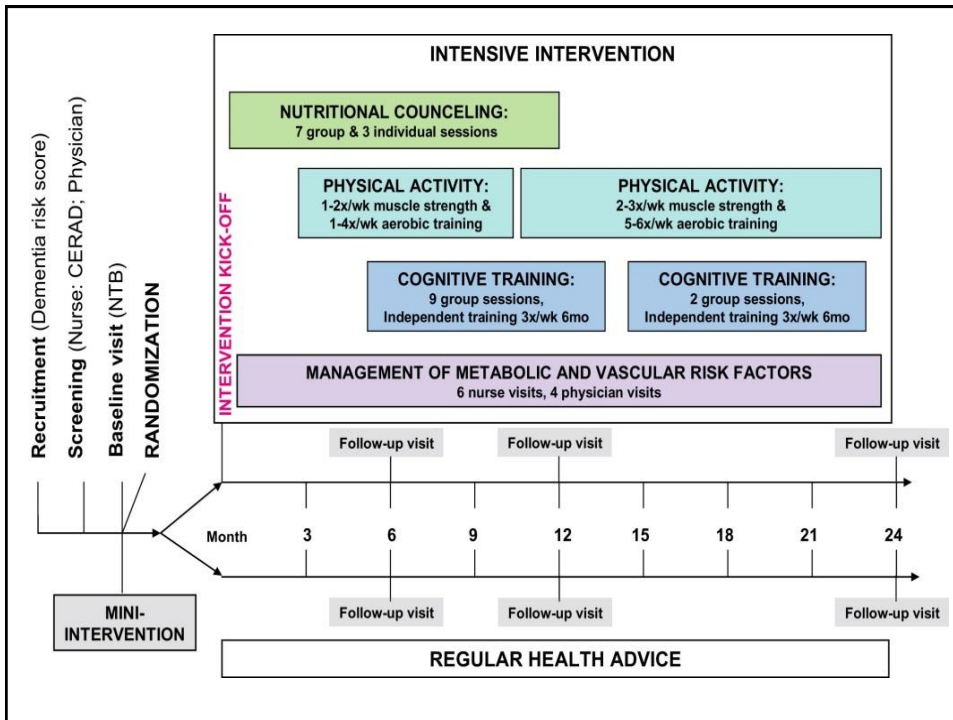
Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)



- 2 year multicenter RCT targeting older adults (60-77) at risk for cognitive decline
- Multi-domain study with cognitively at risk individuals
 - All provided information on diet, exercise, cognitive training, and vascular risk factors management
 - Intervention group received training and additional support

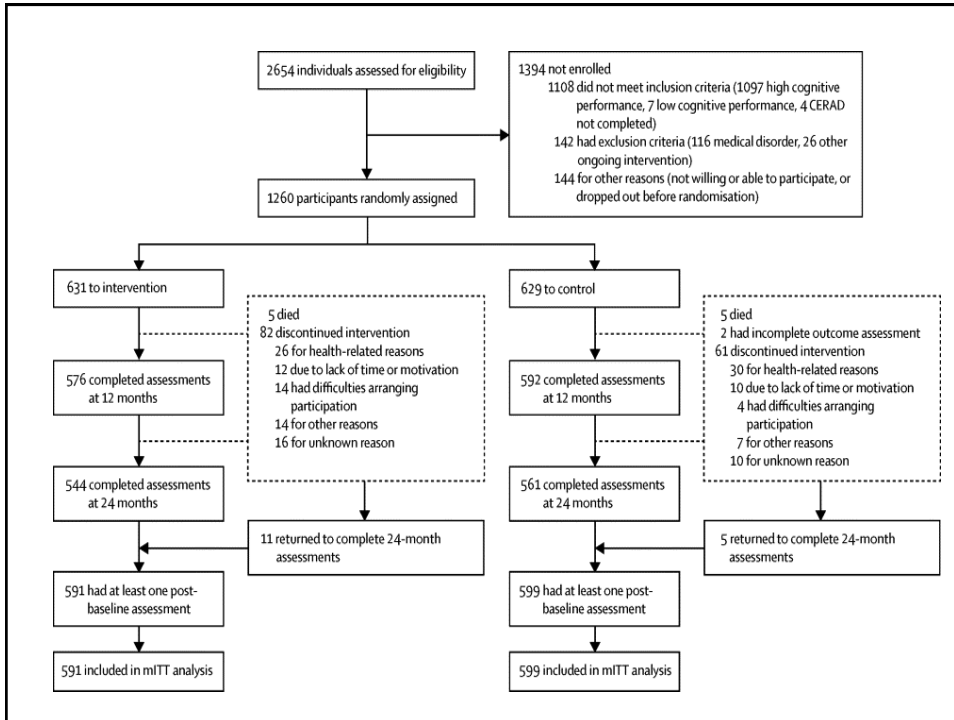
FINGER

- Inclusion/exclusion criteria:
 - Elevated dementia risk score (age, education, HTN, hypercholesterolemia, obesity, and physical inactivity)
 - Normal to near normal cognition
 - Safe to engage in exercise, no major disability, medical stability
- Intervention components
 - Nutrition: National guidelines at the time: high veg/fruit, whole grains rather than processed, low fat, fish
 - Exercise: strength and balance training, aerobic exercise
 - Cognitive training and cognitive/social stimulation: computerized cognitive training targeting memory, exec, speed, WM
 - Management of vascular risks: individual and group meetings to manage HTN, cholesterol, blood sugars, weight



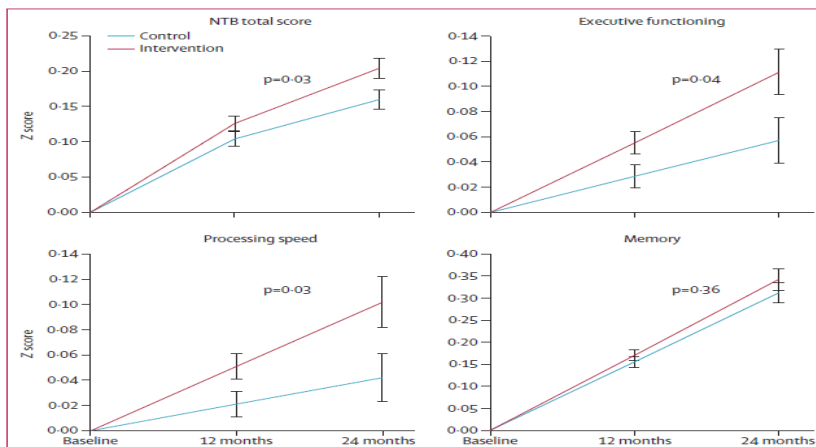
FINGER

- Initial study screening in 2009-2011; study completed in 2014; participants will be followed an additional five years
- Drop out rates similar across tx (14%) and control (11%)
- Primary outcome: cognitive performance (global)
- Secondary outcomes: cognitive domain scores (memory, exec, speed), incident dementia, disability, vascular risk outcomes, physical activity levels, diet, depression, QoL
- Exploratory outcomes: biomarkers (structural and functional imaging)



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

Tiina Ngandu, Jenni Lehtisalo, Aina Solomon, Esko Levälihti, Satu Ahtiluoto, Riitta Antikainen, Lars Backman, Tuomo Hämmänen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Pelttonen, Rainer Raatzma, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Mikko Soininen, Milla Kivipelto



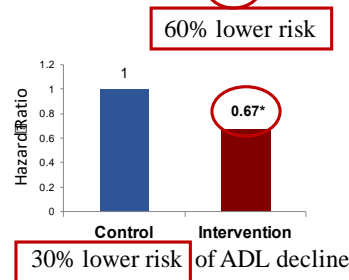
A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Timo Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Leväjähti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangiavacche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauman, Arno Stigsdotter-Nyely, Timo Strandberg, Jaakko Tuomi, Elina Hänninen, Mikko Kivipelto

- Other results
 - BMI was lower in the tx group compared to controls at end of 2 years
 - Dietary habits were better
 - Physical activity was higher

Subsequent Findings

Intervention vs. Control group	Hazard Ratio	95% CI
1+ chronic disease	0.80	0.66-0.98
2+ chronic disease	0.74	0.51-1.06
3+ chronic disease	0.38	0.16-0.88



Kulmala et al., in press; Ngandu et al., Lancet 2015
Marengoni et al., JAMDA 2017



- FINGER-like multidomain interventions will be adapted and tested across cultures
- Goals include harmonization of methods and outcomes across sites
- Data sharing and collaboration across sites to produce robust results on a large scale
- Develop prevention strategies and programs that are accessible, feasible, sustainable and cost effective



U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk (U.S. POINTER)

- 2 year multidomain behavioral intervention
- Funded by the Alzheimer’s Association
- Randomly assigned to evaluate two lifestyle interventions: Structured vs Self-guided
- Target: Older adults at risk (ages 60-79)
 - Sedentary, poor diet, ≥ 1 vascular risks, normal cognition, family hx of memory impairment
- N = 2000
- Multisite (5)
 - Wake Forest
 - University of California, Davis
 - 3 more TBD



Interventions



Self-Guided Lifestyle Intervention



- **Education & Support:**
Group meetings **2-3 times** per year for presentations, general information about healthy lifestyle, and for support



- **Guideline-Based Health Monitoring:**
Annual physical exam & blood tests

Structured Lifestyle Intervention



- **Exercise** (mostly aerobic): 4x per week **primarily** at a YMCA
- **Nutrition:** MIND diet (modified Mediterranean)
- **Cognitive Stimulation:**
Computer cognitive training (**BrainHQ**), group meetings to encourage social/intellectual challenge
- **Guideline-Based Health Coaching:** Frequent exams, blood tests, review of health numbers & goal-setting

Other innovate aspects of the intervention

- Participants organized into teams (~12)
 - Provide social support and reinforcement
 - Group meetings
 - Exercise together
- Each team has a 'navigator' – intervention coach – works with the team and individuals
- Interventionalists will have specialized training in each intervention component



Outcomes

- Primary Outcomes
 - Global cognitive composite
- Secondary Outcomes
 1. Separate composites of episodic memory, executive function, and processing speed
 2. Everyday function (ECog, IADLs, CDR)
 3. Change in lifestyle (physical activity, cognitive activity, social engagement, diet)
 4. Cardiometabolic health metrics
 5. Impact of other characteristics:
 - APOE4
 - Baseline cognitive and health characteristics
 - Adherence overall, and by intervention component



U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk

Study Team

- **Wake Forest:** Laura Baker, Mark Espeland, Jeff Williamson, Nancy Woolard, Jing Su, Scott Rushing, Jeff Katula, Julia Robertson, Iris Leng, Dan Beavers, **Ben Williams**
- **UC Davis:** Rachel Whitmer, Charlie DeCarli, Sarah Farias
- **FINGER team:** Miia Kivipelto, Tiia Ngandu, Aina Solomon
- **Rush University:** Martha Clare Morris, Jennifer Ventrelle
- **USC/ATRI:** Rema Raman, Gustavo Jimenez, Maggiora Robert Rissman
- **Brigham & Women's Hospital/Harvard:** Kate Papp, **Dorene Rentz, Yakeel Quiroz**
- **Y-USA:** Valerie Lawson
- **Alzheimer's Association:** Maria Carrillo, Heather Snyder, Bill Fisher, Glenda Berry, Kenann Cassidy, Elizabeth Edgerly, Katherine Lambert, Claire Day



Industry Partners:

- BrainHQ (Posit Science)
- Digital Cognition Technologies
- Cogstate
- Wellpepper
- FitBit
- YMCA



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Thank You!

