Minimizing Your Risk for Alzheimer's Disease

Mehul Trivedi, PhD,
Assistant Professor, Department of Psychiatry
SIU School of Medicine, Springfield, IL.

08.November.2019

No Financial Disclosures

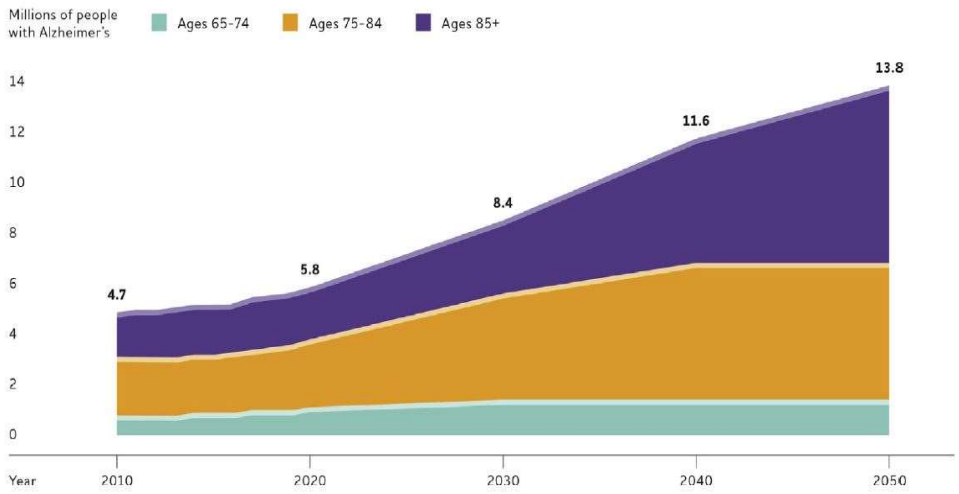
LEARNING OBJECTIVES

- Identify hereditary and lifestyle risk factors associated with increased risk for Alzheimer's disease (AD).
- Highlight current research focused on understanding preclinical neurobiological and cognitive changes in individuals at risk for AD.
- Introduce recent clinical trials focused on delaying or preventing the onset of AD.

ALZHEIMER'S DISEASE (AD)

- Progressive neurodegenerative condition.
- Most common form of dementia in older adults (>65) (70%).
- 10% of individuals aged 65 or older have AD.
- Learning and remembering new information is the first and worst symptom.
  - Other cognitive and/or behavior problems begin to emerge later.
    - Language, executive functions, visuospatial skills, personality changes, etc……
- Memory and other cognitive problems are significant enough to disrupt instrumental daily living skills (IADLs)
  - shopping, housekeeping, accounting, food preparation/meds, telephone/transportation.

PREVALENCE RATES ARE INCREASING OVER TIME

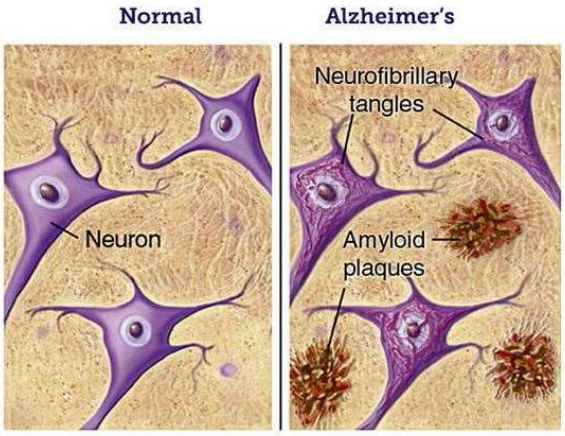


Alzheimer's Association Facts and Figures 2019

NEUROPATHOLOGY OF AD

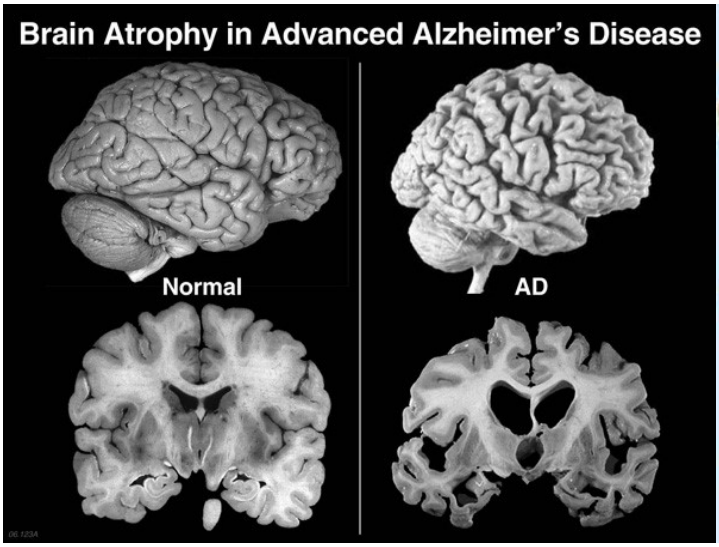
Beta Amyloid Plaques and Neurofibrillary Tangles are the Hallmarks of AD

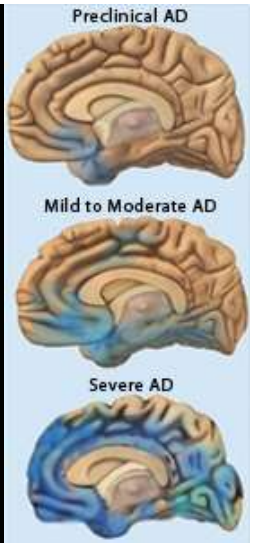
Normal vs. Alzheimer's Diseased Brain



https://www.brightfocus.org/alzheimers-disease/infographic/amyloid-plaques-and-neurofibrillary-tangles

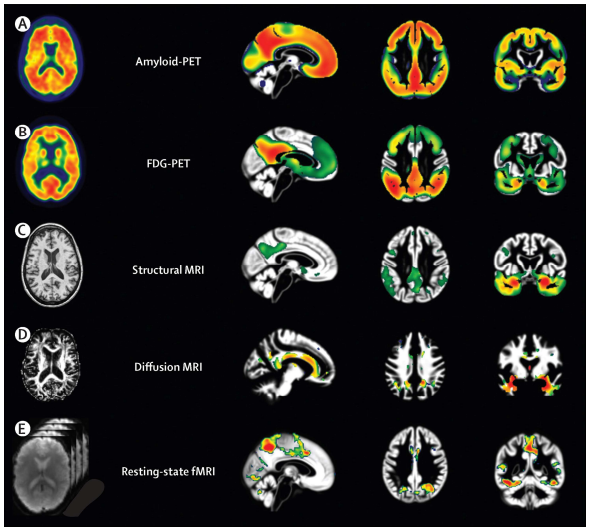
ATROPHY IN AD





IN-VIVO NEUROIMAGING IN AD

- A long preclinical phase where brain changes begin in middle age, 10-20 years before cognitive decline in individuals at greatest risk.



Teipel et al., 2015

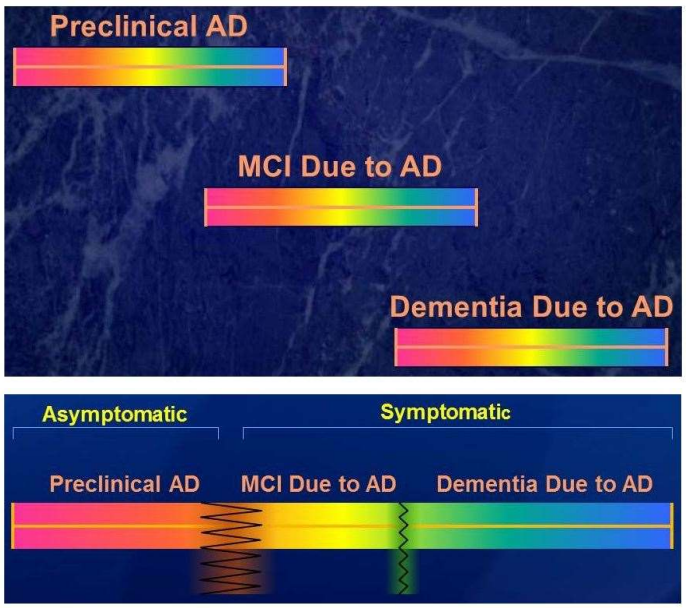
RISK FACTORS FOR AD

- Clinical risk factors.
  - Amnestic mild cognitive impairment.
- Non-modifiable risk factors.
- Modifiable risk factors.

MILD COGNITIVE IMPAIRMENT

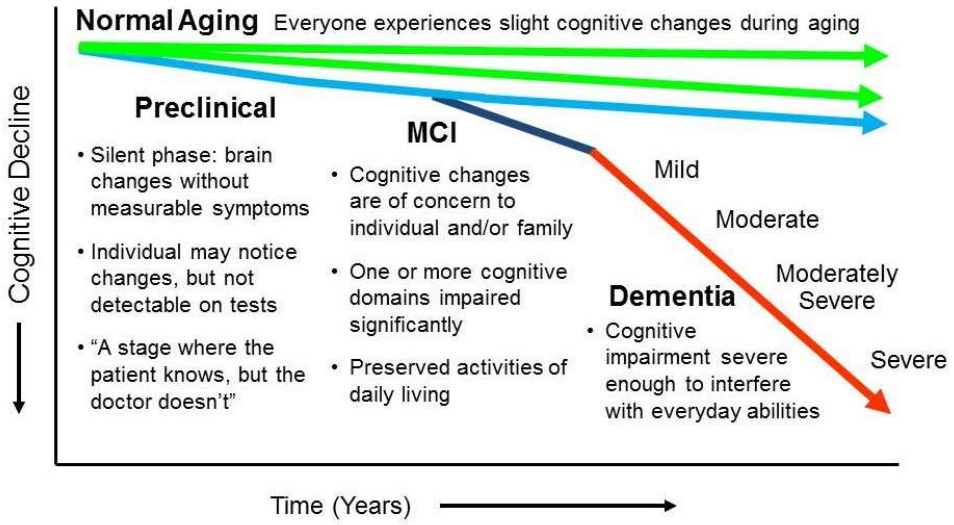
- Amnestic Mild Cognitive Impairment (aMCI)
  - Impairments in learning and remembering new information that are not significant enough to significantly disrupt IADLs.
- ***Continuum Perspective: Every patient with AD goes through an aMCI phase, but not every patient with aMCI goes on to develop AD.***
  - aMCI: annual conversion rate to AD of 10-15%
  - A small percentage of individuals with aMCI, remain aMCI for years without converting to AD, others revert back to normal.
  - Time course of decline is variable.
- aMCI might be too late in the disease process to prevent decline to AD.

A CONTINUUM PERSPECTIVE



https://aspe.hhs.gov/advisory-council-april-2016-meeting-presentation-terminology-heterogeneity

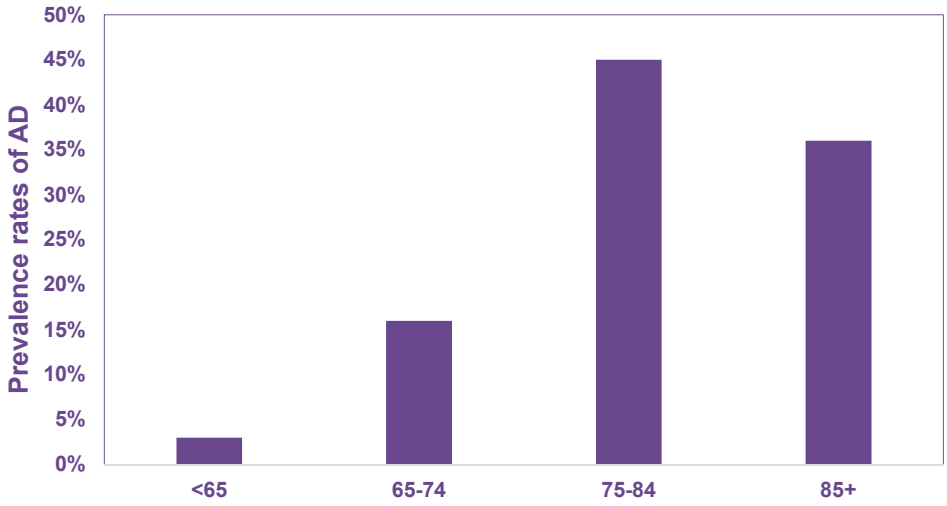
A CONTINUUM PERSPECTIVE



http://www.mind.uci.edu/wp-content/uploads/2013/08/Normal-aging-to-dementia.jpg

NON-MODIFIABLE RISK FACTORS

- **INCREASING AGE:** #1 risk factor for late-onset AD



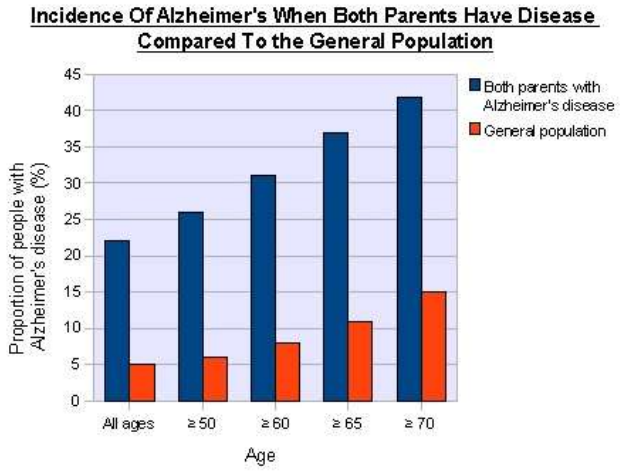
adapted Alzheimer's Association Facts and Figures 2019

NON-MODIFIABLE RISK FACTORS

- **FAMILY HISTORY OF AD**
- People *without* a family history also develop AD.
- But, having a parent or sibling with AD increases risk.
  - The more relatives with AD, the greater the risk.
  - Risk is greater in children versus siblings.

NON-MODIFIABLE RISK FACTORS

- **FAMILY HISTORY OF AD**



Data from: "Conjugal Alzheimer Disease: Risk in Children When Both Parents Have Alzheimer Disease" – Archives of Neurology, 2008

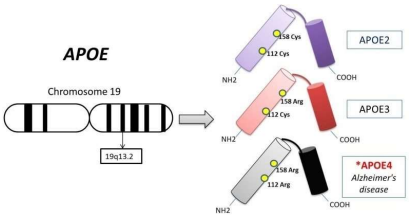
NON-MODIFIABLE RISK FACTORS

- **APOE GENOTYPE**
  - APOE gene is a protein involved in the metabolism of fats in the body.
  - 3 alleles (e2, e3, e4), 6 genotypes.
    - e2/2, e2/3, e3/3, e2/4, e3/4, e4/4
  - Inheriting one copy of the e4 allele is associated with increased risk for developing aMCI and AD.

Estimated percentages of the U.S. population with the six possible e2, e3 and e4 pairs of the apolipoprotein E (*APOE*) gene

APOE pair	Percentage
e2/e2	0.5
e2/e3	11
e2/e4	2
e3/e3	61
e3/e4	23
e4/e4	2

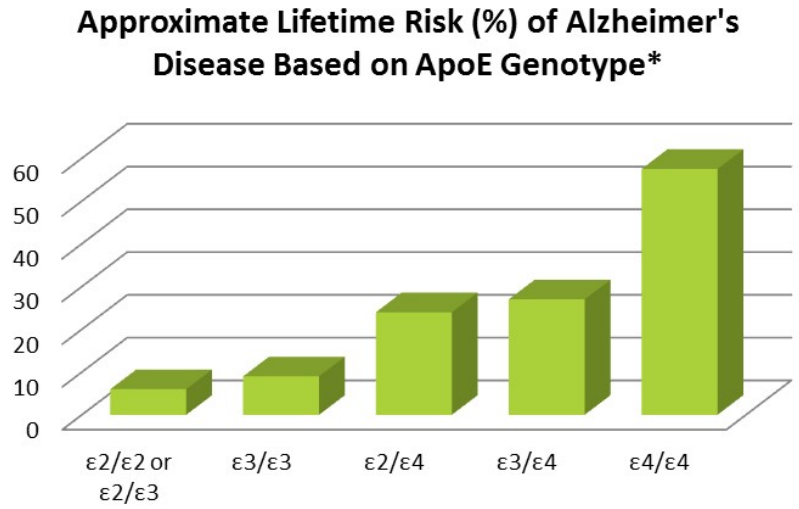
NOTE. Created from data from Raber and colleagues [40]. Percentages do not total 100 due to rounding.



- 20+ other genes increase risk for AD, none as great as the e4 allele (www.alzgene.org).

Alzheimer's Association Facts and Figures 2017

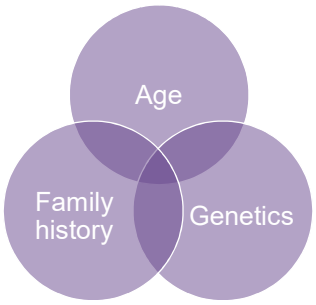
NON-MODIFIABLE RISK FACTORS



*data adapted from Genin *et al.*, Molec Psych (2011) 16:903, https://adxhealthcare.com/apoe-information/

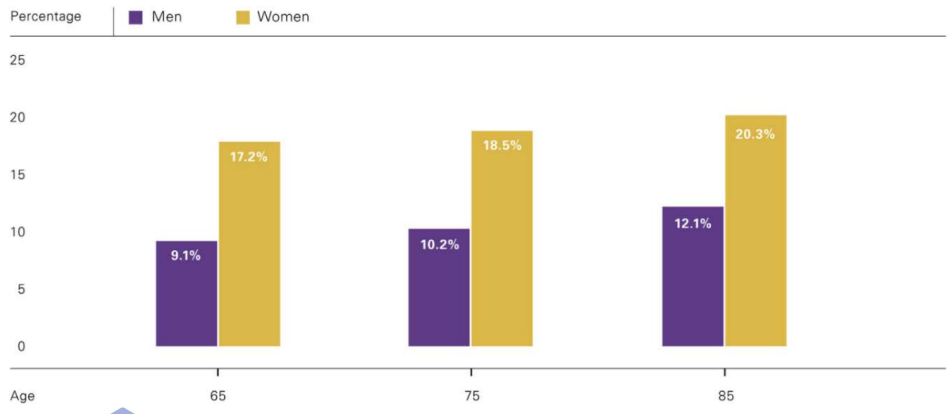
NON-MODIFIABLE RISK FACTORS

- **INDEPENDENT AND INTERACTIVE EFFECTS**
  - APOE e4 allele is more common in the children of individuals with AD.
    - 47% (Wisconsin Registry for Alzheimer's Prevention).
    - 27% in the general population.
  - Lower age at onset of AD symptoms in e4 carriers.



GENDER

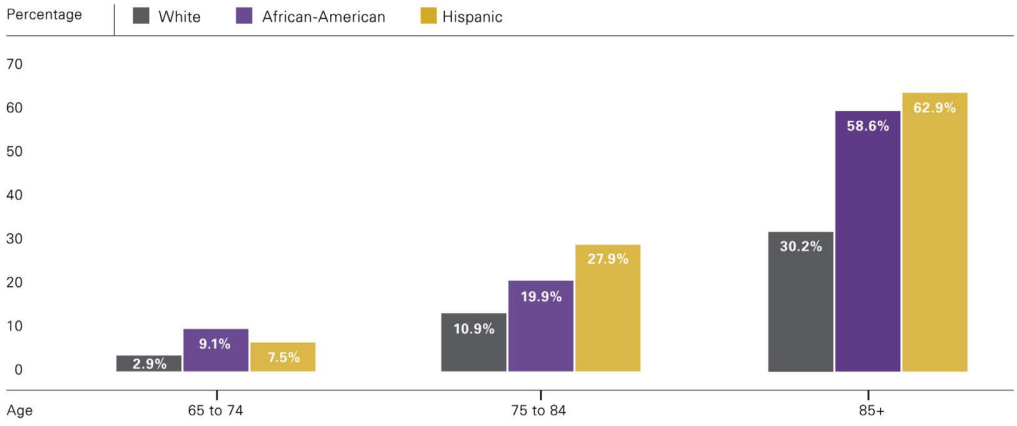
- Women are at greater risk for AD
  - Not just related to longer life expectancy for women.
- Almost two-thirds of US citizens with AD are women.



Alzheimer's Association Facts and Figures 2015

RACE AND ETHNICITY

- Older African-Americans and Hispanic Americans are 1.5-2 times more likely to develop AD compared to older not-Hispanic/White Americans.



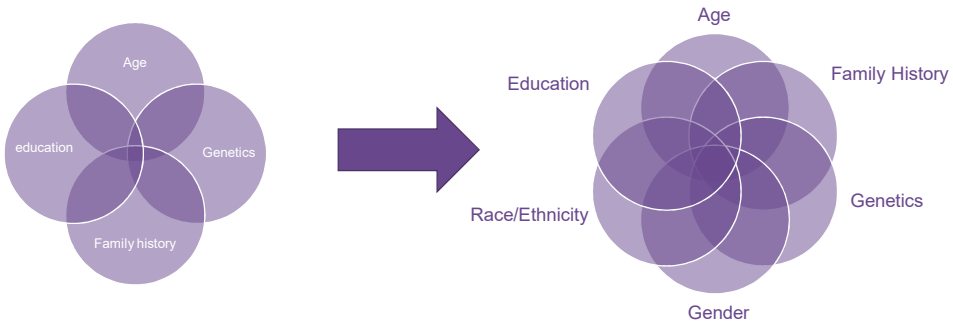
Alzheimer's Association Facts and Figures 2014, 2017

RACE AND ETHNICITY

- APOE e4 allele less strongly associated with AD in African-Americans.
- Other genetic factors might be more strongly associated with greater risk for AD in African Americans.
- *Modifiable risk factors*, health disparities.
  - Variations in health, lifestyle and socioeconomic risk factors across racial groups likely account for most of the differences in risk for AD.

Alzheimer's Association Facts and Figures 2019

COMPLEX INTERACTIONS AMONG NON-MODIFIABLE RISK FACTORS



MODIFIABLE RISK FACTORS FOR AD

- Up to 50% of all cases of AD may be due to potentially modifiable AD risk factors.
- Midlife: a ***critical*** period where many modifiable risk factors influence the development of AD later in life.
  - Supported by epidemiological, neuropsychological, and neuroimaging studies.

IS MIDLIFE A CRITICAL PERIOD IN THE DEVELOPMENT OF AD IN LATE LIFE?

Review Article

Is late-onset Alzheimer's disease really a disease of midlife?

Karen Ritchie[a,b,*,1], Craig W. Ritchie[c,d,1], Kristine Yaffe[e], Ingmar Skoog[f], Nikolaos Scarmeas[g,h]

[a]Institut National de la Santé et de la Recherche Médicale, U1061 Neuropsychiatry, Montpellier, France
[b]Faculty of Medicine, University of Montpellier, France
[c]Faculty of Medicine, Imperial College London, UK
[d]Department of Psychiatry, University of Edinburgh, UK
[e]University of California at San Francisco, USA
[f]Centre for Health and Ageing (AgeCap), Institute of Neuroscience and Physiology, Sahlgrenska Academy at the University of Gothenburg, Sweden
[g]Department of Social Medicine, Psychiatry and Neurology, National and Kapodistrian University of Athens, Greece
[h]Taub Institute for Research in Alzheimer's Disease and the Aging Brain, the Gertrude H. Sergievsky Center, Department of Neurology, Columbia University, New York, NY, USA

- Considerable evidence suggests that exposure to AD risk factors and brain changes appear to already be present in midlife.
- Promotion of cardiovascular health during midlife in persons with a family history of AD may considerably reduce disease risk.
- Strong need for dedicated prospective biomarker studies in middle-age, at risk populations.

Ritchie et al., 2015, Alzheimer & Dementia: Translational Research & Clinical Interventions (2015) 122-130

MODIFIABLE RISK FACTORS FOR AD

Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective

Matthew Baumgart[a], Heather M. Snyder[b,*], Maria C. Carrillo[b], Sam Fazio[c], Hye Kim[a], Harry Johns[d]

[a]Division of Public Policy, Alzheimer's Association, Washington, DC, USA
[b]Division of Medical & Scientific Relations, Alzheimer's Association, Chicago, IL, USA
[c]Division of Constituent Relations, Alzheimer's Association, Chicago, IL, USA
[d]President & CEO, Alzheimer's Association, Chicago, IL, USA

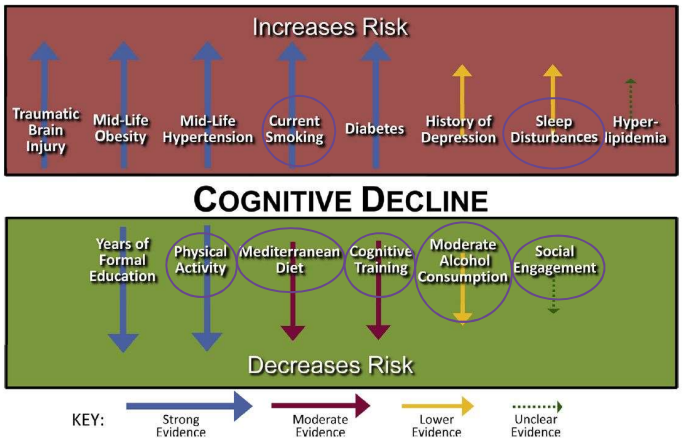


Fig. 1. Strength of evidence on risk factors for cognitive decline.

Baumgart et al. (2015) *Alzheimer's and Dementia*, 11, 718-26

MODIFIABLE RISK FACTORS FOR AD

Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective

Matthew Baumgart[a], Heather M. Snyder[b,*], Maria C. Carrillo[b], Sam Fazio[c], Hye Kim[a], Harry Johns[d]

[a]Division of Public Policy, Alzheimer's Association, Washington, DC, USA
[b]Division of Medical & Scientific Relations, Alzheimer's Association, Chicago, IL, USA
[c]Division of Constituent Relations, Alzheimer's Association, Chicago, IL, USA
[d]President & CEO, Alzheimer's Association, Chicago, IL, USA

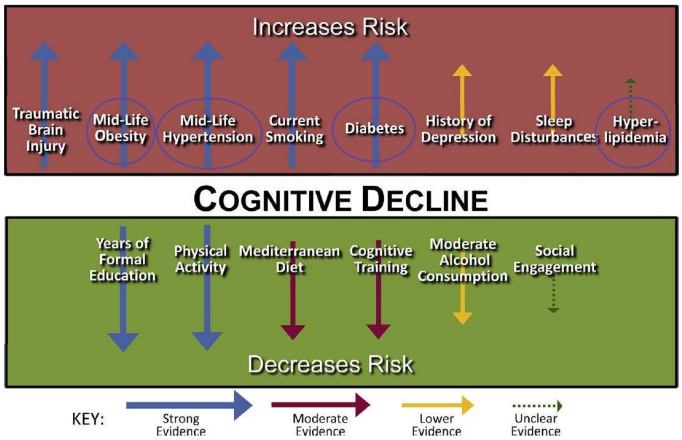


Fig. 1. Strength of evidence on risk factors for cognitive decline.

Baumgart et al. (2015) *Alzheimer's and Dementia*, 11, 718-26

MODIFIABLE RISK FACTORS FOR AD

Potential for primary prevention of Alzheimer's disease: an analysis of population-based data

Sam Norton, Fiona E Matthews, Deborah E Barnes, Kristine Yaffe, Carol Brayne

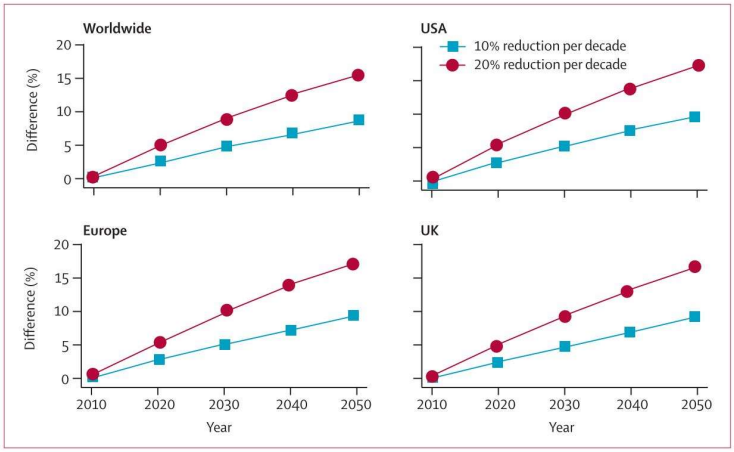


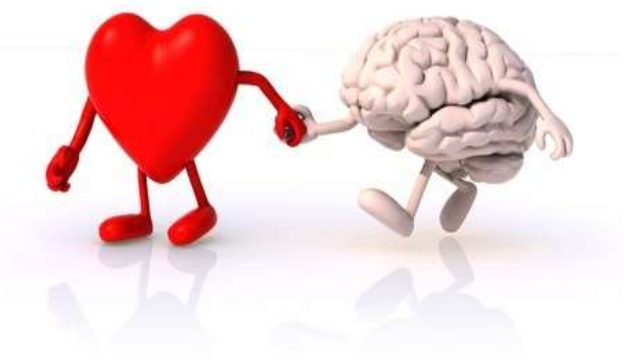
Figure: Projected percentages of Alzheimer's disease cases that could be prevented, with 10% or 20% reductions per decade in each risk factor

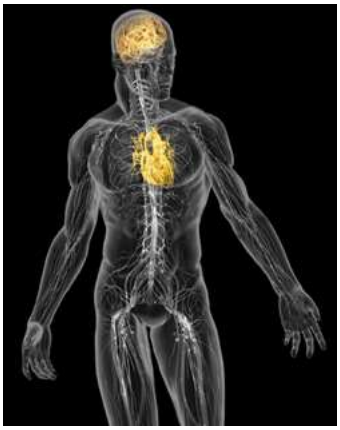
Norton et al., Lancet Neurol. 2014 Sep;13:788-94.

MODIFIABLE RISK FACTORS FOR AD ARE ALSO HEART DISEASE AND STROKE RISK FACTORS

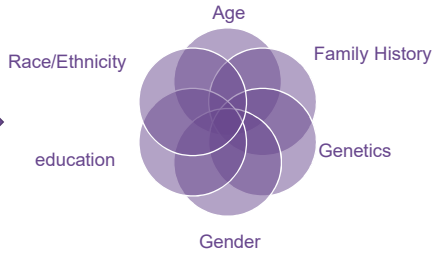
- Modifiable risk factors tend to aggregate in individuals.
- ***Metabolic syndrome***: 3 or more of hypertension, obesity, hyperlipidemia, diabetes.

WHAT'S GOOD FOR THE HEART IS GOOD FOR THE MIND





COMPLEX INTERACTIONS BETWEEN MODIFIABLE AND NON-MODIFIABLE RISK FACTORS



RISK FACTORS FOR ALZHEIMER'S DISEASE IN MIDLIFE PREDICT DEMENTIA IN LATE LIFE

Midlife risk score for the prediction of dementia four decades later

Lieza G. Exalto[a,b], Charles P. Quesenberry[a], Deborah Barnes[c], Miia Kivipelto[d], Geert Jan Biessels[a], Rachel A. Whitmer[b,*]

[a]Kaiser Permanente Division of Research, Oakland, CA, USA
[b]Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Centre Utrecht, Utrecht, Netherlands
[c]University of California, San Francisco, CA, USA
[d]Karolinska Aging Research Centre, Karolinska University, Stockholm Sweden

Higher aggregate CAIDE risk factor scores in midlife predict the development of dementia 40 years later.

- Age
- Education
- Hypertension
- Body mass index (BMI)
- Hyperlipidemia

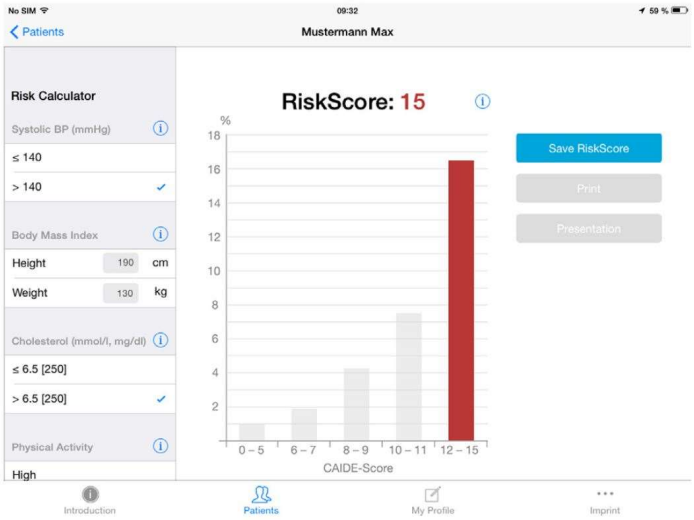
Associations of CAIDE Dementia Risk Score with MRI, PIB-PET measures, and cognition

Ruth Stephen[a,b,*], Yawu Liu[a,c], Tiia Ngandu[d,e], Juha O. Rinne[f,g], Nina Kemppainen[g], Riitta Parkkola[f], Tiina Laatikainen[d,h], Teemu Paajanen[i], Tuomo Hänninen[j], Timo Strandberg[k,l], Riitta Antikainen[l,m], Jaakko Tuomilehto[d,n,o,p,q,r], Sirkka Keinänen Kiukaanniemi[l,m], Ritva Vanninen[c], Seppo Helisalmi[a], Esko Levälahti[d], Miia Kivipelto[a,d,e], Hilkka Soininen[a,b] and Alina Solomon[a,e]

Higher CAIDE scores at midlife are associated with Alzheimer's disease brain changes 30 years later.

- Greater white matter disease
- Reduced cortical and hippocampal volume
- Worse cognitive function.

CAIDE APP



https://itunes.apple.com/us/app/caide-risk-score-app/id897853817

PROSPECTIVE, COHORT STUDIES IN MIDDLE AGED INDIVIDUALS AT RISK FOR AD

- Not many, very expensive, very long follow-up time.
- Wisconsin Registry for Alzheimer's Prevention (WRAP)

ELSEVIER

CrossMark

Alzheimer's & Dementia

Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 10 (2018) 130-142

Diagnostic Assessment & Prognosis

The Wisconsin Registry for Alzheimer's Prevention: A review of findings and current directions

Sterling C. Johnson[a,b,c,*], Rebecca L. Koscik[a], Erin M. Jonaitis[a], Lindsay R. Clark[a,b,c], Kimberly D. Mueller[a], Sara E. Berman[b], Barbara B. Bendlin[a,b], Corinne D. Engelman[a,b], Ozioma C. Okonkwo[a,b], Kirk J. Hogan[a], Sanjay Asthana[b,c], Cynthia M. Carlsson[a,b,c], Bruce P. Hermann[a], Mark A. Sager[a]

[a]Wisconsin Alzheimer's Institute, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
[b]Wisconsin Alzheimer's Disease Research Center, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
[c]Geriatric Research Education and Clinical Center, Wm. S. Middleton Veterans Hospital, Madison WI, USA

WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION (WRAP)

Cardiorespiratory fitness is associated with brain structure, cognition, and mood in a middle-aged cohort at risk for Alzheimer's disease

Elizabeth A. Boots • Stephanie A. Schultz • Jennifer M. Oh • Jordan Larson • Dorothy Edwards • Dane Cook • Rebecca L. Koscik • Maritza N. Dowling • Catherine L. Gallagher • Cynthia M. Carlsson • Howard A. Rowley • Barbara B. Bendlin • Asenath LaRue • Sanjay Asthana • Bruce P. Hermann • Mark A. Sager • Sterling C. Johnson • Ozioma C. Okonkwo

Meeting physical activity recommendations may be protective against temporal lobe atrophy in older adults at risk for Alzheimer's disease

Ryan J. Dougherty[a,b], Laura D. Ellingson[a,c], Stephanie A. Schultz[d,e,f], Elizabeth A. Boots[d,e,f], Jacob D. Meyer[a,g], Jacob B. Lindheimer[a,b], Stephanie Van Riper[a,b], Aaron J. Stegner[a,b], Dorothy F. Edwards[b,e,f], Jennifer M. Oh[d,e,f], Rebecca L. Koscik[f], Maritza N. Dowling[h], Catherine L. Gallagher[d,e], Cynthia M. Carlsson[d,e], Howard A. Rowley[e], Barbara B. Bendlin[d,e,f], Sanjay Asthana[d,e], Bruce P. Hermann[e,f,i], Mark A. Sager[e,f], Sterling C. Johnson[d,e,f], Ozioma C. Okonkwo[d,e,f], Dane B. Cook[a,b,*]

Boots et al., 2014, Dougherty et al., 2016

INTERVENTIONS TO PREVENT COGNITIVE DECLINE

Comparative Effectiveness Review
Number 188

Interventions To Prevent Age-Related Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer's-Type Dementia

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

Contract No. 290-2015-00008-I

Prepared by:
Minnesota Evidence-based Practice Center
Minneapolis, MN

Investigators:
Robert L. Kane, M.D.
Mary Butler, Ph.D., M.B.A.
Howard A. Fink, M.D., M.P.H.
Michelle Brasure, Ph.D., M.L.I.S.
Heather Davila, M.P.A.
Priyanka Desai, M.H.P.
Eric Jutkowitz, B.A.
Ellen McCreedy, Ph.D.
Victoria A. Nelson, M.Sc.
J. Riley McCarten, M.D.
Collin Calvert, B.A.
Edward Ratner, M.D.
Laura S. Hemmy, Ph.D.
Terry Barclay, Ph.D., L.P.

Kane, R. L., et al. (2017). AHRQ Comparative Effectiveness Reviews.

INTERVENTIONS TO PREVENT COGNITIVE DECLINE

- 263 eligible studies (primarily in older adults); 13 classes of interventions were identified:
  - cognitive training
  - physical activity
  - nutraceuticals
  - diet
  - multimodal interventions
  - hormone therapy
  - vitamins
  - antihypertensive treatment
  - lipid lowering treatment
  - nonsteroidal anti-inflammatory drugs (NSAIDs)
  - anti-dementia drugs
  - diabetes treatment
  - "other interventions"

INTERVENTIONS TO PREVENT COGNITIVE DECLINE

- **NO** high-strength evidence for any intervention to delay cognitive decline.
- Moderate-strength evidence that cognitive training in older adults improves performance in the domain that was trained (memory, processing speed).
  - Benefits did not transfer to other cognitive areas.
  - Little evidence for benefit beyond 2 years after trial conclusion.
- Low-strength evidence for physical activity, antihypertensive medications, NSAIDs, B vitamins, nutraceuticals, and multimodal interventions.
- Methodological limitations were prominent.
  - Lack of consistent cognitive outcome measures, longer follow-up duration needed, and participant attrition in longer duration interventions.
- Recommended testing interventions that address modifiable risk factors can help to establish their causative role in MCI and AD.

FINGER STUDY

Recruitment and Baseline Characteristics of Participants in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)—A Randomized Controlled Lifestyle Trial †

Tiia Ngandu [1,2]*, Jenni Lehtisalo [1], Esko Levälahti [1], Tiina Laatikainen [1,3], Jaana Lindström [1], Markku Peltonen [1], Alina Solomon [2,4,5], Satu Ahtiluoto [1], Riitta Antikainen [6,7,8], Tuomo Hänninen [9], Antti Jula [1], Francesca Mangialasche [5], Teemu Paajanen [10], Satu Pajala [11], Rainer Rauramaa [12], Timo Strandberg [6,13], Jaakko Tuomilehto [14,15,16,17], Hilkka Soininen [4,9] and Miia Kivipelto [1,2,4,5]

- 1,260 cognitively normal, older adults in Finland between the ages of 60-77 completed a 2-year multi-domain intervention (diet, exercise, cognitive training, vascular risk monitoring).
- Outcome measures: cognition, dementia (after extended follow-up), disability, vascular risk factors and outcomes, depressive symptoms, quality of life, and neuroimaging measures.

Ngandu et al. (2014) Int. J. Environ. Res. Public Health, 11, 9345-9360
Ngandu et al. (2015) Lancet, 385, 2255-63

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

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

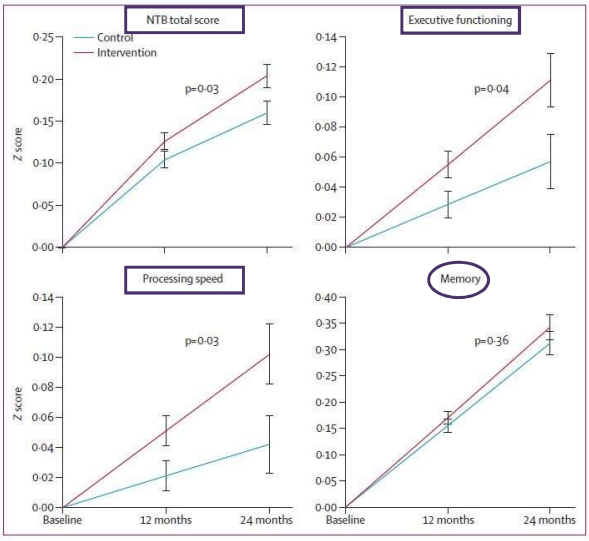


Figure 2: Change in cognitive performance during the 2 year intervention

U.S.POINTER

alzheimer's association®

Intervention Methods will Include:

Recruitment began in 2018

https://alz.org/us-pointer/overview.asp

WORLD WIDE FINGERS

A GLOBAL COLLABORATION FOR FUTURE GENERATIONS

The World Wide FINGERS (WW-FINGERS) is an interdisciplinary network to share experiences, harmonize data and plan joint international initiatives for the prevention of cognitive impairment or dementia.

WORLD WIDE FINGERS

alzheimer's association®

https://alz.org/us-pointer/overview.asp

WORLD WIDE FINGERS

https://www.coalitionforbetterhealth.org/advisors_partners

GRAY MATTERS STUDY

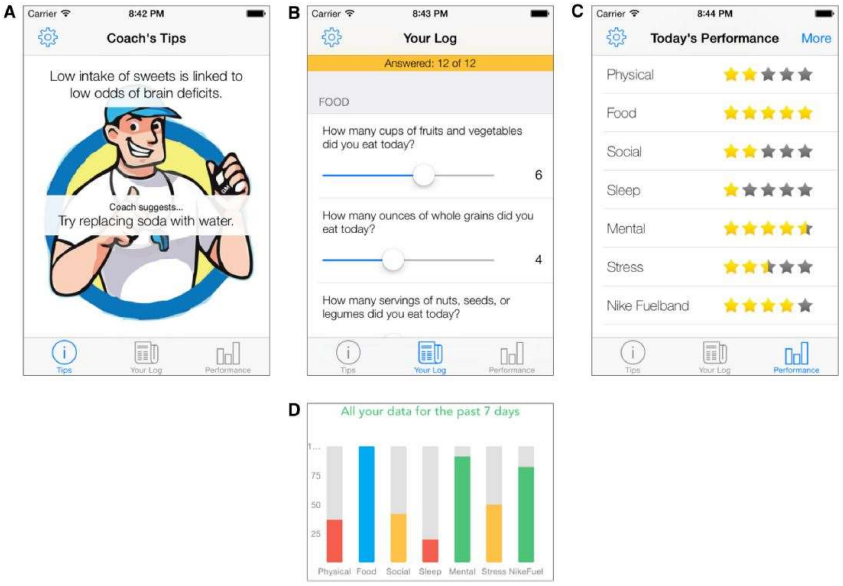
The design and progress of a multidomain lifestyle intervention to improve brain health in middle-aged persons to reduce later Alzheimer's disease risk: The Gray Matters randomized trial

Maria C. Norton[a,b,*], Christine J. Clark[a], JoAnn T. Tschanz[b], Phillip Hartin[c], Elizabeth B. Fauth[a], Julie A. Gast[d], Travis E. Dorsch[a,d], Heidi Wengreen[e], Chris Nugent[c], W. David Robinson[a], Michael Lefevre[e], Sally McClean[f], Ian Cleland[c], Sydney Y. Schaefer[d], Sheryl Aguilar[e]

[a]Department of Family Consumer and Human Development, Utah State University, Logan, UT, USA
[b]Department of Psychology, Utah State University, Logan, UT, USA
[c]School of Computing and Mathematics, University of Ulster, Londonderry, UK
[d]Department of Health, Physical Education and Recreation, Utah State University, Logan, UT, USA
[e]Department of Nutrition, Dietetics and Food Sciences, Utah State University, Logan, UT, USA
[f]School of Computing and Information Engineering, University of Ulster, Londonderry, UK

- 6-month multimodal intervention conceptually similar to FINGER and POINTER studies but in middle aged adults with much smaller sample size (N=144).
- Increase in positive health behavior changes across intervention trial was associated with improved vascular health.
  - Lower Body mass index.
  - Higher HDL (good cholesterol).
  - Greater motivation to engage in physical activity and make healthy food choices.

GRAY MATTERS STUDY



http://graymattersapp.org/

PRECISION MEDICINE AND RISK REDUCTION

ELSEVIER

Check for updates

Alzheimer's & Dementia 14 (2018) 1663–1673

Alzheimer's & Dementia

Perspective

The clinical practice of risk reduction for Alzheimer's disease: A precision medicine approach

Richard S. Isaacson[a,*], Christine A. Ganzer[b], Hollie Hristov[a], Katherine Hackett[c], Emily Caesar[d], Randy Cohen[e], Robert Kachko[f], Josefina Meléndez-Cabrero[g], Aneela Rahman[a], Olivia Scheyer[a], Mu Ji Hwang[h], Cara Berkowitz[i], Suzanne Hendrix[j], Monica Mureb[a], Matthew W. Schelke[k], Lisa Mosconi[a], Alon Seifan[l], Robert Krikorian[m]

- Precision Medicine is focused on identifying treatment approaches for chronic diseases that will be effective for different groups of patients based on genetic, environmental, and lifestyle factors.
- Applying these evidence-based principles of precision medicine to tailor individualized recommendations, follow patients longitudinally to continually refine the interventions, and evaluate "N-of-1 effectiveness."
- Preliminary results (N=600) suggest that the clinical practice of AD risk reduction is feasible with measurable improvements in cognition and biomarkers of AD risk.

INDIVIDUALIZED CLINICAL MANAGEMENT OF PATIENTS AT RISK FOR AD

ELSEVIER

Alzheimer's & Dementia ■ (2019) 1-15

Alzheimer's & Dementia

Featured Article

Individualized clinical management of patients at risk for Alzheimer's dementia

Richard S. Isaacson[a,*], Hollie Hristov[a], Nabeel Saif[a], Katherine Hackett[b], Suzanne Hendrix[c], Juan Melendez[d], Joseph Safdieh[a], Matthew Fink[a], Madhav Thambisetty[e], George Sadek[a], Sonia Bellara[a], Paige Lee[f], Cara Berkowitz[a], Aneela Rahman[a], Josefina Meléndez-Cabrero[g], Emily Caesar[h], Randy Cohen[i], Pei-lin Lu[j], Samuel P. Dickson[c], Mu Ji Hwang[a], Olivia Scheyer[k], Monica Mureb[a], Matthew W. Schelke[l], Kellyann Niotis[a], Christine E. Greer[m], Peter Attia[n], Lisa Mosconi[a], Robert Krikorian[o]

- Multimodal individualized intervention focused on patient education, genetic counseling, pharmacological approaches, nonpharmacological approaches in individuals with AD risk factors (N=174).
- Cognition, AD/vascular risk factors, and serum biomarkers were measured at baseline and after 18-month follow-up.
- Individuals in the intervention group demonstrated improved cognition and reduced AD/vascular risk factor scores.

PREVALENCE OF PRECLINICAL AD

ELSEVIER

CrossMark

Alzheimer's & Dementia 14 (2018) 121-129

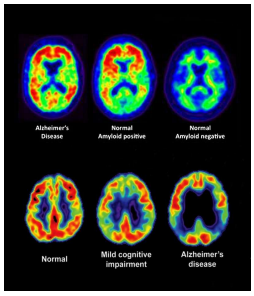
Alzheimer's & Dementia

Featured Article

Forecasting the prevalence of preclinical and clinical Alzheimer's disease in the United States

Ron Brookmeyer[a,*], Nada Abdalla[a], Claudia H. Kawas[b,c,d], María M. Corrada[b,d,e]

[a]Department of Biostatistics, University of California, Los Angeles, CA, USA
[b]Department of Neurology, University of California, Irvine, CA, USA
[c]Department of Neurobiology and Behavior, University of California, Irvine, CA, USA
[d]Institute for Memory Impairments and Neurological Disorders, University of California, Irvine, CA, USA
[e]Department of Epidemiology, University of California, Irvine, CA, USA



- 6.08 million with AD or mild cognitive impairment due to AD in 2017.
- 46.7 million Americans with preclinical AD including amyloidosis, neurodegeneration, or both.
- Critical need for both primary prevention in individuals without preclinical AD and secondary prevention of developing AD in individual with preclinical AD.

RESEARCH ARTICLE Open Access

Formulation of evidence-based messages to promote the use of physical activity to prevent and manage Alzheimer's disease

Kathleen A. Martin Ginis[1*], Jennifer Heisz[2], John C. Spence[3], Ilana B. Clark[2], Jordan Antflick[4], Chris I. Ardern[5], Christa Costas-Bradstreet[6], Mary Duggan[7], Audrey L. Hicks[2], Amy E. Latimer-Cheung[8], Laura Middleton[9], Kirk Nylen[4], Donald H. Paterson[10], Chelsea Pelletier[11] and Michael A. Rotondi[5]

"Regular participation in physical activity is associated with a reduced risk of developing Alzheimer's disease. Among older adults with Alzheimer's disease and other dementias, regular physical activity can improve performance of activities of daily living and mobility, and may improve general cognition and balance."

10 Ways to Love Your Brain

Growing evidence indicates that people can reduce their risk of cognitive decline by adopting key lifestyle habits. When possible, combine these habits to achieve maximum benefit for the brain and body. Start now. It's never too late or too early to incorporate healthy habits.

Break a sweat

Engage in regular cardiovascular exercise that elevates your heart rate and increases blood flow to the brain and body. Several studies have found an association between physical activity and reduced risk of cognitive decline.

Hit the books

Formal education in any stage of life will help reduce your risk of cognitive decline and dementia. For example, take a class at a local college, community center or online.

Butt out

Evidence shows that smoking increases risk of cognitive decline. Quitting smoking can reduce that risk to levels comparable to those who have not smoked.

Follow your heart

Evidence shows that risk factors for cardiovascular disease and stroke — obesity, high blood pressure and diabetes — negatively impact your cognitive health. Take care of your heart, and your brain just might follow.

Heads up!

Brain injury can raise your risk of cognitive decline and dementia. Wear a seat belt, use a helmet when playing contact sports or riding a bike, and take steps to prevent falls.

https://www.alz.org/help-support/brain_health/10_ways_to_love_your_brain

10 Ways to Love Your Brain

Buddy up

Staying socially engaged may support brain health. Pursue social activities that are meaningful to you. Find ways to be part of your local community — if you love animals, consider volunteering at a local shelter. If you enjoy singing, join a local choir or help at an after-school program. Or, just share activities with friends and family.

Stump yourself.

Challenge and activate your mind. Build a piece of furniture. Complete a jigsaw puzzle. Do something artistic. Play games, such as bridge, that make you think strategically. Challenging your mind may have short and long-term benefits for your brain.

Fuel up right

Eat a healthy and balanced diet that is lower in fat and higher in vegetables and fruit to help reduce the risk of cognitive decline. Although research on diet and cognitive function is limited, certain diets, including Mediterranean and Mediterranean-DASH (Dietary Approaches to Stop Hypertension), may contribute to risk reduction.

Catch some Zzz's

Not getting enough sleep due to conditions like insomnia or sleep apnea may result in problems with memory and thinking.

Take care of your mental health

Some studies link a history of depression with increased risk of cognitive decline, so seek medical treatment if you have symptoms of depression, anxiety or other mental health concerns. Also, try to manage stress.

https://www.alz.org/help-support/brain_health/10_ways_to_love_your_brain

SUMMARY

- AD is the most common cause of age-related dementia.
- Non-modifiable and modifiable risk factors.
- Reducing prevalence rates of modifiable risk factors by 10-20% could reduce prevalence rates of AD by up to 15%.
  - Midlife is a critical period.
- Intervention studies to date have yet to produce high or moderate evidence to support their use in prevention of AD.
- Some support for physical activity and multimodal interventions in improving cognition in older adults.
  - FINGER and POINTER studies.
- Higher levels of physical activity are associated with improved vascular health and reduced AD biomarkers in middle aged adults at risk for AD.

REFERENCES

- Alzheimer's disease facts and figures. Alzheimers Dement. 2019, 15, 321-87.
- Alzheimer's disease facts and figures. Alzheimers Dement. 2017, 13, 325-73.
- Alzheimer's disease facts and figures. Alzheimers Dement. 2015, 11(3):332-84.
- Alzheimer's disease facts and figures. Alzheimers Dement. 2014, Mar;10(2):e47-92.
- Baumgart, M., et al. (2015). "Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective." Alzheimers Dement **11**(6): 718-726.
- Boots, E. A., et al. (2015). "Cardiorespiratory fitness is associated with brain structure, cognition, and mood in a middle-aged cohort at risk for Alzheimer's disease." Brain Imaging Behav **9**(3): 639-649.
- Dougherty, R. J., et al. (2016). "Meeting physical activity recommendations may be protective against temporal lobe atrophy in older adults at risk for Alzheimer's disease." Alzheimers Dement (Amst) **4**: 14-17.
- Exalto et al. Midlife risk score for the prediction of dementia four decades later. Alzheimers Dement. 2014 Sep;10(5):562-70.
- Ginis, K. A., et al. (2017). "Formulation of evidence-based messages to promote the use of physical activity to prevent and manage Alzheimer's disease." BMC Public Health **17**(1): 209.

REFERENCES

- Hartin, P. J., et al. (2016). "The Empowering Role of Mobile Apps in Behavior Change Interventions: The Gray Matters Randomized Controlled Trial." JMIR Mhealth Uhealth **4**(3): e93.
- Isaacson, R. S., et al. (2019). "Individualized clinical management of patients at risk for Alzheimer's dementia." Alzheimers Dement.
- Jayadev, S., et al. (2008). "Conjugal Alzheimer disease: risk in children when both parents have Alzheimer disease." Arch Neurol **65**(3): 373-378.
- Kane, R. L., et al. (2017). AHRQ Comparative Effectiveness Reviews. Interventions to Prevent Age-Related Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer's-Type Dementia. Rockville (MD), Agency for Healthcare Research and Quality (US).
- Norton, S., et al. (2014). "Potential for primary prevention of Alzheimer's disease: an analysis of population-based data." Lancet Neurol **13**(8): 788-794.
- Ngandu, T., et al. (2014). "Recruitment and baseline characteristics of participants in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)-a randomized controlled lifestyle trial." Int J Environ Res Public Health **11**(9): 9345-9360.
- Ngandu, T., et al. (2015). "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 **385**(9984): 2255-2263.
- Sindi, S., et al. (2015). "The CAIDE Dementia Risk Score App: The development of an evidence-based mobile application to predict the risk of dementia." Alzheimers Dement (Amst) **1**(3): 328-333.

REFERENCES

- Stephen, R., et al. (2017). "Associations of CAIDE Dementia Risk Score with MRI, PIB-PET measures, and cognition." J Alzheimers Dis **59**(2): 695-705.
- Vuorinen, M., et al. (2015). "Midlife CAIDE dementia risk score and dementia-related brain changes up to 30 years later on magnetic resonance imaging." J Alzheimers Dis **44**(1): 93-101.