

# IL CONTRIBUTO DEI CENTRI PER I DISTURBI COGNITIVI E LE DEMENZE NELLA GESTIONE INTEGRATA DEI PAZIENTI



**XII Convegno**  
**15 – 16 novembre 2018**  
***Aula Pocchiari***  
***Istituto Superiore di Sanità***  
***Viale Regina Elena, 299 Roma***

***V Sessione - STRATEGIE DI PREVENZIONE***  
***Moderatrice: M. Gasparini***

**La dieta mediterranea**

**G. Bruno**



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# Capitalising on modifiable risk factors for Alzheimer's disease

Geert Jan Biessels

www.thelancet.com/neurology Vol 13 August 2014

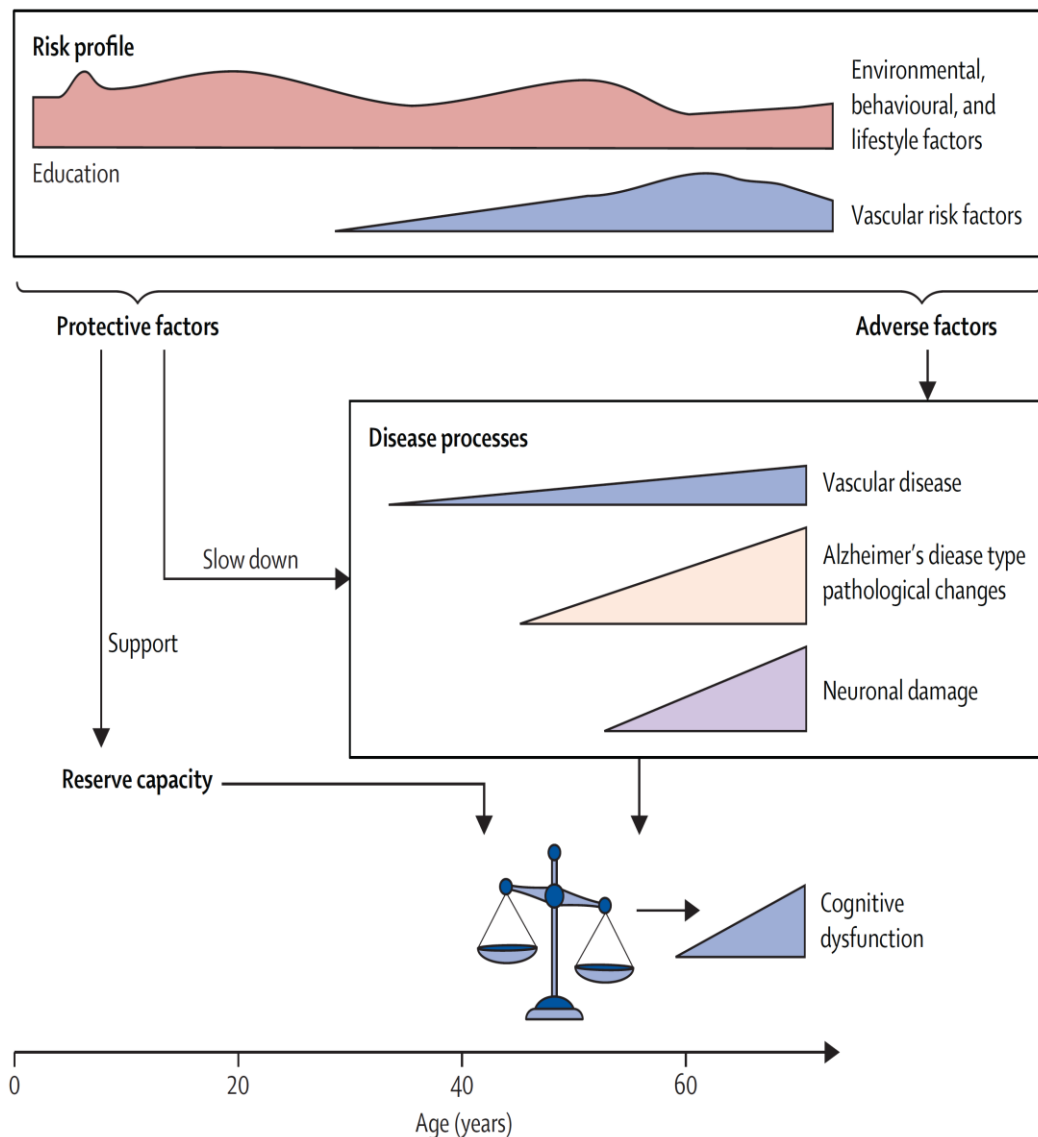
An individual's profile of modifiable factors includes **adverse and protective factors**.

These factors include factors that:

- **fluctuate over the course of life** (education, environmental, behavioural, lifestyle factors, depression)
- **occur from midlife onwards** (diabetes, hypertension, obesity)

**Adverse factors** induce disease processes in the brain that generally start to develop later in life.

**Protective factors** might attenuate disease processes and can also contribute to cerebral reserve capacity.

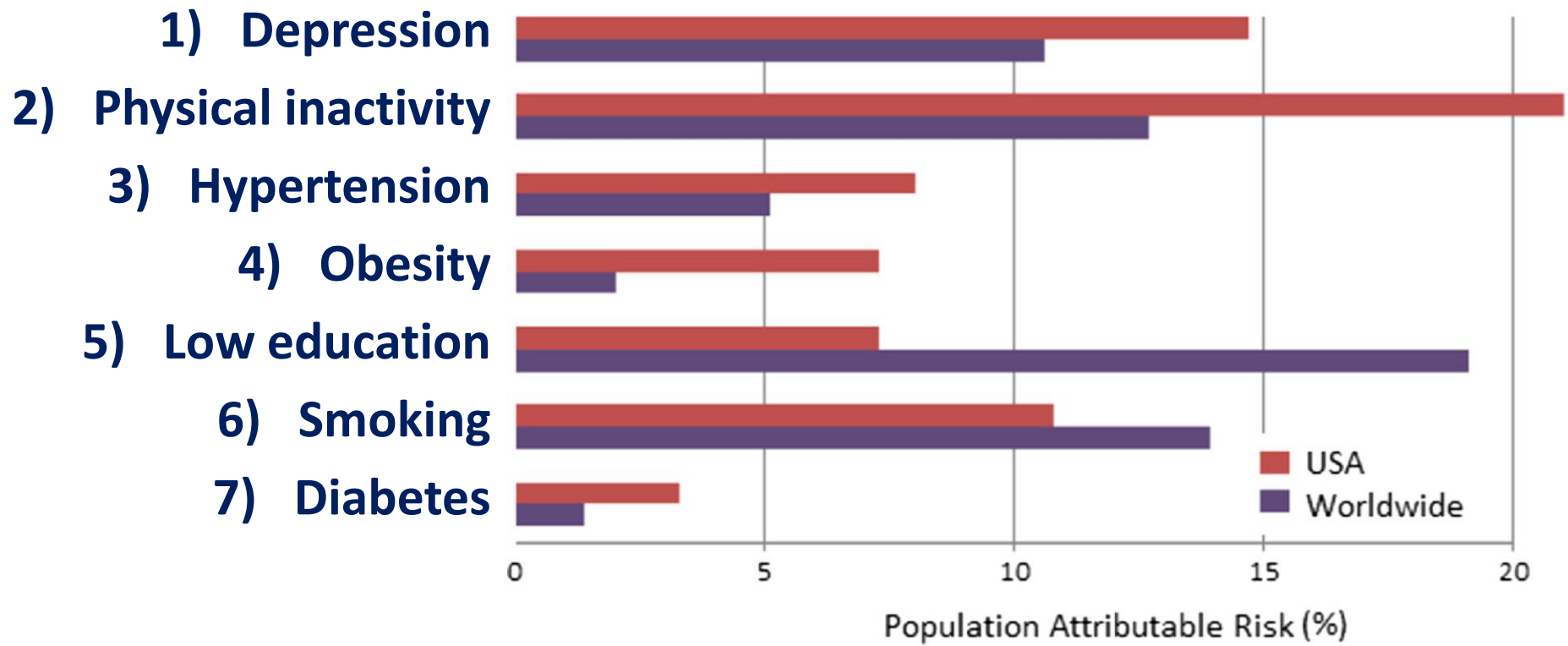




# The projected effect of risk factor reduction on Alzheimer's disease prevalence

Lancet Neurol 2011; 10: 819-28

Deborah E Barnes, Kristine Yaffe

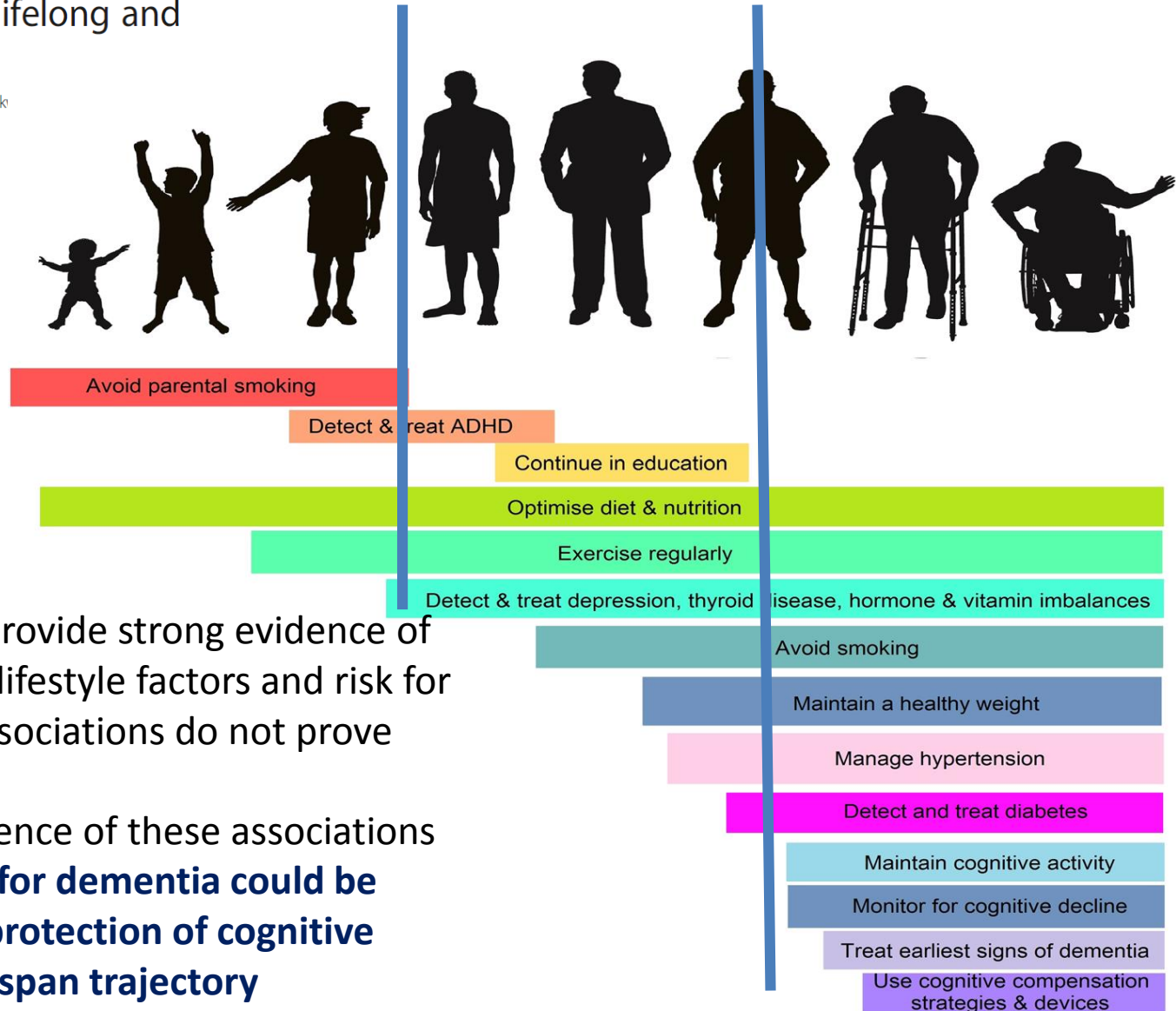


OPINION

Open Access

# Cognitive health begins at conception: addressing dementia as a lifelong and preventable condition

Jennifer H Barnett<sup>1,2\*</sup>, Vladimir Hachinski<sup>3</sup> and Andrew D Black



Epidemiological data provide strong evidence of **associations** between lifestyle factors and risk for dementia but these associations do not prove **causality**.

Nonetheless, the existence of these associations does suggest that **risk for dementia could be reduced through the protection of cognitive health throughout lifespan trajectory**



# Nutrition and prevention of cognitive impairment

Nikolaos Scarmeas, Costas A Anastasiou, Mary Yannakoulia

*Lancet Neurol* 2018; 17: 1006–15

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Nutrition is an important lifestyle factor that can modify the risk of future cognitive impairment and dementia. Some, but not conclusive, evidence (mostly from observational studies and infrequently from clinical trials) exists of a protective association between certain nutrients (eg, folate, flavonoids, vitamin D, and certain lipids) or food groups (eg, seafood, vegetables, and fruits, and potentially moderate alcohol and caffeine consumption) and cognitive outcomes in older people. For some nutrients and food groups, protection might be greater in individuals with either deficiencies in certain nutrients or a genetic predisposition to cognitive impairment. Identification of potentially different associations between such subgroups should be a priority for future research. At present, evidence of an association between nutrition and cognitive outcomes is somehow stronger for healthy dietary patterns, such as the Mediterranean-type diet, than for individual nutrients and food groups, possibly because of the cumulative beneficial effects of the many ingredients in these diets. Multidomain interventions (including a nutrition component) might also hold some promise for the prevention of cognitive impairment and dementia, but their effectiveness is still uncertain. Use of advanced technologies for nutrition assessment (eg, metabolomics and innovative methods of dietary intake assessment) and recently identified biomarkers of nutrition and neurobiological outcomes will be important to achieve this goal.

## Introduction

An analysis of population-based data suggested that a third of Alzheimer's disease cases worldwide might be attributable to potentially modifiable risk factors.<sup>1</sup> Nutrition is a modifiable environmental factor that has been associated with many non-communicable diseases

## Nutrients and biologically active compounds

### B vitamins

B vitamins have been studied for their potential effect on cognitive function because of their role in homocysteine metabolism and the well established association between homocysteine concentrations and cognitive decline

Observational studies

Clinical trials

**Nutrients**

B vitamins

B6



B12



Folate



B vitamins combination



Antioxidants

Carotenoids



Vitamin C



Vitamin E



Selenium



Copper



Flavonoids/polyphenols



Anthocyanidins



Multiantioxidant supplementation



Vitamin D



Macronutrients

Total carbohydrates



Total proteins



Total dietary fat



Saturated fatty acids



Total polyunsaturated fatty acids



Monounsaturated fatty acids



n-3 polyunsaturated fatty acids



Trans fatty acids



Cholesterol



Observational studies

Clinical trials

Food groups and beverages

Alcohol

Moderate total intake vs abstinence



Moderate vs high total intake



Moderate wine consumption



Moderate beer consumption



Moderate other spirit consumption



Coffee and tea

Coffee



Tea



Caffeine



Food groups

Fish and seafood



Meat



Vegetables



Fruits



Fruits and vegetables



Juices



Legumes



Dairy



Olive oil



Nuts



Observational studies

Clinical trials

Dietary patterns

Mediterranean diet



DASH diet



MIND diet



Alternative Healthy Eating Index



Dietary Quality Score



WHO's Healthy Diet Indicator



Healthy Eating Index



Nordic diet



Low-carbohydrate, high-protein diet



Population-specific prudent diet patterns



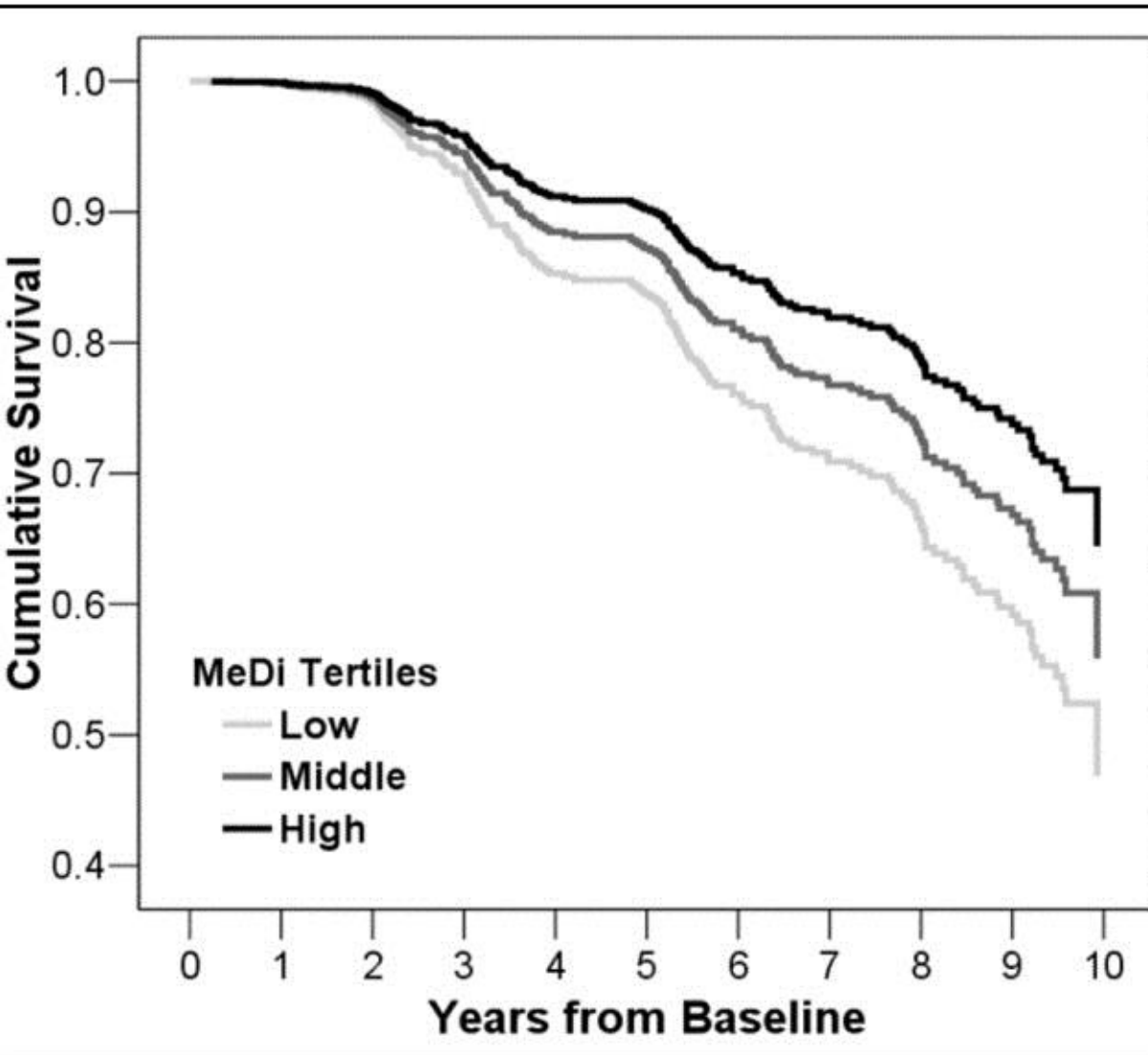
Multidomain interventions





# Mediterranean diet and risk for AD

Scarmeas N et al: Ann Neurology 2006



- 2258 soggetti non dementi di New York valutati per un periodo di 4 anni
- Una maggiore aderenza ad un modello alimentare mediterraneo è correlata ad una riduzione del rischio di comparsa di AD



# Adherence to a Mediterranean Diet, Cognitive Decline, and Risk of Dementia

JAMA. 2009;302(6):638-648

Catherine Féart, PhD

Cécilia Samieri, MPH

Virginie Rondeau, PhD

Hélène Amieva, PhD

Florence Portet, MD, PhD

Jean-François Dartigues, MD, PhD

Nikolaos Scarmeas, MD

Pascale Barberger-Gateau, MD, PhD

- Prospective cohort study of 1410 adults (65 years) from Bordeaux (F) included in the Three-City cohort in 2001- 2002 and reexamined at least once over 5 years.
- Adjusting for age, sex, education, marital status, energy intake, physical activity, depressive symptomatology, taking 5 medications/d or more, apolipoprotein E genotype, CV risk factors, and stroke, ....

.... higher Mediterranean diet score was associated with fewer MMSE errors ( $\beta = -0.006$ ; 95% CI,  $-0.01$  to  $-0.0003$ ;  $p=0.04$  for 1 point of the Mediterranean diet score)



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# Adherence to a Mediterranean-type dietary pattern and cognitive decline in a community population<sup>1-3</sup>

*Am J Clin Nutr* 2011;93:601-7.

Christine C Tangney, Mary J Kwasny, Hong Li, Robert S Wilson, Denis A Evans, and Martha Clare Morris

- Adherence to a Mediterranean diet may afford some protection against cognitive decline in older black and white adults while adherence to the Healthy Eating Index (HEI-2005) pattern scores was not related to cognitive change

⇐ emphasis on different dietary components (points attributed to red meat, full-fat dairy component alcohol consumption, solid fats, and added sugars)

Estimated effects ( $\beta$  coefficients) of MedDiet scores, MedDiet wine scores, and Healthy Eating Index-2005 (HEI-2005) scores on global cognitive scores at baseline (cross-sectional) and on rates of change in global cognitive scores among 3790 Chicago Health and Aging Project (CHAP) participants followed for an average of 7.6 y<sup>1</sup>

| Score indicators   | Cross-sectional model <sup>2</sup> |                | Rate of change model <sup>3</sup> |                |
|--------------------|------------------------------------|----------------|-----------------------------------|----------------|
|                    | $\beta$ (SEE)                      | <i>P</i> value | $\beta$ (SEE)                     | <i>P</i> value |
| MedDiet score      | 0.0070 (0.0022)                    | 0.0013         | 0.0014 (0.0004)                   | 0.0004         |
| MedDiet wine score | 0.0050 (0.0022)                    | 0.0231         | 0.0014 (0.0004)                   | 0.0009         |
| HEI-2005 score     | -0.0011 (0.001)                    | 0.236          | 0.0002 (0.0002)                   | 0.214          |

<sup>1</sup> Values are presented as  $\beta$  or regression coefficients (SEE) and the corresponding *P* value.

<sup>2</sup> Values reflect adjustment for age, sex, race, education, participation in cognitive activities, and total energy intake in mixed linear models.

<sup>3</sup> Scores were entered into the mixed models with adjustment for age, sex, race, education, participation in cognitive activities, total energy intake, and the interaction between time and each dietary quality score.

Review

# Nutrition and Dementia: Evidence for Preventive Approaches?



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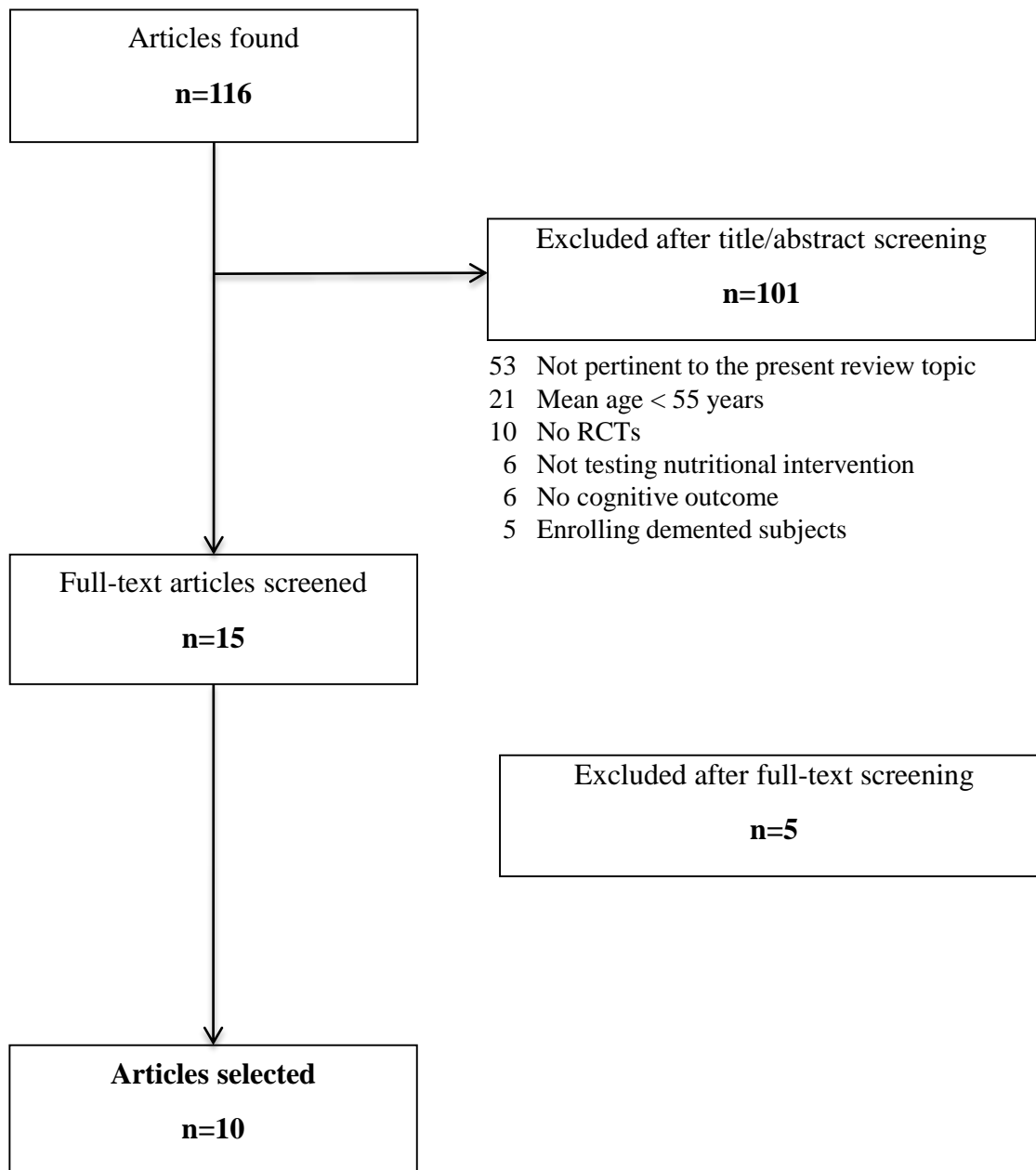
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Received: 17 January 2016; Accepted: 29 February 2016; Published: 4 March 2016

**Abstract:** In recent years, the possibility of favorably influencing the cognitive trajectory through promotion of lifestyle modifications has been increasingly investigated. In particular, the relationship between nutritional habits and cognitive health has attracted special attention. The present review is designed to retrieve and discuss recent evidence (published over the last 3 years) coming from randomized controlled trials (RCTs) investigating the efficacy of nutritional interventions aimed at improving cognitive functioning and/or preventing cognitive decline in non-demented older individuals. A systematic review of literature was conducted, leading to the identification of 11 studies of interest. Overall, most of the nutritional interventions tested by the selected RCTs were found to produce statistically significant cognitive benefits (defined as improved neuropsychological test scores). Nevertheless, the clinical meaningfulness of such findings was not adequately discussed and appears controversial. In parallel, only 2 studies investigated between-group differences concerning



| Reference                           | Study sample   | Intervention(s)   | Duration         | Cognitive Outcome(s)  | Main results   |
|-------------------------------------|--|---|------------------|---|--|
| <b>Alves2013 [14]</b>               | n=56 healthy older women (mean age 66.8 y)                   | 1) Creatine (20 g/d for 5 days, then 5 g/d)<br>2) Creatine + strength training<br>3) Placebo<br>4) Placebo + strength training  | 24 weeks         | MMSE; Stroop test; TMT;<br>Digit Span; Delayed recall test                                  | Creatine supplementation did not promote any significant cognitive benefit   |
| <b>Bin Sayeed 2013 [15]</b>         | n=40 healthy elderly males (mean age 55.8 y)                 | 1) <i>Nigella sativa</i> Linn. Seeds (1000 mg/d)<br>2) Placebo  | 9 weeks          | WMS; Digit Span; ROCF;<br>LCT; TMT; Stroop test;<br>Logical memory test                     | Significant improvement of all the cognitive scores in the <i>Nigella sativa</i> group                             |
| <b>Brickman 2014 [16]</b>           | n=37 healthy, sedentary older subjects (mean age 57.7 y)     | 1) High flavanol intake (900 mg cocoa flavanols and 138 mg of (-)-epicatechin/d)+ exercise<br>2) High flavanol intake<br>3) Low flavanol intake (10 mg cocoa flavanols and <2 mg (-)-epicatechin/d)+ exercise<br>4) Low flavanol intake | 12 weeks         | ModBent task  | A high-flavanol intervention had a significant effect on ModBent performance, independent of exercise              |
| <b>Kean 2015 [17]</b>               | n=37 healthy older subjects (mean age 66.7 y)                | 1) High flavanone drink (305 mg/d)<br>2) Low flavanone drink (37 mg/d)  | 8 weeks          | CERAD; SWM; DSST; LM;<br>Go-NoGo; Letter Fluency;<br>Serial sevens; WMS                     | Significant improvement of global cognitive function in the high flavanone group                                   |
| <b>Màrtinez-Lapiscina 2013 [18]</b> | n=268 older subjects at high vascular risk (mean age 74.1 y) | 1) <b>MedDiet + EVOO (1 L/w)</b><br>2) MedDiet + mixed nuts (30 g/d)<br>3) Control diet (advice to reduce dietary fat)  | <b>6.5 years</b> | MMSE; CDT; WMS; FAS;<br>RAVLT; ROCF; BNT; CDR;<br>TMT; WAIS; Digit span<br>Cognitive status | <b>Significant improvement of fluency and memory tasks in MedDiet + EVOO group</b><br><b>Reduced MCI incidence</b> |



|                                 |   |   |                    |  |  |
|---------------------------------|---|---|--------------------|--|--|
| <b>Ngandu 2015 [19]</b>         | n=1260 older subjects at high risk of cognitive decline (mean age 69.3 y) | 1) Diet (Finnish Nutrition Recommendations) + exercise + cognitive training+ vascular risk monitoring<br>2) General health advice | 2 years            | Comprehensive neuropsychological test battery (CERAD)                  | Significant improvement of global cognition, executive functioning and processing speed                        |
| <b>Nilsson 2012 [20]</b>        | n=40 healthy older subjects (mean age 63.3 y)                             | 1) Fish oil n-3 PUFA (3 g/d)<br>2) Placebo  | 5 weeks            | Working memory and selective attention tests                           | n-3 PUFA intervention significantly improved working memory  |
| <b>Valls-Pedret 2015 [11]</b>   | n=447 cognitively healthy older subjects (mean age 66.9 y)                | 1) MedDiet+ EVOO (1 L/w)<br>2) MedDiet+ mixed nuts (30 g/d)<br>3) Control diet (advice to reduce dietary fat)                     | 4.1 years (median) | MMSE; WMS; RAVLT; WAIS; CTT; FAS; Digit span<br>Cognitive status       | Significant improvement of all the cognitive functions in the 2 MedDiet groups. No difference in MCI incidence |
| <b>van de Rest 2014 [21]</b>    | n=127 frail or pre-frail older subjects (mean age 79 y)                   | 1) Protein (30 g/d)<br>2) Protein + exercise<br>3) Placebo<br>4) Placebo + exercise   | 24 weeks           | MMSE; TMT; Stroop test; WMS; WLT; VFT; Reaction time tasks; Digit span | Exercise training in combination with protein supplementation improved information processing speed            |
| <b>van der Zwaluw 2014 [22]</b> | n=65 frail or pre-frail older subjects (mean age 79 y)                    | 1) Protein (30 g/d)<br>2) Placebo   | 24 weeks           | MMSE; TMT; Stroop test; WMS; WLT; VFT; Reaction time tasks; Digit span | Improvement of reaction time in the protein supplementation group  |



# The role of Mediterranean diet on the Amyloid burden

Rainey-Smith et al. *Translational Psychiatry* (2018)8:238  
DOI 10.1038/s41398-018-0293-5

Translational Psychiatry

ARTICLE

Open Access

## Mediterranean diet adherence and rate of cerebral A $\beta$ -amyloid accumulation: Data from the Australian Imaging, Biomarkers and Lifestyle Study of Ageing

Stephanie R. Rainey-Smith<sup>1,2</sup>, Yian Gu<sup>3,4</sup>, Samantha L. Gardener<sup>1,2</sup>, James D. Doecke<sup>5,6</sup>, Victor L. Villemagne<sup>7</sup>, Belinda M. Brown<sup>2,8</sup>, Kevin Taddei<sup>1,2</sup>, Simon M. Laws<sup>6,9,10</sup>, Hamid R. Sohrabi<sup>1,2,11</sup>, Michael Weinborn<sup>1,2,12</sup>, David Ames<sup>13,14</sup>, Christopher Fowler<sup>15</sup>, S. Lance Macaulay<sup>5</sup>, Paul Maruff<sup>5,16</sup>, Colin L. Masters<sup>15</sup>, Olivier Salvado<sup>5</sup>, Christopher C. Rowe<sup>7</sup>, Nikolaos Scarmeas<sup>3,4,17,18</sup> and Ralph N. Martins<sup>1,2,11,19</sup>

### ABSTRACT

Accumulating research has linked Mediterranean diet (MeDi) adherence with slower cognitive decline and reduced Alzheimer's disease (AD) risk. However, no study to-date has examined the relationship between MeDi adherence and accumulation of cerebral A $\beta$ -amyloid (A $\beta$ ; a pathological hallmark of AD) in older adults. Cognitively normal healthy control participants of the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study of Ageing completed the Cancer Council of Victoria Food Frequency Questionnaire at baseline, which was used to construct a MeDi score for each participant (score range 0–9; higher score indicating higher adherence). Cerebral A $\beta$  load was quantified by Pittsburgh Compound B positron emission tomography at baseline, 18 and 36 months: Only individuals categorised as “A $\beta$  accumulators”, and thus considered to be on the AD pathway, were included in the analysis ( $N = 77$ ). The relationship between MeDi adherence, MeDi components, and change in cerebral A $\beta$  load (baseline to 36 months) was evaluated using Generalised Linear Modelling, accounting for age, gender, education, Apolipoprotein E  $\epsilon 4$  allele status, body mass index and total energy intake. Higher MeDi score was associated with less A $\beta$  accumulation in our cohort ( $\beta = -0.01 \pm 0.004$ ,  $p = 0.0070$ ). Of the individual MeDi score components, a high intake of fruit was associated with less accumulation of A $\beta$  ( $\beta = -0.04 \pm 0.01$ ,  $p = 0.00036$ ). Our results suggest MeDi adherence is associated with reduced cerebral AD pathology accumulation over time. When our results are considered collectively with previous data linking the MeDi to slower cognitive decline, it is apparent that MeDi adherence warrants further investigation in the quest to delay AD onset.



- 77 cognitively healthy individuals, categorised as “A $\beta$  accumulators” as calculated by the SUVR (standardised uptake value ratio), derived from PiB-PET imaging;
- 18 and 36-month follow-up assessments;
- MeDi score: 1 point when (0-9)
  - caloric-adjusted consumption of **fruits, vegetables, legumes, cereals** and fish is at or above the cohort sex-specific median;
  - caloric-adjusted consumption of **meat** and **dairy** is below the sex-specific median;
  - the **ratio of monounsaturated to saturated fats** is at or above the median;
  - **alcohol consumption** is >5 to <25 g per day for females and >10 to <50 g per day for males.

| <i>Model / Variable</i>  | $\beta$ coefficient | SE      | t-value  | p-value        |
|--|---------------------|---------|----------|----------------|
| <i>Initial model including total MeDi score (without MeDi score components):</i> |                     |         |          |                |
| (Intercept)  | -0.02905            | 0.06602 | -0.44006 | 0.66120        |
| MeDi Score   | -0.01015            | 0.00366 | -2.77308 | <b>0.00704</b> |
| APOE $\epsilon$ 4 allele status  | 0.03134             | 0.01228 | 2.55229  | <b>0.01279</b> |
| Age  | 0.00164             | 0.00086 | 1.90979  | 0.06009        |
| <i>Second model including MeDi score components (without total MeDi score):</i>  |                     |         |          |                |
| (Intercept)  | -0.08644            | 0.06313 | -1.36934 | 0.17527        |
| Fruit intake (0/1)   | -0.03802            | 0.01091 | -3.48617 | <b>0.00085</b> |
| Age  | 0.00225             | 0.00083 | 2.71501  | <b>0.00834</b> |
| APOE $\epsilon$ 4 allele status  | 0.03061             | 0.01147 | 2.66877  | <b>0.00945</b> |
| Meat intake (0/1)  | -0.02215            | 0.01144 | -1.93659 | 0.05683        |
| Cereals intake (0/1)   | -0.01758            | 0.01150 | -1.52890 | 0.13080        |
| Dairy intake (0/1)   | 0.01705             | 0.01118 | 1.52563  | 0.13161        |
| <i>Second model (reduced)</i>  |                     |         |          |                |
| (Intercept)  | -0.07342            | 0.06033 | -1.217   | 0.22760        |
| Fruit intake (0/1)   | -0.04143            | 0.01107 | -3.744   | <b>0.00036</b> |
| Age  | 0.00196             | 0.00082 | 2.385    | <b>0.01967</b> |
| APOE $\epsilon$ 4 allele status  | 0.02749             | 0.01170 | 2.350    | <b>0.02148</b> |
| <i>Interaction model (Total MeDi score)</i>                                      |                     |         |          |                |
| (Intercept)  | -0.03027            | 0.06612 | -0.458   | 0.64850        |
| MeDi score   | -0.01245            | 0.00447 | -2.786   | <b>0.00681</b> |
| Age  | 0.00178             | 0.00087 | 2.037    | <b>0.04532</b> |
| APOE $\epsilon$ 4 allele status  | 0.00157             | 0.03526 | 0.045    | 0.96453        |
| MeDi score * APOE $\epsilon$ 4 allele status                                     | 0.00701             | 0.00780 | 0.901    | 0.37061        |

All beta ( $\beta$ ) coefficients ( $\pm$  SE) from the GLM are shown. Bold indicates statistical significance ( $p < 0.05$ )  
 APOE apolipoprotein E, GLM generalised linear model, MeDi Mediterranean diet, SE standard error, SUVR standardised uptake value ratio

- MeDi score is negatively related with the SUVR value ( $\beta = -0.01015$ ,  $p$ -value = 0.00704), representing the amyloid load;
- Fruit intake turned out to give the greatest benefits among the MeDi components ( $\beta = -0.03802$ ,  $p$ -value = 0.00085).

Featured Article

Mediterranean diet, micronutrients and macronutrients, and MRI measures of cortical thickness

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**Abstract** **Introduction:** The Mediterranean diet (MeDi) is associated with reduced risk of cognitive impairment, but it is unclear whether it is associated with better brain imaging biomarkers. **Methods:** Among 672 cognitively normal participants (mean age, 79.8 years, 52.5% men), we investigated associations of MeDi score and MeDi components with magnetic resonance imaging measures of cortical thickness for the four lobes separately and averaged (average lobar). **Results:** Higher MeDi score was associated with larger frontal, parietal, occipital, and average lobar cortical thickness. Higher legume and fish intakes were associated with larger cortical thickness: legumes with larger superior parietal, inferior parietal, precuneus, parietal, occipital, lingual, and fish with larger precuneus, superior parietal, posterior cingulate, parietal, and inferior parietal. Higher carbohydrate and sugar intakes were associated with lower entorhinal cortical thickness. **Discussion:** In this sample of elderly persons, higher adherence to MeDi was associated with larger cortical thickness. These cross-sectional findings require validation in prospective studies. © 2016 the Alzheimer's Association. Published by Elsevier Inc. All rights reserved.

**Keywords:** Cortical thickness; Diet; Fish; Fruit; Legumes; Macronutrients; Nutrition; Sugar; Vitamins; Cross-sectional studies; Biomarkers; Magnetic resonance imaging; Structural brain changes

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Genentech, Inc., Biogen, Inc., Eli Lilly and Co.; and receives publishing royalties from *Mild Cognitive Impairment* (Oxford University Press, 2003), and receives research support from the NIH. Dr. Jack serves on the scientific advisory board for Eli Lilly & Company; receives research support from the NIH/NIA and the Alexander Family Alzheimer's Disease Research Professorship of the Mayo Foundation; and holds stock in Johnson & Johnson.

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# Mediterranean diet, micronutrients and macronutrients, and MRI measured of cortical thickness

*“The absence of effective disease-modifying treatments for cognitive impairment underscores the need for preventive measures to reduce the burden of late life cognitive impairment including mild cognitive impairment (MCI) and Alzheimer’s dementia (AD). Certain diets show promising, preventive effects on brain aging and cognitive impairment”*

### Inclusion criteria:

- Healthy (**n=672**) (non-demented, non-hospitalized, non-terminally ill) > 70 years old participants who completed a brain MRI and the Food Frequency Questionnaire (FFQ).

**Period:** MRI scans were performed from August 2005, while FFQ were mailed to participants from 2006.

### Measurement of dietary food intake:

-**FFQ:** Respondents indicated the usual portion size (small, medium, and large; the medium portion was specified), and how often they consumed the food (never or ,1 per month, 1–3 per month, 1 per week, 2–4 per week, 5–6 per week, 1 per day, 2–3 per day, 4–5 per day, 6 per day).\*

### Limitations:

- Cross-sectional design
- FFQ was not administered concurrently with MRI
- The analysis was not adjusted for multiple comparisons to reduce the likelihood of falsely rejecting potentially relevant associations.
- Significant differences in age, education and vascular comorbidity across MRI study group and non-included participants.

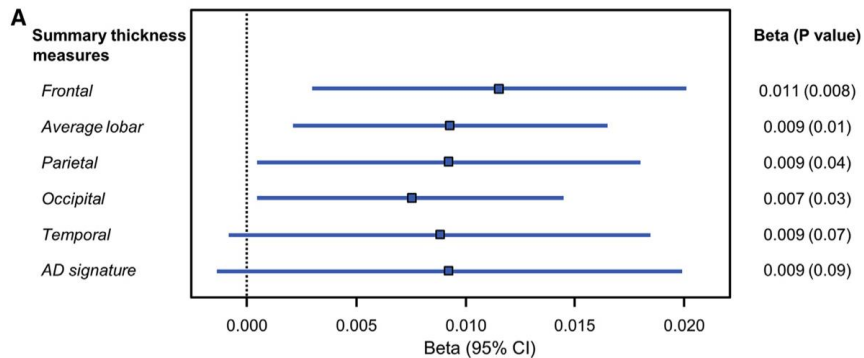
### Clinical evaluation:

- Interview (education, memory complaints, Functional activities questionnaire and CDR) weight and height.
- Neuropsychometric test.
- Short Test of Mental status.
- Neurologic examination

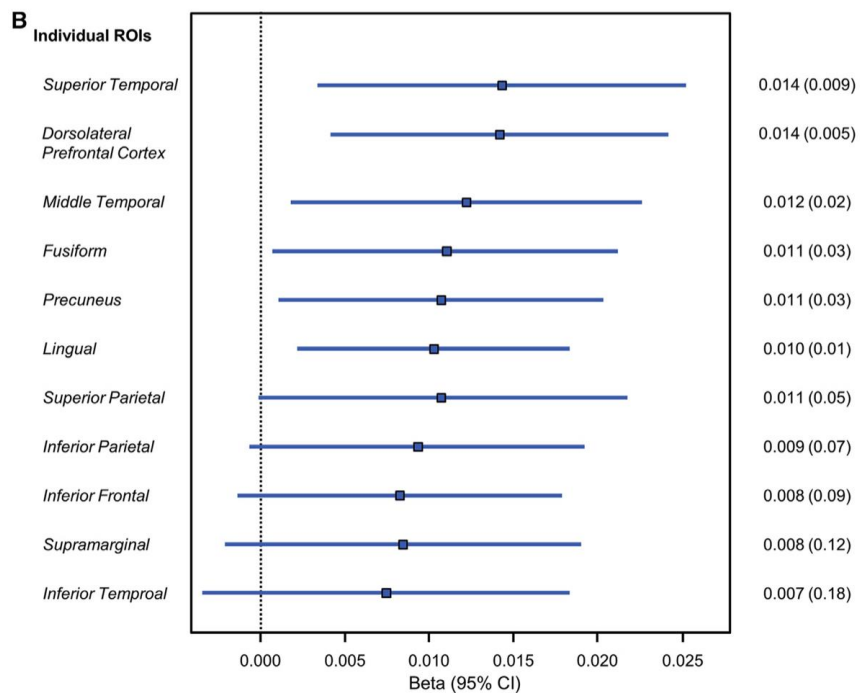
Using a sex-specific median cutoff, a value of 0 was assigned for consumption below and 1 for values at or above the median for beneficial foods (**vegetables, legumes, fruit, cereal/grains, and fish**). Inversely was done for foods considered unfavorable in excess (**meat and dairy products**). Fat intake was estimated from the ratio of **MUFA** to saturated fats (SFA); a value of 1 was assigned for a ratio at or above the median and 0 otherwise. **Alcohol** intake was included: a score of 1 was assigned for intake of 5 to ,25 g/d for women and 10 to ,50 g/d for men, and

-**The total MeDi score** ranged from 0 to 9 (maximum adherence).

\*The questionnaire data were analyzed using The Food Processor SQL nutrition analysis software program (version 10.0.0; ESHA Research, Salem, Oregon, USA).

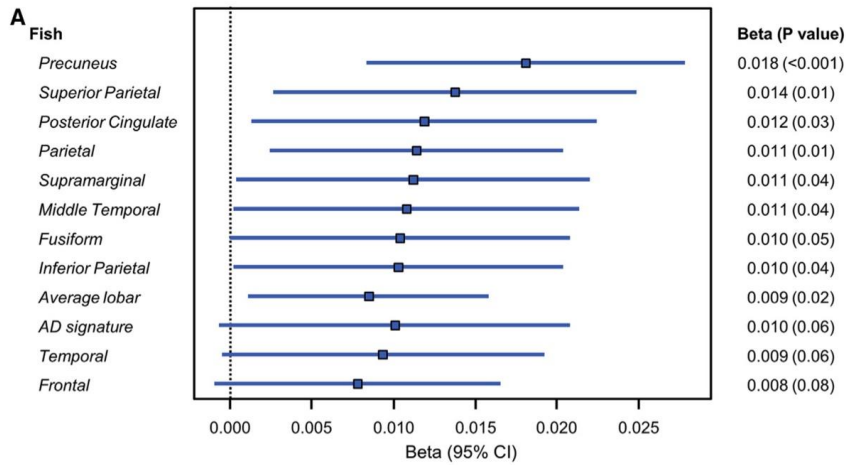


A positive associations of total MeDi score and beneficial components of MeDi (fish, vegetables, legumes, and whole grains/cereals) were observed with average cortical thickness especially in **parietal** and **frontal** lobes.

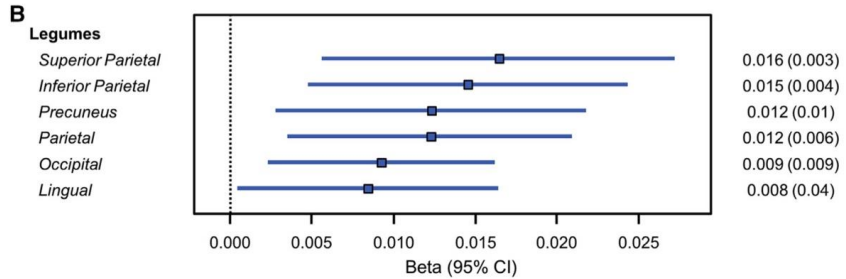


A positive associations of total MeDi score and beneficial components of MeDi were observed ROIs such as superior temporal, dorsolateral prefrontal, entorhinal, and fusiform ROIs that mediate or support **memory, executive function, attention, and language** and are associated with atrophy in dementia

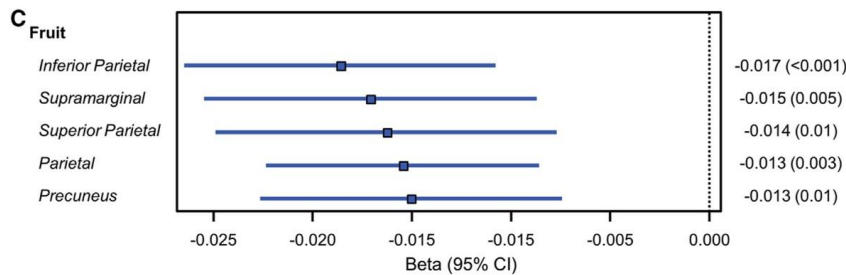
These cross-sectional findings suggest that a healthy or MeDi dietary pattern is associated with larger cortical thickness in several brain regions.



**Fish** (fatty fish in particular) is an important source of omega-3 fatty acid that is reported to have beneficial effects on brain structure and function. Indeed, fish, omega3 fatty acids, and linolenic acid (**an omega-3 PUFA**) were associated with larger cortical thickness in the present study



Higher intake of **legumes** was associated with larger parietal and occipital CT, and with larger thickness in ROIs for superior parietal, inferior parietal, precuneus, and lingual CT. legumes may be important because of their high micronutrient content (vitamins, minerals, and phytochemicals), anti-oxidant, and anti-inflammatory effects as well as other factors.



**Fruit**, on the other hand, is a beneficial MeDi component and a source of antioxidants and vitamins but was negatively associated with cortical thickness. Several fruits have a high content of simple sugars and a **high glycemic index** that may offset the benefits at high intakes.

High-percentage intakes of daily calories derived from carbohydrate and sugar might associate with an increased risk of MCI.

## Panel 2: Future research directions

### Dietary assessment

- Use of improved, validated dietary tools and multiple measures (multiple short-term quantitative measures with or without non-quantitative information about usual consumption), possibly improved by new technologies<sup>95,96</sup>
- Use of social media applications and other technologies to record dietary information (although computer literacy is a prerequisite)
- Use of a more extensive list of nutrient biomarkers, possibly aided by new omics approaches, to assess the independent and combined effects of many nutrients and food ingredients
- Exploration of many aspects of the diet not studied thus far (eg, fluid intake and chronobiology of nutrition, such as timing or distribution of food intake during the day)
- Focus on dietary patterns

### Study design

- Consideration of pertinent confounders not related to diet
- Studies with long-term follow-up or in various periods of life using multiple dietary assessments
- Emphasis on populations susceptible to diet inadequacy, cognitive decline, or both
- Careful selection of populations with neurobiological pathologies that are reasonably homogeneous
- Replication of findings in populations with different genetic backgrounds and exposures to environmental factors
- Implementation of pilot, biomarker-guided clinical trials, with feasibility components
- Clinical trials targeting earlier windows of exposure, before onset of age-related cognitive decline or neurodegeneration
- Implementation of large-scale preventive interventions based on already identified brain healthy dietary patterns
- Examination of potential sex differences in the effect of dietary components on cognitive outcomes

# Ancel Keys

epidemiologo e fisiologo USA 1904-2004

- 1957, Seven Country Study (USA, Finlandia, Olanda, Italia, Jugoslavia, Grecia, Giappone) osservazionale, prospettico, >12000 soggetti seguiti dall'età di 40-59 anni per un periodo di oltre 50 anni, valutazioni ogni 5 anni
- Contrapposte popolazioni del nord a quelle del sud, pattern alimentari e stili di vita diversi.
- 1990, pattern mediterraneo è stabilito essere favorevole per la prevenzione della malattia coronarica (OMS e FAO)



# Dieta Mediterranea

## principi generali

- Le caratteristiche della dieta mediterranea sono:

Abbondanti **alimenti di origine vegetale** (frutta, verdura, ortaggi, pane e cereali, soprattutto integrali, patate, fagioli e altri legumi, noci, semi), freschi al naturale, di stagione, di origine locale; frutta fresca come dessert giornaliero; dolci contenenti zuccheri raffinati o miele poche volte alla settimana; **olio di oliva come principale fonte di grassi**; latticini (principalmente formaggi e yogurt) consumati giornalmente in modesta-moderata quantità; pesce e pollame consumato in quantità abbastanza bassa; da 0 a 4 uova la settimana; carni rosse in minime quantità; vino consumato in quantità modesta-moderata generalmente durante il pasto.

- Questa dieta ha un contenuto basso in grassi saturi (inferiore al 7-8%), ed un contenuto totale di grassi da meno del 25 a meno del 35% a seconda delle zone. Inoltre originariamente era associata a regolare attività fisica lavorativa, ad esempio nei campi o in casa.

# Dieta Mediterranea

## principi generali

- Il contenuto calorico della dieta mediterranea nelle indagini di popolazione non superava le **2500 Kcal per l'uomo e le 2000 Kcal per la donna**, comunque l'introito calorico non andava oltre il consumo metabolico con l'attività fisica. In sostanza si trattava della dieta di una popolazione rurale povera e frugale.
- Come dieta mediterranea di riferimento nel Seven Country Study è stata considerata quella di Nicotera; i vari componenti di essa, espressi come percentuali dell'apporto calorico totale (in rilievi della durata di sette giorni in differenti stagioni del 1960) sono: cereali 50-59%, olio di oliva extravergine 13-17%, vegetali 2,2-3,6%, patate 2,3-3,6%, legumi 3-6%, frutta 2,6-3,6%, pesce 1,6-2%, vino rosso 1-6%, carne 2,6-5%, latticini 2-4%, uova e grassi animali molto scarsi.

# UNESCO » Culture » Intangible Heritage » Lists » Mediterranean diet

## Mediterranean diet

**Cyprus, Croatia, Spain, Greece, Italy, Morocco and Portugal**

Inscribed in 2013 on the Representative List of the Intangible Cultural Heritage of Humanity

The Mediterranean diet involves a set of skills, knowledge, rituals, symbols and traditions concerning crops, harvesting, fishing, animal husbandry, conservation, processing, cooking, and particularly the sharing and consumption of food. Eating together is the foundation of the cultural identity and continuity of communities throughout the Mediterranean basin. It is a moment of social exchange and communication, an affirmation and renewal of family, group or community identity. The Mediterranean diet emphasizes values of hospitality, neighbourliness, intercultural dialogue and creativity, and a way of life guided by respect for diversity. It plays a vital role in cultural spaces, festivals and celebrations, bringing together people of all ages, conditions and social classes. It includes the craftsmanship and production of traditional receptacles for the transport, preservation and consumption of food, including ceramic plates and glasses. Women play an important role in transmitting knowledge of the Mediterranean diet: they safeguard its techniques, respect seasonal rhythms and festive events, and transmit the values of the element to new generations. Markets also play a key role as spaces for cultivating and transmitting the Mediterranean diet during the daily practice of exchange, agreement and mutual respect.