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Blanchette Rockefeller Neurosciences Institute
West Virginia University

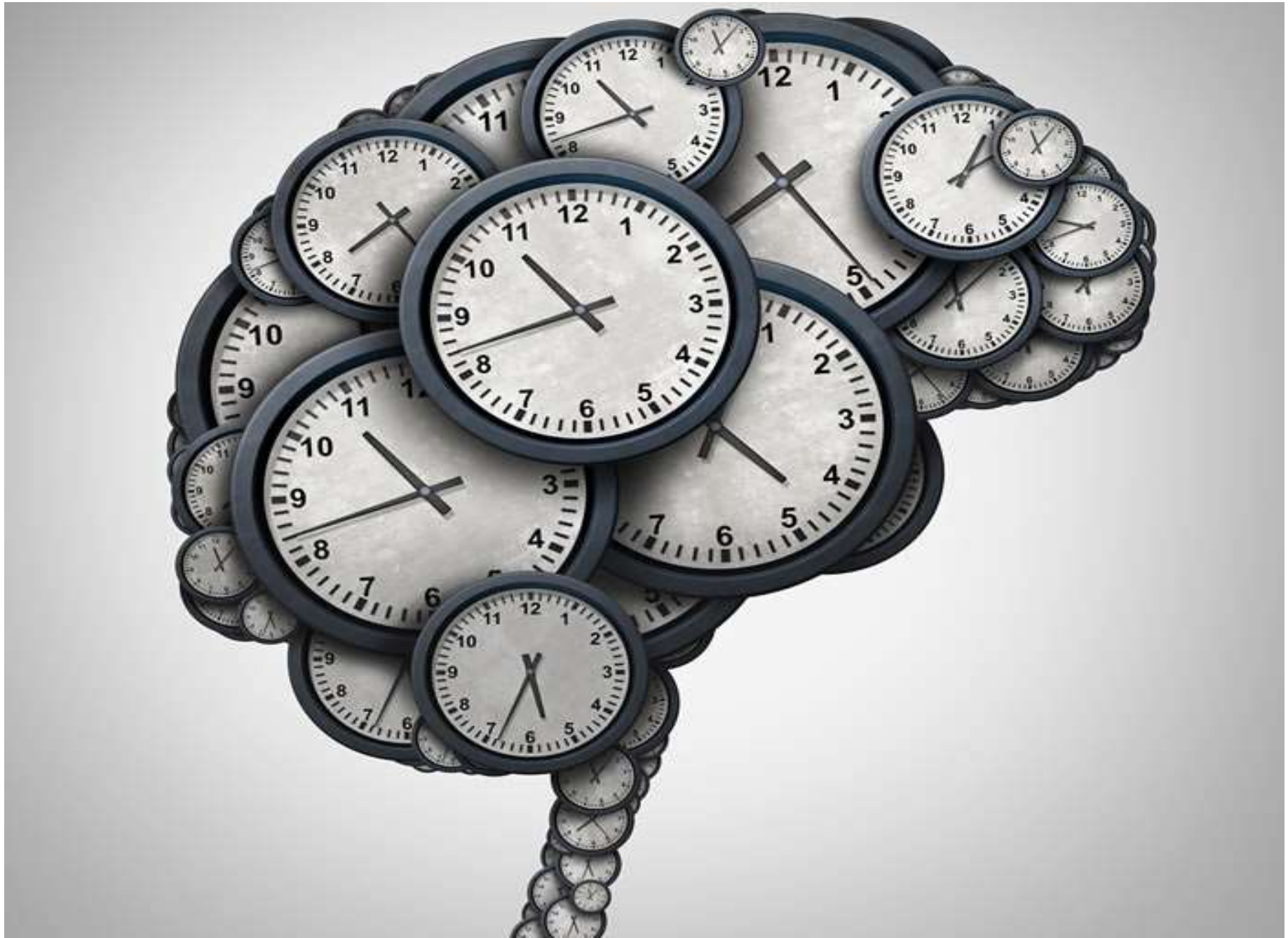
CONSIGLIO NAZIONALE DELLE RICERCHE
ISTITUTO DI SCIENZE NEUROLOGICHE

SINut
Società Italiana di Nutraceutica

Nutrizione e nutraceutica nel brain aging: Mind Diet e nutrizione preventiva tramite Med Diet e Dash Diet

Giovanni Scapagnini, MD, PhD

The human brain is a time machine

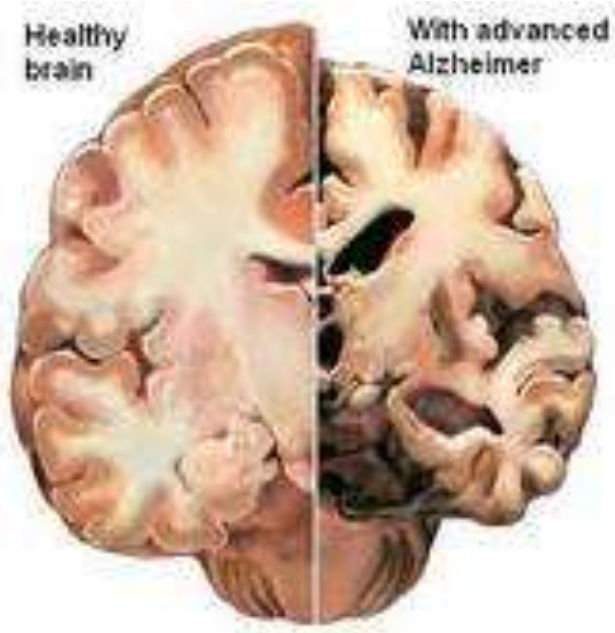


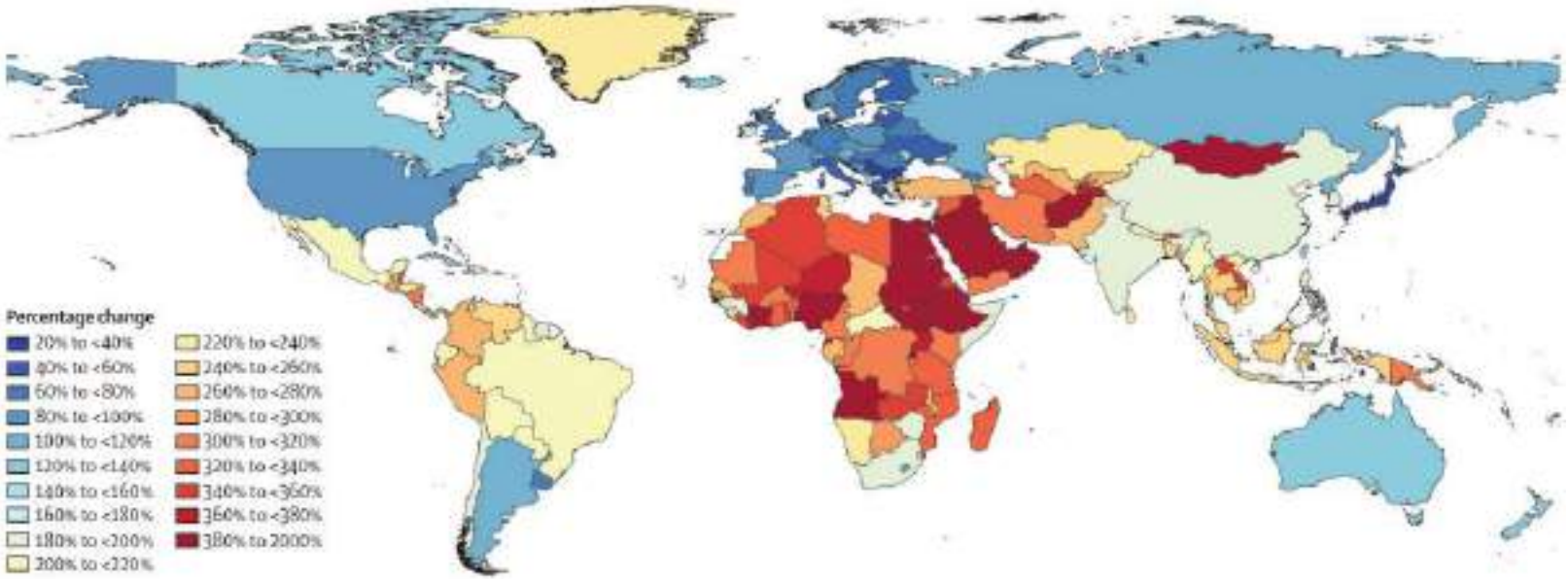
www.thelancet.com/public-health Vol 7 February 2022

Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019

*GBD 2019 Dementia Forecasting Collaborators**

The number of people with dementia would increase from 57·4 (95% uncertainty interval 50·4–65·1) million cases globally in 2019 to 152·8 (130·8–175·9) million cases in 2050



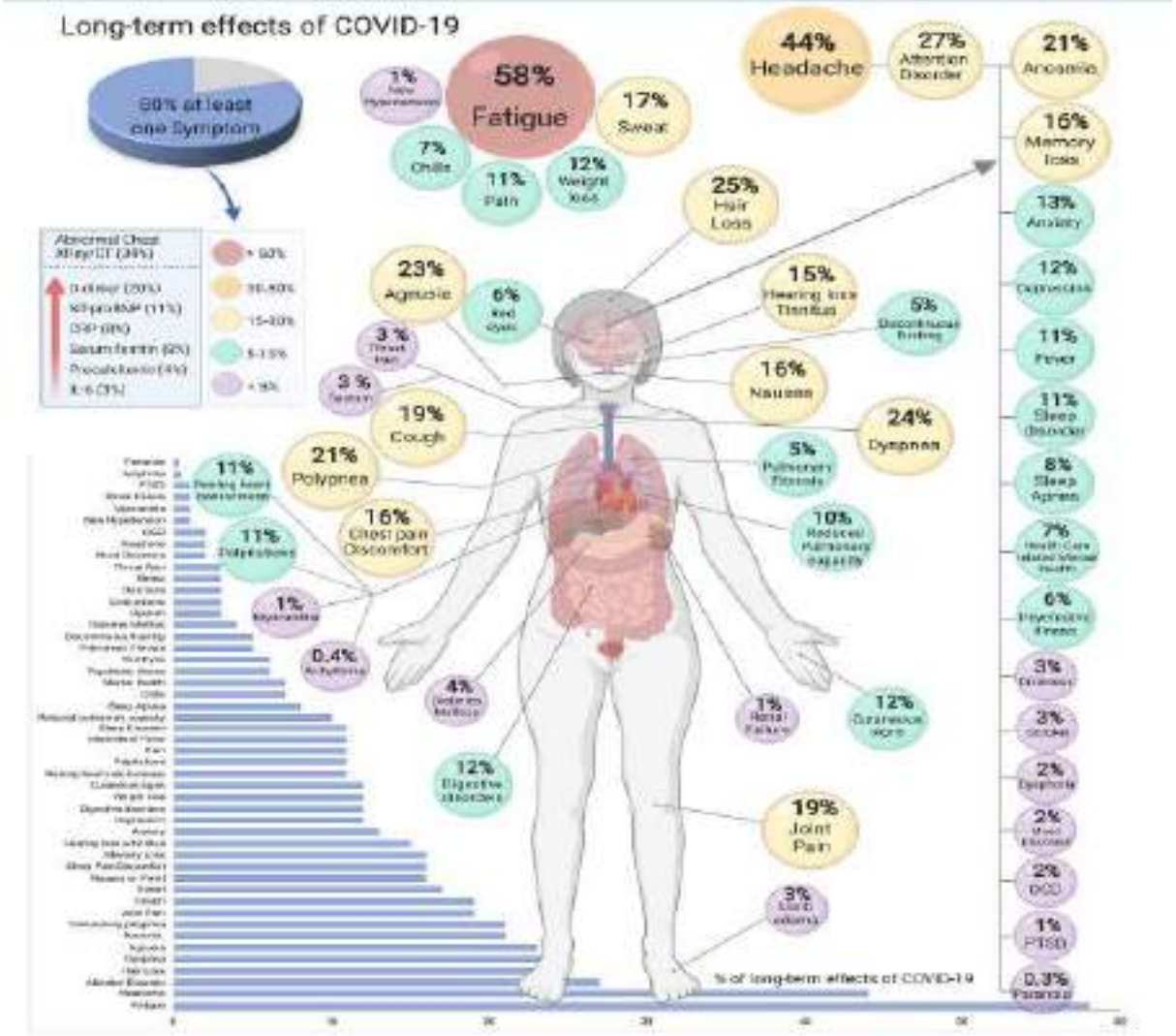


Scientific Reports | (2021) 11:16144

More than 50 long-term effects of COVID-19: a systematic review and meta-analysis

Sandra Lopez-Leon[1], Talia Wegman-Ostrosky[2], Carol Perelman[3], Rosalinda Sepulveda[4], Paulina A. Rebolledo[5,6], Angelica Cuapio[7] & Sonia Villapol[8,9]

Studies included in review
(n = 15) 55
Total Persons n= 47,910
Long-Term COVID19 effects

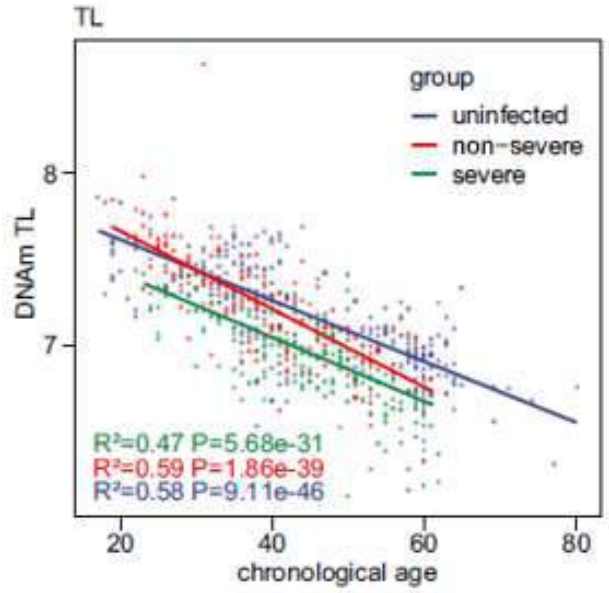


nature COMMUNICATIONS

Accelerated biological aging in COVID-19 patients

(2022) 13:2135

Xue Cao[1,2,3], Wenjuan Li[4], Ting Wang[5], Dongzhi Ran[6,7], Veronica Davalos[8], Laura Planas-Serra[9,10], Aurora Pujol[9,10,11], Manel Esteller[8,11,12,13], Xiaolin Wang[2] & Huichuan Yu[2,3]

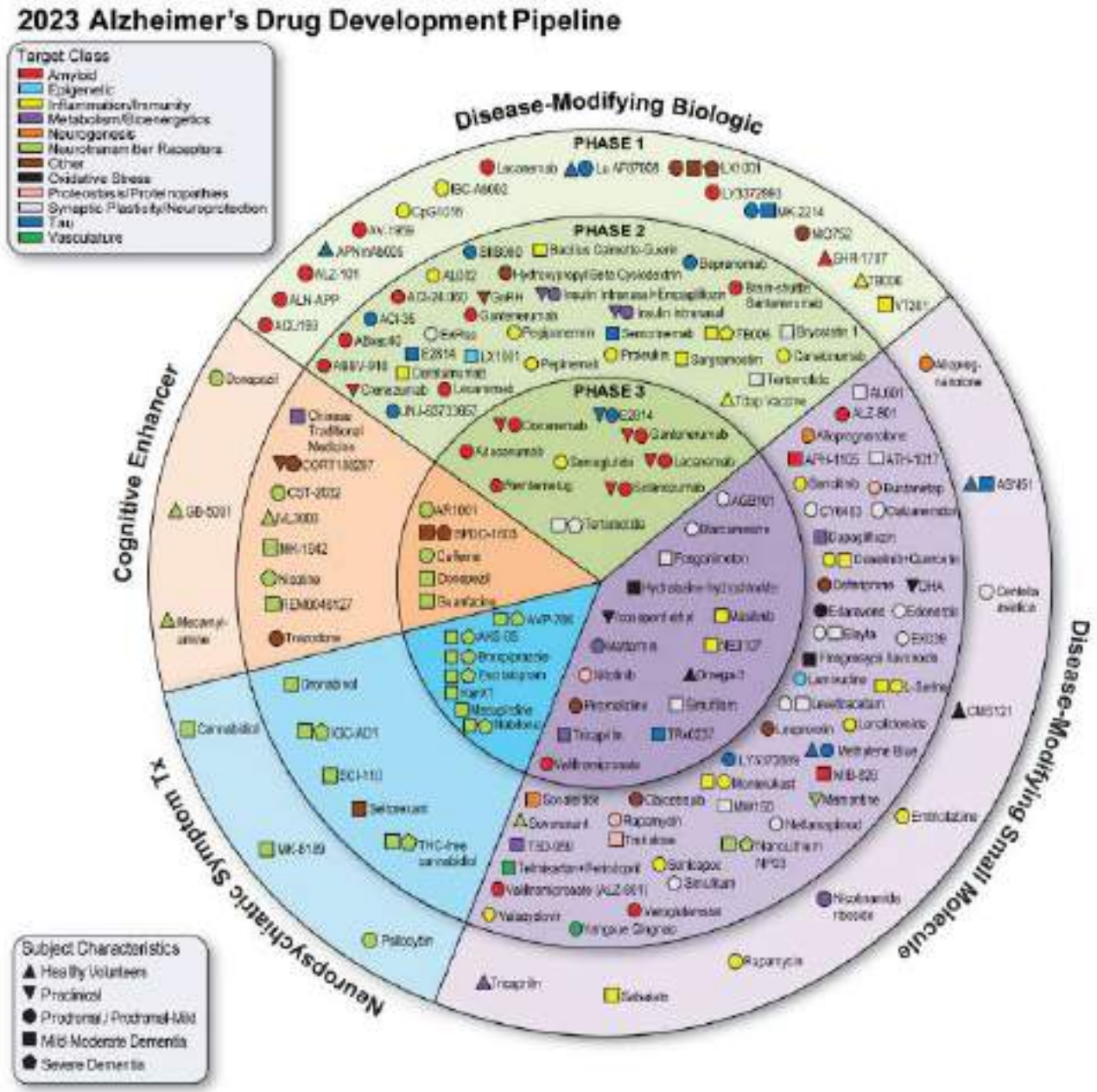


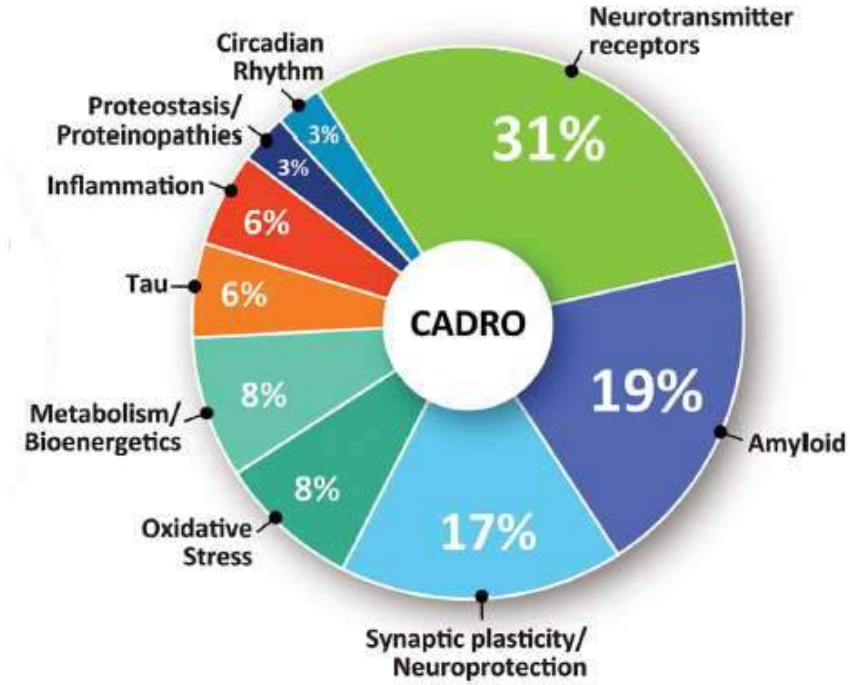
Assessment of DNA methylation-based telomere length estimator in patient cohorts

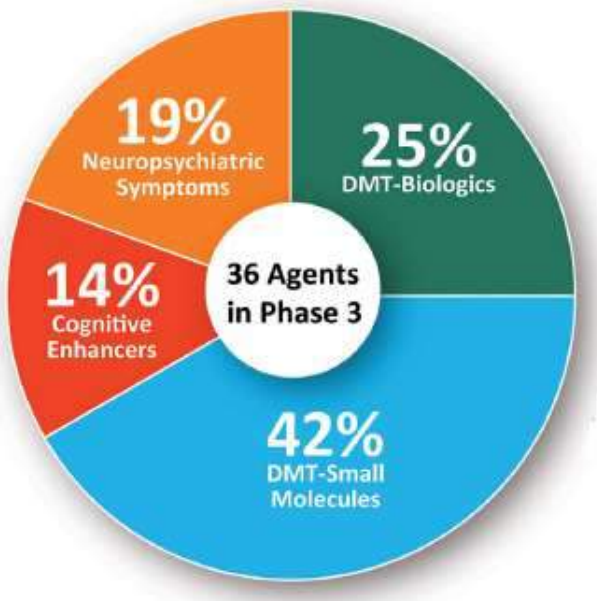
Accelerated epigenetic aging is associated with the risk of SARS-CoV-2 infection and developing severe COVID-19. In addition, the accumulation of epigenetic aging from COVID-19 may contribute to the post-COVID-19 syndrome among survivors.

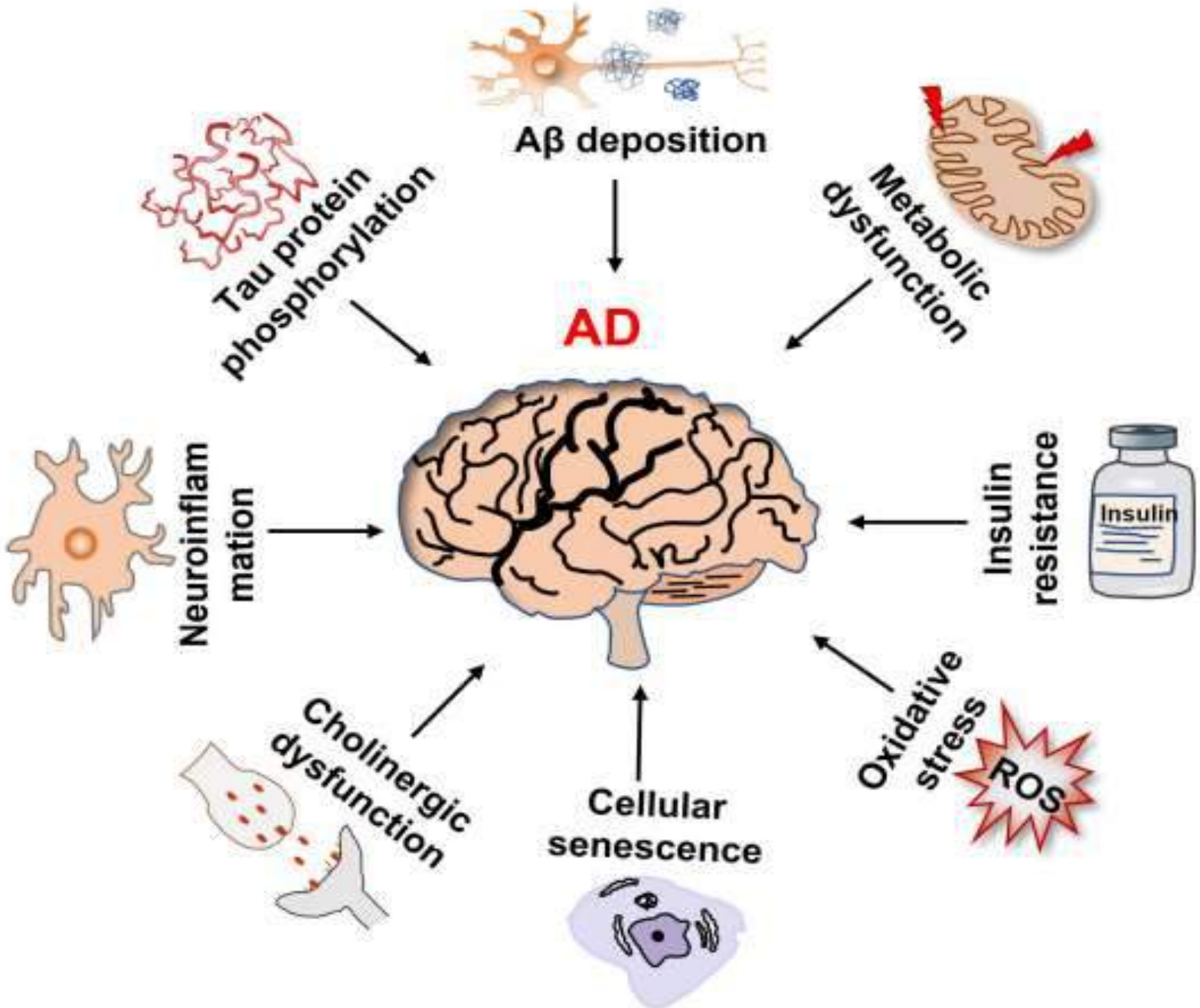
Alzheimer's Dement. 2023;9:e12385.

Alzheimer's disease drug development pipeline: 2023

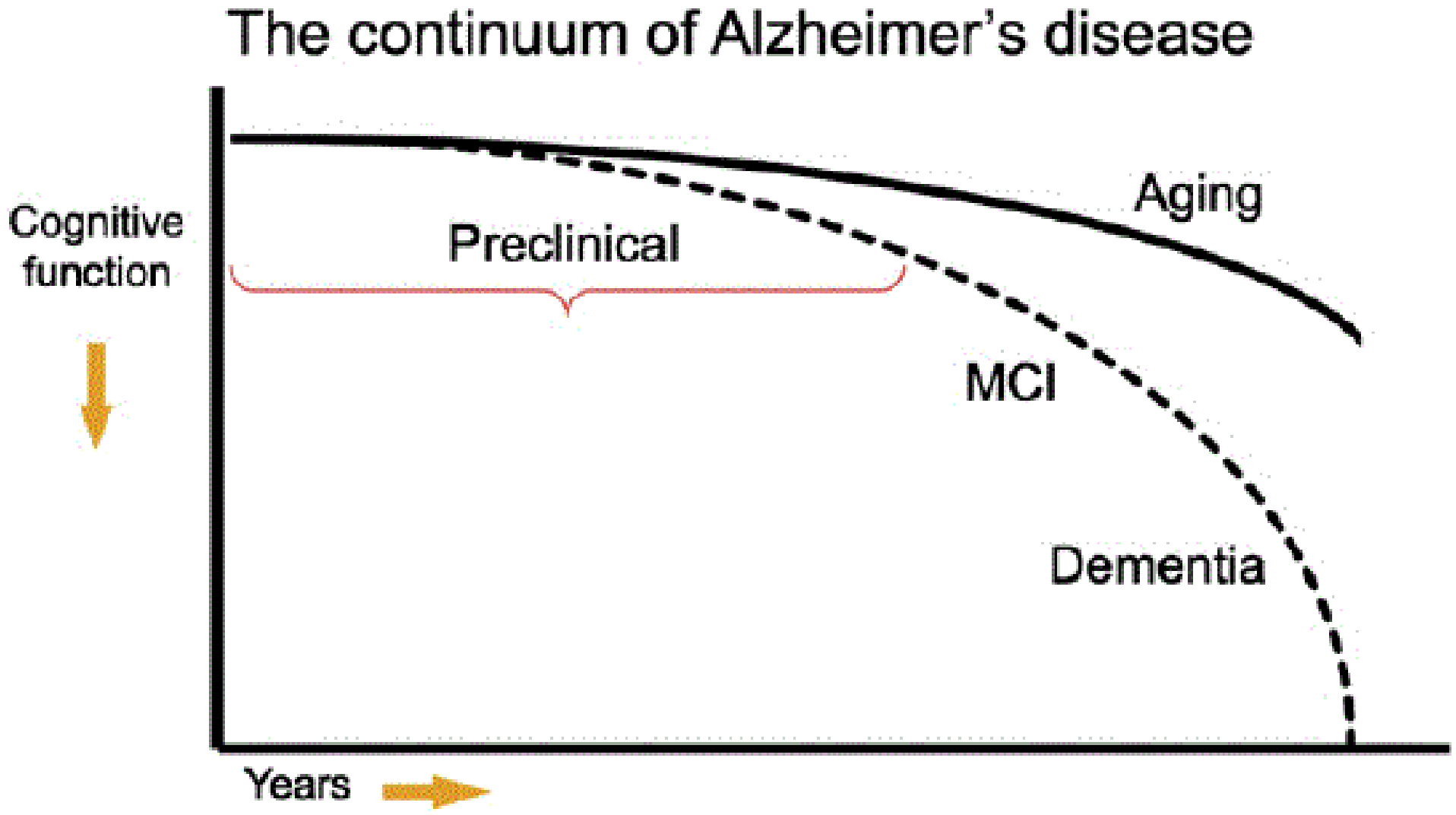


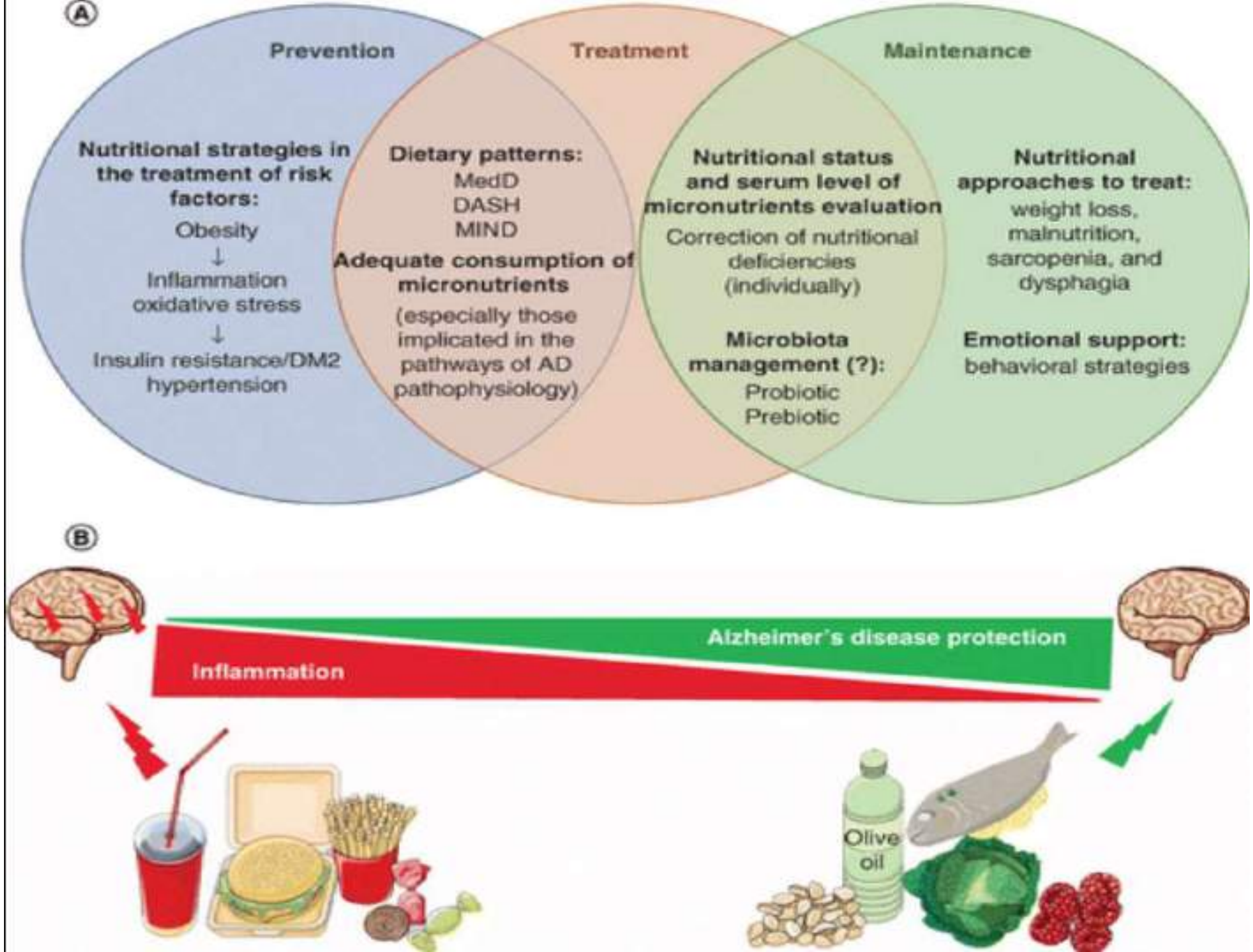




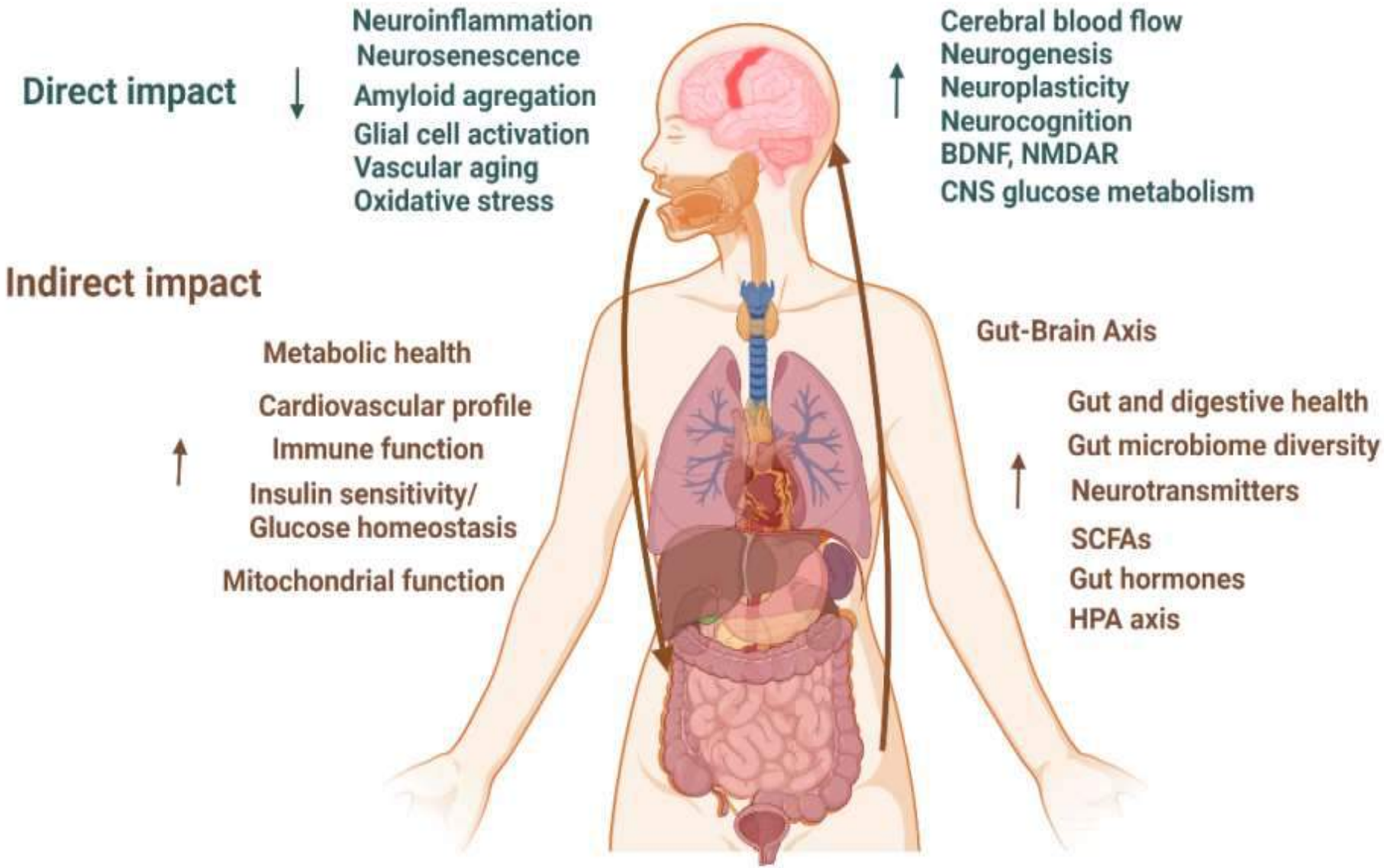

Aβ deposition
Tau protein phosphorylation
Metabolic dysfunction
AD
Neuroinflam mation
Insulin resistance
Insulin
Cholinergic dysfunction
Cellular senescence
Oxidative stress
ROS

Toward defining the preclinical stages of Alzheimer's disease:
Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup




A
Prevention
Treatment
Maintenance
Nutritional strategies in the treatment of risk factors:
Obesity
↓
Inflammation
oxidative stress
↓
Insulin resistance/DM2
hypertension
Dietary patterns:
MedD
DASH
MIND
Adequate consumption of micronutrients
(especially those implicated in the pathways of AD pathophysiology)
Nutritional status and serum level of micronutrients evaluation
Correction of nutritional deficiencies (individually)
Microbiota management (?):
Probiotic
Prebiotic
Nutritional approaches to treat:
weight loss, malnutrition, sarcopenia, and dysphagia
Emotional support:
behavioral strategies
B
Inflammation
Alzheimer's disease protection
Olive oil

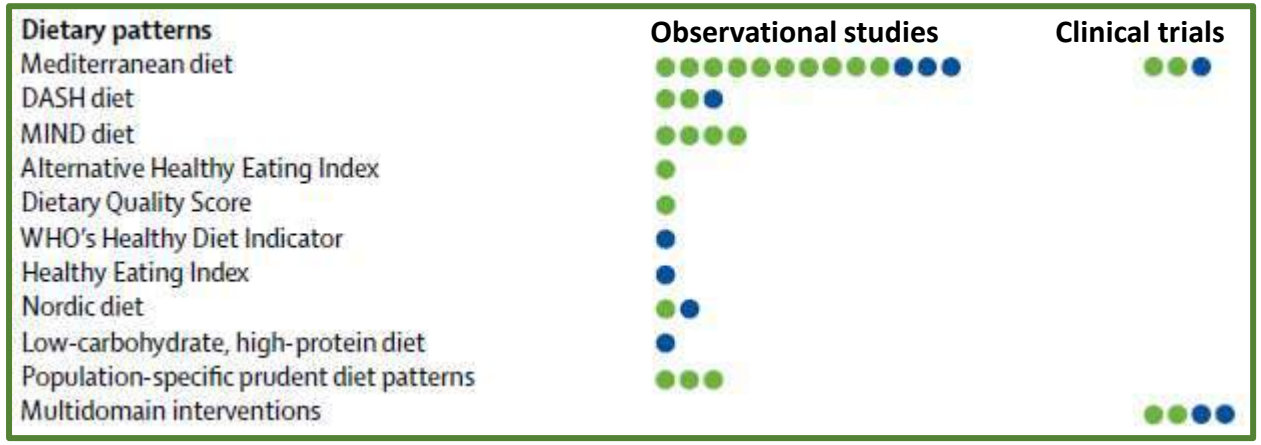
Direct and indirect impacts of dietary patterns on brain aging



Nutrition and prevention of cognitive impairment

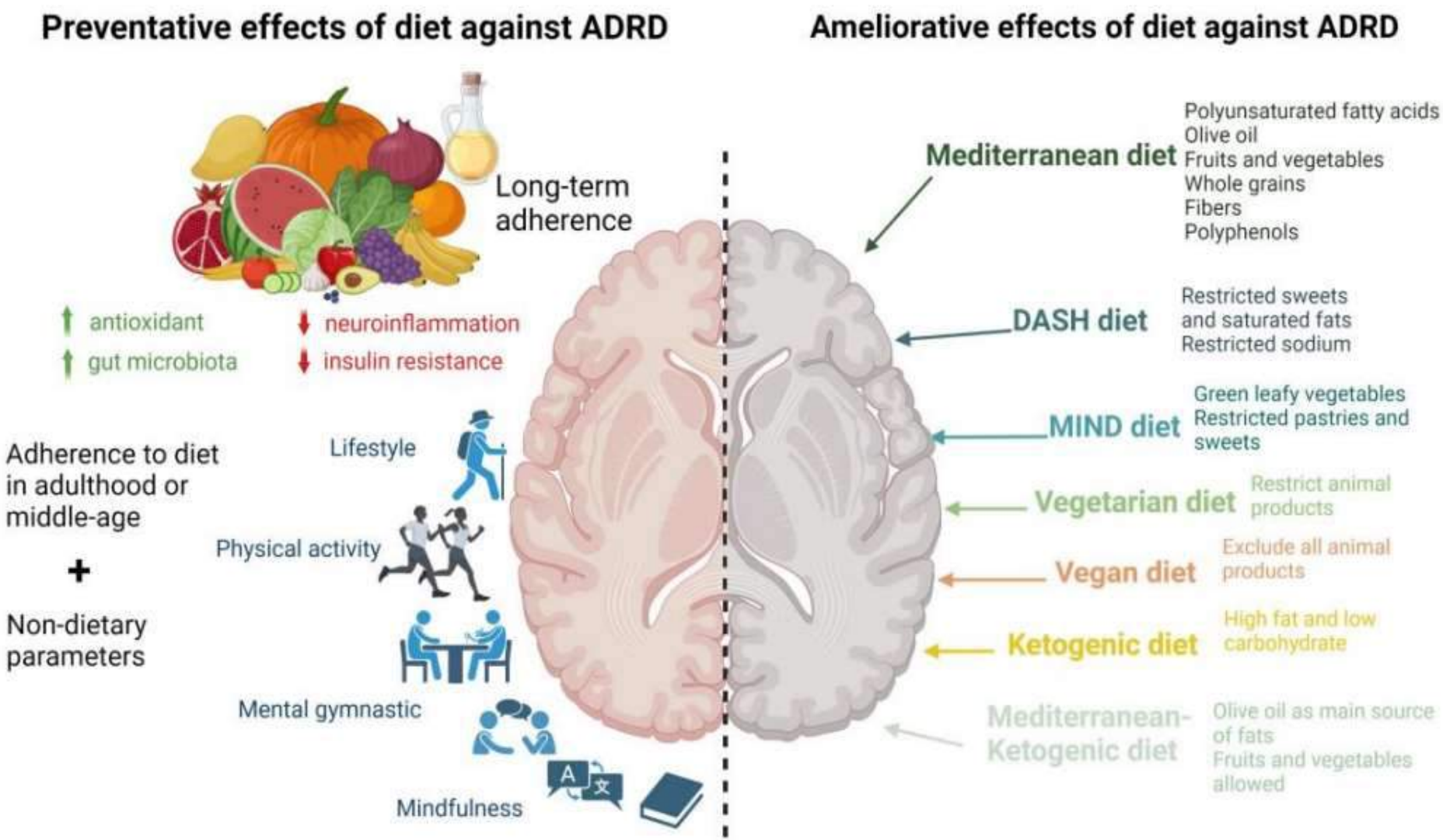
Lancet Neurol 2018; 17: 1006–15

Nikolaos Scarmeas, Costas A Anastasiou, Mary Yannakoulia



Antioxidants	
Vitamin C[14]	Fruits (berries, citrus fruits, kiwis, lychees, and papayas), vegetables (Brussels sprouts, cauliflowers, cabbages, sweet peppers, and tomatoes), and herbs and spices (parsley, sorrel, and chives)
Vitamin E[15]	Vegetable oils and fat spreads from vegetable oils, nuts and seeds, some fatty fish (eg, sardines, salmon, herring, swordfish, and trout), egg yolk, and wholegrain cereals
Carotenes[16]	Yellow or orange vegetables (sweet potatoes, carrots, and pumpkins), dark leafy vegetables (spinach, broccoli, and endives), and yellow or orange fruits (apricots, peaches, mangoes, and melons)
Flavonoids[17]	Fruits (mainly citrus fruits, bananas, and berries), vegetables (parsley and onions), tea (black and brewed)
Vitamin D[18]	Fish (especially fatty fish) and fish liver, full-fat dairy products (or fortified low-fat ones), egg yolk, meat and meat products, and offal (particularly liver)
n-3 fatty acids[19]	Fish (for eicosapentaenoic acid and docosahexaenoic acid) and some vegetable oils and nuts (eg, linseeds, rapeseed oil, and walnuts for α-linolenic acid)

Nutrients related to cognitive function


Preventative effects of diet against ADRD
Ameliorative effects of diet against ADRD
Long-term adherence
antioxidant
gut microbiota
neuroinflammation
insulin resistance
Adherence to diet in adulthood or middle-age
+
Non-dietary parameters
Lifestyle
Physical activity
Mental gymnastic
Mindfulness
Mediterranean diet
Polyunsaturated fatty acids
Olive oil
Fruits and vegetables
Whole grains
Fibers
Polyphenols
DASH diet
Restricted sweets and saturated fats
Restricted sodium
MIND diet
Green leafy vegetables
Restricted pastries and sweets
Vegetarian diet
Restrict animal products
Vegan diet
Exclude all animal products
Ketogenic diet
High fat and low carbohydrate
Mediterranean-Ketogenic diet
Olive oil as main source of fats
Fruits and vegetables allowed

Mediterranean diet, a story of positive biology

EMBO reports VOL 13 | NO 3 | 2012

science & society

‘Positive biology’ as a new paradigm for the medical sciences

Focusing on people who live long, happy, healthy lives might hold the key to improving human well-being

Colin Farrelly

The 7 Seven Countries Study

From 1984, focus of investigations shifted to healthy ageing

Mediterranean diet related to low all-cause mortality

- All-cause mortality
- Mental health
- Functional status

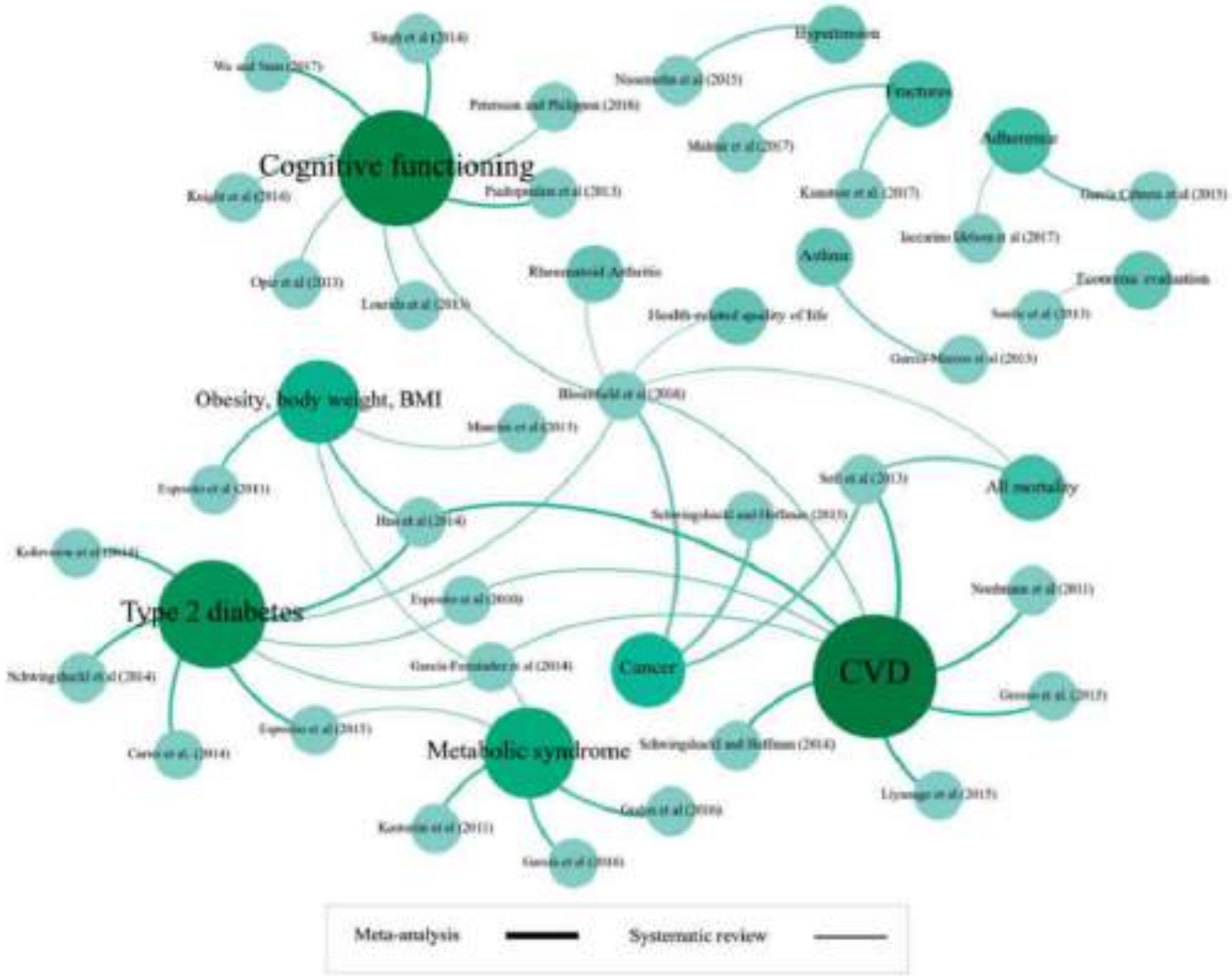
Mediterranean diet and health outcomes: a systematic meta-review

European Journal of Public Health, 2018, 1–6

Roberto Martinez-Lacoba[1,2], Isabel Pardo-Garcia[1,2], Elisa Amo-Saus[1], Francisco Escribano-Sotos[1,2]

Twenty-four meta-analyses and nine systematic reviews and 636 studies were included; this research included results from 636 studies.

MeDi has been shown to be a healthy dietary pattern that may reduce risk related to NCD. The effect is larger if the pattern is combined with physical activity, and tobacco and excessive alcohol consumption are avoided.



BMJ 2014;349:g6674 doi: 10.1136/bmj.g6674 (Published 2 December 2014)

Mediterranean diet and telomere length in Nurses' Health Study: population based cohort study

Marta Crous-Bou *postdoctoral research fellow*[1] *research fellow*[2], Teresa T Fung *associate professor*[3] *adjunct associate professor*[4], Jennifer Prescott *instructor in medicine*[1], Bettina Julin *postdoctoral research fellow*[1] *research fellow*[2], Mengmeng Du *postdoctoral research fellow*[1] *research fellow*[5], Qi Sun *assistant professor*[1 4], Kathryn M Rexrode *associate professor*[7], Frank B Hu *professor*[1 2 4], Immaculata De Vivo *associate professor*[1 2]

Results Greater adherence to the Mediterranean diet was associated with longer telomeres after adjustment for potential confounders. Least squares mean telomere length z scores were −0.038 (SE 0.035) for the lowest Mediterranean diet score groups and 0.072 (0.030) for the highest group (P for trend=0.004).

Conclusion In this large study, greater adherence to the Mediterranean diet was associated with longer telomeres. These results further support the benefits of adherence to the Mediterranean diet for promoting health and longevity.

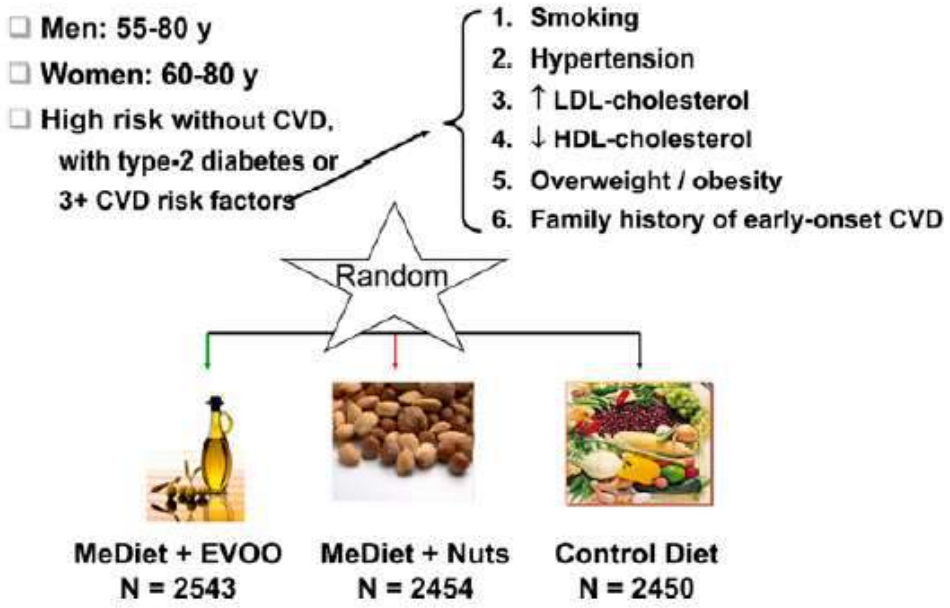
The NEW ENGLAND JOURNAL of MEDICINE

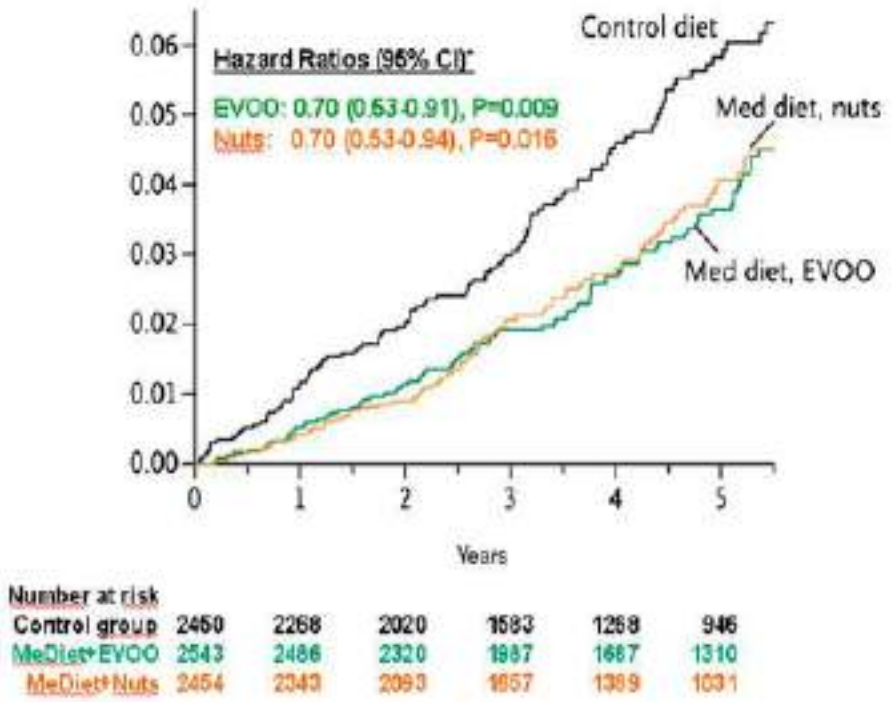
ESTABLISHED IN 1812 APRIL 4, 2013 VOL. 368 NO. 14

the PREDIMED Study

Università degli Studi del Molise

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet





Design of the PREDIMED (Prevención con Dieta Mediterránea) study.
CVD, cardiovascular disease; EVOO, extravirgin olive oil; MeDiet, Mediterranean diet.

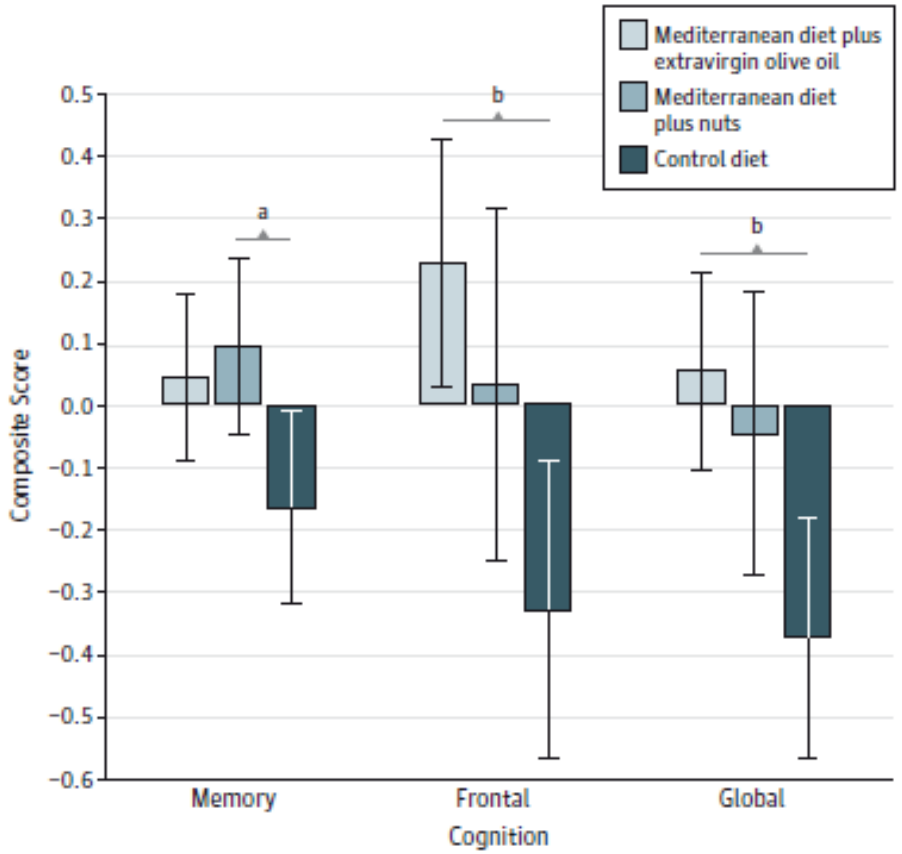
Incidence of cardiovascular disease by intervention group in the PREDIMED (Prevención con Dieta Mediterránea) study.

Original Investigation

JAMA Internal Medicine Published onlineMay 11, 2015

Mediterranean Diet and Age-Related Cognitive Decline
A Randomized Clinical Trial

Cinta Valls-Pedret, MSc; Aleix Sala-Vila, DPharm, PhD; Mercè Serra-Mir, RD; Dolores Corella, DPharm, PhD; Rafael de la Torre, DPharm, PhD; Miguel Ángel Martínez-González, MD, PhD; Elena H. Martínez-Lapiscina, MD, PhD; Montserrat Fitó, MD, PhD; Ana Pérez-Heras, RD; Jordi Salas-Salvadó, MD, PhD; Ramon Estruch, MD, PhD; Emilio Ros, MD, PhD



INTERVENTIONS

Participants were randomly assigned to a Mediterranean diet supplemented with extravirgin olive oil (1 L/wk), a Mediterranean diet supplemented with mixed nuts (30 g/d), or a control diet (advice to reduce dietary fat).

CONCLUSIONS AND RELEVANCE

In an older population, a Mediterranean diet supplemented with olive oil or nuts is associated with improved cognitive function.

Description of the DASH Eating Plan

The DASH eating plan requires no special foods and instead provides daily and weekly nutritional goals. This plan recommends:

- Eating vegetables, fruits, and whole grains
- Including fat-free or low-fat dairy products, fish, poultry, beans, nuts, and vegetable oils
- Limiting foods that are high in saturated fat, such as fatty meats, full-fat dairy products, and tropical oils such as coconut, palm kernel, and palm oils
- Limiting sugar-sweetened beverages and sweets

Based on these recommendations, the following table shows examples of daily and weekly servings that meet DASH eating plan targets for a 2,000-calorie-a-day diet.

Food Group	Daily Servings
Grains	6–8
Meats, poultry, and fish	6 or less
Vegetables	4–5
Fruit	4–5
Low-fat or fat-free dairy products	2–3
Fats and oils	2–3
Sodium	2,300 mg*
	Weekly Servings
Nuts, seeds, dry beans, and peas	4–5
Sweets	5 or less

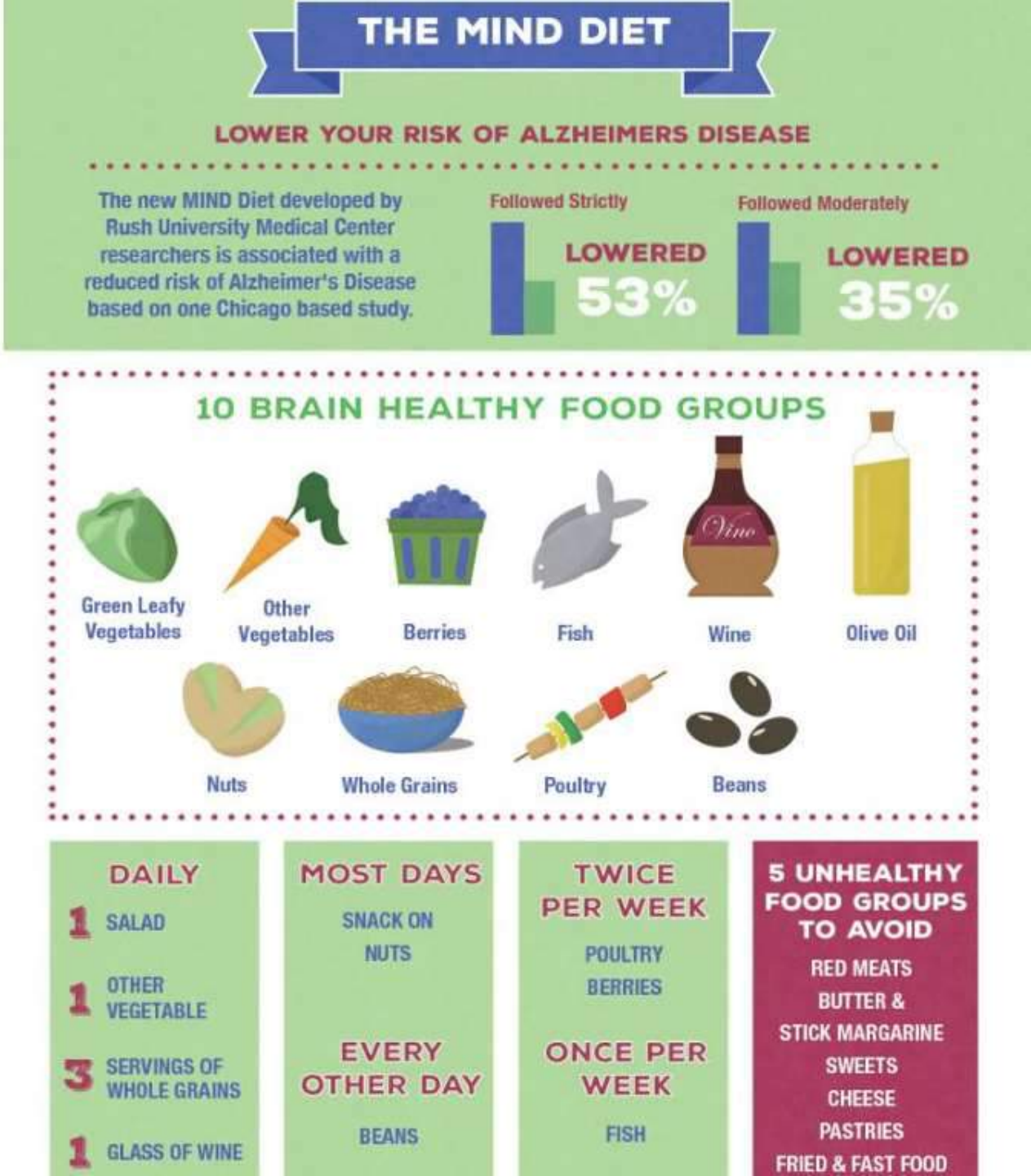
*1,500 milligrams (mg) sodium lowers blood pressure even further than 2,300 mg sodium daily.

When following the DASH eating plan, it is important to choose foods that are:

- Low in saturated and *trans* fats
- Rich in potassium, calcium, magnesium, fiber, and protein
- Lower in sodium

What is the MIND diet?

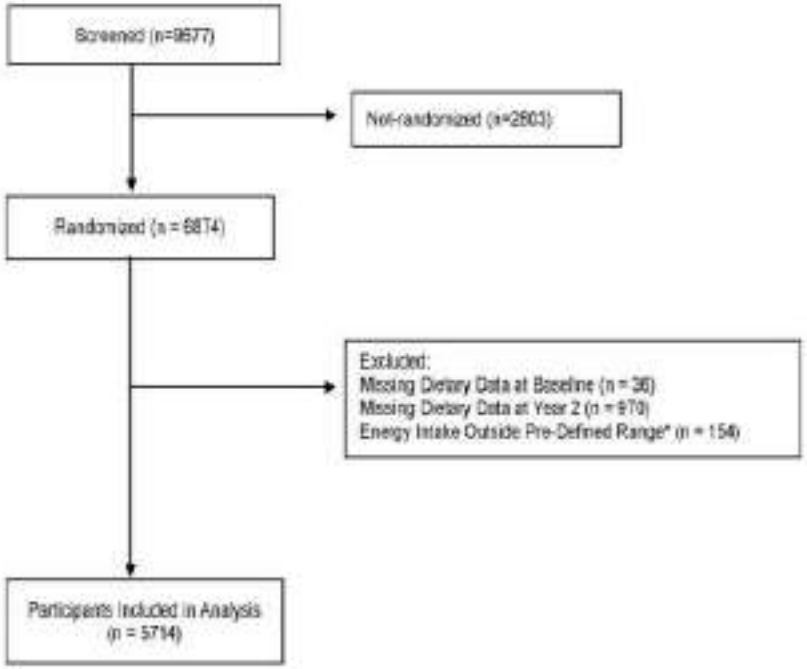
- **M**editerranean-DASH **I**ntervention for **N**eurodegenerative **D**elay
- Developed by Rush University Medical Center's nutritional epidemiologist Dr. Martha Clare Morris & colleagues
- Made by modifying and combining **Mediterranean and DASH diets**
  - largely plant-based & limits high-fat foods
- May promote brain health and reduce an individual's risk of developing Alzheimer's disease (AD)
- Generally nutritious eating plan & good for overall health



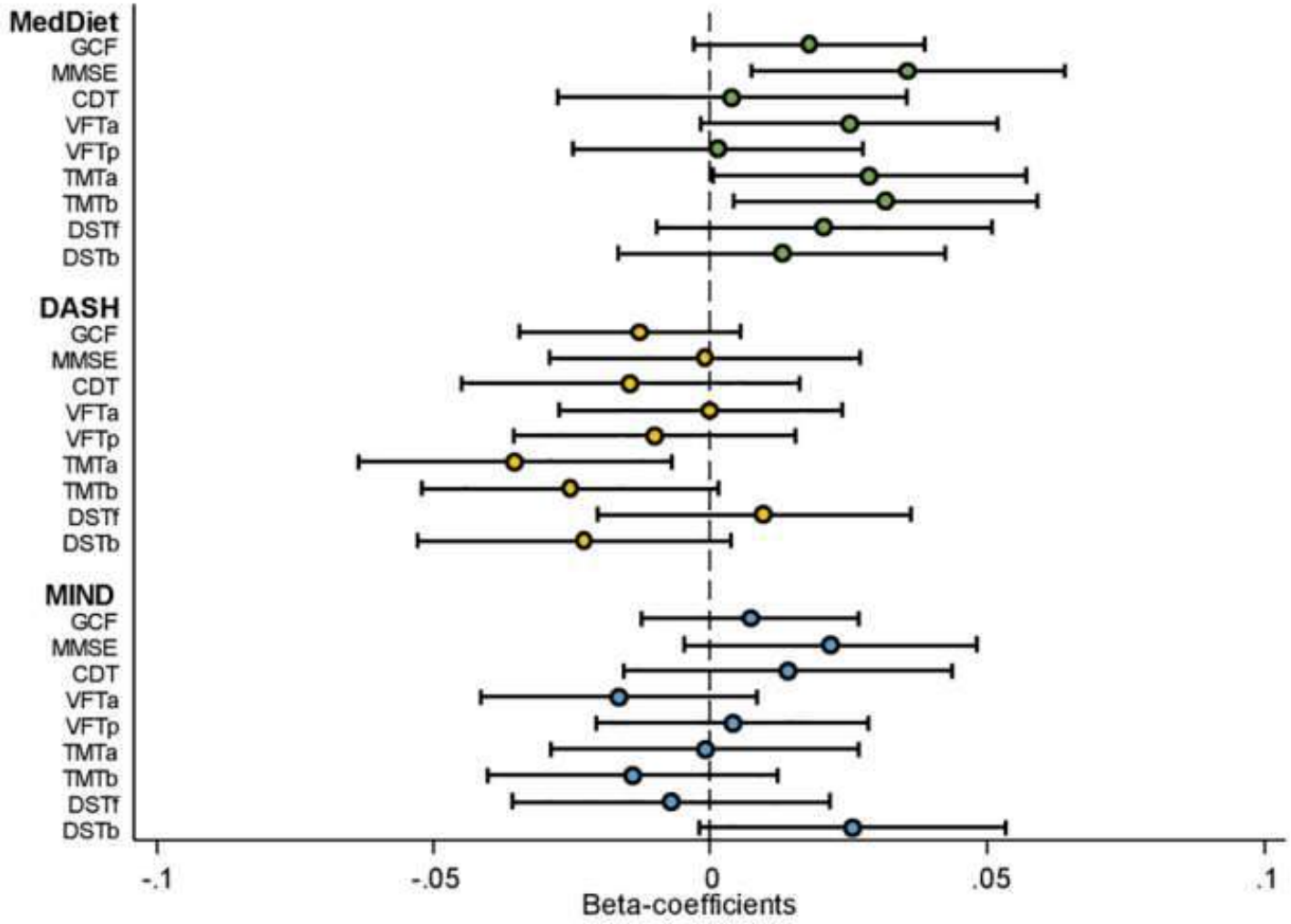
frontiers in Aging Neuroscience

December 2021 | Volume 13 | Article 782067

Mediterranean, DASH, and MIND Dietary Patterns and Cognitive Function: The 2-Year Longitudinal Changes in an Older Spanish Cohort



Cognitive function assessment by dietary pattern adherence

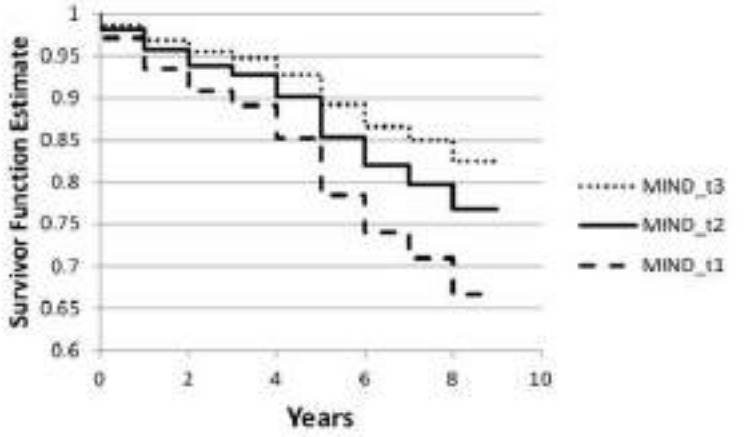


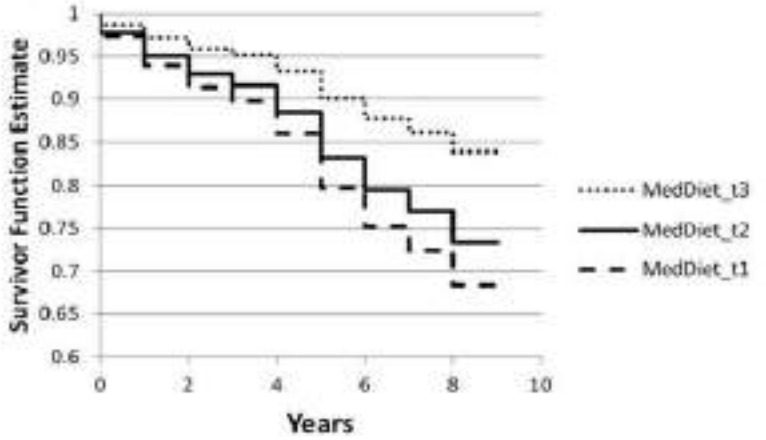
Alzheimer's & Dementia ■ (2015) 1-8

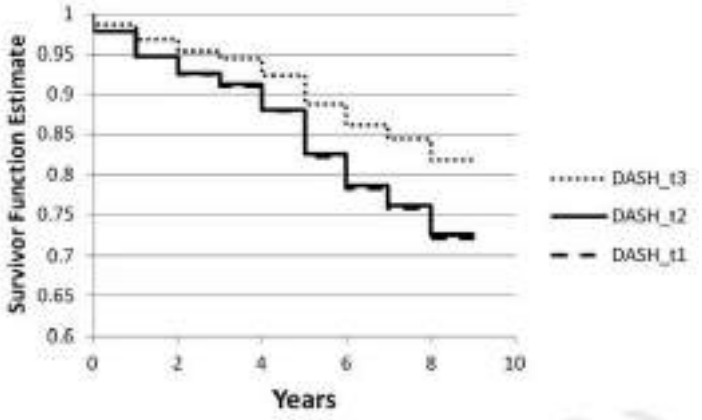
MIND diet associated with reduced incidence of Alzheimer's disease

Baseline characteristics of 923 MAP participants by tertile of MIND diet score

	MIND diet score		
Baseline characteristic	Tertile 1	Tertile 2	Tertile 3
MIND diet score, mean (minimum, maximum)	5.6 (2.5, 6.5)	7.5 (7.0, 8.0)	9.6 (8.5, 12.5)
Age, mean years	81.7	81.4	80.4
Males, percent	26	25	22
Education, mean years	14.3	15.1	15.6
APOE-ε4, percent	21	27	21
Total Energy Intake, mean calories	1644	1777	1792
Cognitive activity frequency, mean rating	3.1	3.2	3.4
Physical activity weekly, mean hours	2.5	3.5	4.3
Depressive symptoms, mean number	1.3	0.9	0.9
Body mass index (BMI)			
Percent BMI ≤20	9	5	7
Percent BMI ≥30	31	22	24
Medical conditions			
Diabetes, percent	24	21	17
Hypertension, percent	79	75	72
Hypertensive medication use, percent	57	53	53
Myocardial infarction, percent	17	11	16
Stroke, percent	10	6	8







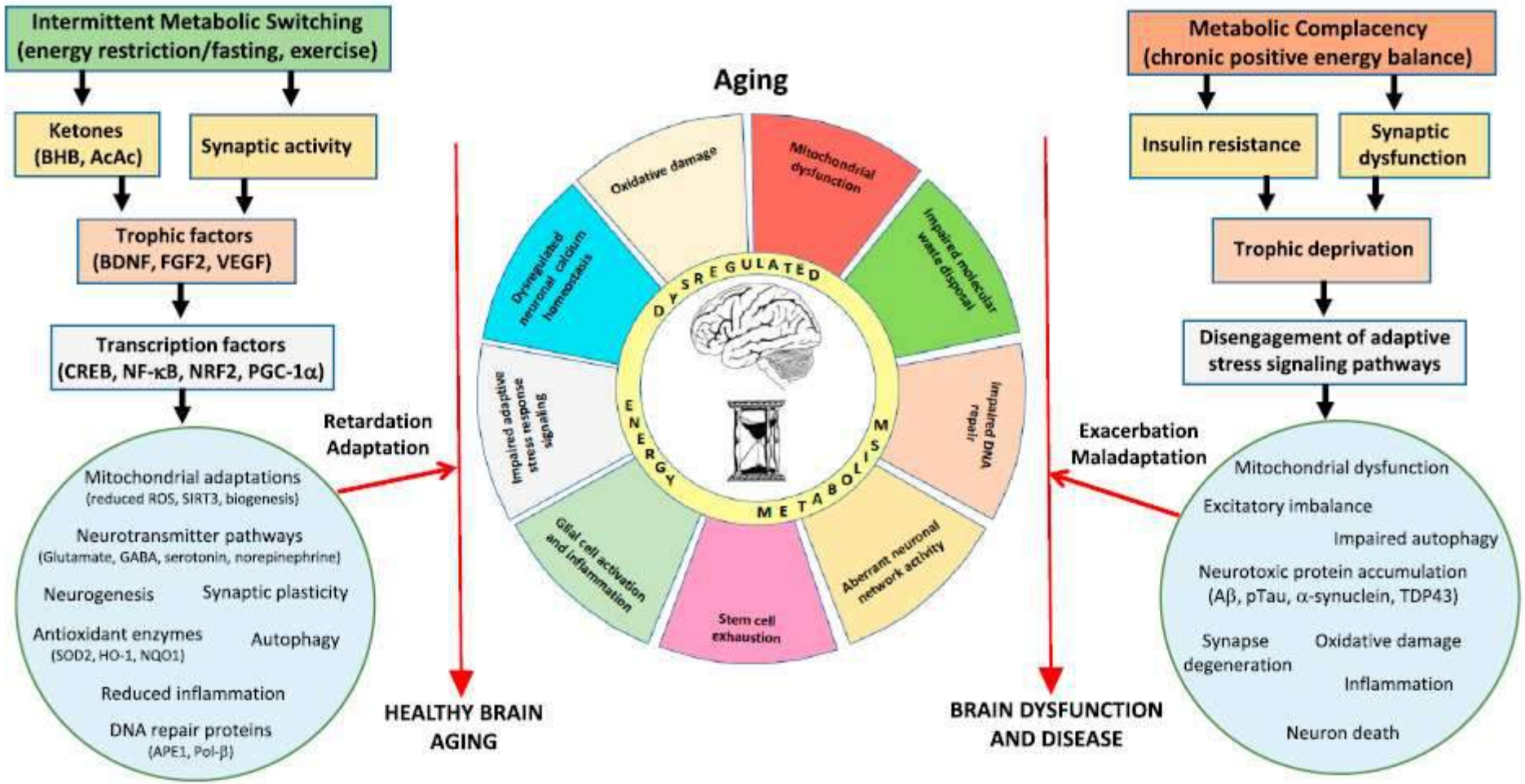
Conclusion: High adherence to all three diets may reduce AD risk. Moderate adherence to the MIND diet may also decrease AD risk

Hallmarks of Brain Aging: Adaptive and Pathological Modification by Metabolic States

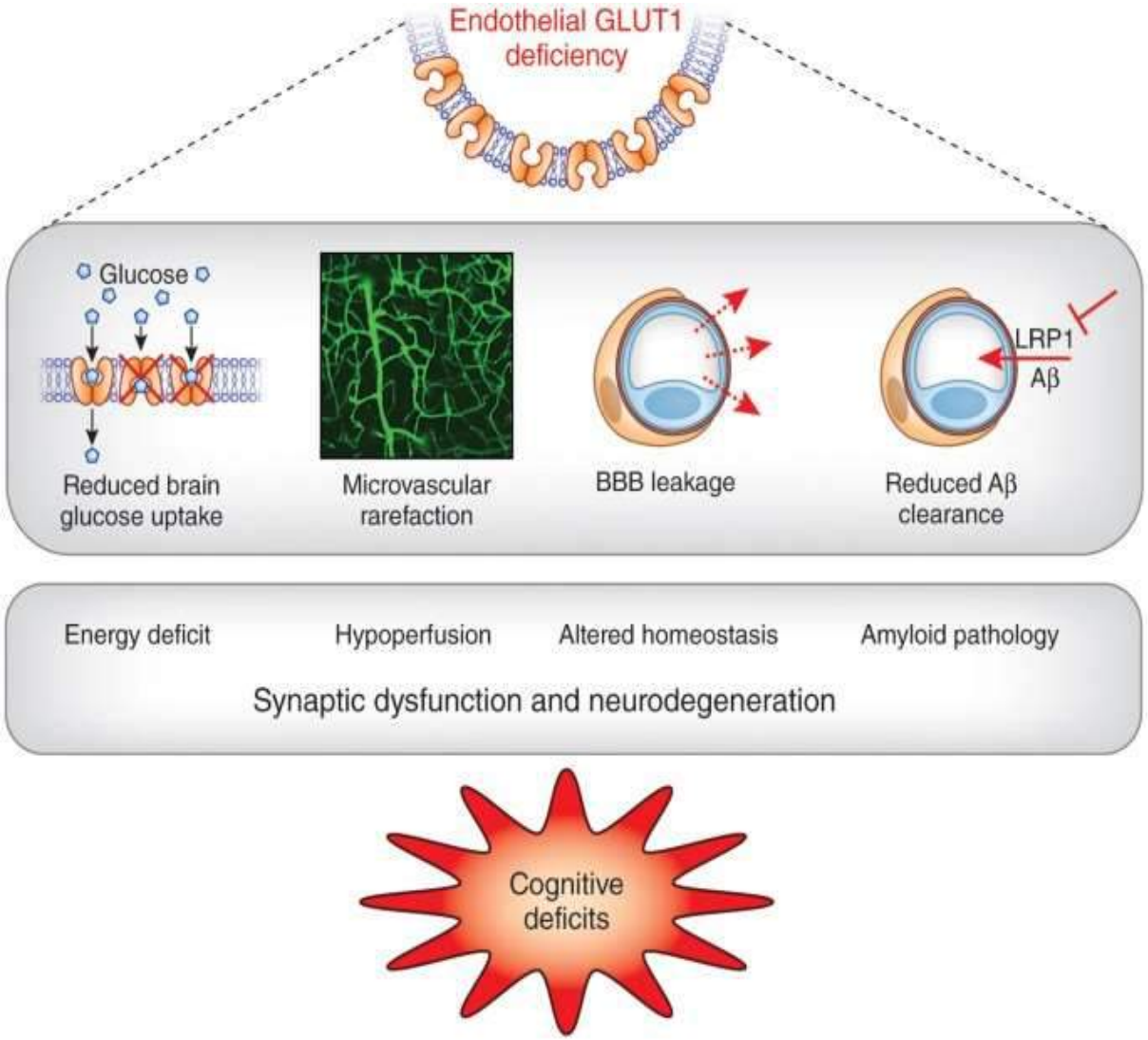
Cell Metabolism 27, June 5, 2018

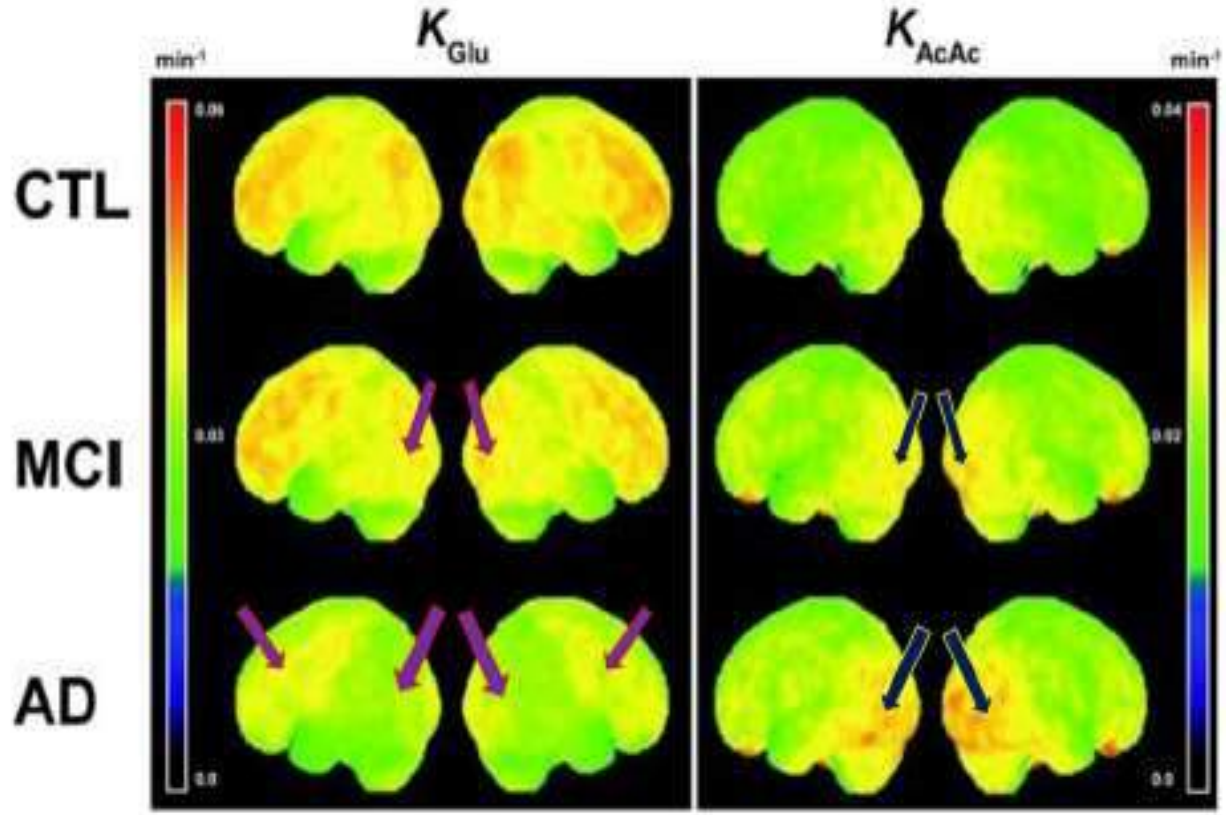
Mark P. Mattson[1,2,*] and Thiruma V. Arumugam[3,4]

CellPress



Working Model for How Intermittent Metabolic Challenges Bolster Brain Health during Aging, Whereas a Chronic Positive Energy Balance Hastens Brain Aging and Associated Brain Diseases

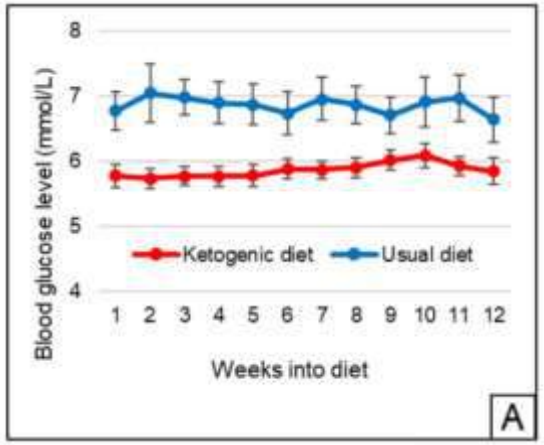

Endothelial GLUT1 deficiency
Glucose
Reduced brain glucose uptake
Microvascular rarefaction
BBB leakage
LRP1
Aβ
Reduced Aβ clearance
Energy deficit
Hypoperfusion
Altered homeostasis
Amyloid pathology
Synaptic dysfunction and neurodegeneration
Cognitive deficits

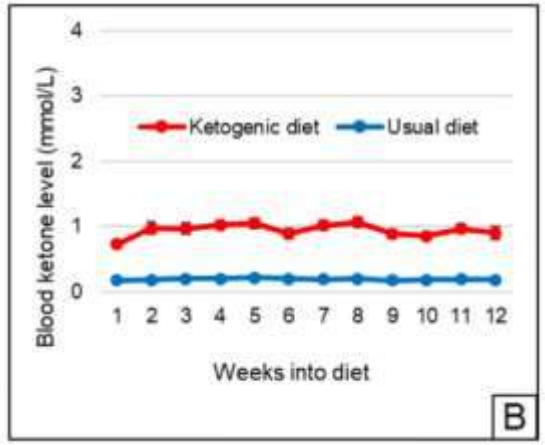

CTL
MCI
AD
K_{Glu}
K_{AcAc}
min⁻¹
min⁻¹

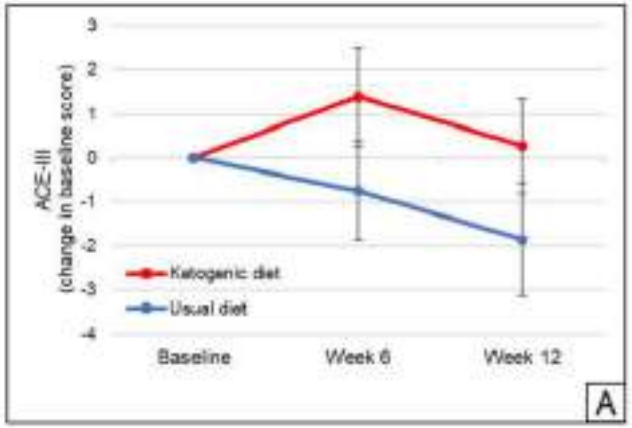
Phillips *et al. Alzheimer's Research & Therapy* (2021) 13:51

Randomized crossover trial of a modified ketogenic diet in Alzheimer's disease

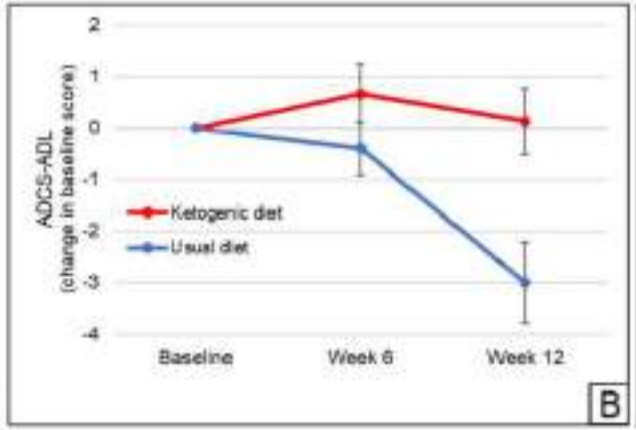
Our findings suggest that high rates of retention and adherence are achievable in applying a 12-week modified ketogenic diet to AD patients. Compared with a usual diet supplemented with low-fat healthy eating guidelines, patients on the ketogenic diet improved in daily function and quality of life, two factors of great importance to people living with dementia.



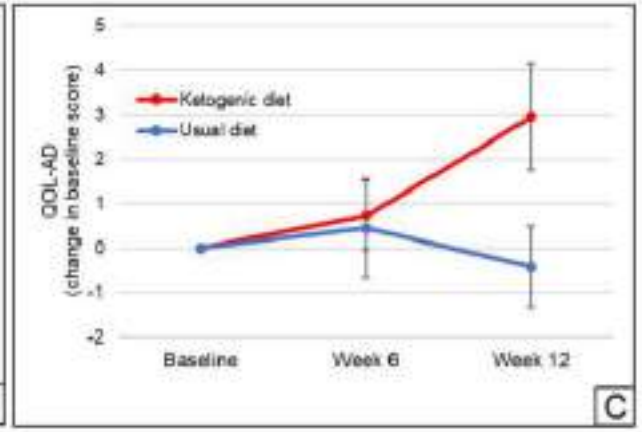




Addenbrookes Cognitive Examination - III (ACE-III)



AD Cooperative Study - Activities of Daily Living (ADCS-ADL) inventory



Quality of Life in AD (QOL-AD) questionnaire