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Università Cattolica del Sacro Cuore

NUTRITION FOR HEALTHY BRAIN AGING

Emanuele Marzetti, MD, PhD

Centro di Medicina dell'Invecchiamento (Ce.M.I.)
Fondazione Policlinico Universitario "Agostino Gemelli", IRCCS
Università Cattolica del Sacro Cuore
Roma

Roma, 27 novembre 2019

CONFLICT OF INTEREST DISCLOSURE

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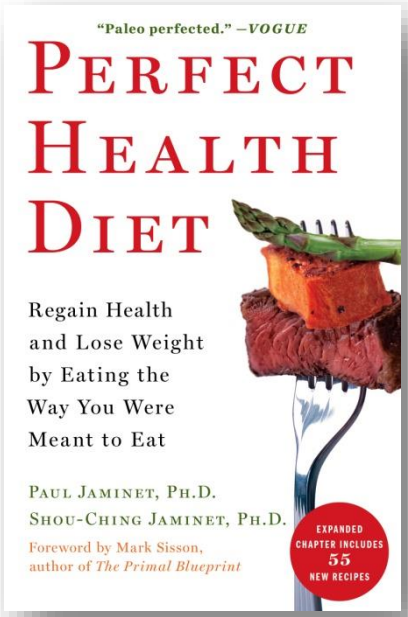
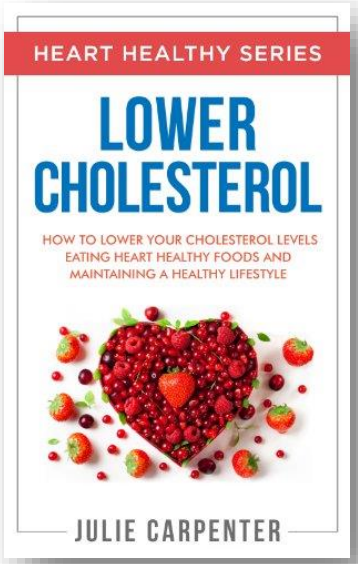
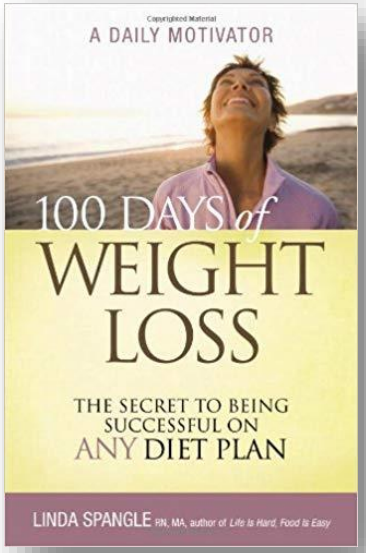
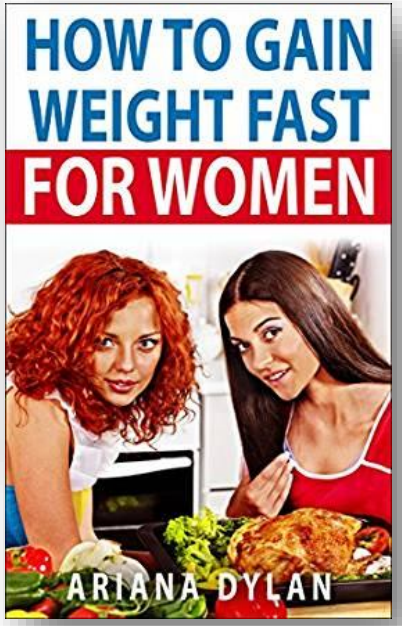
- Consultant for
  - Abbott
  - Acsel Health
  - Biophytis
  - Genactis
  - Huron Consulting Group
  - Nestlè
  - Novartis
  - Nutricia
- Academic Leader of Work-Package 8 (analysis of results) of the SPRINTT Project (IMI–JU 115621)

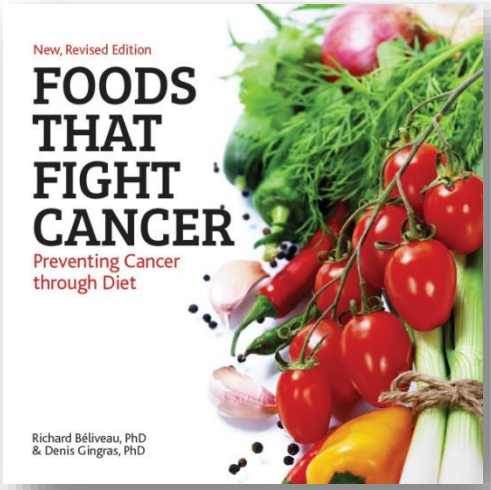
THE WORLD IS ON DIET


"Paleo perfected." —VOGUE
PERFECT HEALTH DIET
Regain Health and Lose Weight by Eating the Way You Were Meant to Eat
PAUL JAMINET, PH.D.
SHOU-CHING JAMINET, PH.D.
Foreword by Mark Sisson, author of The Primal Blueprint
EXPANDED CHAPTER INCLUDES 55 NEW RECIPES

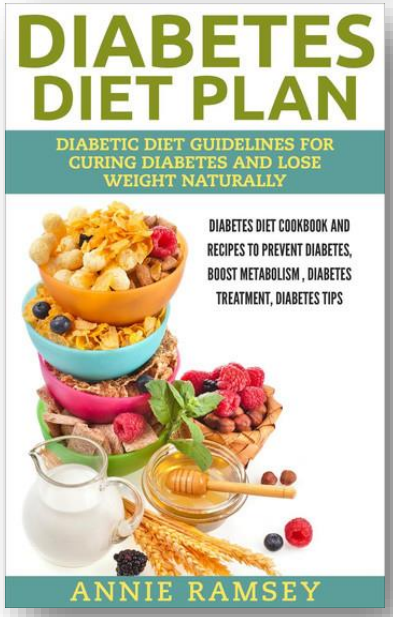

HEART HEALTHY SERIES
LOWER CHOLESTEROL
HOW TO LOWER YOUR CHOLESTEROL LEVELS EATING HEART HEALTHY FOODS AND MAINTAINING A HEALTHY LIFESTYLE
JULIE CARPENTER

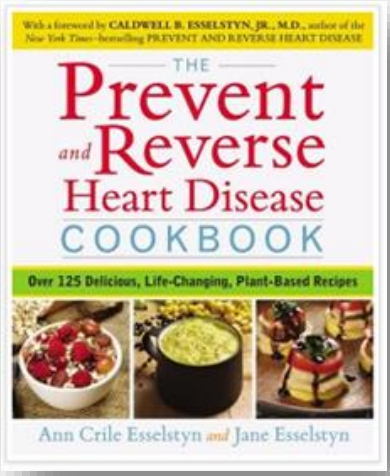

A DAILY MOTIVATOR
100 DAYS of WEIGHT LOSS
THE SECRET TO BEING SUCCESSFUL ON ANY DIET PLAN
LINDA SPANGLE RN, MA, author of Life Is Hard, Food Is Easy


HOW TO GAIN WEIGHT FAST FOR WOMEN
ARIANA DYLAN


New, Revised Edition
FOODS THAT FIGHT CANCER
Preventing Cancer through Diet
Richard Béliveau, PhD
& Denis Gingras, PhD


SESAME SEEDS
POMEGRANATES
SAFFRON
AT A GLANCE: ANTI-AGEING FOODS
ORANGES
GHEE
OLIVES
GREEN TEA


DIABETES DIET PLAN
DIABETIC DIET GUIDELINES FOR CURING DIABETES AND LOSE WEIGHT NATURALLY
DIABETES DIET COOKBOOK AND RECIPES TO PREVENT DIABETES, BOOST METABOLISM , DIABETES TREATMENT, DIABETES TIPS
ANNIE RAMSEY


With a foreword by CALDWELL B. ESSELSTYN, JR., M.D., author of the New York Times–bestselling PREVENT AND REVERSE HEART DISEASE
THE Prevent and Reverse Heart Disease COOKBOOK
Over 125 Delicious, Life-Changing, Plant-Based Recipes
Ann Crile Esselstyn and Jane Esselstyn

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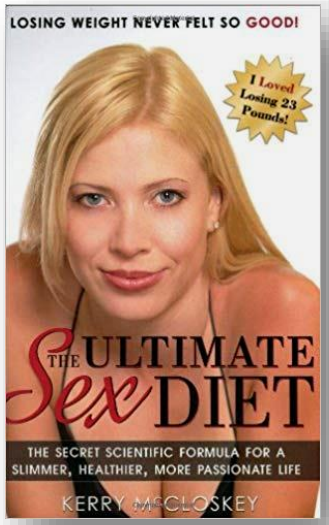

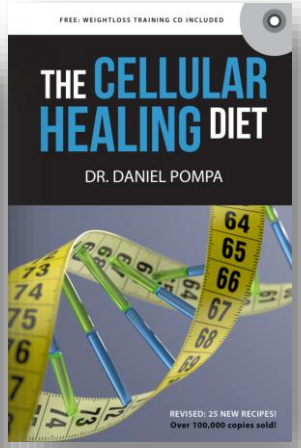

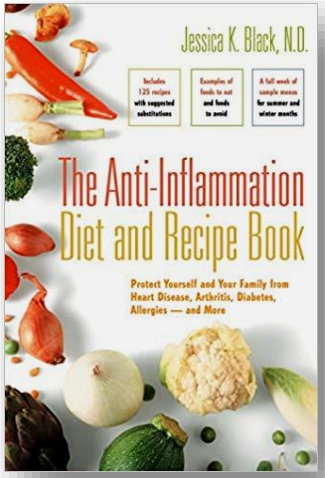

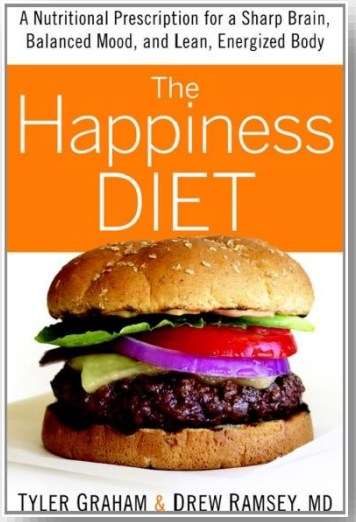

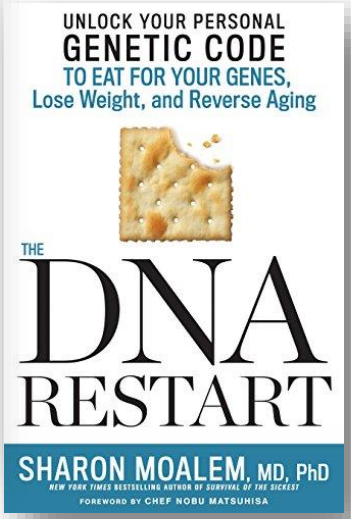

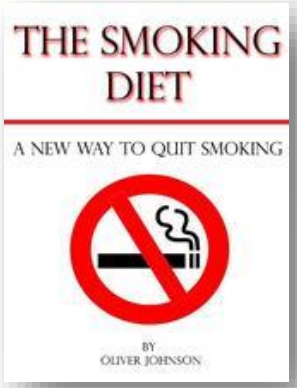

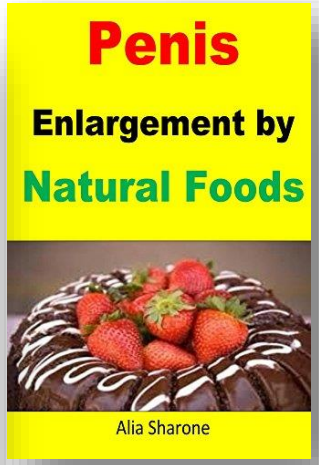

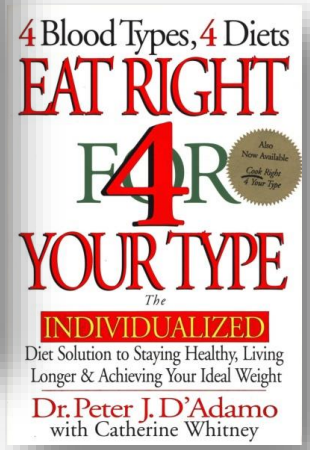

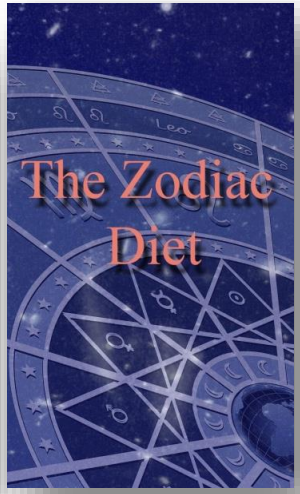

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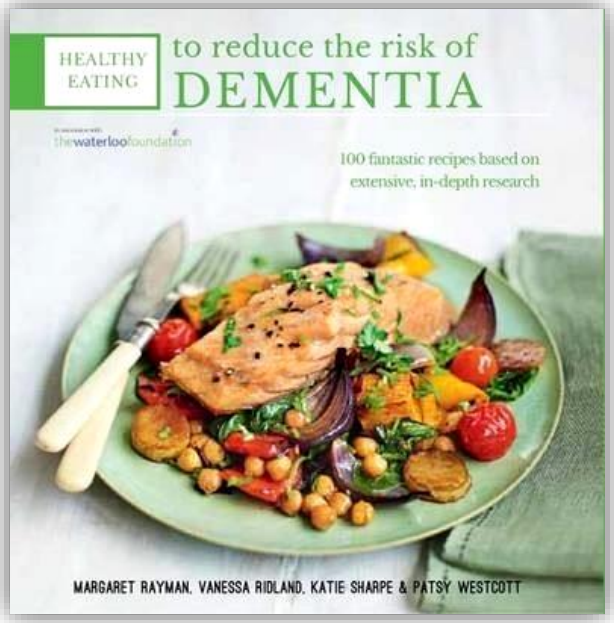
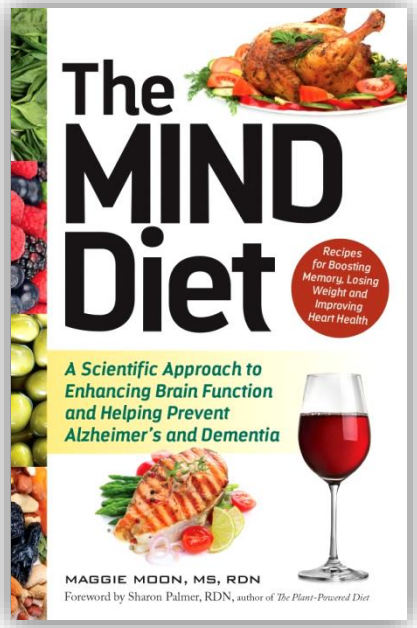
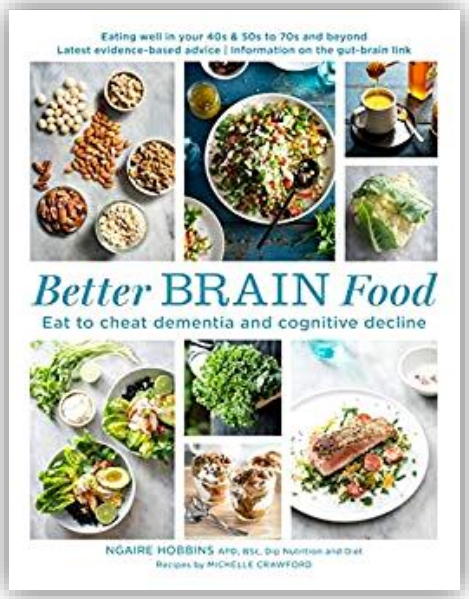
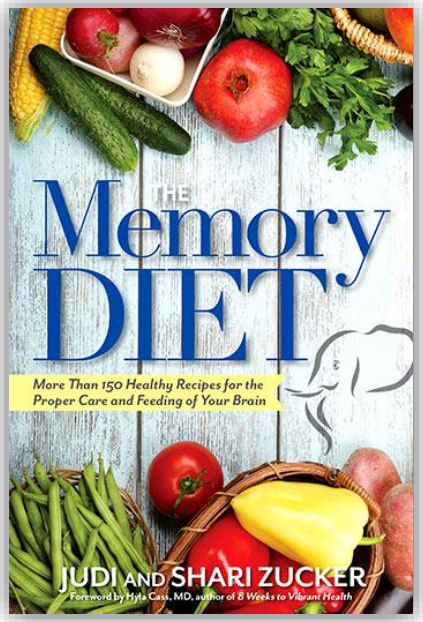
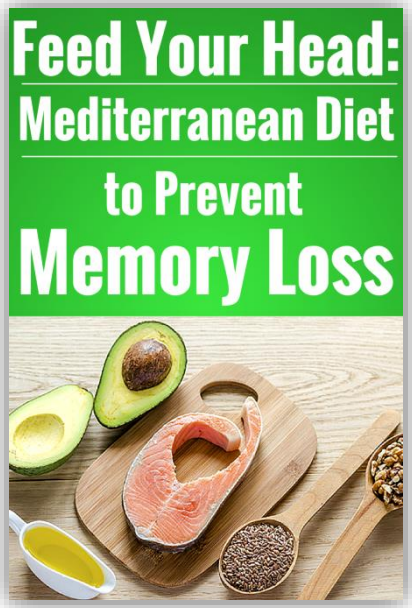
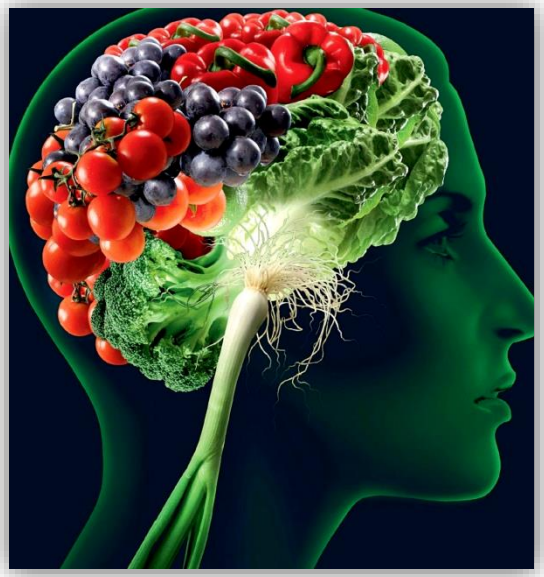


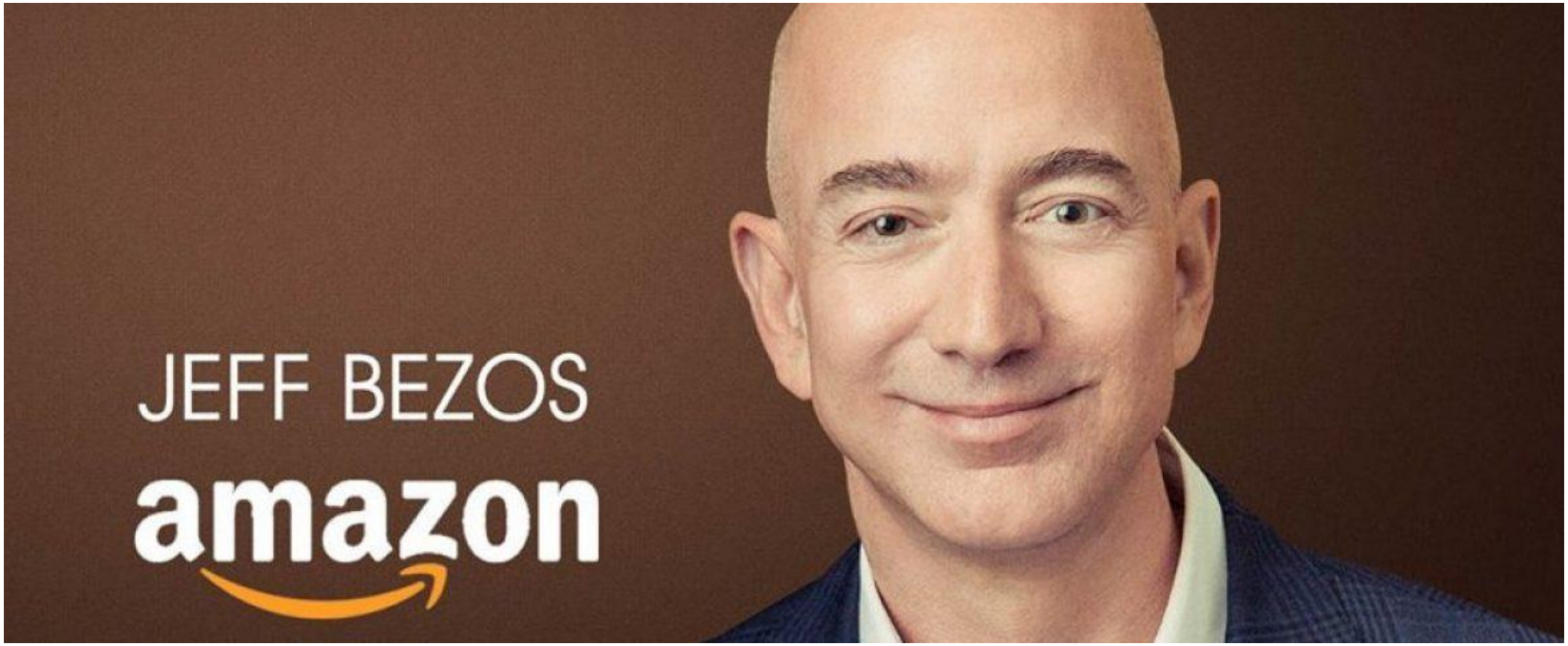


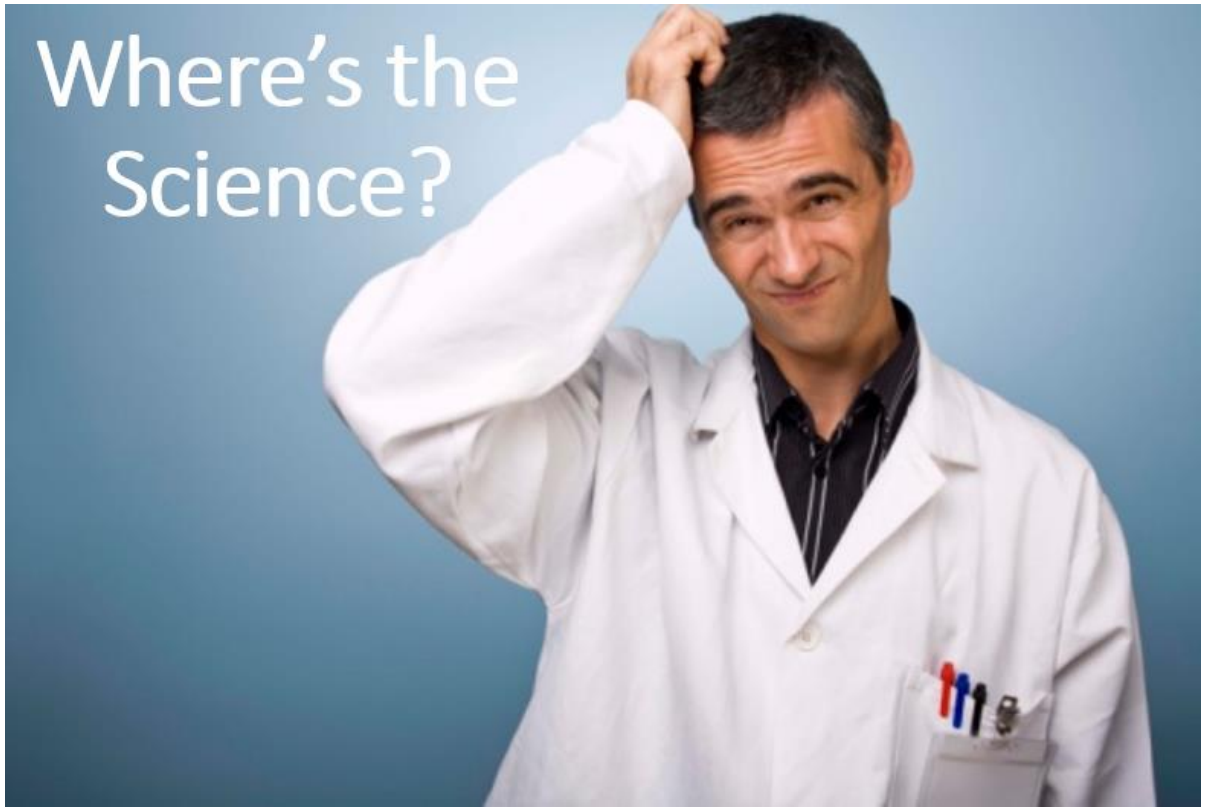









JEFF BEZOS
amazon


Where's the
Science?

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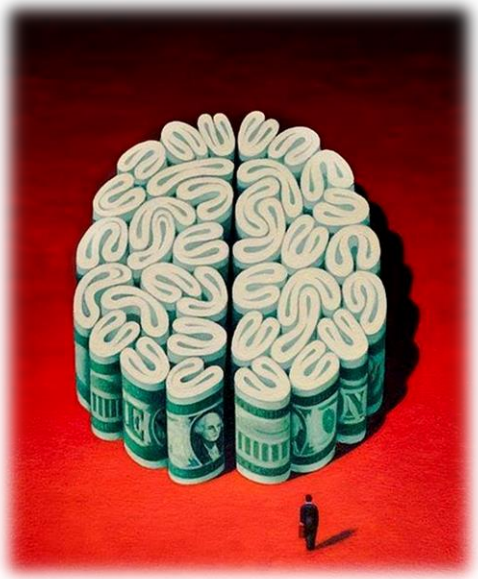
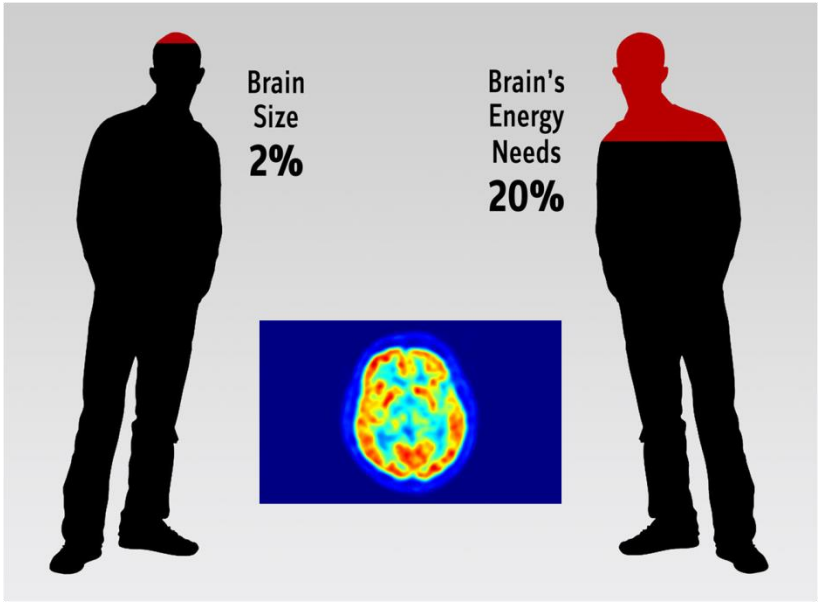
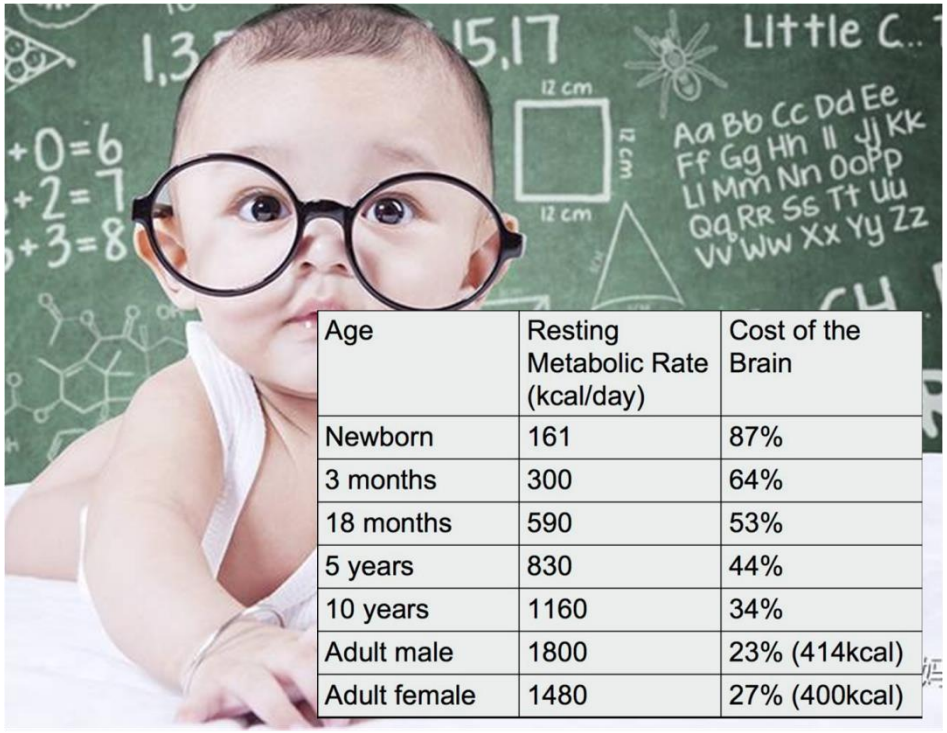
BRAIN IS A COSTLY ORGAN



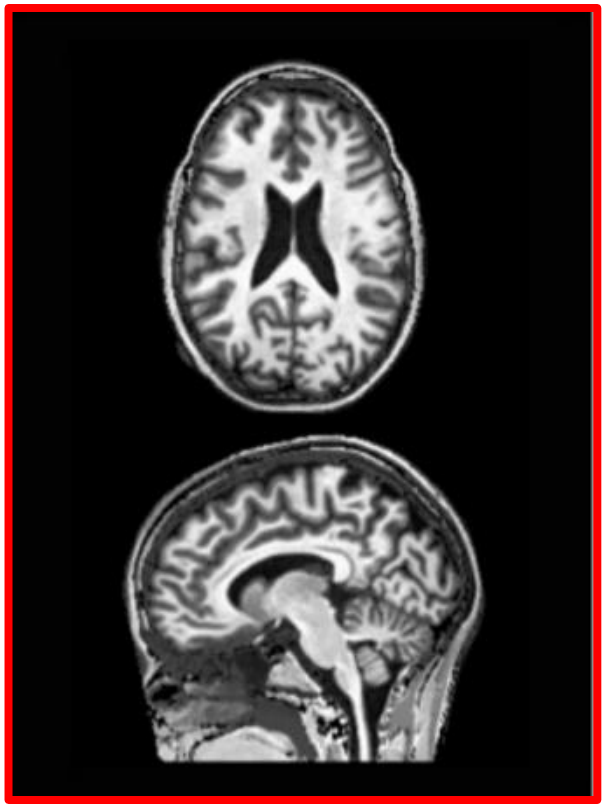




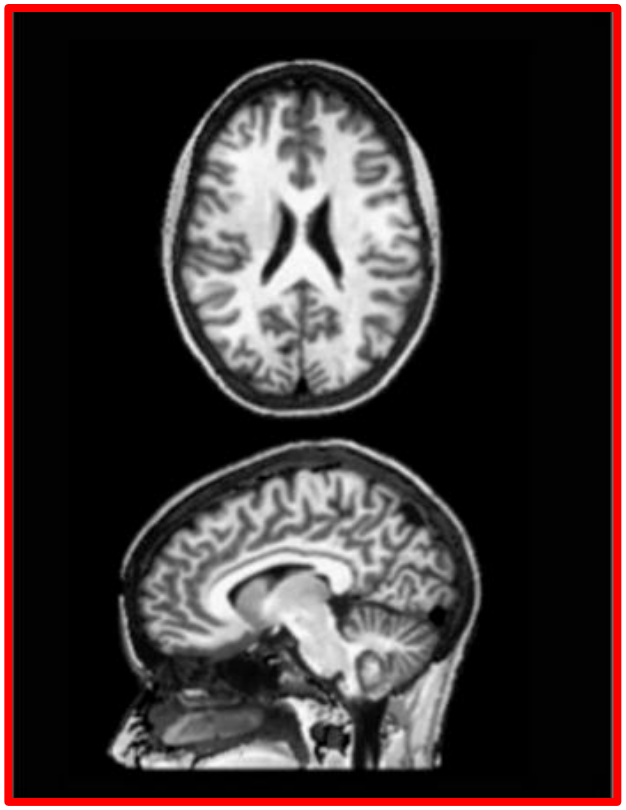
Age	Resting Metabolic Rate (kcal/day)	Cost of the Brain
Newborn	161	87%
3 months	300	64%
18 months	590	53%
5 years	830	44%
10 years	1160	34%
Adult male	1800	23% (414kcal)
Adult female	1480	27% (400kcal)


My brain really IS bigger than yours
Yes, but mine is actually switched on

27-year-old woman with anorexia nervosa



27-year-old normal-weight woman



Tooth Loss, Apolipoprotein E, and Decline in Delayed Word Recall

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Stein et al., J Dent Res 2010

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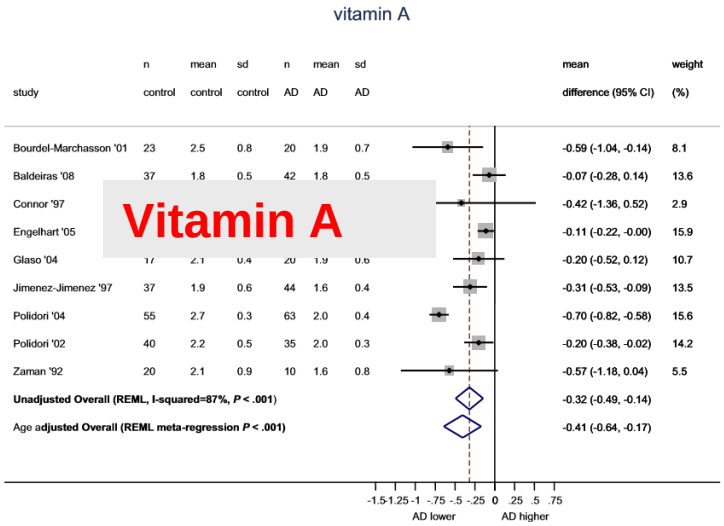
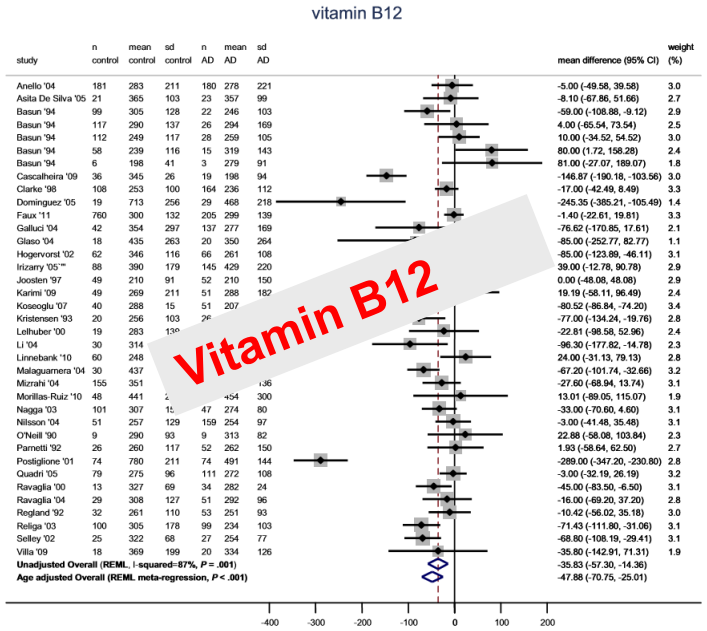
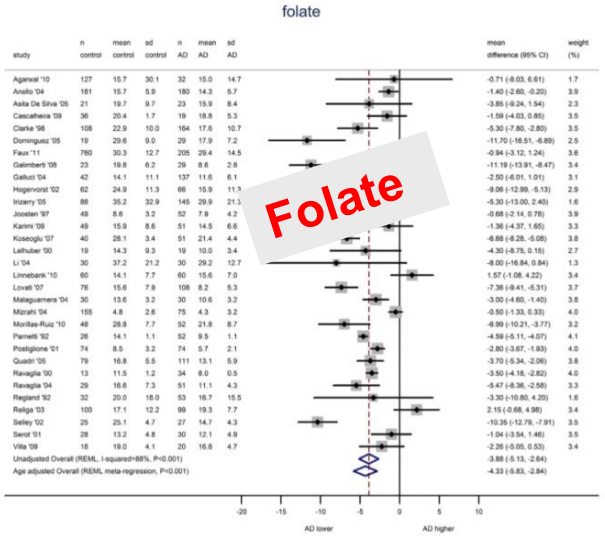
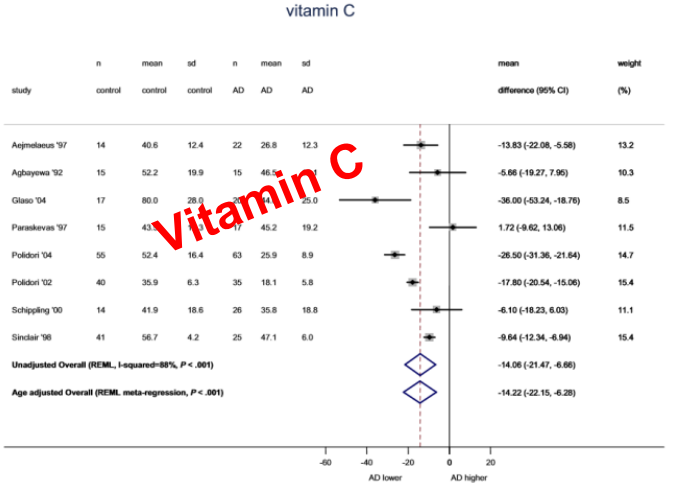
Plasma nutrient status of patients with Alzheimer's disease: Systematic review and meta-analysis









Lopes da Silva et al., Alzheimers Dement 2014

Alzheimer's & Dementia

Plasma nutrient status of patients with Alzheimer's disease: Systematic review and meta-analysis

Sofia Lopes da Silva[a,b], Bruno Vellas[c], Saskia Elemans[a], José Luchsinger[d], Patrick Kamphuis[a,b], Kristine Yaffe[e], John Sijben[a,*], Martine Groenendijk[a], Theo Stijnen[f]

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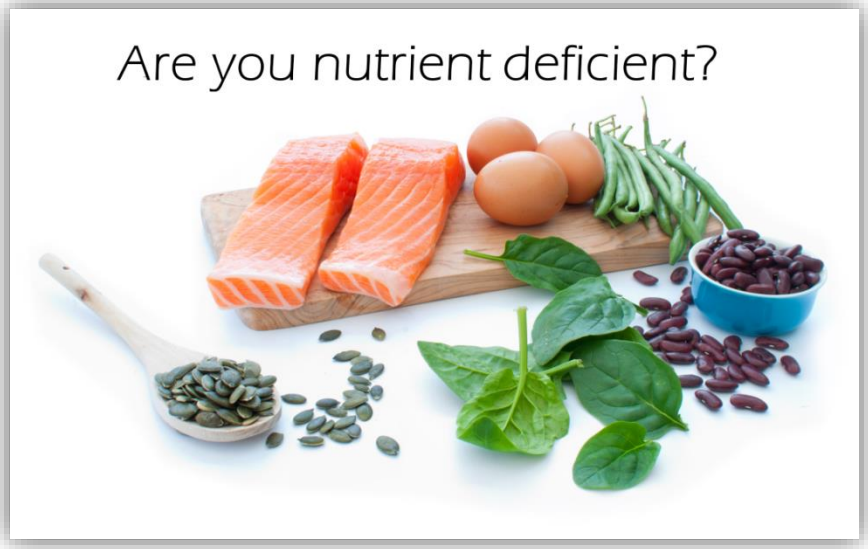
"The lower plasma nutrient levels indicate that patients with AD have impaired systemic availability of several nutrients. This difference appears to be unrelated to the classic malnourishment that is well known to be common in AD, suggesting that **compromised micronutrient status may precede protein and energy malnutrition**. Contributing factors might be AD-related alterations in feeding behavior and intake, nutrient absorption, alterations in metabolism, and increased utilization of nutrients for AD pathology-related processes. Given the potential role of nutrients in the pathophysiological processes of AD, the utility of nutrition may currently be underappreciated and offer potential in AD management".



Vitamin B12 deficiency

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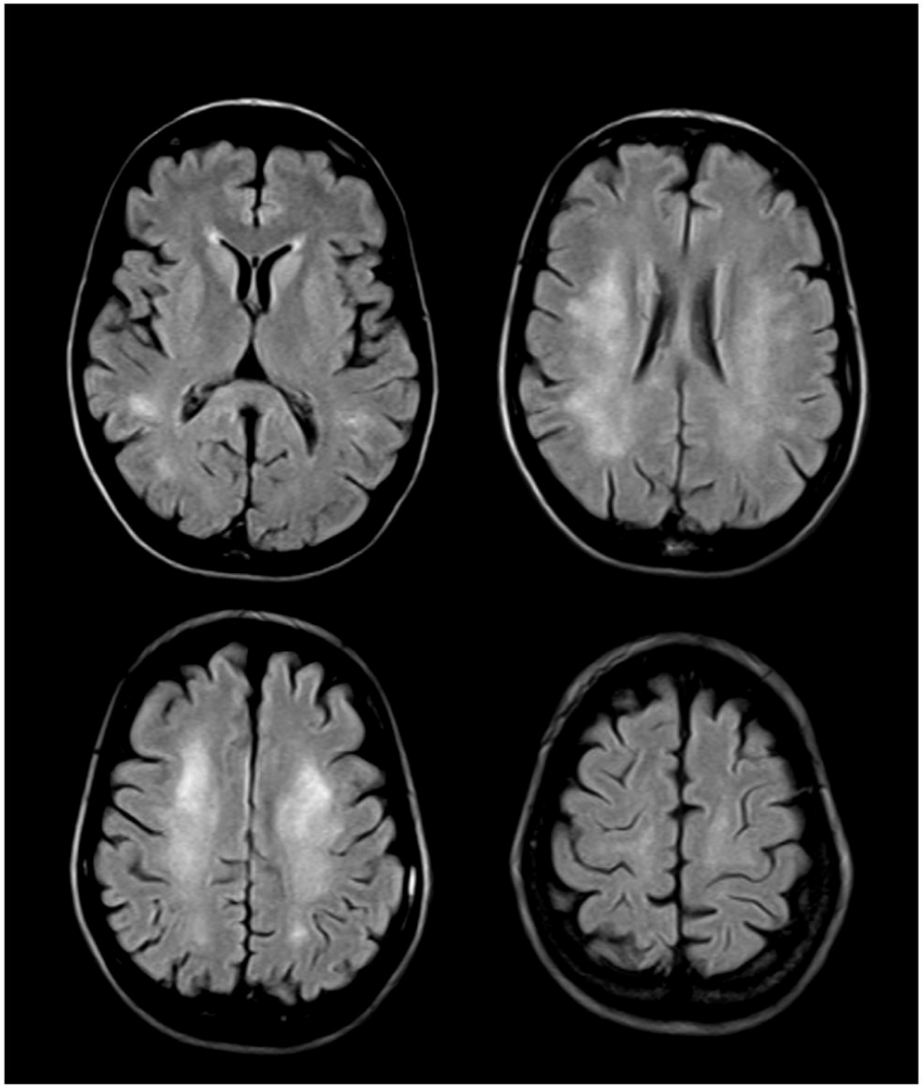
Brain MRI of a 45-year-old female presenting with slowly progressive cognitive impairment. Axial attenuated inversion recovery (FLAIR) images disclose **diffuse and symmetric white matter signal hyperintensity**.



Briani et al., Nutrients 2013

Age Group, yr*	pH Mean (±SD)
<35 (n = 124)	2.72 (1.23)
35–39 (n = 90)	2.77 (1.24)
40–44 (n = 92)	2.85 (1.27)
45–49 (n = 111)	2.91 (1.29)
50–54 (n = 96)	3.05 (1.40)
55–59 (n = 61)	3.30 (1.54)
60–64 (n = 59)	3.28 (1.49)
65–69 (n = 42)	3.07 (1.56)
≥70 (n = 64)	3.23 (1.56)

Shih et al., Am J Gastroenterol 2003

Therapeutic Advances in Gastroenterology

Original Research

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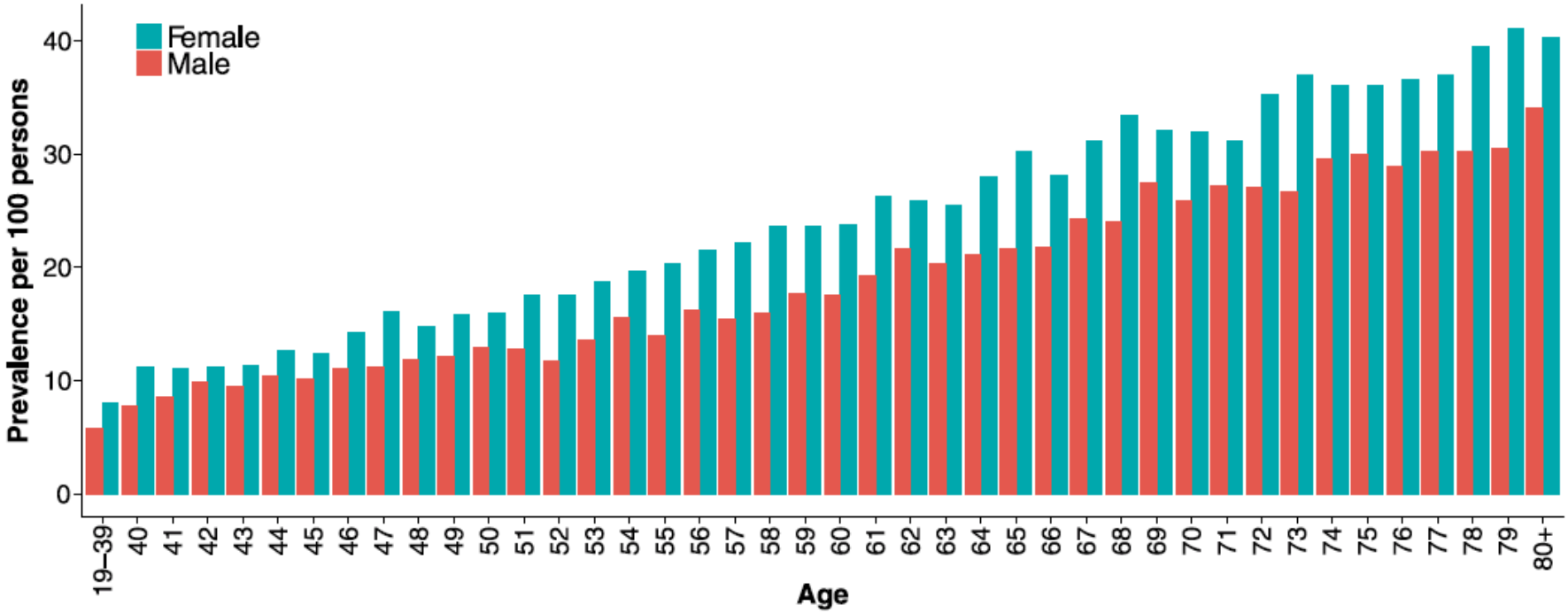
Proton-pump inhibitors among adults: a nationwide drug-utilization study

Ther Adv Gastroenterol
2018, Vol. 11: 1–11
DOI: 10.1177/1756284818777943

Óskar Ö. Hálfdánarson, Anton Pottegård, Einar S. Björnsson, Sigrún H. Lund, Margret H. Ogmundsdottir, Eiríkur Steingrímsson, Helga M. Ogmundsdottir and Helga Zoega



Therapeutic Advances in Gastroenterology

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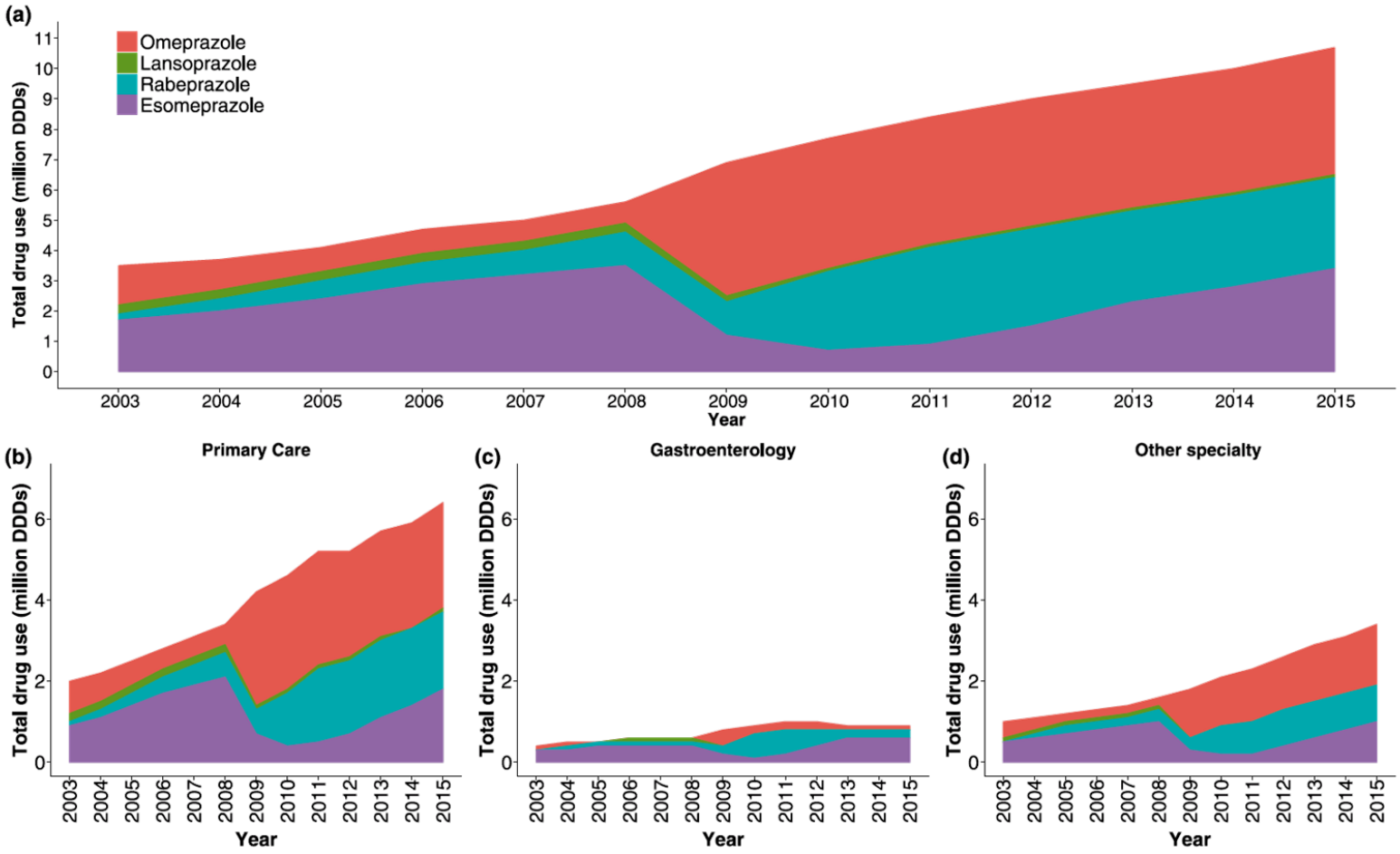

JAMA Neurology

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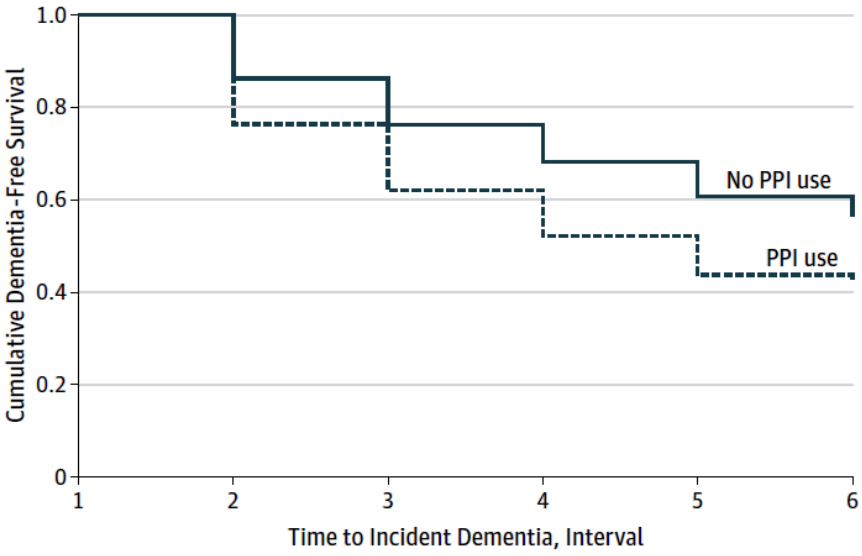
Original Investigation

Association of Proton Pump Inhibitors With Risk of Dementia
A Pharmacoepidemiological Claims Data Analysis

Willy Gomm, PhD; Klaus von Holt, MD, PhD; Friederike Thomé, MSc; Karl Broich, MD; Wolfgang Maier, MD; Anne Fink, MSc; Gabriele Doblhammer, PhD; Britta Haenisch, PhD

Figure 2. Dementia-Free Survival by Use of Proton Pump Inhibitors (PPIs)



- Some PPIs (e.g., lansoprazole and omeprazole) can cross the BBB and might promote Aβ deposition.
- PPIs might impair degradation of Aβ by lysosomes in microglia.
- PPI use is associated with vitamin B12 deficiency.

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JOURNAL
OF THE
AMERICAN
GERIATRICS
SOCIETY

The Association Between Cognition and Histamine-2 Receptor Antagonists in African Americans

Malaz Boustani, MD, MPH,[*†‡] *Kathleen S. Hall, PhD,*[§] *Kathleen A. Lane, MS,*[¶] *Hisham Aljadhey, PharmD,*[‖] *Sujuan Gao, PhD,*[¶**] *Frederick Unverzagt, PhD,*[§] *Michael D. Murray, PharmD, MPH,*[†‖] *Adesola Ogunniyi, MD,*[††] *and Hugh Hendrie, MB, ChB, DSc (Med)*[*†§]

CONCLUSION: H2As might be a risk factor for the development of cognitive impairment in African Americans. This finding requires confirmation from future studies.

JAMA The Journal of the American Medical Association

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Original Investigation

Proton Pump Inhibitor and Histamine 2 Receptor Antagonist Use and Vitamin B_{12} Deficiency

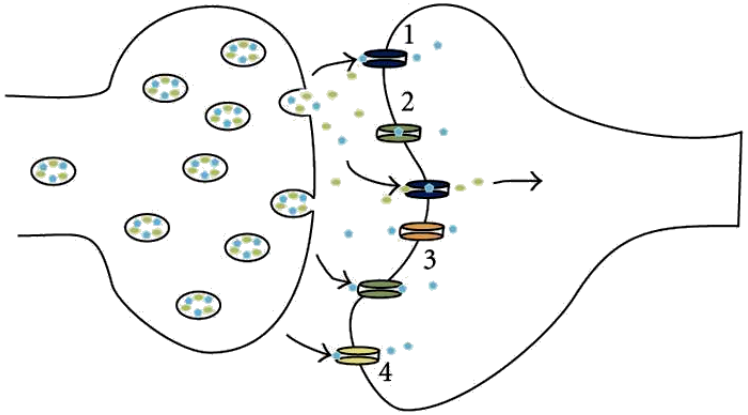
Jameson R. Lam, MPH; Jennifer L. Schneider, MPH; Wei Zhao, MPH; Douglas A. Corley, MD, PhD

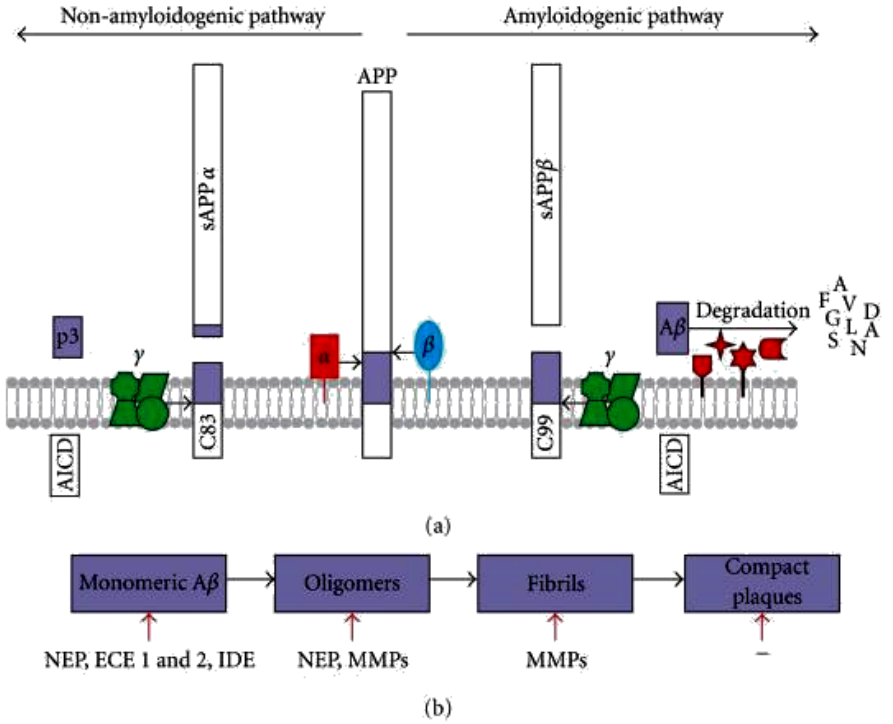
This study found an association between the use of PPIs and H_2RAs for 2 or more years and a subsequent diagnosis of vitamin B_{12} deficiency.

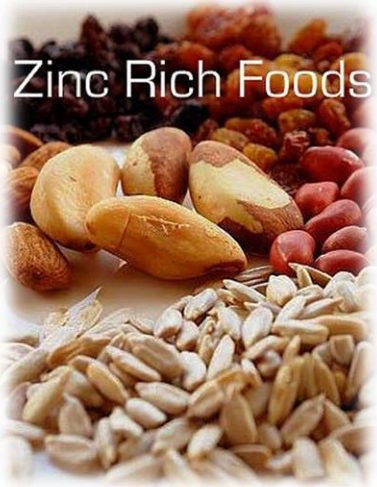
SAGE-Hindawi Access to Research
International Journal of Alzheimer's Disease
Volume 2011, Article ID 971021, 10 pages
doi:10.4061/2011/971021

The Role of Zinc in Alzheimer's Disease

Nicole T. Watt, Isobel J. Whitehouse, and Nigel M. Hooper







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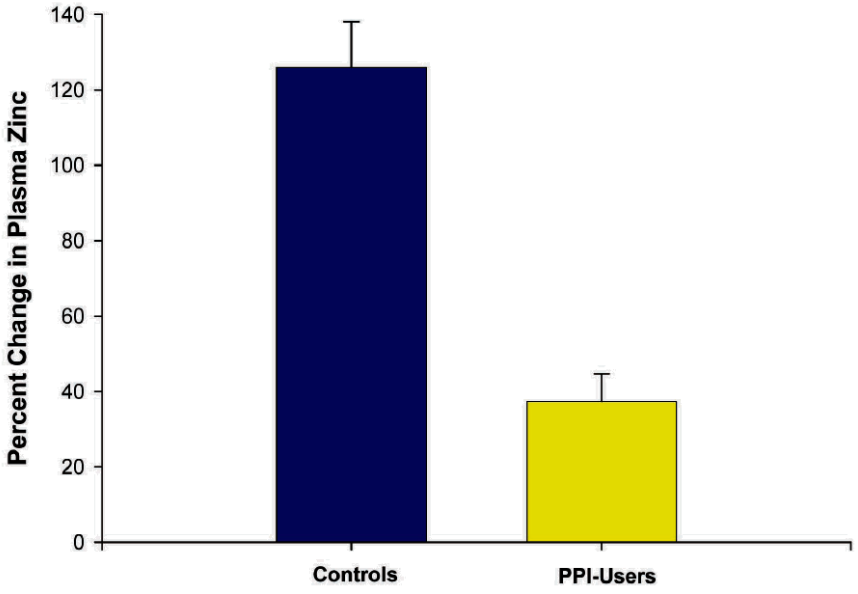

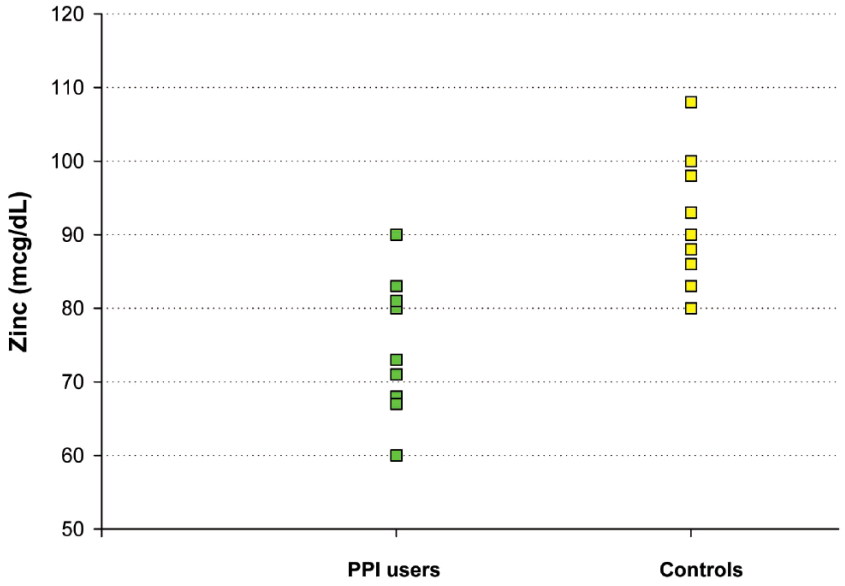

Farrell et al., Gastroenterology Res 2011

nutrients

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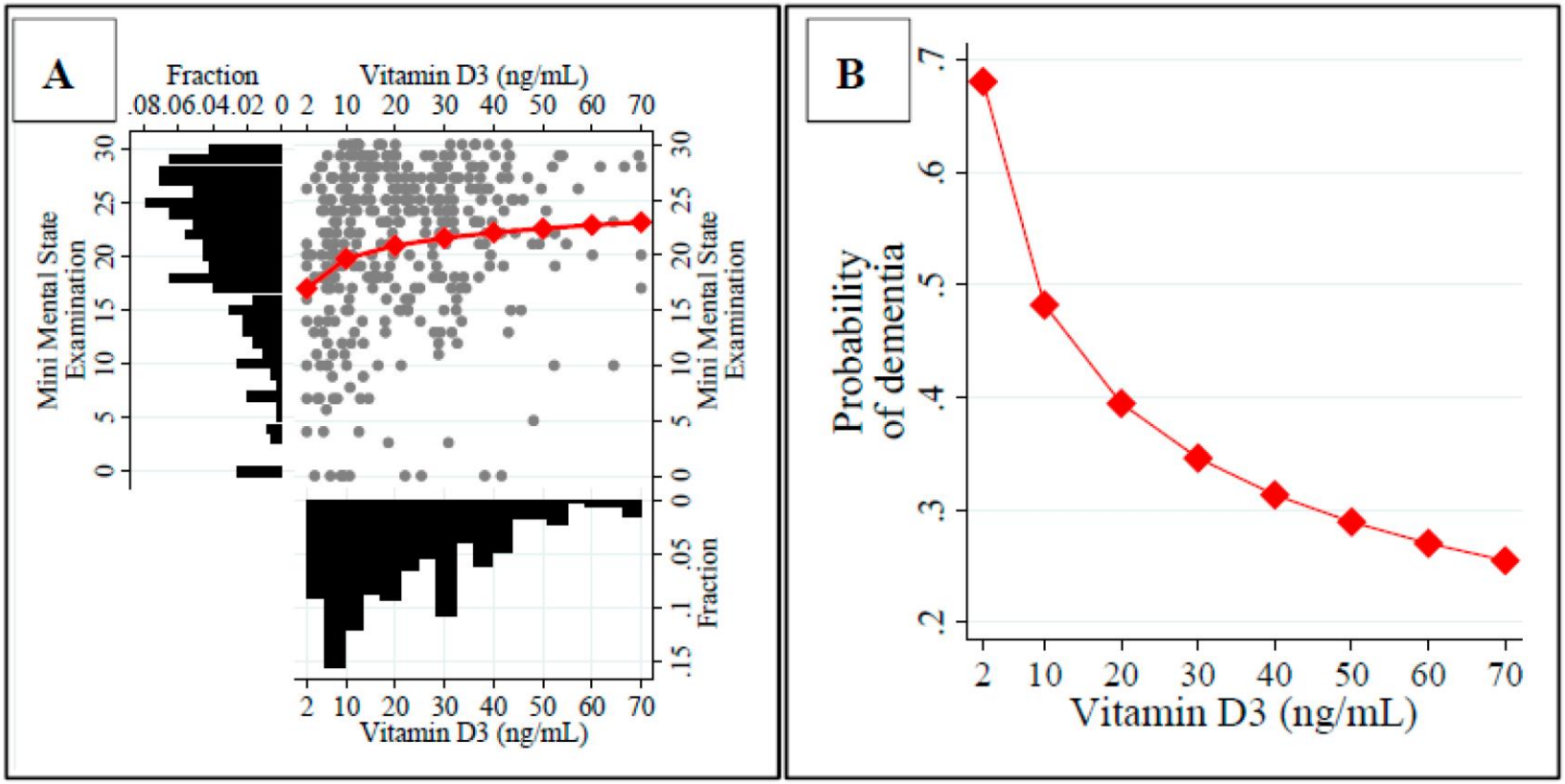
Article

Cognitive Functioning of Geriatric Patients: Is Hypovitaminosis D the Next Marker of Cognitive Dysfunction and Dementia?

Ewelina Łukaszyk [1,2,*], Katarzyna Bień-Barkowska [3] and Barbara Bień [1,2]



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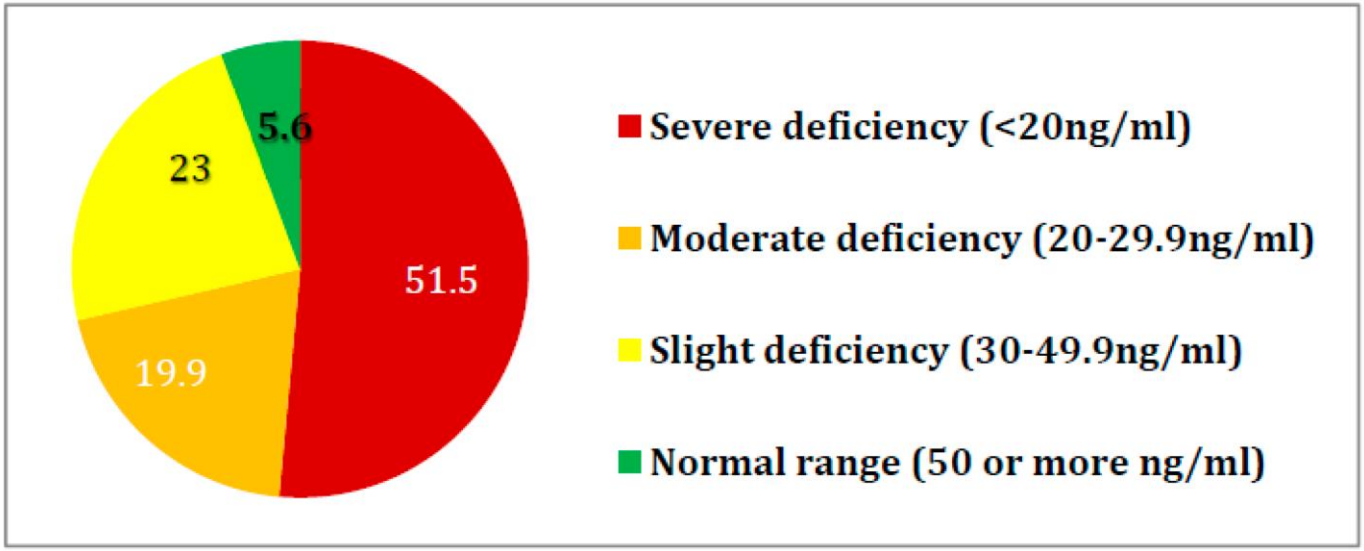
Article

Cognitive Functioning of Geriatric Patients: Is Hypovitaminosis D the Next Marker of Cognitive Dysfunction and Dementia?

Ewelina Łukaszyk [1,2,*], Katarzyna Bień-Barkowska [3] and Barbara Bień [1,2]

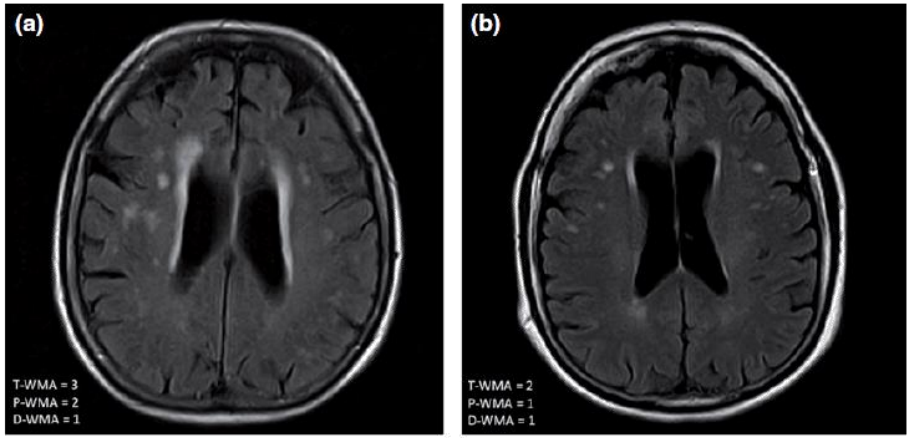


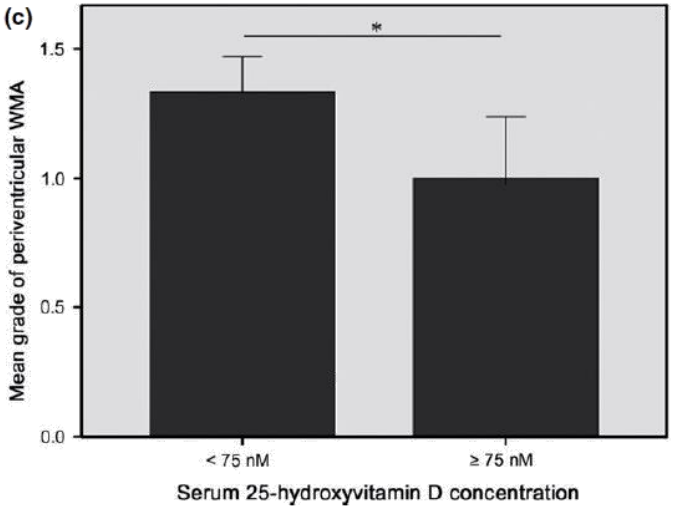
European Journal of Neurology 2014, **21:** 1436–1442 doi:10.1111/ene.12511

CME ARTICLE

Vitamin D and white matter abnormalities in older adults: a cross-sectional neuroimaging study

C. Annweiler[a,b,c], T. Annweiler[d], R. Bartha[c], F. R. Herrmann[e], R. Camicioli[f] and O. Beauchet[a,b,g]





Neuro
-epidemiology

Methods in Neuroepidemiology

Neuroepidemiology 2011;37:249–258
DOI: 10.1159/000334177

Received: May 4, 2011
Accepted: September 28, 2011
Published online: December 7, 2011

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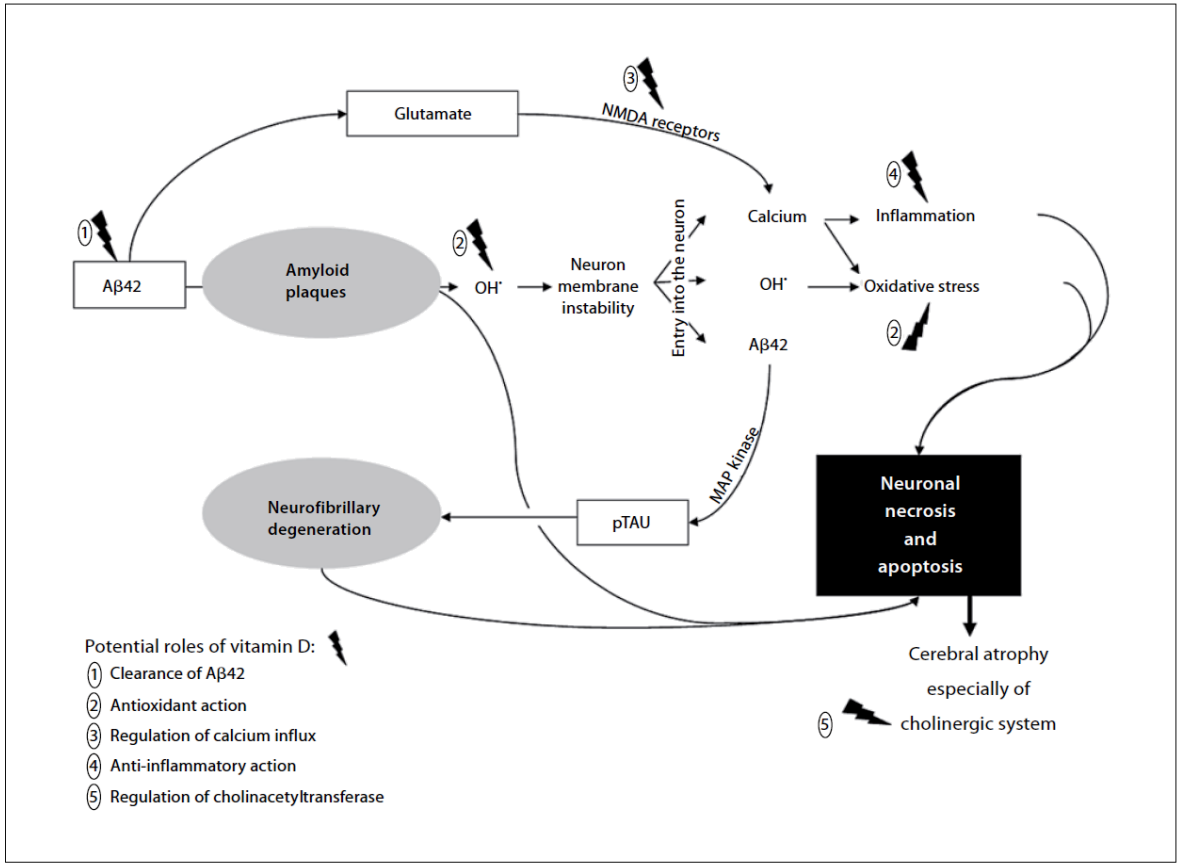
Vitamin D-Mentia: Randomized Clinical Trials Should Be the Next Step

Cédric Annweiler Olivier Beauchet



Journal of
Neurology, Neurosurgery
& Psychiatry

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Effects of vitamin D supplementation on cognitive function and blood Aβ-related biomarkers in older adults with Alzheimer's disease: a randomised, double-blind, placebo-controlled trial

Jingya Jia,[1] Jing Hu,[1] Xiaoxu Huo,[1] Rujuan Miao,[1] Yanping Zhang,[2] Fei Ma[1]

Conclusions Daily oral vitamin D supplementation (800 IU/day) for 12 months may improve cognitive function and decrease Aβ-related biomarkers in elderly patients with AD. Larger scale longer term randomised trials of vitamin D are needed.

Journal of the AMERICAN GERIATRICS SOCIETY

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Cognition and Vitamin D in Older African-American Women–Physical performance and Osteoporosis prevention with vitamin D in older African Americans Trial and Dementia

Jeanette E. Owusu, MD, Shahidul Islam, MPH,* Subhashini S. Katumuluwa, MD, MPH,* Alexandra R. Stolberg, MD, MPH,* Gianina L. Usera, MD,† Ayesha A. Anwarullah, MD,‡ Albert Shieh, MD,§ Ruban Dhaliwal, MD, MPH,¶ Louis Ragolia, PhD,* Mageda B. Mikhail, MD,* and John F. Aloia, MD**

CONCLUSION: There was no difference in cognition over time between older African-American women with serum concentrations of 25(OH)D of 30 ng/mL and greater than those taking placebo. There is no evidence to support vitamin D intake greater than the recommended daily allowance in this population for preventing cognitive decline. J Am Geriatr Soc 67:81–86, 2019.

Physiology & Behavior 213 (2020) 112689

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/physbeh

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Silibinin ameliorates STZ-induced impairment of memory and learning by up- regulating insulin signaling pathway and attenuating apoptosis

Panwen Liu[a], Lingyu Cui[a], Bo Liu[a], Weiwei Liu[a], Toshihiko Hayashi[a,b], Kazunori Mizuno[c], Shunji Hattori[c], Yuko Ushiki-Kaku[c], Satoshi Onodera[d], Takashi Ikejima[a,e,*]

Neurochemical Research (2019) 44:1818–1829
https://doi.org/10.1007/s11064-019-02816-2

ORIGINAL PAPER

Silibinin Alleviates the Learning and Memory Defects in Overtrained Rats Accompanying Reduced Neuronal Apoptosis and Senescence

Bo Liu[1] · Weiwei Liu[1] · Panwen Liu[1] · Xiumin Liu[1] · Xiaoyu Song[1,2] · Toshihiko Hayashi[1,3] · Satoshi Onodera[4] · Takashi Ikejima[1,5]

Single nutrient interventions in MCI and AD: No effect on cognitive function

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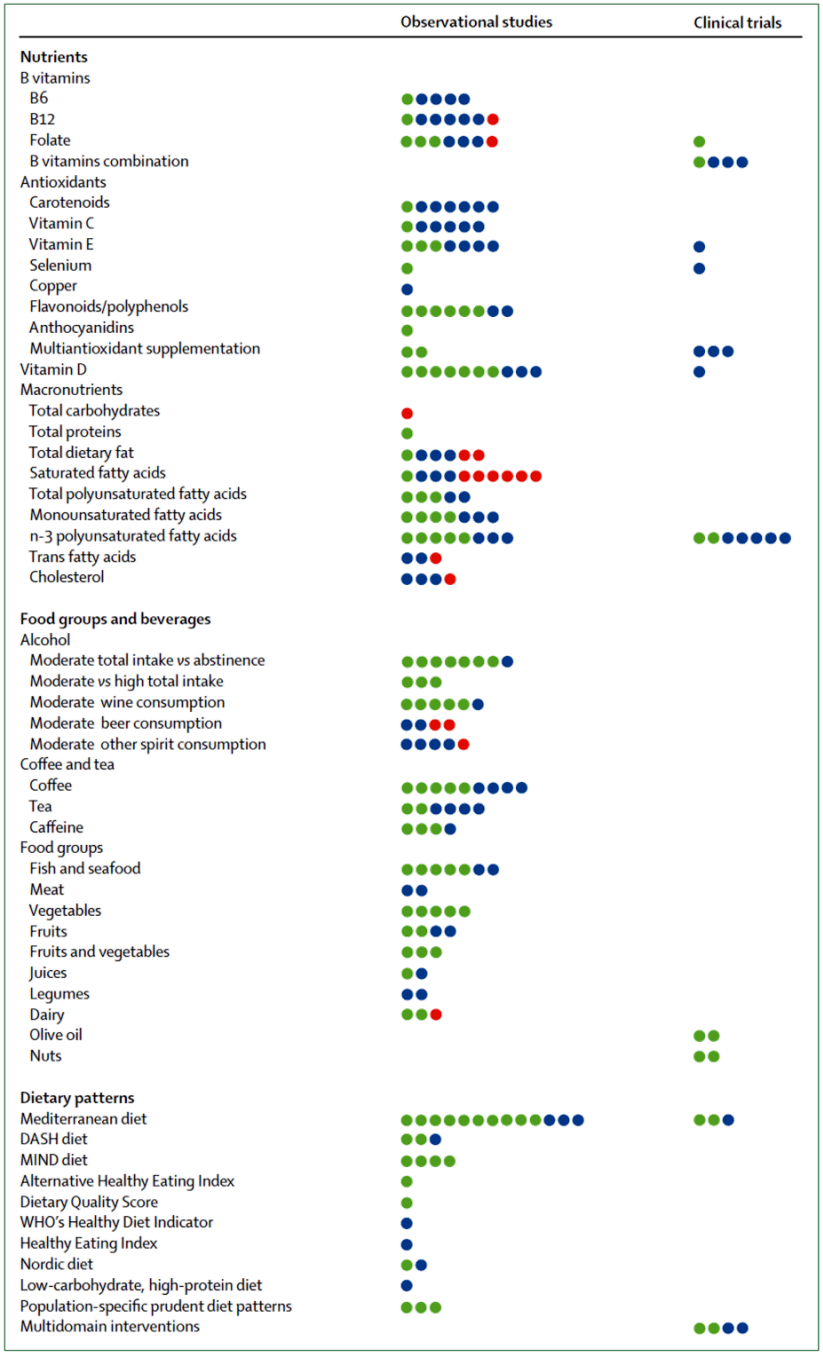
Author	Journal	Nutrient	#Subjects/ Duration	Outcome
Stein 2011	J Alz Dis	Vitamin D2	32 8 weeks	We conclude that high-dose vitamin D provides no benefit for cognition or disability over low-dose vitamin D in mild-moderate AD
DeKosky 2008	JAMA	Ginkgo biloba	3069 median f-up 6.1 Y	Ginkgo biloba at 120 mg twice a day was not effective in reducing either the overall incidence rate of dementia or AD incidence in elderly individuals with normal cognition or those with MCI
Aisen 2008	JAMA	B-vitamins	409 18 months	This regimen of high-dose B vitamin supplements does not slow cognitive decline in individuals with mild to moderate AD
McMahon 2006	N Eng J Med	B-vitamins	276 24 months	The results of this trial do not support the hypothesis that homocysteine lowering with B vitamins improves cognitive performance
Petersen 2005	N Eng J Med	Vitamin E	769 36 months	Vitamin E had no benefit in patients with mild cognitive impairment



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Scarmeas et al., Lancet Neurol 2018

Ann Intern Med. 2013;159:850-851.

EDITORIAL | Annals of Internal Medicine

Enough Is Enough: Stop Wasting Money on Vitamin and Mineral Supplements

(…) "Most supplements do not prevent chronic disease or death, their use is not justified, and they should be avoided". (…)

(…) "β-carotene, vitamin E, and possibly high doses of vitamin A supplements are harmful. Other antioxidants, folic acid and B vitamins, and multivitamin and mineral supplements are ineffective for preventing mortality or morbidity due to major chronic diseases". (…)


NO HOPE
SLAVE LABOR
Raoul
MAN, I'M SO STONED.

Lancet Neurol 2017; 16: 965–75

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24-month intervention with a specific multinutrient in people with prodromal Alzheimer's disease (LipiDiDiet): a randomised, double-blind, controlled trial

*Hilkka Soininen, Alina Solomon, Pieter Jelle Visser, Suzanne B Hendrix, Kaj Blennow, Miia Kivipelto, Tobias Hartmann, on behalf of the LipiDiDiet clinical study group**

Combination of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), uridine monophosphate, choline, vitamins B12, B6, C, E, and folic acid, phospholipids, and selenium administered once daily over 24 months.

Interpretation The intervention had no significant effect on the NTB primary endpoint over 2 years in prodromal Alzheimer's disease. However, cognitive decline in this population was much lower than expected, rendering the primary endpoint inadequately powered. Group differences on secondary endpoints of disease progression measuring cognition and function and hippocampal atrophy were observed. Further study of nutritional approaches with larger sample sizes, longer duration, or a primary endpoint more sensitive in this pre-dementia population, is needed.

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EPIDEMIOLOGY

Mediterranean Diet, Cognitive Function, and Dementia

A Systematic Review

Ilianna Lourida,[a] *Maya Soni,*[b] *Joanna Thompson-Coon,*[a] *Nitin Purandare,*[a†] *Iain A. Lang,*[a,c] *Obioha C. Ukoumunne,*[a] *and David J. Llewellyn*[b]

Conclusions: Published studies suggest that greater adherence to Mediterranean diet is associated with slower cognitive decline and lower risk of developing Alzheimer disease.


Switzerland
Slovenia
Zagreb
Croatia
Sarajevo
Italy
FAST
FOOD

Mediterranean Adequacy Index (MAI)

$$MAI = \frac{\%\ \text{total energy from typical Mediterranean food groups}}{\%\ \text{total energy from non-typical Mediterranean food groups}}$$

Fidanza & Fidanza, Public Health Nutr 2004

JPAD The Journal of Prevention of Alzheimer's Disease

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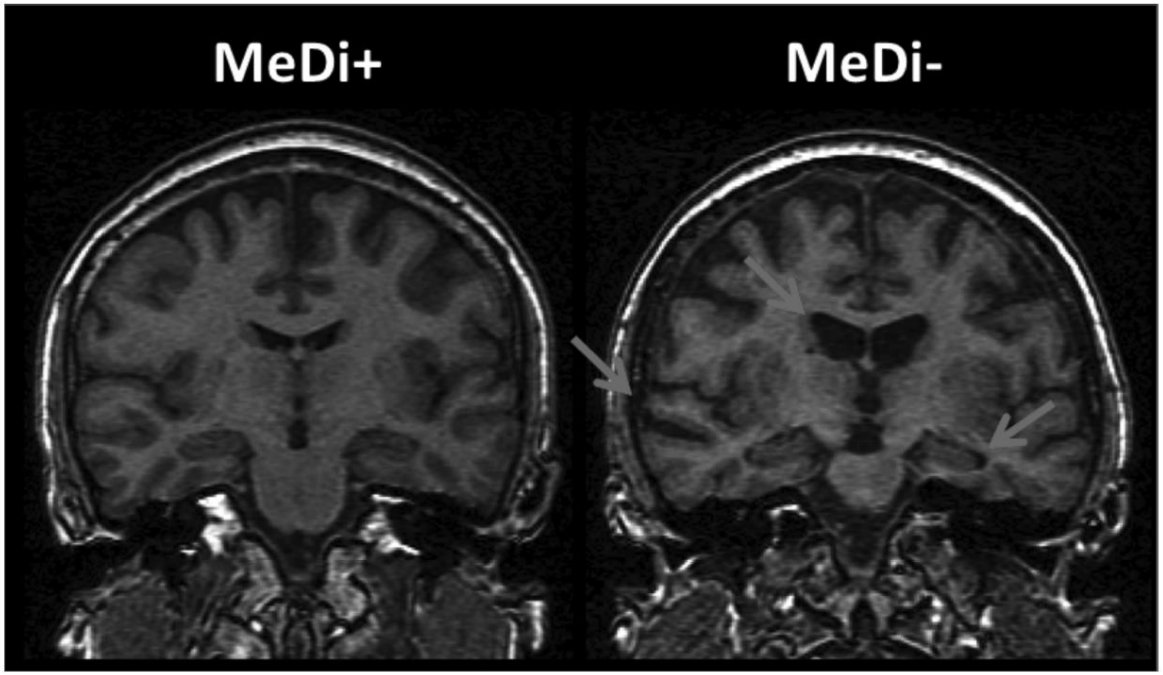
Mediterranean Diet and Magnetic Resonance Imaging-Assessed Brain Atrophy in Cognitively Normal Individuals at Risk for Alzheimer's Disease

L. Mosconi, J. Murray, W.H. Tsui, Y. Li, M. Davies, S. Williams, E. Pirraglia, N. Spector, R.S. Osorio, L. Glodzik, P. McHugh, and M.J. de Leon



Neurology

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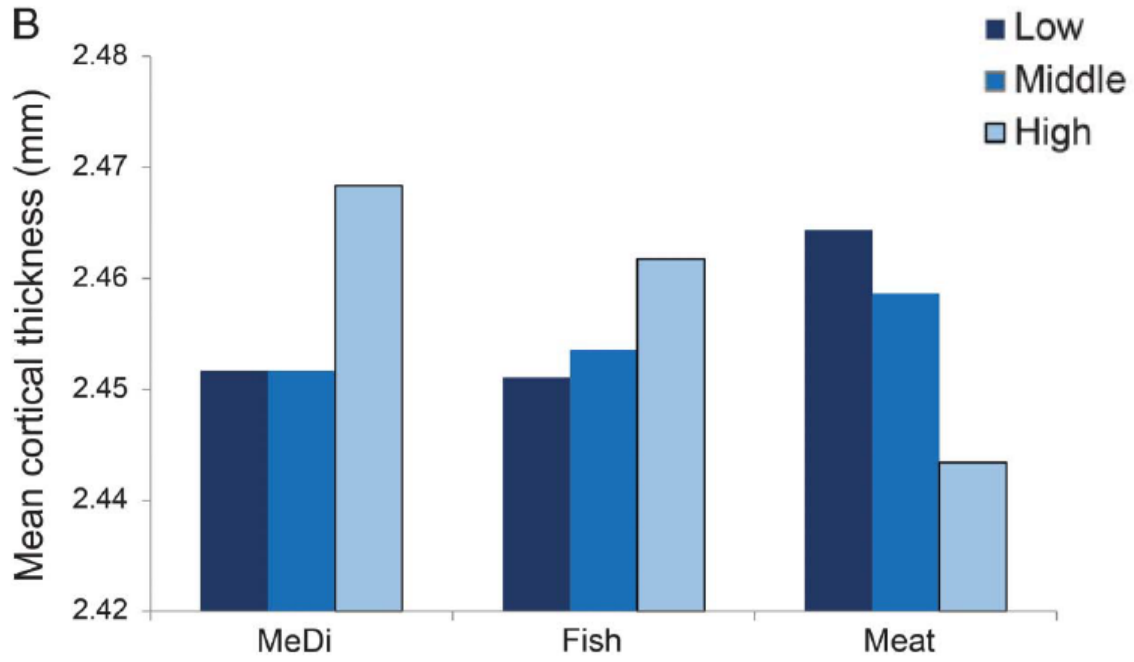
Mediterranean diet and brain structure in a multiethnic elderly cohort



Conclusions: Among older adults, MeDi adherence was associated with less brain atrophy, with an effect similar to 5 years of aging. Higher fish and lower meat intake might be the 2 key food elements that contribute to the benefits of MeDi on brain structure. *Neurology*® 2015;85:1–8

JAMA Internal Medicine

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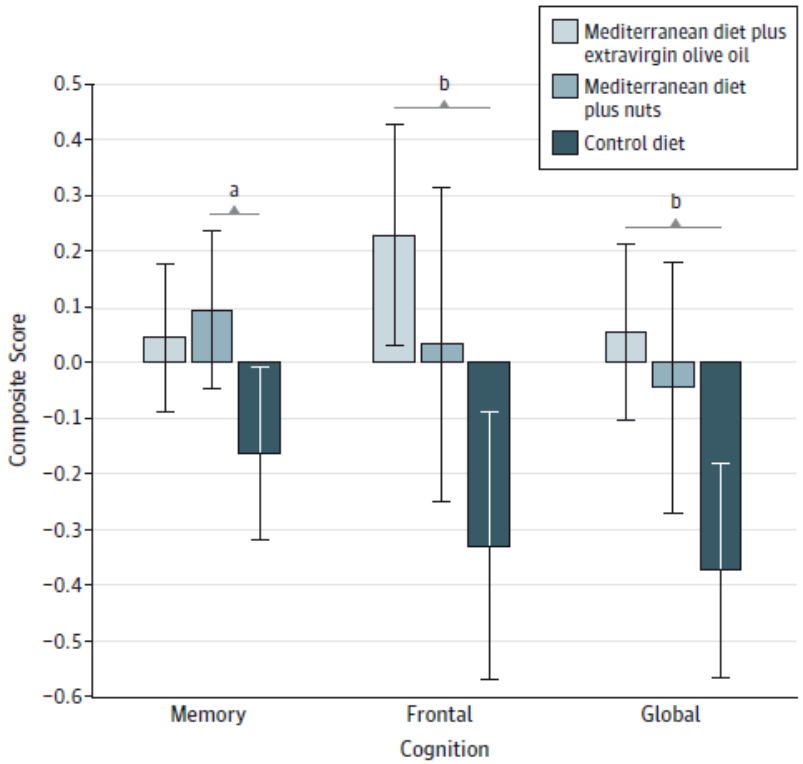
Mediterranean Diet and Age-Related Cognitive Decline
A Randomized Clinical Trial

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).



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Published by THE LANCET

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Research paper

Modified Mediterranean-ketogenic diet modulates gut microbiome and short-chain fatty acids in association with Alzheimer's disease markers in subjects with mild cognitive impairment

Ravinder Nagpal [a,b], Bryan J. Neth [c,d], Shaohua Wang [a,b], Suzanne Craft [c,**], Hariom Yadav [a,b,*]

- The gut microbiome signature differs in participants with mild cognitive impairment compared with cognitively normal counterparts.
- Modified Mediterranean-ketogenic diet alters the gut microbiome signature and SCFAs, and these changes are associated with improved cerebrospinal fluid AD biomarkers (amyloid β-40 and 42, total tau, and phosphorylated tau-181).

	Nutrients	Food groups
Mediterranean diet[73-75]	High intake of folate, vitamin E, carotenoids, flavonoids and other antioxidants, dietary fibre, and monounsaturated fatty acids; balanced intake of unsaturated fatty acids; reasonably high intake of n-3 fatty acids; and low intake of saturated fatty acids	High consumption of fruits, vegetables, wholegrains, and olive oil; everyday consumption of fermented dairy, nuts, seeds, herbs or spices; emphasis on plant proteins (legumes) and seafood instead of red meat; wine in moderation; and daily consumption of herbal infusions
DASH diet[76]	High in potassium, magnesium, calcium, fibre, and protein; low in saturated fatty acids, total lipids, cholesterol, and sodium; and high intake of folate, vitamin E, carotenoids, flavonoids, and other antioxidants	High consumption of fruits, vegetables, low-fat dairy products, and wholegrains; reasonably high consumption of lean animal protein but low consumption of red meat; and emphasis on foods that are low in saturated and trans lipids, sodium, and sugar
MIND diet[77]	High intake of folate, vitamin E, carotenoids, flavonoids and other antioxidants, dietary fibre, and monounsaturated fatty acids, and low intake of saturated and trans fatty acids	Increased consumption of green leafy or other vegetables, nuts, berries, beans, wholegrains, fish, poultry, olive oil, and wine, and decreased consumption of red meats, butter and stick margarine, cheese, pastries, sweets, and fried or fast foods

DASH=Dietary Approaches to Stop Hypertension. MIND=Mediterranean-DASH Intervention for Neurodegenerative Delay.

Table 2: **Dietary patterns related to cognitive function**

Scarmeas et al., Lancet Neurol 2018

Alzheimers Dement. 2015 September ; 11(9): 1007–1014. doi:10.1016/j.jalz.2014.11.009.

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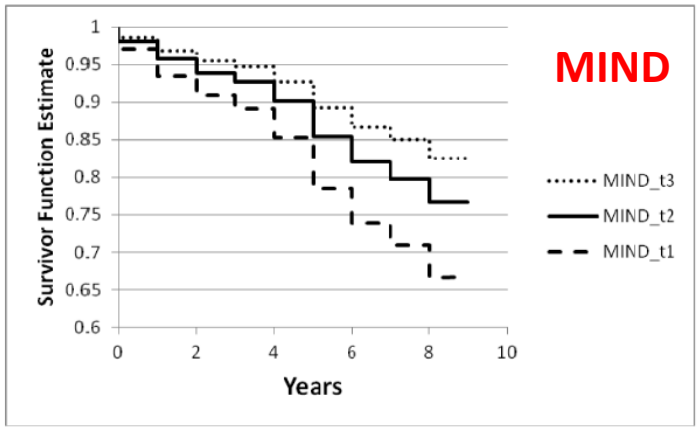
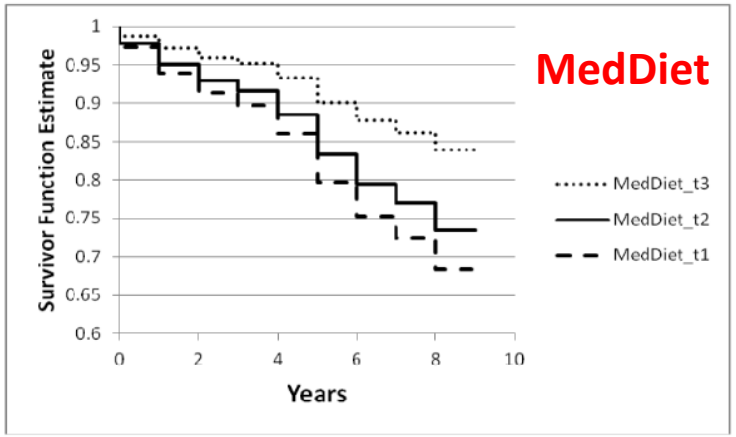
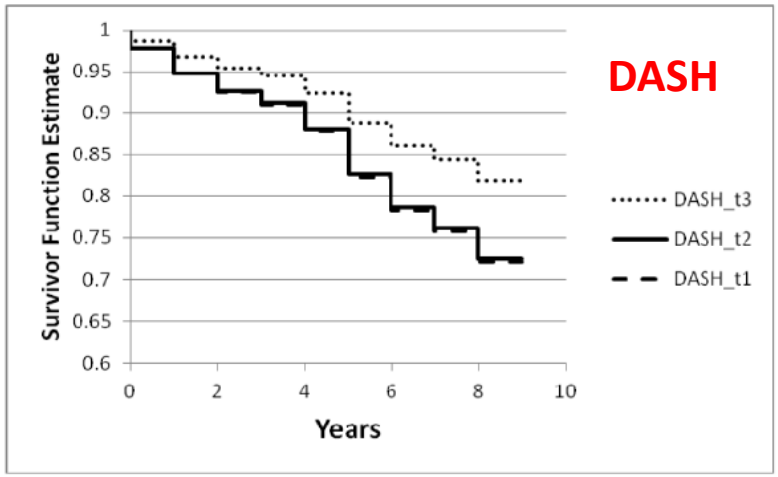
MIND Diet Associated with Reduced Incidence of Alzheimer's Disease

Martha Clare Morris, S.D.[1], **Christy C. Tangney, Ph.D.**[2], **Yamin Wang, Ph.D.**[1], **Frank M. Sacks, M.D.**[5], **David A Bennett, M.D.**[3,4], and **Neelum T. Aggarwal, M.D.**[3,4]







Annals of NEUROLOGY
An Official Journal of the American Neurological Association and the Child Neurology Society

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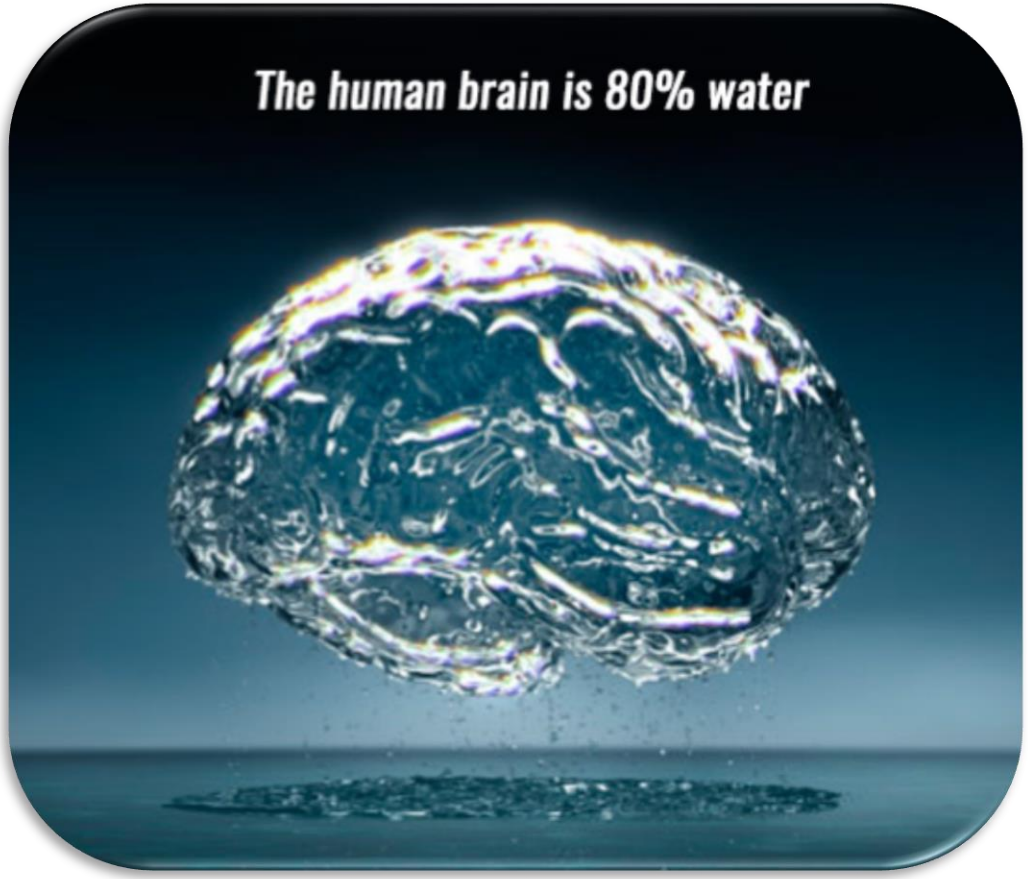
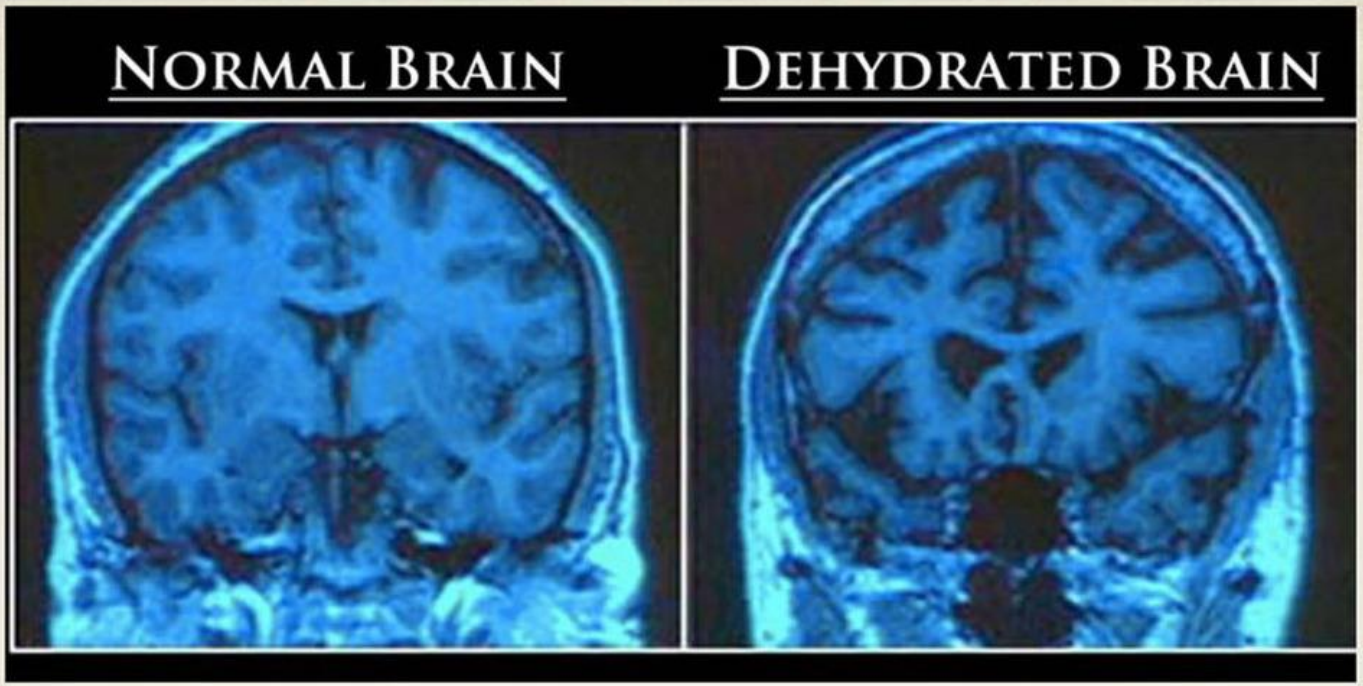
Mediterranean Diet and Magnetic Resonance Imaging–Assessed Cerebrovascular Disease

Nikolaos Scarmeas, MD,[1,2,3] José A. Luchsinger, MD,[1,4] Yaakov Stern, PhD,[1,2,3] Yian Gu, MD,[1,2] Jing He, PhD,[5] Charlie DeCarli, MD,[5] Truman Brown, PhD,[6] and Adam M. Brickman, PhD[1,2,3]

- High-resolution structural MRI was collected on 707 elderly 65 years or older community residents.
- Participants were divided into 3 groups of adherence to MeDi (low, middle, and high tertiles).
- Compared to the low adherence group, those in the moderate MeDi adherence group had a 22% reduced odds of having an infarct, while participants in the highest MeDi adherence group had a 36% reduced odds.
- Higher adherence to the MeDi is associated with reduced cerebrovascular disease burden.


The human brain is 80% water

BRAIN DEHYDRATION



nutrients

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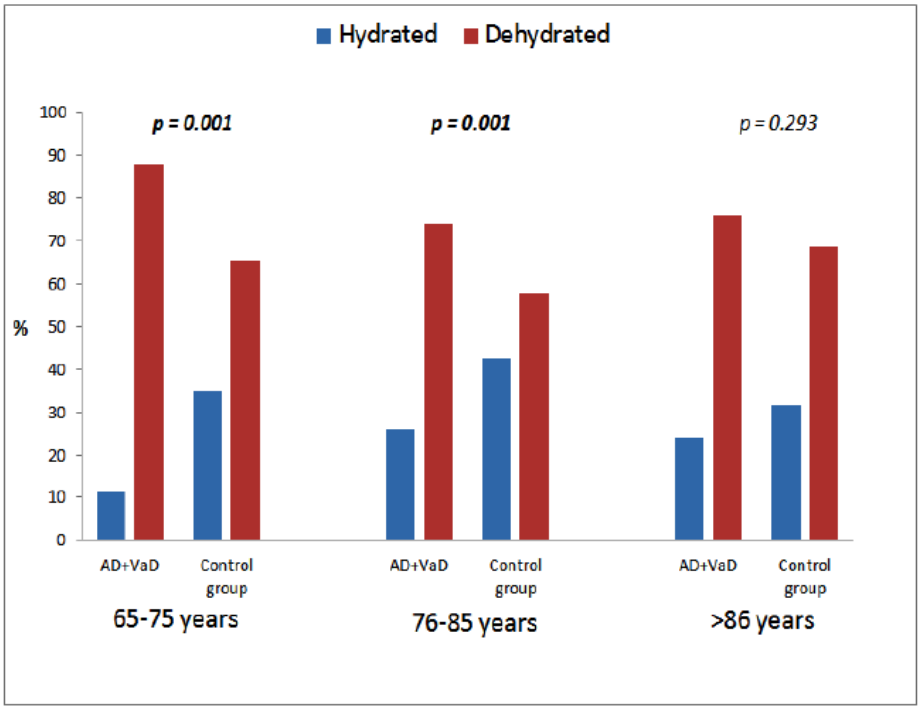
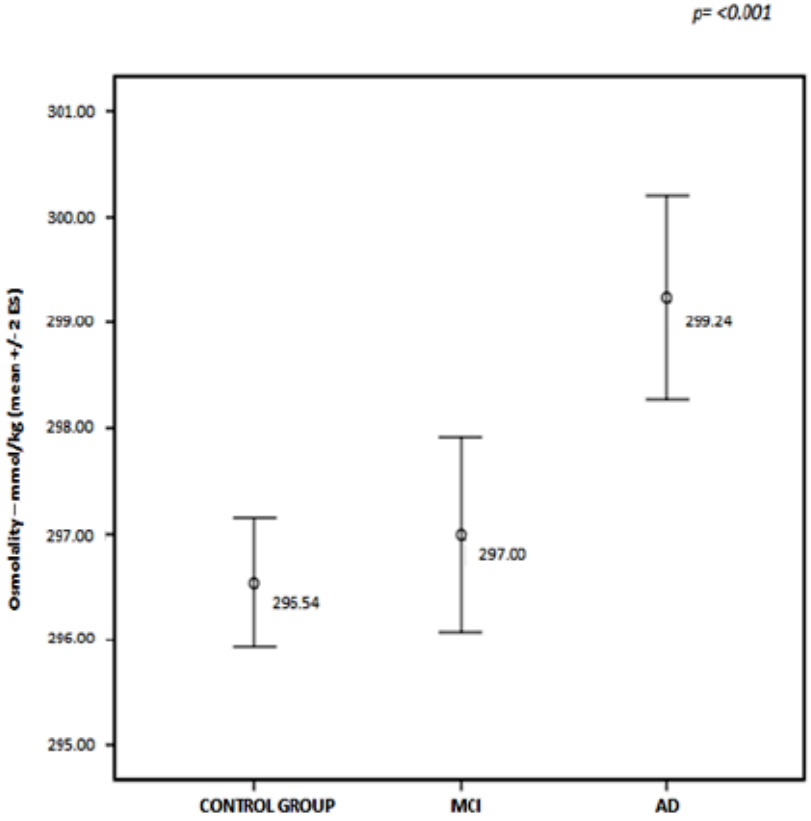
Article

Neurocognitive Disorders and Dehydration in Older Patients: Clinical Experience Supports the Hydromolecular Hypothesis of Dementia

Michele Lauriola, Antonio Mangiacotti, Grazia D'Onofrio *, Leandro Cascavilla, Francesco Paris, Giulia Paroni, Davide Seripa *, Antonio Greco and Daniele Sancarlo





CHALLENGES AND UNANSWERED QUESTIONS

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Method of nutritional status assessment

- Dietary assessments (Food Frequency Questionnaire limitations) are limited by requirements for memory and averaging tasks, prespecified food lists, and absence of information about meal patterns and combinations of foods
- Biomarkers are available for few nutrients, expensive, reflect only short-term habits, and provide no information about other aspects of nutrition (eg, chronobiology of diet, eating with company, and social and cultural aspects affecting food choice)

Timing of assessment (duration of follow-up)

- Dietary intake assessed at a specific timepoint but might change over time in long-term follow-up
- Short-term follow-up might not capture early subclinical stages
- Counterbalancing might produce often unconscious changes in dietary intake in clinical trials

Confounding of non-dietary factors

- Physical activity
- Aspects of cognitive reserve (eg, education, occupation, socioeconomic status, intellect, and social activities)

Sample selection

- Many participants have adequate nutrition and some of them might not cognitively benefit from nutrition
- Populations include individuals with variable risk of cognitive decline, which might limit power to detect an association between nutrition and cognition

Multidimensionality of diet

- Multiple nutrients, foods, and food groups that are not eaten in isolation
- Observed effect of a dietary factor might simply reflect the simultaneous intake of another factor

Multidimensionality of underlying mechanisms

- Many causal biological pathways, known and unknown have potentially different (even opposing) effects of each nutritional element on each pathway

Multidimensionality of cognitive function

- Multiple cognitive domains and respective neuropsychological evaluations and tests, apart from the clinical diagnoses

Scarmeas et al., Lancet Neurol 2018

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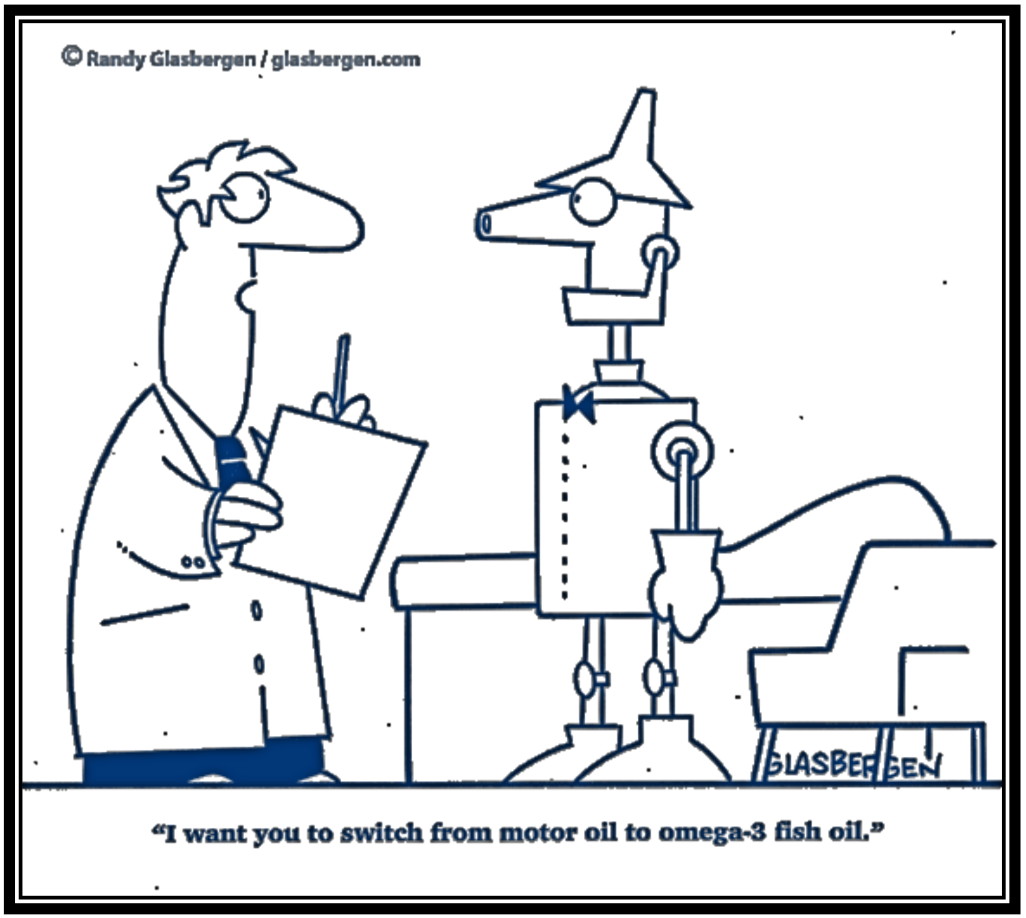
THANK YOU FOR YOUR ATTENTION!



emanuele.marzetti@policlinicogemelli.it