

Debunking 'Cures, Preventions & Treatments' of Alzheimer's disease

Dementia Care Training
October 21, 2020

Tamara LeCaire, MS, PhD

Associate Scientist, Wisconsin Alzheimer's Institute



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

No Disclosures

Objectives

- Background
- Debunk or discuss commonly asked about alternative therapies (and ~risk factors)
 - Latest research show?
 - Talking points
- Evidenced-based 'healthy-brain' actions

Alzheimer's disease therapies

- Alzheimer's disease has no cure
- Medications may lessen or stabilize symptoms temporarily

Medication and supplement use in older adults

- 88% of adults 62-85 years used prescription medications
- 72% used OTC or supplements at same time
- 67% use 5 or more medications or supplements – polypharmacy
- Risk for adverse drug events, interactions



Alternative therapies sought

- Limited treatments
- Want to prevent, delay onset or treat
- Increasingly accessible generic and OTC products
- Independently sought out 'brain health' interventions

“Pseudomedicine”

- “Supplements can exist within the law, promoted as scientifically supported” with little or no valid data on achievable benefits (efficacy)
- “Protocols may re-package” tested interventions and add untested components, such as supplements
- Evidence appears scientific but lacks key study features that address bias that may otherwise explain findings

Bias, Correlation without Causation

- Systematic error in a study
- Not controlling or adjusting for factors resulting from that error may influence an association, causing us to over or under-estimate a true association between measured factors

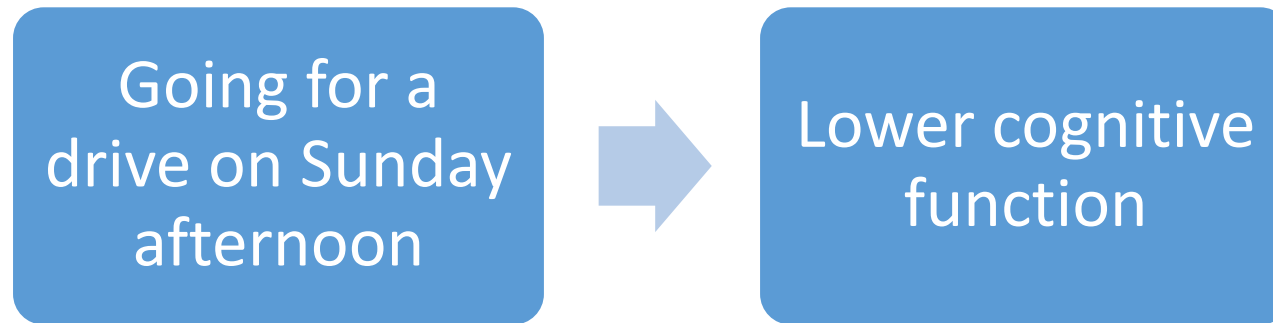


Wisconsin Alzheimer's Institute

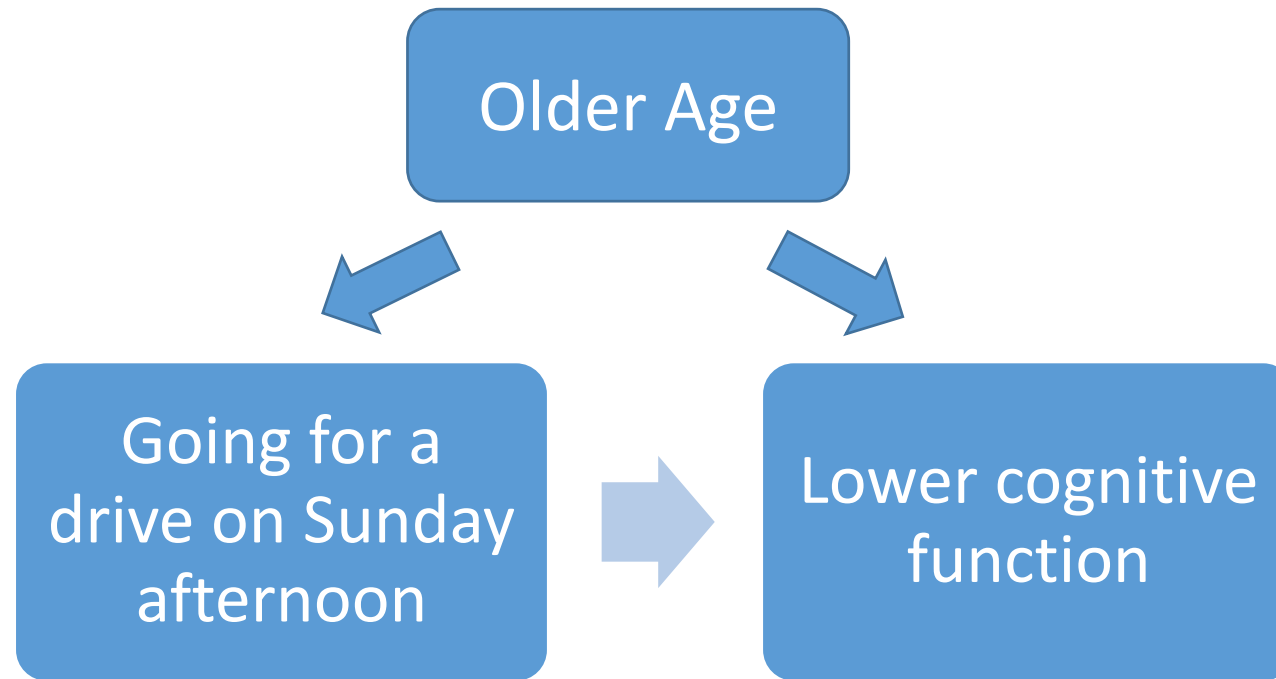
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Bias, Correlation without Causation

- Example –
 - Going for a drive on a Sunday afternoon
 - Lower cognitive function



Bias, Correlation without Causation



Science directing alternative therapies

- Estimated that 1/3 of AD worldwide due to nutrition and lifestyle dependent risk factors
- Cardiometabolic risk reduction is target for current food guidelines and recommendations
- Cardiometabolic health important for cognitive function – Hypertension, Type 2 diabetes, Obesity



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Diet and Supplements



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Supplements

- Debunk vs. hold promise?
 - Prevagen
 - Neuriva
 - Resveratrol
 - Ginkgo Biloba
 - Turmeric/Curcumin
 - Fish Oil/Omega-3
 - Coconut oil

Prevagen

- Aequorin (apoaequorin) – calcium-binding protein from jellyfish
- ? Help regulate calcium in the brain and reduce memory loss and decline since similar structure to calcium-binding proteins in humans
- **DEBUNK** – no known role in human memory, would likely be digested before reaching the brain
 - “Company-sponsored study used data dredging to find/report on favorable results”
 - FTC lawsuit for false advertising; separate class action lawsuit settled – company will change claims on product label
 - Expensive - \$50-100/month

Data dredging, data fishing, p-hacking

- Misuse of data analysis to find significant patterns
- Reporting only those results that are found significant
- “Significance” here refers to statistical significance in data analysis
 - P-value as a measure of statistical significance – the probability that the observed result is due to ‘chance’
 - We want a very small probability that ‘chance’ explains a result to accept a finding as scientifically ‘true’



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Prevagen Talking Points

- No good scientific evidence to support it's use;
lawsuit for false advertising
- In addition – Prevagen is very expensive –
 - Dr. Carlsson instead “spend \$ towards blood pressure measurement or medication, shoes for walking or other exercising...” goals proven to be beneficial for cognition

Many other supplements



Qualia Mind Nootropic Brain - \$70
Brain & Memory Power Boost - \$60
Neuriva - \$50-30
Neuro-Mag - \$30
Per month...
And so on....

Double or triple the monthly cost of
some blood pressure medications

Example: Neuriva

- Neuriva – combination of two ingredients (phosphatidylserine and coffee cherry extract)
- Coffee cherry extract – increased brain-derived neurotrophic factors (BDNF) in a single study, one-time dose, no placebo/control group – and BDNF is a biomarker – correlated but not causal for MCI
- Phosphatidylserine – inconsistent study findings
- **DEBUNK** – Combination is untested

Example: Qualia Mind

- Science page describing using “Complexity Systems Science” to decide what numerous compounds to include
- **DEBUNK** - Pilot study: cognitive testing on day of first dose and 5 days later, share partial results from 6/12 tests performed, no placebo control group
- Add the disclaimer: *“Given that this study did not have a placebo control, we cannot conclusively determine whether or not Mind is the cause of the increased scores. Further placebo controlled studies will be required.”*

<https://neurohacker.com/>



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Plant-based: Resveratrol



- Antioxidant, cardioprotective, anticarcinogenic, antitumor and estrogenic/antiestrogenic activity; neuroprotective?
- A natural polyphenol detected in > 70 plant species in some red wines, foods
- Meta-analysis of several studies showed [no significant effect on memory and cognitive performance](#)
- [Studies are ongoing...](#)



Plant-based - Ginkgo Biloba



- Leaves of Ginkgo tree, thought to have preventive properties for Alzheimer's disease
- Two large RCTs in adults followed 5-6 years - normal cognition and MCI
- **DEBUNK** - no difference in Alzheimer's disease or all cause dementia; no difference in rate of cognitive decline
- **Not enough evidence for recommending use for preventing or treating ADRD**

Turmeric/Curcumin

- Low incidence of Alzheimer's disease in Asia often attributed to high intake of turmeric (Curry)
- Curcumin – active in turmeric root; anti-inflammatory and anti-oxidant properties; used in traditional Indian and Chinese medicine



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Curcumin Talking Points

- Animal studies show curcumin may stabilize or prevent cognitive decline
- Findings from animal studies don't always translate to humans
- Human studies limited (n=5) and inconclusive
- Seek guidance from healthcare provider – adverse events possible
 - Likely to cause GI problems in high doses
 - Can inhibit antitumor activity of chemotherapies

Fish Oil/Omega-3 Fatty Acids

- Long-chain omega-3 fatty acids (docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), prevalent in oily fish
- May decrease beta-amyloid deposition, prevent neuronal loss, improve cognition, and reduce inflammation (animal models)
- Several large RCTs with omega-3 supplementation; “no benefit for treating Alzheimer's disease symptoms; insufficient evidence for supplement reducing risk.”

Bartochowski A et al. Curr Nutr Rep 2020 Sep; 9(3):210-225.



Fish Oil/Omega-3 Fatty Acids Talking Points

- “Omega-3 fatty acid DHA in fish or from supplements may lower the risk of developing dementia, but clinical studies have shown no benefit for treating Alzheimer's disease symptoms to-date.”
- Supplementation with omega-3 fatty acids may cause GI problems; Consider healthier diet which includes fish as alternative
- Studies are ongoing...BRAVE-EPA – studying whether EPA may have vascular benefits...improve blood flow in the brain and impact cognition in veterans at risk for AD



Coconut Oil

- Fatty acids in coconut oil; hypothesis of metabolism of FAs providing alternative energy source for the brain
- Saturated fats – increased cardiovascular risk through high cholesterol, so may be detrimental to AD
- **DEBUNK** - No support for prevention or treatment of Alzheimer's disease; no clinical studies (trial was halted in 2017; insufficient subjects)
- Eat in moderation



<https://curealz.org/news-and-events/myth-busting-why-coconut-oil-is-not-a-cure-for-alzheimers-disease/><https://www.alzheimers.org.uk/about-dementia/treatments/alternative-therapies/coconut-oil-and-dementia>



Wisconsin Alzheimer's Institute
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Supplement Talking Points - Disclaimers

- “These statements *have not been evaluated by the Food and Drug Administration (FDA)*. This product is not intended to diagnose, treat, cure, or prevent any disease.”
- “This information is for educational purposes only and is neither intended to nor implied to be a *substitute for professional medical advice*.”
- “Always seek the advice of your physician or other qualified health provider prior to using a dietary supplement or with questions regarding a medical condition.”



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Supplements Talking Points

- Remember:
 - Dietary supplements do not undergo FDA testing, review for safety or efficacy.
 - A reason for supplement disclaimer: “This product is not intended to diagnose, treat, cure, or prevent any disease.”
- Older adults at increased risk for adverse effects, drug interactions
 - “Always seek the advice of your physician or other qualified health provider prior to using a dietary supplement or with questions regarding a medical condition.”
 - If interested in an alternative therapy, consider a Clinical Trial with your healthcare provider



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Supplements Talking Points

- Consider sources – not all sources contain reliable medical information
- “If seems too good to be true...switch stations” Shmerling, RH. [Harvard Health Blog](https://www.health.harvard.edu/blog); <https://www.health.harvard.edu/blog>
- [Science-Based Medicine](https://sciencebasedmedicine.org), website, respected source of information about alternative therapies and medical controversies (not specific to ADRD); <https://sciencebasedmedicine.org>
- U.S. National Library of Medicine, [MedlinePlus](https://medlineplus.gov/evaluatinghealthinformation.html) <https://medlineplus.gov/evaluatinghealthinformation.html>



Diet vs. Supplements

- Food sources instead of supplements?
 - WHO advocates for whole diet approaches to delay or prevent cognitive decline
- Lower risk for Alzheimer's disease with (more closely) following healthier, 'diets with plant-based origin'
- Healthy diet may provide some protection against a high dementia genetic risk score

Mediterranean Diet

What is the Mediterranean Diet?



"Mediterranean diet" is a generic term based on the traditional eating habits in the countries bordering the Mediterranean Sea. There's not one standard Mediterranean diet. At least 16 countries border the Mediterranean. Eating styles vary among these countries and even among regions within each country because of differences in culture, ethnic background, religion, economy, geography and agricultural production. However, there are some common factors.

Eat Smart

American Heart Association
Cookbooks

Eat Smart Month

Fats

Nutrition Basics

5 Tips to Deal with Picky Eaters (Both Kids
& Adults)

The American Heart Association Diet and
Lifestyle Recommendations

Is drinking alcohol part of a healthy
lifestyle?

Caffeine and Heart Disease

Can Processed Foods Be Healthy
Infographic

Carbohydrates

Daily Tips to Help Your Family Eat Better

Dairy Products - Milk Yogurt and Cheese

Dietary Recommendations for Healthy
Children

Eat Healthy on a Budget by Planning
Ahead

Food as Fuel Before, During and After

- Olive Oil
- Fish
- Whole grains
(breads/cereals)
- Fruits
- Vegetables
- Legumes, Beans
- Nuts, Seeds

MIND Diet

Morris MC, et al. Alzheimer's Dement 2015;11:1015–22.



THE MIND DIET FOR HEALTHY BRAIN AGING

10 things to incorporate	5 things to limit
Green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil, wine (especially red)	Red meat, butter and margarine, cheese, pastries and sweets, fried or fast food

Ketogenic Diets

- Diet adjusts fat/carbohydrate + protein ratio
- When glucose is not readily available – metabolic switch to breakdown stored fat to release and use ketone bodies for energy
- Used to lose weight, T2DM (insulin sensitivity)
- Improve insulin resistance, insulin signaling tied to β -amyloid, pTau



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Ketogenic Diet Talking Points

- Some clinical trials of diet or intake of specific ketone; several show positive outcomes on cognition (but not all), smaller and only over the short-term
- Need larger trials with longer follow-up with cognitive and neuroimaging outcomes, especially in those with MCI/early AD
- Risk for malnutrition in older adults; contraindicated in kidney disease
- Discuss with your healthcare provider



Axona/Medical Foods for Alzheimer's disease

- Prescription dietary supplement as energy source for brain instead of glucose
- Further study is needed. Company funded study found benefit for memory and cognition. Another study showed this might have a small benefit for certain individuals with AD
- A medical food for conditions with nutritional deficiencies – however FDA does not consider AD as such a condition
- [Do not use Axona or medical foods for treatment of AD until more is known](#)



Lifestyle modification

- FINGER Study – Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability
 - Cognitive function protected:
 - physical activity
 - nutrition
 - cognitive training, social activities
 - management of cardiovascular risk
- U.S. Pointer Study – U.S. Study to Protect Brain Health through Lifestyle Intervention to Reduce Risk

Bredesen MEND Protocol

- Personalized program – MEND protocol (metabolic enhancement for neurodegeneration)
- Several lifestyle changes employed - also involves the use of several unproven supplements
- Small case study – N=10 persons with varying levels of cognitive function and other factors – findings due to chance or other factors?
- ReCODE (not a trial) with N=30 cases is ongoing


Bredesen MEND Protocol Talking Points

- Elements of the protocol that may be beneficial for Alzheimer's disease and cognitive decline:
 - Aerobic exercise, Mediterranean diet, cognitive and social engagement, and management of cerebrovascular risk factors
- Standard of care to educate patients on lifestyle interventions that may be beneficial
- **DEBUNK** – Example of 'pseudomedicine' – protocol repackages known interventions but adds various unproven supplements for \$\$\$\$
- “No evidence that intensive, costly regimens of dietary supplements are effective.”



Others are referencing the Breseden MEND protocol...

- Reduce sugar intake/blood sugar
- Reduce environmental toxin exposure (oxidative stress)
- ‘De-stress’ diet - organic to avoid pesticides, avoid fried foods
- Get proper sleep
- Supplements to improve autophagy and neuroplasticity
- Exercise your brain



But scary as that is, **neuroplasticity CAN be restored.** And when the brain is back to its normal, flexible self, it can heal itself – making Alzheimer’s a reversible condition.


6 Steps to Reverse Alzheimer’s Through Lifestyle Changes

Just as we each have unique stress exposures and an individual set of genes, every person with cognitive impairment has a different set of circumstances that led them to develop their condition. For that reason, the precise path to recovery from Alzheimer’s differs somewhat from person to person.

That said, below is a list of six primary areas that I, as a medical professional, always address when working with a patient seeking to prevent or reverse Alzheimer’s.

STEP 1: Reduce sugar intake/blood sugar

Over-consumption of sugar and/or carbs overwhelms our body’s ability to manage glucose. This makes us more



Lifestyle modifications

- Reduce sugar intake/blood sugar
- Cites 'Bredesen Protocol' as proof for supplements
- markets supplements, books, consulting
- Cites 'Bredesen Protocol' as proof for supplements
- Cites 'Bredesen Protocol' as proof for supplements
- Supplements to improve autophagy and neuroplasticity
- Exercise your brain

'Reversal' of Alzheimer's disease

But scary as that is, new research says that cognitive function CAN be restored. And when the brain is back to its normal, flexible self, it can heal itself – making Alzheimer's a reversible condition.

6 Steps to Reverse Alzheimer's Through Lifestyle Changes

Just as we each have unique stress exposures and an individual set of genes, every person with cognitive impairment has a different set of circumstances that led them to develop their condition. For that reason, the precise path to recovery from Alzheimer's differs somewhat from person to person.

Instead: Follow a healthy lifestyle through diet and exercise



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Things to remember on studying diet and supplements, alternative therapies

- Positive effects of individual components probably require **longer term exposure and in those with low regular intake**
- Healthy diet patterns may provide a **synergistic effect of several components** to affect many processes and signaling pathways impacting cognitive function and decline
- Healthy diet may have more of an impact **on those who don't already have diagnosed dementia** – before extensive damage
- **Different patterns** of protection for **different dementia subtypes?**



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Therapies

- Treat hypertension
- Physical activity; Aerobic exercise
- (Diet – MIND)
- Cognitive stimulation



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Cognitive Stimulation

- Crosswords, word and number puzzles - are memory training – strengthening type of memory used – some benefits noted in observational studies
- Most beneficial - new, varied and targeted stimulation activities, speed of processing training; cross-train your brain – work on something you are not good at.
- Education as a cognitive buffer – resilience/reserve to prevent/reduce risk; engage in life-long learning
- Several studies ongoing...



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Debunking Risk Factors - Aluminum

- First introduced in 60's-70's as possible risk factor
- Animal (rat) studies still studying underlying mechanisms
- Human studies - higher post-mortem brain levels (β -amyloid is sticky); observational studies – moderate association of aluminum in drinking water and risk; but no strong evidence that aluminum exposures directly cause Alzheimer's disease
- Not a major focus in AD research
- DEBUNK - Aluminum from food or cookware, everyday sources, unlikely to cause Alzheimer's disease



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Debunk vs. hold promise

- Prevacen
- Neuriva
- Resveratrol
- Ginkgo Biloba
- Turmeric/Curcumin
- Fish Oil/Omega-3
- Coconut oil
- Medi-Diet/MIND Diet
- Ketogenic Diet
- Breseden MEND Protocol

Be Skeptical

- Be cautious when reading about alternative treatments
- Is there reference to curing, reversing or preventing Alzheimer's?
– remember there are no proven cures currently
- Science presented – published scientific review of several studies including randomized controlled trials? (vs. case studies only)
- If expensive, invest money otherwise towards supporting proven beneficial activities, actions



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Alzheimer's Disease Therapies and Risk

- <https://www.nia.nih.gov/health/what-causes-alzheimers-disease>
- <https://www.nia.nih.gov/health/assessing-risk-alzheimers-disease>
- <https://www.alz.org/alzheimers-dementia/what-is-alzheimers/myths>
- <https://www.alzheimers.org.uk/about-dementia/treatments/alternative-therapies>
- <https://www.mayoclinic.org/diseases-conditions/alzheimers-disease/diagnosis-treatment/drc-20350453>



Wisconsin Alzheimer's Institute

UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Be Hopeful

- Refer individuals to Clinical Trials
- Only through participation in Clinical Trials will we find and prove benefits of therapies for Alzheimer's disease and other dementias

Clinical Trial Resources

- **Wisconsin Alzheimer's Research Center (ADRC)**
 - <http://www.adrc.wisc.edu/>
- **Clinical Trials in Alzheimer's disease**
 - <http://clinicaltrials.gov/>
- **Alzheimer's Association TrialMatch**
 - http://www.alz.org/research/clinical_trials/find_clinical_trials_trialmatch.asp

Thank you!

References

- Campos M. Ketogenic diet: Is the ultimate low-carb diet good for you? Harvard Health Blog. Posted 7/27/2017, updated 4/14/2020. <https://www.health.harvard.edu/blog/ketogenic-diet-is-the-ultimate-low-carb-diet-good-for-you-2017072712089>
- Jennings A, Cunnane SC, Minihane AM. Can nutrition support healthy cognitive ageing and reduce dementia risk? *BMJ*. 2020 Jun 26;369:m2269
- Hellmuth, J., Rabinovici, G.D., Miller, B.L. The rise of pseudomedicine for de-mentia and brain health. *JAMA* 2019; 321:543–544.
- Morris MC, Tangney CC, Wang Y, Sacks FM, Barnes LL, Bennett DA, Aggarwal NT. MIND diet slows cognitive decline with aging. *Alzheimer's Dement* 2015;11:1015–22.
- Qato, D.M., Wilder, J., Schumm, L.P., Gillet, V., Alexander, G.C., 2016. Changes in prescription and over-the-counter medication and dietary supplement use among older adults in the United States, 2005 vs 2011. *JAMA Intern. Med.* 176, 473–482.
- Schmerling RH. FDA curbs unfounded memory supplement claims. Posted 5/31/2019, updated 9/29/2020. <https://www.health.harvard.edu/blog/fda-curbs-unfounded-memory-supplement-claims-2019053116772>
- U.S. National Library of Medicine. <https://medlineplus.gov/evaluatinghealthinformation.html>
- van den Brink AC, Brouwer-Brolsma EM, Berendsen AAM, van de Rest O. The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diets Are Associated with Less Cognitive Decline and a Lower Risk of Alzheimer's Disease-A Review. *Adv Nutr.* 2019 Nov 1;10(6):1040-1065..
- Voulgaropoulou SD, van Amelsvoort TAMJ, Prickaerts J, Vingerhoets C. The effect of curcumin on cognition in Alzheimer's disease and healthy aging: A systematic review of pre-clinical and clinical studies. *Brain Res.* 2019 Dec 15;1725:146476.