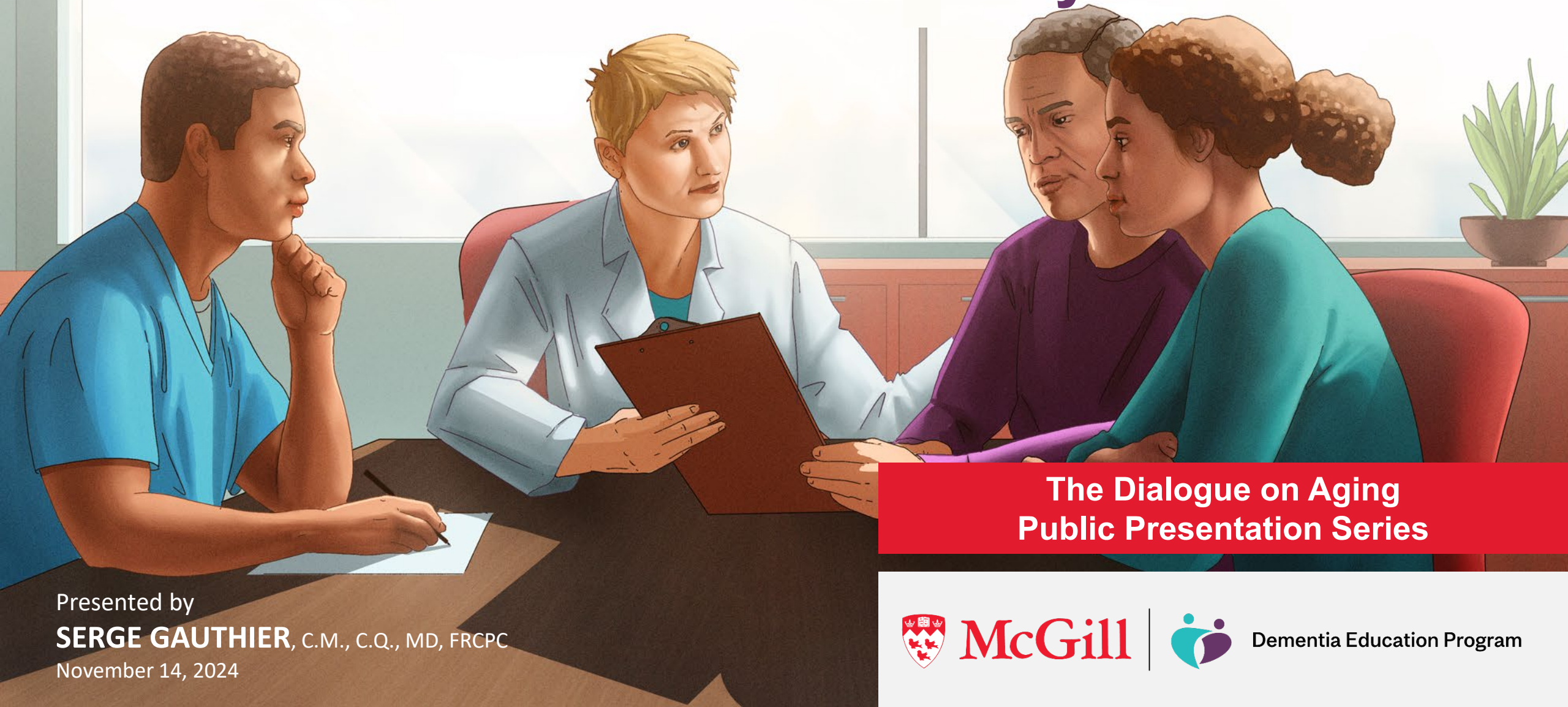
Can we translate modifiable risk factors for dementia into our lifestyle? Yes!



The Dialogue on Aging
Public Presentation Series

Presented by
SERGE GAUTHIER, C.M., C.Q., MD, FRCPC
November 14, 2024

McGill | Dementia Education Program

Serge Gauthier, C.M., C.Q., MD, FRCPC

Professor Emeritus, Department of Neurology & Neurosurgery and Department of Psychiatry

Academic Co-Lead, Dementia Education Program

McGill University

McGill | Dementia Education Program

Overview

In July, the Lancet Commission launched its 2024 report on dementia prevention, intervention and care.

I will explain the new findings on modifiable risk factors for dementia, and how addressing them can prevent or delay disease progression.

Risk factors for dementia that you cannot control

Age

- Dementia is not a normal part of aging. However, age is the strongest known risk factor for dementia. The older you become, the higher the risk.
- **One in 20 Canadians over age 65** has Alzheimer's disease, the most common form of dementia.
- After 65, the risk of developing Alzheimer's disease doubles approximately every five years, with one in four Canadians over 85 having Alzheimer's disease.
- While rare, dementia can affect people under 65. This is known as young-onset dementia.

Source: Alzheimer Society of Canada
https://alzheimer.ca/en/about-dementia/how-can-i-reduce-risk-dementia/risk-factors-dementia

Risk factors for dementia that you cannot control

Sex and gender

- Women have a higher risk of developing Alzheimer's disease than men. While the reasons for this are still unclear, some of the potential contributors include women generally living longer on average than men and changes in estrogen levels over many women's lifetimes.
- For types of dementia other than Alzheimer's disease, men and women have the same risk. There is not much data yet available on non-binary people and dementia, though some research is in progress.

Source: Alzheimer Society of Canada
https://alzheimer.ca/en/about-dementia/how-can-i-reduce-risk-dementia/risk-factors-dementia

Risk factors for dementia that you cannot control

Genetics

- We don’t yet fully understand the role of genes in the development of dementia. We do know that most cases of Alzheimer’s disease are sporadic, meaning they do not run in families. Only rare instances of Alzheimer’s disease are inherited or familial, accounting for **two to five percent** of all cases.
- Scientists have found over 70 genes that may increase the risk of developing Alzheimer’s disease. Three of these genes directly cause Alzheimer’s disease: PSEN1, PSEN2, and APP.
- If a person has an alteration in any of these genes, they will almost certainly develop familial Alzheimer’s disease, often well before the age of 65. If a parent has any of these changed genes, their children have a 50% chance of inheriting the disease.
- The other genes associated with Alzheimer’s disease increase the risk, but don’t guarantee that Alzheimer’s disease will develop. Some other forms of dementia also have familial forms, such as some forms of frontotemporal dementia.

Source: Alzheimer Society of Canada
https://alzheimer.ca/en/about-dementia/how-can-i-reduce-risk-dementia/risk-factors-dementia

J Prev Alz Dis 2024;
Published online June 7, 2024, http://dx.doi.org/10.14283/jpad.2024.105

Original Research

Potentially Modifiable Dementia Risk Factors in Canada: An Analysis of Canadian Longitudinal Study on Aging with a Multi-Country Comparison

S. Son[1,2], M. Speechley[1], G.Y. Zou[1,3], M. Kivipelto[4,5,6,7], F. Mangialasche[4,6], H.H. Feldman[8,9], H. Chertkow[10,11], S. Belleville[12,13], H. Nygaard[14], V. Hachinski[1,3,15], F. Pieruccini-Faria[2,16], M. Montero-Odasso[1,2,16]

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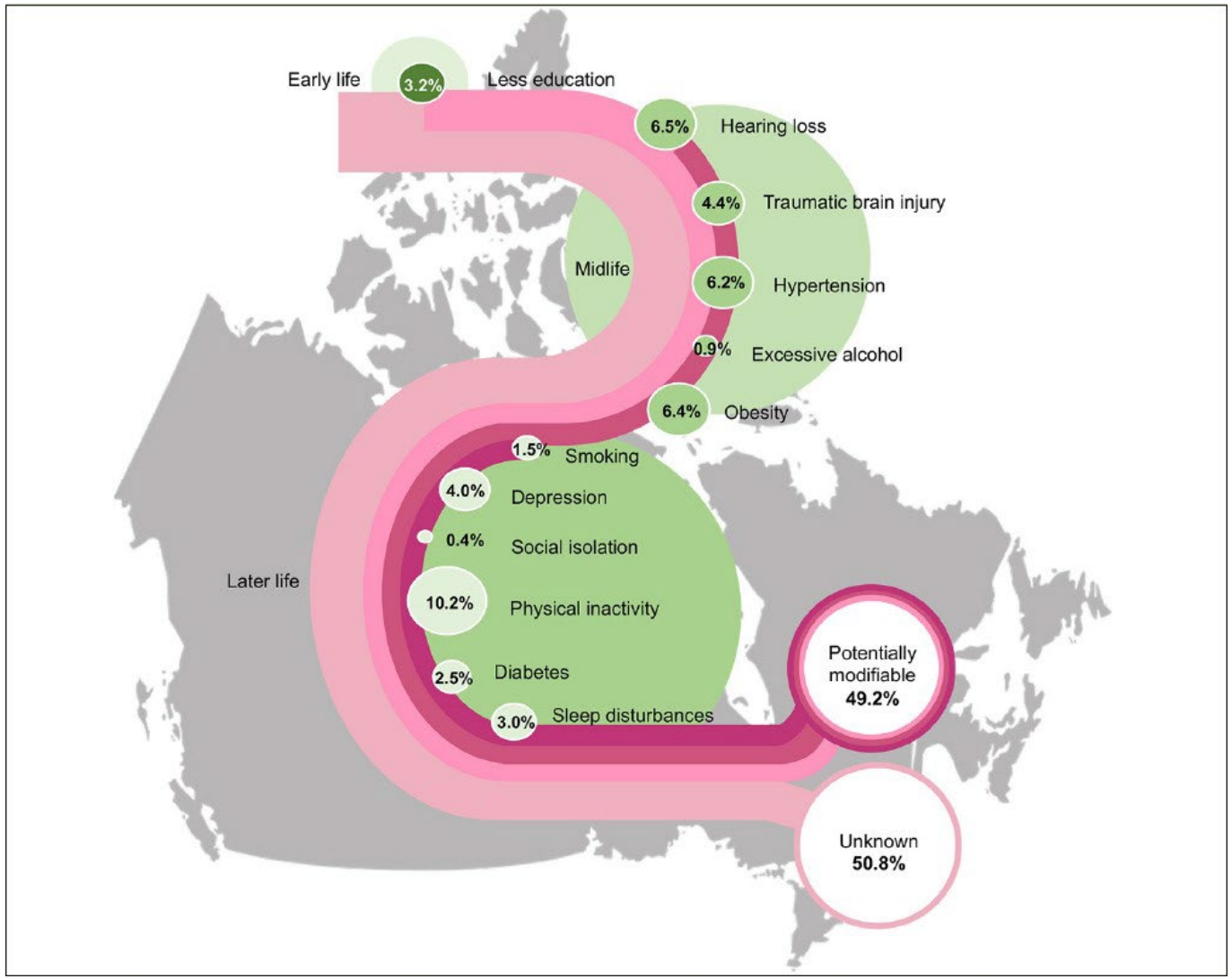
Potentially Modifiable Dementia Risk Factors in Canada: An Analysis of Canadian Longitudinal Study on Aging with a Multi-Country Comparison

Figure 1. Weighted population attributable fraction for 12 potentially modifiable risk factors for dementia in Canada

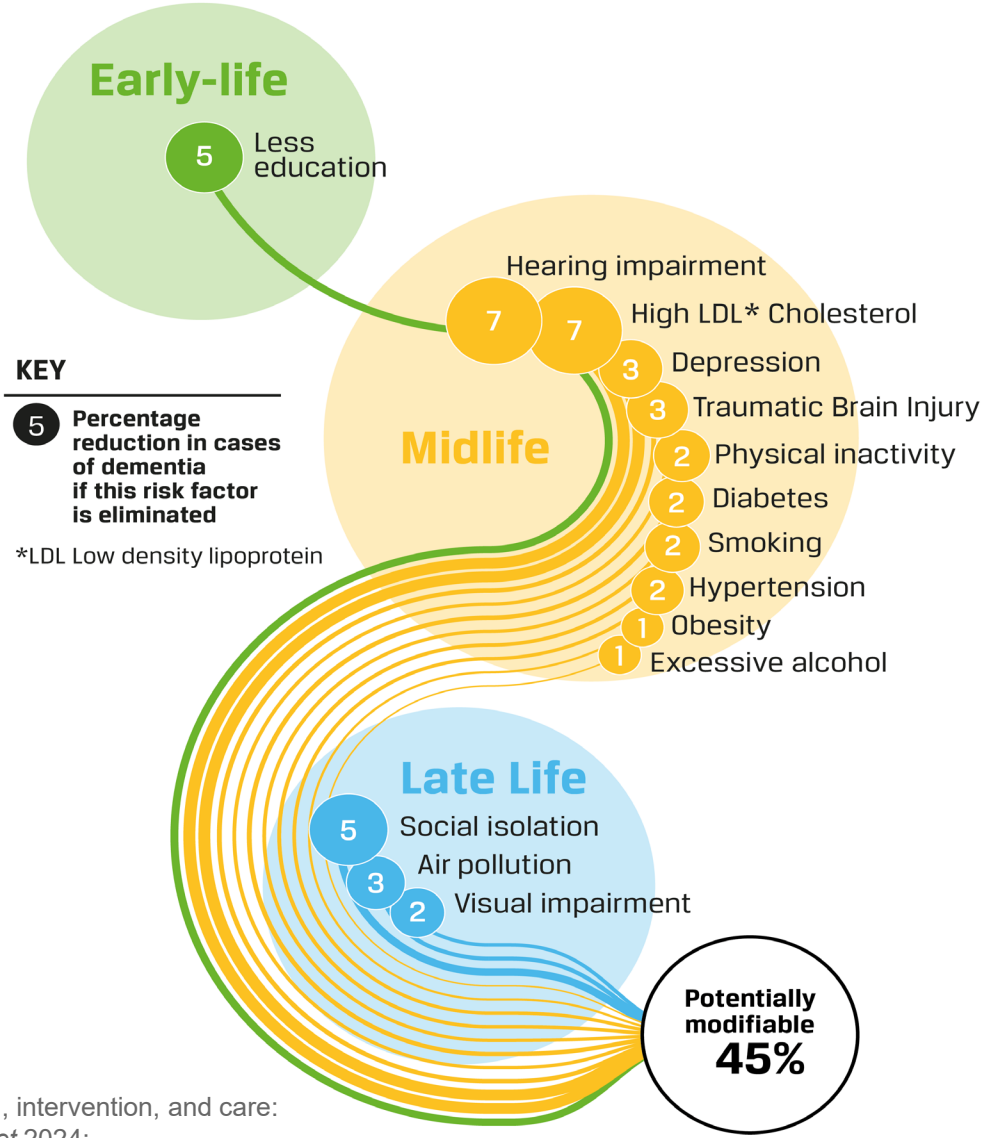


The 2024 Lancet Commission update

As life expectancies increase, the number of people living with dementia worldwide continues to rise. The 2024 report of the Lancet Commission on dementia prevention, intervention, and care adds compelling new evidence that untreated vision loss and high LDL cholesterol are risk factors for dementia. Overall, around 45% of cases of dementia are potentially preventable by addressing 14 modifiable risk factors at different stages during the life course.

Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *The Lancet* 2024; published online July 31. https://doi.org/10.1016/S0140-6736(24)01296-0.

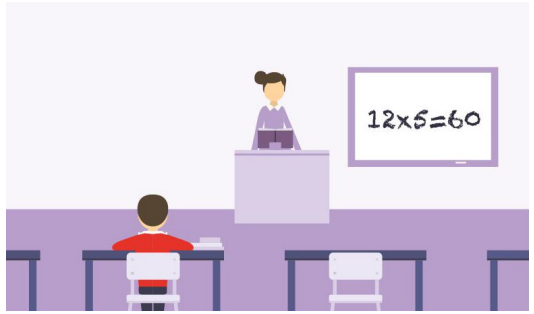
Population attributable fraction of potentially modifiable risk factors for dementia



Livingston G, Huntley J, Liu KY, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *The Lancet* 2024; published online July 31. https://doi.org/10.1016/S0140-6736(24)01296-0.

Modifiable Risk Factors
Less Education

- A low level of education in early life affects cognitive reserve and is one of the most significant risk factors for dementia.
- Midlife cognitive stimulation at work reduces risk of dementia.



5%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Ensure good quality education is available for all and encourage cognitively stimulating activities in midlife to protect cognition.

Source:Illustrations and content for the 14 risk factors
Alzheimer's Disease International
Based on findings from the Lancet Commission
www.alzint.org/about/risk-factors-risk-reduction

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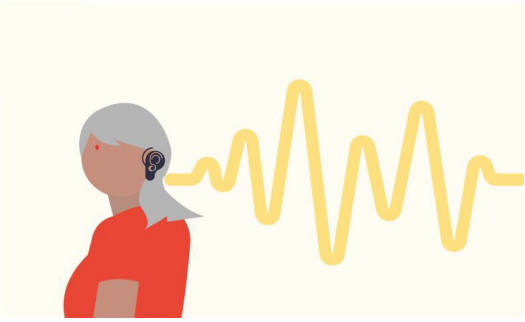
Modifiable Risk Factors
Hearing Impairment

- People with hearing loss have a significantly increased risk of dementia.
- Using hearing aids reduces dementia risk in people at risk, including doubling the time between MCI and dementia.
- As hearing loss is one of the risk factors which affects the most people, addressing it could result in a large impact on the number of people developing dementia.



7%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Make hearing aids accessible for people with hearing loss and decrease harmful noise exposure to reduce hearing loss.

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Modifiable Risk Factors
High Low-Density Lipoprotein (LDL) Cholesterol

- It is common to have high cholesterol
- There is increased evidence that high LDL cholesterol in midlife is a risk for dementia
- Statin use in midlife can lower the risk of dementia and Alzheimer's disease versus untreated high cholesterol
- Clear opportunity to prevent dementia with statins for high cholesterol

7%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation
Detect and treat high LDL cholesterol from midlife.

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Modifiable Risk Factors
Depression

- Depression is associated with dementia incidence. Depression is part of the prodrome of dementia (a symptom that occurs before the symptoms that are used for diagnosis). It is not clear to what extent dementia may be caused by depression or the reverse, and both may be the case. In any case, it is important to manage and treat depression because is associated with increased disability, physical illnesses and worse outcomes for people with dementia.
- Midlife depression increases risk for dementia.
- New commission meta-analysis finds a 2.2 risk reduction of dementia 10 years after depression.
- UKB cohort study finds drugs, psychotherapy for or spontaneous remission of depression decreases the risk.

3%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation
Treat depression effectively.

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Modifiable Risk Factors
Traumatic Brain Injury

- Head injuries are most commonly caused by car, motorcycle, and bicycle accidents; military exposures; boxing, football, hockey and other sports; firearms and violent assaults; and falls.
- Policymakers should use public health and other policy measures to reduce head injuries.

3%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation
Encourage use of helmets and head protection in contact sports and on bicycles.

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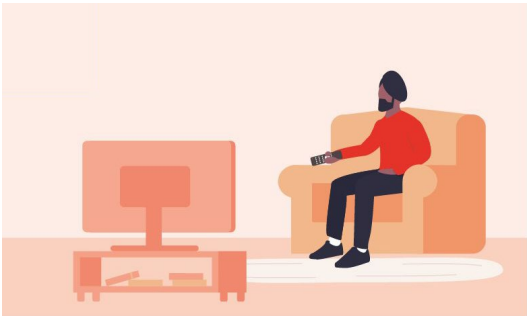
Modifiable Risk Factors
Physical Inactivity

- Regular physical activity is one of the best ways to reduce your risk of dementia. It's good for your heart, circulation, weight and mental well-being.
- It is recommended that adults aim for either 150 minutes of moderate aerobic activity or 75 minutes of vigorous aerobic activity each week.
- Reduction in risk was greatest when moving from extreme sedentariness to some physical activity.
- Exercise at any age appears to be helpful for cognition but little benefit in randomized clinical trials – duration and type which are best are unclear.



2%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Encourage exercise because people who participate in sport and exercise are less likely to develop dementia.

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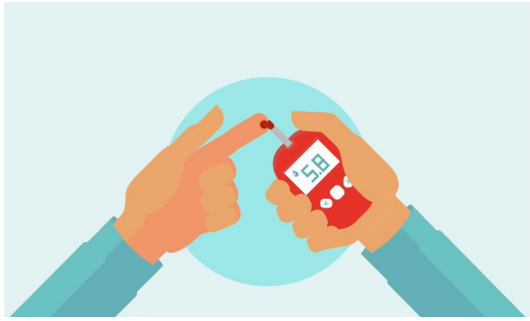
Modifiable Risk Factors
Diabetes

- Type 2 diabetes is a clear risk factor for development of future dementia.
- Whether any particular medication helps with this is unclear, but treatment of diabetes is important for other health reasons.



2%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Maintain a healthy weight and treat obesity as early as possible, which also helps to prevent diabetes.

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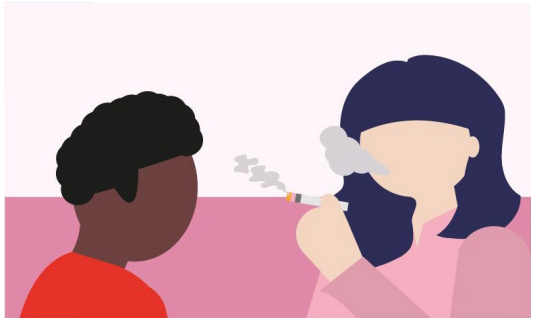
Modifiable Risk Factors
Smoking

- Smoking greatly increases your risk of developing dementia. You're also increasing your risk of other conditions, including type 2 diabetes, stroke, and lung and other cancers.
- It's never too late – stopping smoking later in life also reduces the risk of dementia.
- There is new evidence that midlife smoking is now a stronger risk factor, possibly because smokers are living longer,
- There are encouraging new findings on the beneficial effects of stopping smoking over two years.



2%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Reduce cigarette smoking through education, price control, and preventing smoking in public places and make smoking cessation advice accessible.

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Modifiable Risk Factors
Hypertension

- Hypertension (high blood pressure) in midlife increases a person's risk of dementia, as well as causing other health problems.
- Medication for hypertension is the only known effective preventive medication for dementia.

2%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Prevent or reduce hypertension and maintain systolic blood pressure of 130 mm Hg or less from age 40 years.

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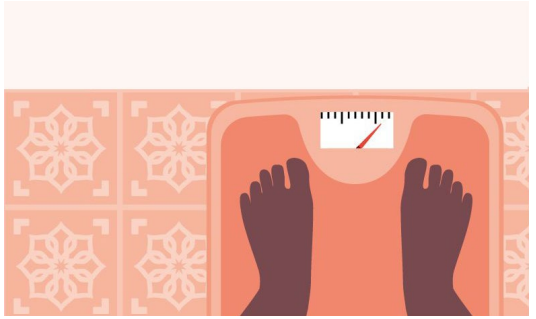
Modifiable Risk Factors
Obesity

- Particularly in midlife, obesity is associated with an increased risk of dementia.
- Obesity can generally be addressed through lifestyle changes such as diet and exercise.



1%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Maintain a healthy weight and treat obesity as early as possible, which also helps to prevent diabetes.

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Modifiable Risk Factors
Excessive Alcohol

- Alcohol misuse and drinking more than 21 units weekly increase the risk of dementia. The harmful use of alcohol is a causal factor in more than 200 disease and injury conditions.
- There is a causal relationship between harmful use of alcohol and a range of mental and behavioural disorders, other noncommunicable diseases as well as injuries.

1%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Reduce high alcohol consumption through price control and increased awareness of levels and risks of overconsumption.

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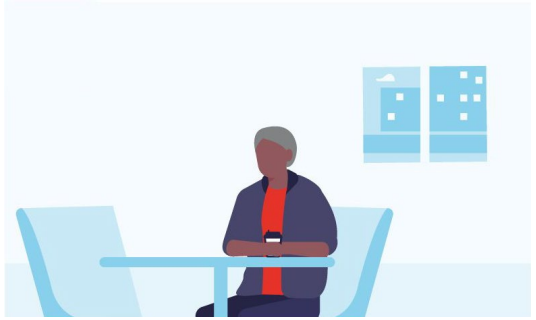
Modifiable Risk Factors
Social Isolation

- It is well established that social connectedness reduces the risk of dementia.
- Social contact enhances cognitive reserve or encourages beneficial behaviours.
- There is not much evidence for any specific activity protecting against dementia.
- Joining a club or community group are good ways to stay socially active.



5%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Prioritize age-friendly and supportive community environments and housing and reduce social isolation by facilitating participation in activities and living with others.

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Modifiable Risk Factors
Air Pollution

- A growing amount of research evidence shows that air pollution increases the risk of dementia.
- Policymakers should expedite improvements in air quality, particularly in areas with high air pollution.

3%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation
Reduce exposure to air pollution.

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Modifiable Risk Factors
Visual Loss

- Vision loss is common, with a global prevalence of 12.5% in people over 50 years old.
- Untreated vision loss of any type is associated with an increased dementia risk of 1.5.
- There is a higher risk for those with increasing vision loss.
- There is a reduced risk for those who have cataract extraction.

2%

reduction in cases of dementia if this risk factor is eliminated

Lancet Standing Commission Recommendation

Make screening and treatment for vision loss accessible for all.

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What do the findings of the Lancet Commission mean?

- There is new evidence about potential dementia prevention at the population level.
- Almost half the risk can be reduced by tackling the 14 risk factors.
- There may be more factors, such as gum hygiene and sleep, but evidence is unclear at the moment.
- **We need more evidence from clinical trials** to demonstrate that interventions makes a difference.
- There is potential for risk reduction at scale through policy changes.
- Changes are often cost saving.
- Risk reduction strategies can help individuals avoid dementia or result in more illness-free years.

Received: 27 February 2024 | Revised: 11 June 2024 | Accepted: 2 July 2024

DOI: 10.1002/dad2.12626

Alzheimer's & Dementia®
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Five-year effects of cognitive training in individuals with mild cognitive impairment

Sylvie Belleville[1,2] | Marc Cuesta[1] | Nathalie Bier[1,2] | Catherine Brodeur[1,2] | Serge Gauthier[3] | Brigitte Gilbert[1] | Sébastien Grenier[1,2] | Marie-Christine Ouellet[4] | Chantal Viscogliosi[5] | Carol Hudon[4,6]

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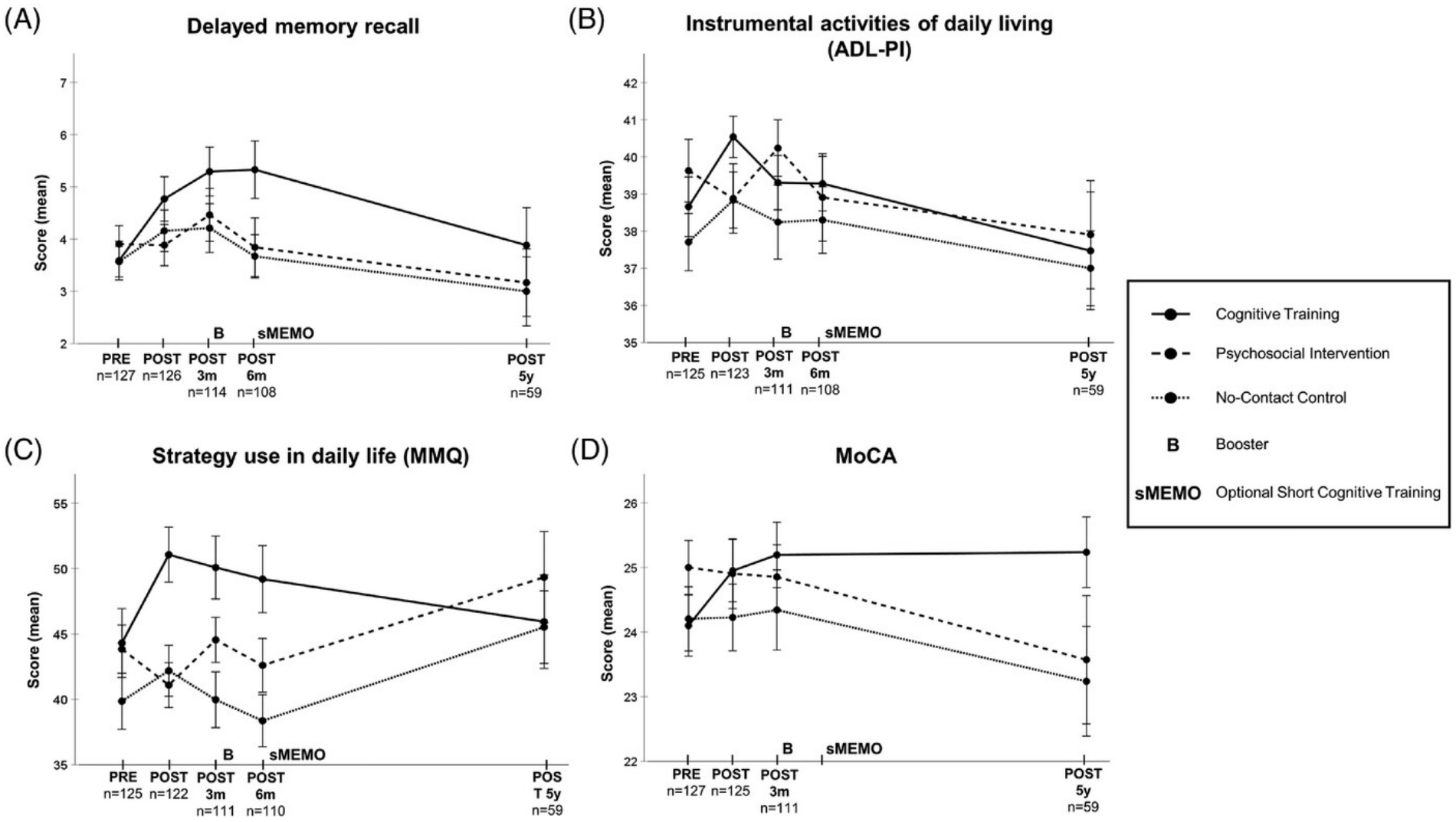
Five-year effects of cognitive training in individuals with mild cognitive impairment

Figure 2



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

FINGER

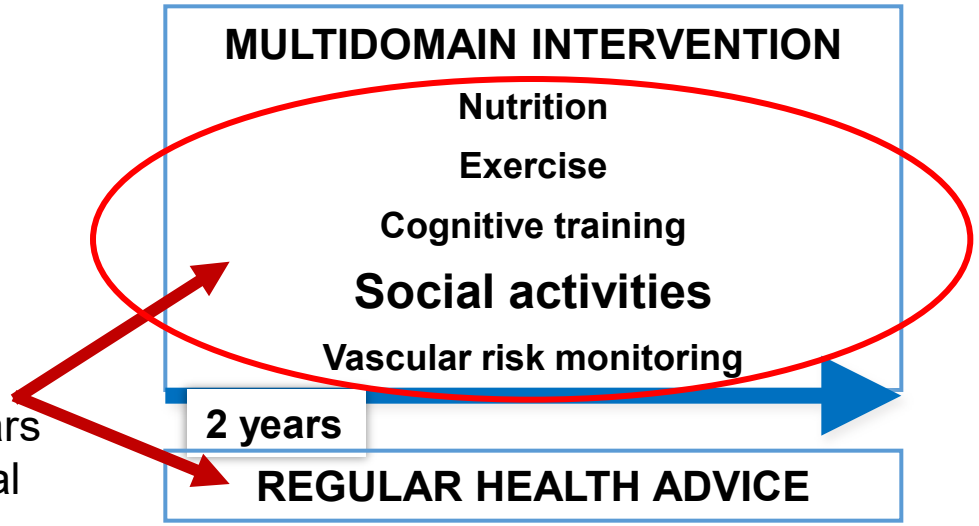
Lancet 2015; 385: 2255–63

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälahti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilkka Soininen, Miia Kivipelto

CAIDE

Dementia Risk Score (midlife)

N = 1260
Age 60-77 years
At risk general population



Kivipelto et al., Lancet Neurology 2006
Alzheimer's and Dementia 2011

Extended 5- & 7-year follow-up finished
11-year follow-up

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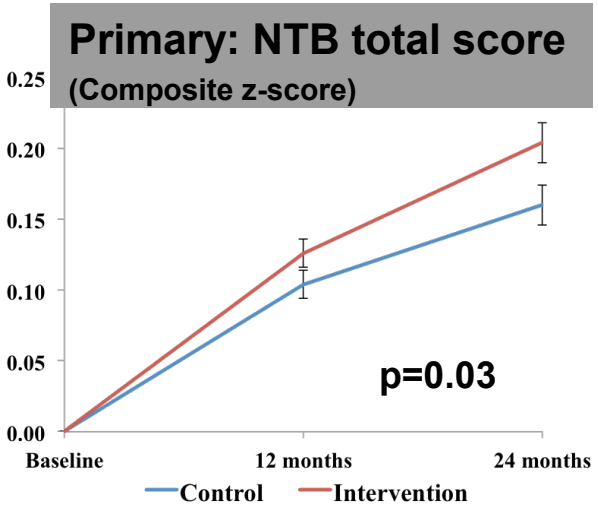
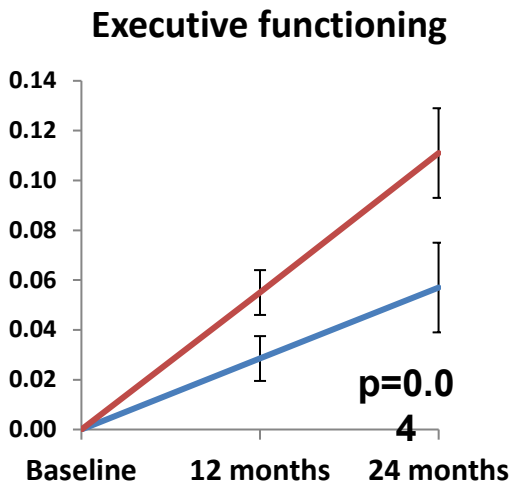
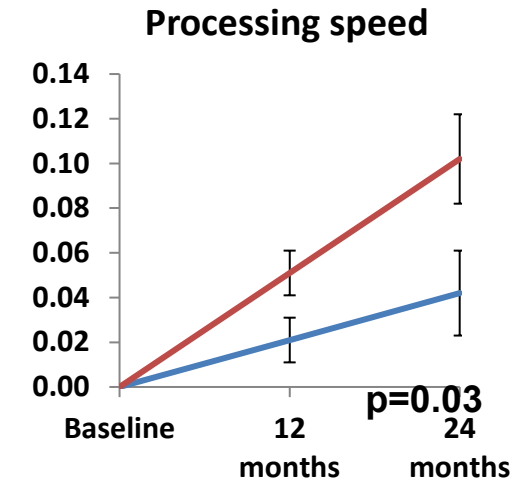
FINGER Trial: summary of primary findings



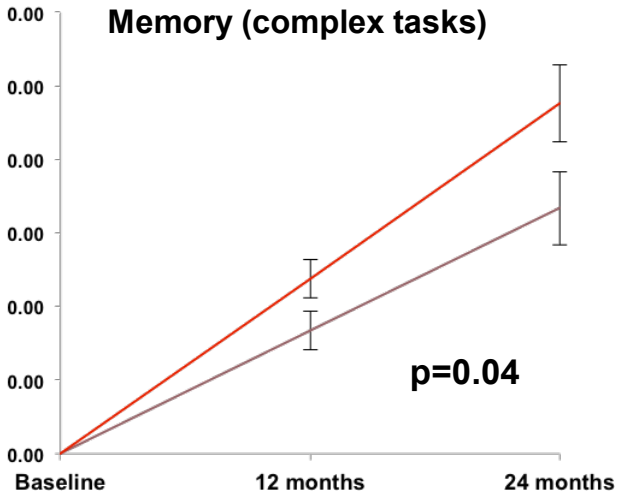
25% higher improvement



83% higher improvement



150% higher improvement



40% higher improvement

Red - intervention
Blue - control

Lines = *estimates for change from baseline to 1 & 2 years*
Error bars = *standard errors*
P-values = *difference in trajectories over time between groups*

Ngandu, Kivipelto et al. Lancet 2015

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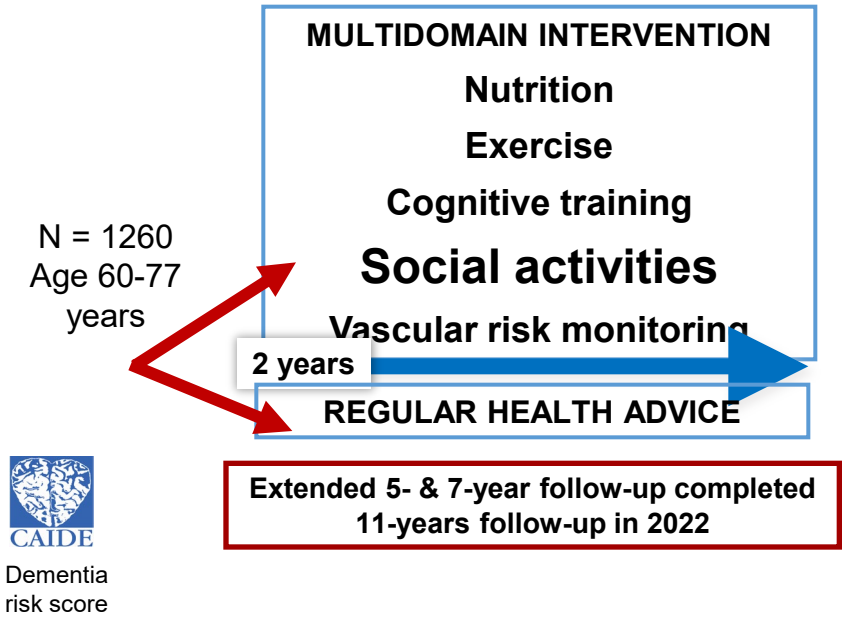
The FINGER model

FINGER



- Cognitive benefits
- 20% lower risk cardiovascular events
- 30% lower risk for functional decline
- 60% lower risk of chronic diseases
- Better health related quality of life
- Health-economical benefits

Lancet 2015; JAMA Neurology 2018, Eur Ger Med 2017, JAMDA 2017, JAGS 2019; Alzheimer's Dementia 2021; European J Cardiology 2022, Alzheimer's Dementia 2022

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Barbera *et al. Alzheimer's Research & Therapy* (2024) 16:23
https://doi.org/10.1186/s13195-023-01355-x

Alzheimer's
Research & Therapy

RESEARCH Open Access

A multimodal precision-prevention approach combining lifestyle intervention with metformin repurposing to prevent cognitive impairment and disability: the MET-FINGER randomised controlled trial protocol

Mariagnese Barbera[1,2*], Jenni Lehtisalo[1,3], Dinithi Perera[2,4], Malin Aspö[5,6], Mary Cross[7], Celeste A. De Jager Loots[2], Emanuela Falaschetti[7], Naomi Friel[2], José A. Luchsinger[8], Hanna Malmberg Gavelin[9], Markku Peltonen[3,4], Geraint Price[2], Anna Stigsdotter Neely[10,11], Charlotta Thunborg[5,6], Jaakko Tuomilehto[3,12,13], Francesca Mangialasche[4,5,6], Lefkos Middleton[2,14], Tiia Ngandu[3,5], Alina Solomon[1,2,5*†], Miia Kivipelto[2,5,6,15†] and on behalf of the MET-FINGER study team

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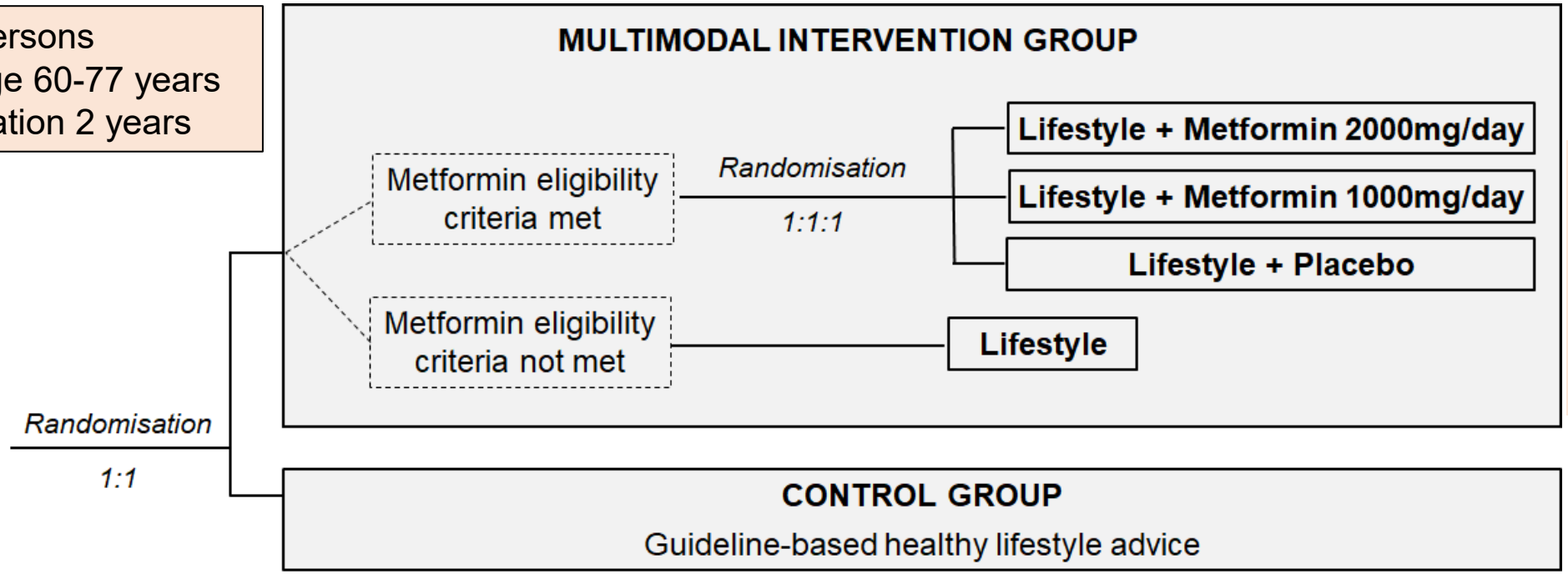
MET-FINGER study diagram

Phase 2b proof of concept trial

Diabetes medicine metformin
Repurposed drug approach

At risk persons
Age range 60-77 years
Trial duration 2 years



Lifestyle domains: *nutrition, exercise, cognitive and social activities, cardiovascular / metabolic risk factors*

Outcomes:
memory and cognition
Brain scans
Alzheimer related biomarkers

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Montero-Odasso *et al. BMC Geriatrics* (2018) 18:93
https://doi.org/10.1186/s12877-018-0782-7

BMC Geriatrics

STUDY PROTOCOL Open Access

SYNERGIC TRIAL (SYNchronizing Exercises, Remedies in Gait and Cognition) a multi-Centre randomized controlled double blind trial to improve gait and cognition in mild cognitive impairment

Manuel Montero-Odasso[1,2,3*], Quincy J. Almeida[4], Amer M. Burhan[5], Richard Camicioli[6], Julien Doyon[7], Sarah Fraser[8], Karen Li[9], Teresa Liu-Ambrose[10], Laura Middleton[11], Susan Muir-Hunter[12], William McIlroy[13], José A. Morais[14], Frederico Pieruccini-Faria[1,3], Kevin Shoemaker[15], Mark Speechley[2], Akshya Vasudev[16], G. Y. Zou[2,17], Nicolas Berryman[18,19], Maxime Lussier[18,20], Leanne Vanderhaeghe[21] and Louis Bherer[9,18,20,22]

NCT02808676 HC6-24-c195918

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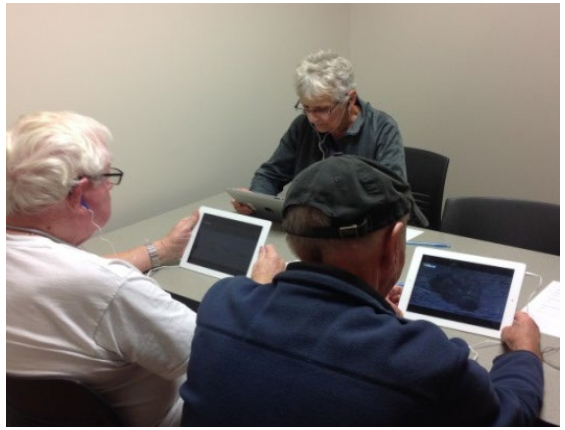
SYNERGIC Trial Interventions

3 interventions… in individuals with MCI

Cognitive training + Physical exercises + Vitamin D



Vitamin D

- 10,000 IU of Vitamin D3 or matching placebo 3 x/week (daily dose: 4,258 IU)
- Maximum daily dose approved by Health Canada as a supplementation is 10,000 IU

JAMA Network Open

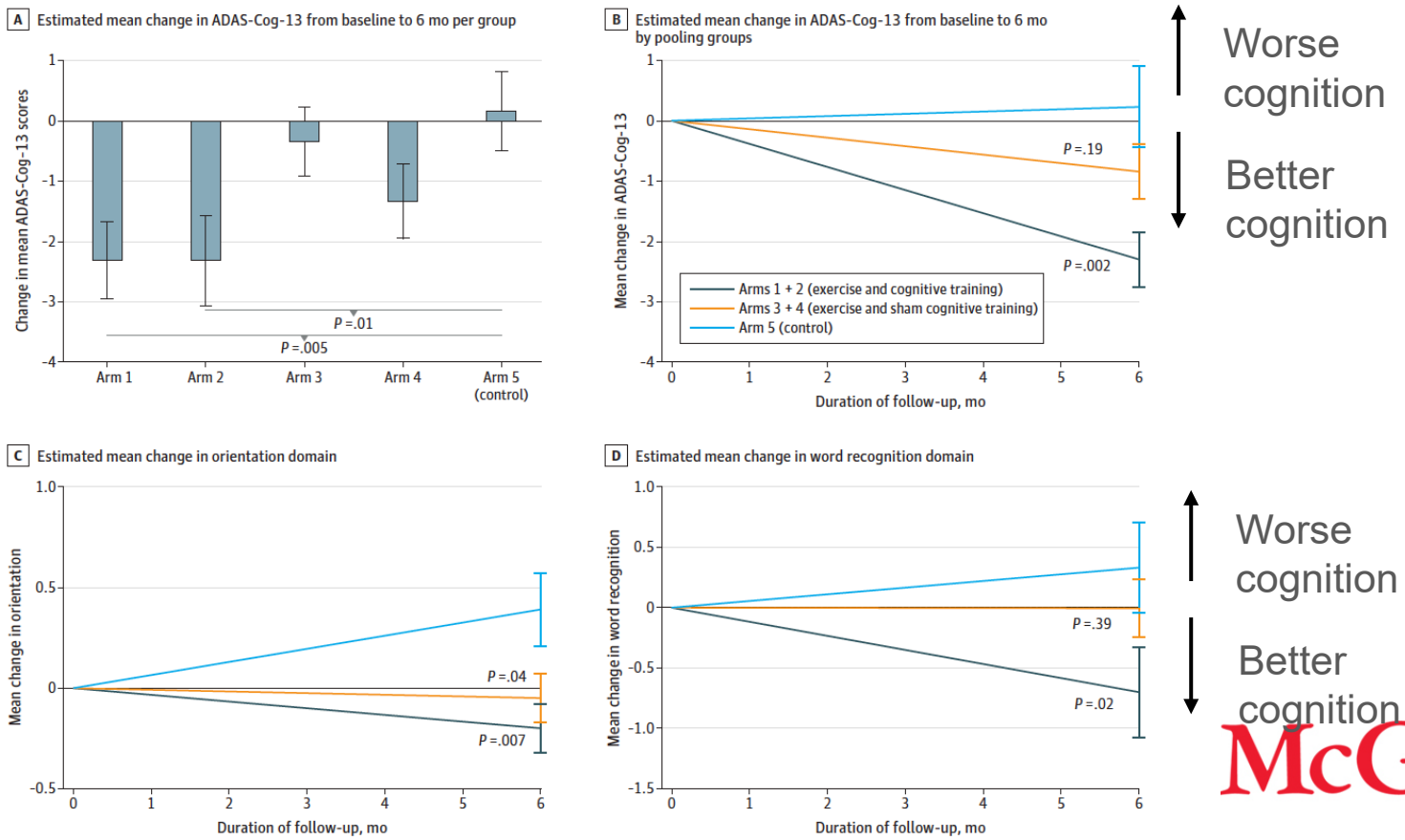
SYNERGIC Trial

Original Investigation | Geriatrics

Effects of Exercise Alone or Combined With Cognitive Training and Vitamin D Supplementation to Improve Cognition in Adults With Mild Cognitive Impairment
A Randomized Clinical Trial

Manuel Montero-Odasso, MD, PhD; Guangyong Zou, PhD; Mark Speechley, PhD; Quincy J. Almeida, PhD; Teresa Liu-Ambrose, PhD; Laura E. Middleton, PhD; Richard Camicioli, MD; Nick W. Bray, PhD; Karen Z. H. Li, PhD; Sarah Fraser, PhD; Frederico Pieruccini-Faria, PhD; Nicolas Berryman, PhD; Maxime Lussier, PhD; J. Kevin Shoemaker, PhD; Surim Son, MSc; Louis Bherer, PhD; for the Canadian Gait and Cognition Network

Figure 2. Change in ADAS-Cog-13 Scores During the 6-Month Intervention



Messages

Exercises + cognitive training synergistically improved cognition in MCI

ADAS-Cog 13 changes were in the medium-large effect size (0.70) and close to clinically significant changes (3-point range)

Adding Vitamin D did not enhance cognition

"*The SYNERGIC Trial demonstrates that people with MCI can do something that may influence their cognitive trajectory*"
said Dr Ronald C. Petersen
(Neurology Today)

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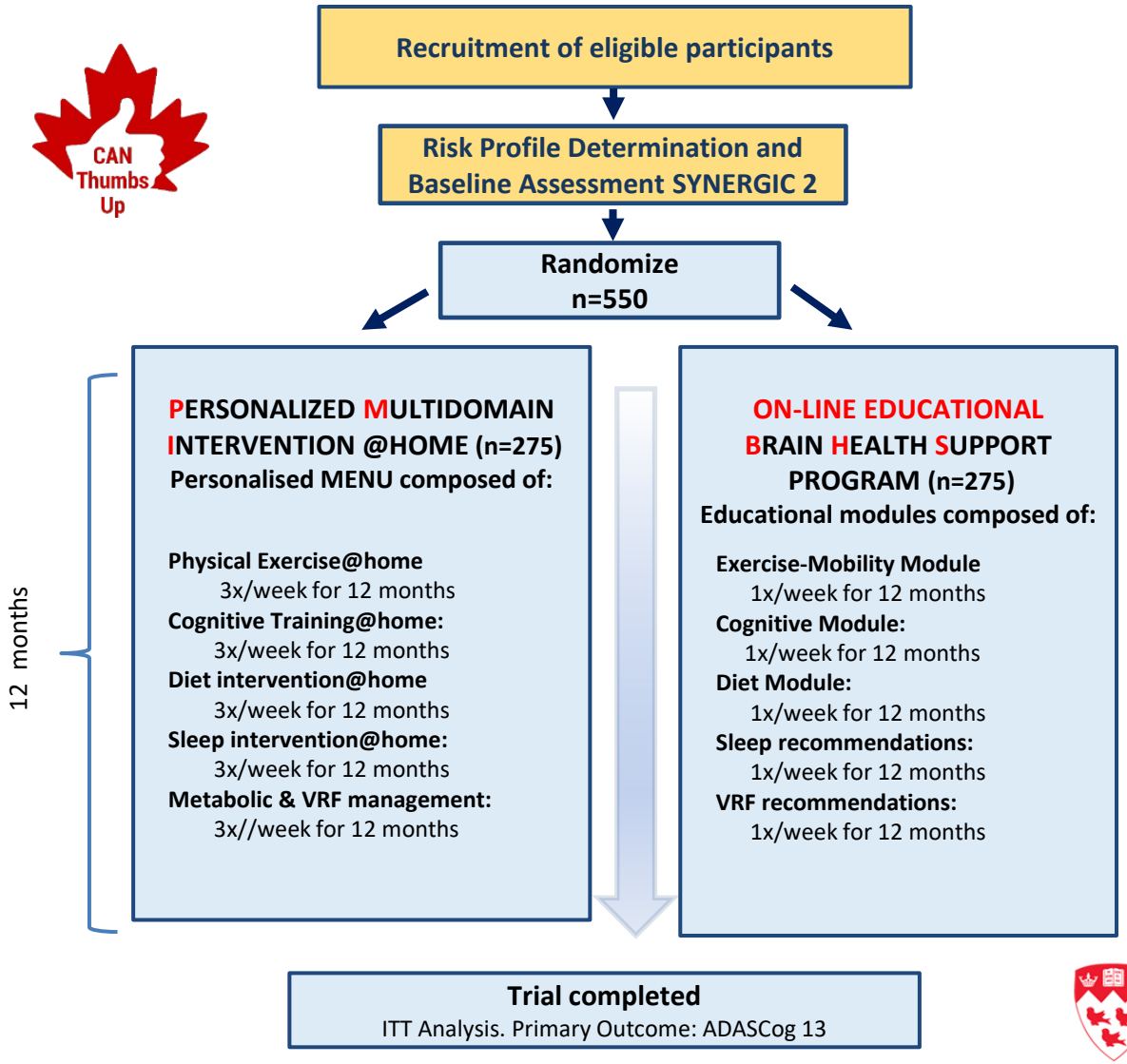
Montero-Odasso et al, 2023, *JAMA Open*

SYNERGIC 2 - Trial Consort Flowchart



RCT, @home Personalized Multidomain lifestyle Interventions for 12 months

Older adults with MCI and ≥2 lifestyle risk factors for dementia

PMI@Home:

-**individually tailored interventions (menu)** based on **patient profiles:** multimodal exercise, cognitive training, and sleep enhancement, diet coaching, metabolic/vascular risk factor coaching,

-effective coaching

Primary Outcome: ADSCog13 at 12 months (PMI group will show a 25% better performance in ADAS-Cog 13 at month 12 with an effect size of 0.22 SD)

Efficacy declared when difference between PMI and BHS in change scores of PO at end point is statistically significant at 2-sided 5% level

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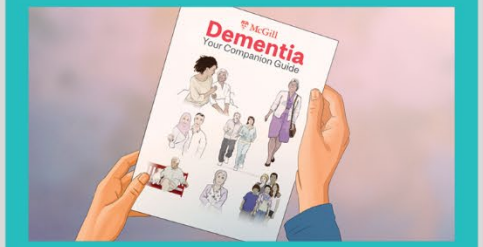
Weston Family Foundation

McGill | Dementia Education Program

www.mcgill.ca/dementia



Dementia, Your Companion Guide

Download our free educational guide, now available in 14 languages!

English, French, Spanish, Italian, Greek, Portuguese, Russian, Ukrainian, Polish, Tagalog, Punjabi, Arabic, Mandarin and Cantonese.

McGill Cares

Watch our free webcast series featuring interviews with leading experts who explore topics related to caring for a person living with dementia.

Over 110 episodes posted on YouTube. Also available as audio podcasts.

World Alzheimer Reports

Read the 2021 and 2022 reports on the diagnosis and post-diagnosis treatment, care and support for people around the world who are living with Alzheimer's disease. This report was delivered by leading experts from our program.

Virtual Support Groups & Forums

The Sharing Room
Caring Conversations
Young Caregiver Community

Join our safe online spaces where care partners can learn from experts, share concerns and ask questions.

Public Lectures

Book a lecture!

We partner with community organizations and private companies to offer lectures that raise awareness and provide basic information on Alzheimer's disease and other forms of dementia.

Trusted Resources

Visit our website to access all of our free resources!

You will also find trusted links to external resources, services and organizations that support people with dementia and their care partners.

Dementia Activity Booklet & Video Capsules

Download our free virtual toolkit and watch our video capsules!

Access over 40 recreational activities designed to engage a person with dementia, and learn how to adapt the activities to the person's needs.

Dementia Education for Care Partners - New Online Program

Register for this free self-guided online course!

It features 10 modules created by experts to educate and support you throughout your journey as a care partner to a person living with dementia.

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