18 – 19 novembre 2024
XVII Convegno
I CENTRI PER I DISTURBI COGNITIVI E LE DEMENZE
E LA GESTIONE INTEGRATA DELLA DEMENZA

Qualità della dieta, consumo di alimenti ultraprocessati e rischio di deterioramento cognitivo e malattie neurodegenerative

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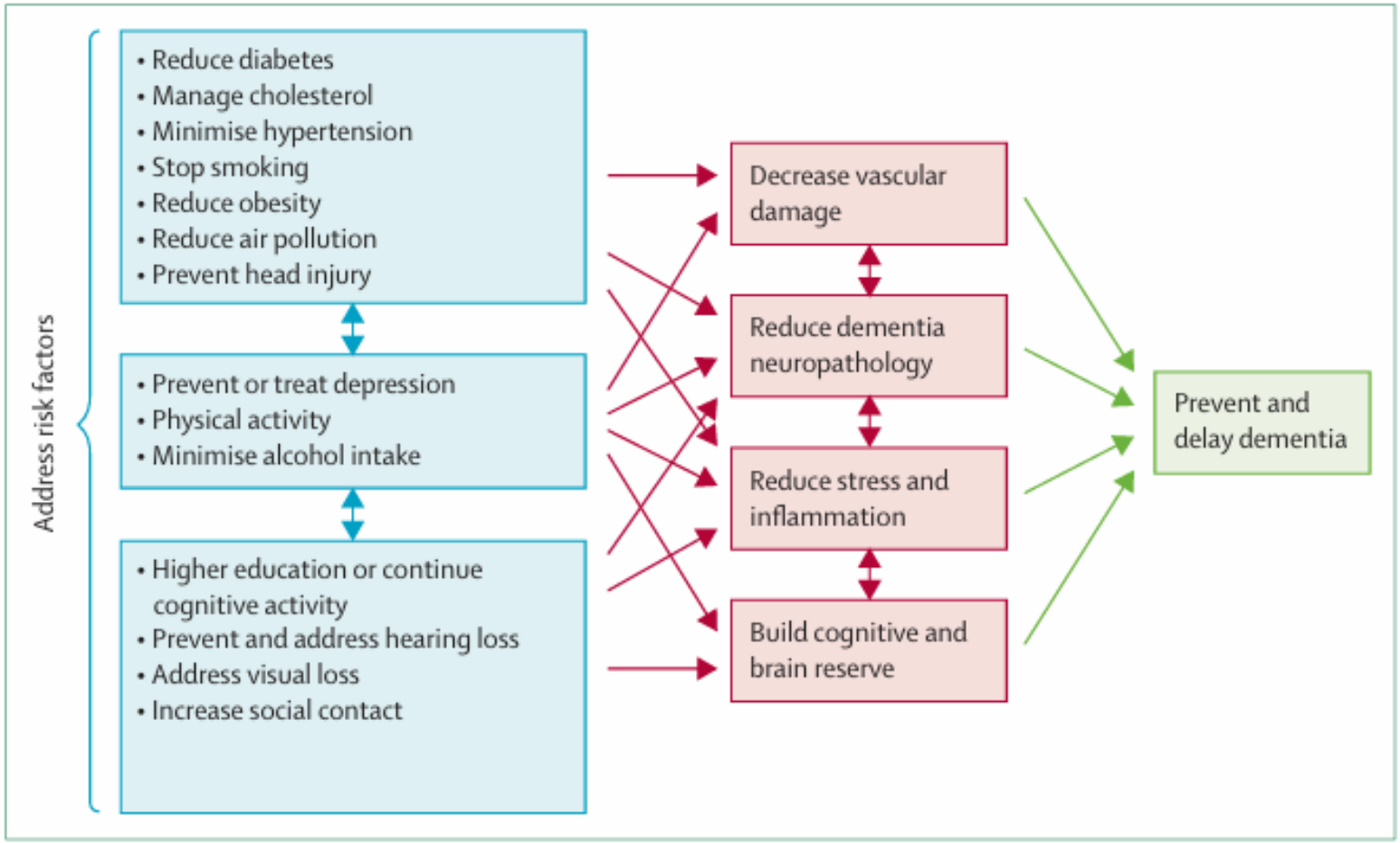
Modifiable risk factors in dementia



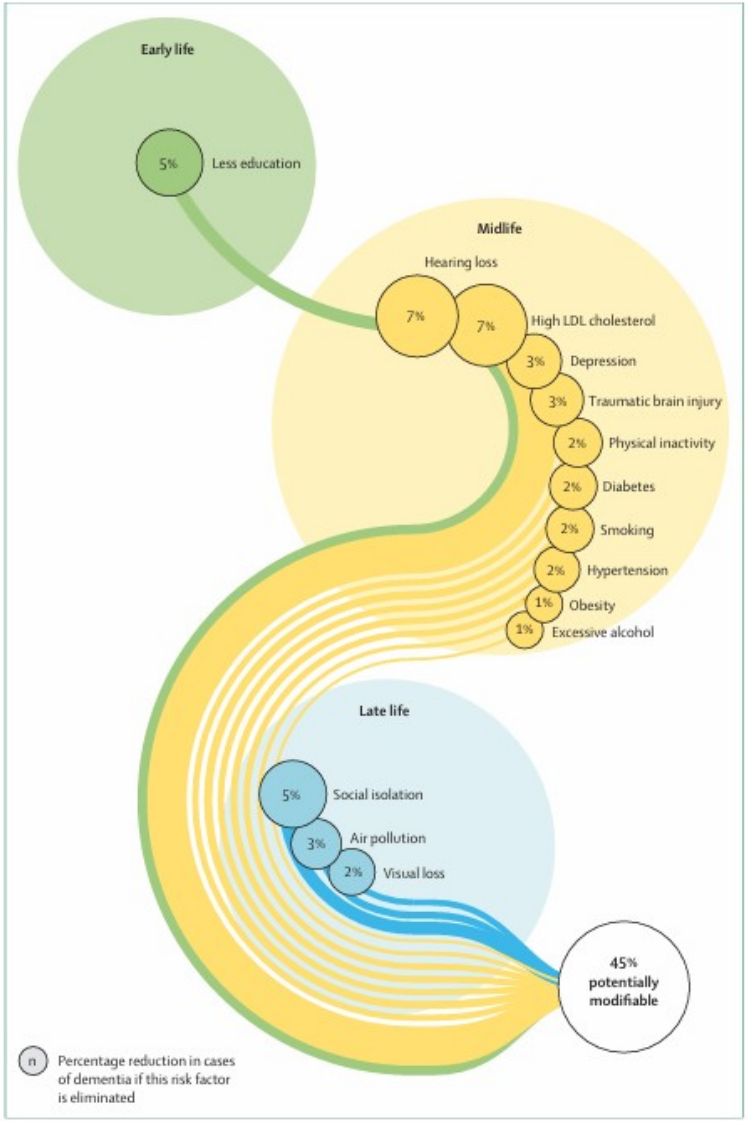
2024 report of the Lancet standing Commission

Specific actions recommended for dementia prevention

2024 report of the Lancet standing Commission

- Ensure **good quality education** is available for all and encourage cognitively stimulating activities in midlife to protect cognition
- Make **hearing aids** accessible for people with hearing loss and decrease harmful noise exposure to reduce hearing loss
- **Treat depression** effectively
- Encourage **use of helmets and head protection** in contact sports and on bicycles
- Encourage **exercise** because people who participate in sport and exercise are less likely to develop dementia
- Reduce **cigarette smoking** through education, price control, and preventing smoking in public places and make smoking cessation advice accessible
- **Prevent or reduce hypertension** and maintain systolic blood pressure of 130 mm Hg or less from age 40 years
- **Detect and treat high LDL cholesterol** from midlife
- Maintain a **healthy weight** and **treat obesity** as early as possible, which also helps to prevent diabetes
- **Reduce high alcohol** consumption through price control and increased awareness of levels and risks of overconsumption
- Prioritise age-friendly and supportive **community environments** and housing and **reduce social isolation by** facilitating participation in activities and living with others
- Make screening and treatment for **vision loss** accessible for all
- Reduce exposure to **air pollution**

Population attributable fraction of potentially modifiable risk factors for dementia



2024 report of the Lancet standing Commission

Major environmental risk factors for dementia and Alzheimer disease

WHO 2019: Conditional racommendation for Mediterranean diet

TO PREVENT

- high blood pressure (hypertension)
- high blood sugar (diabetes)
- being overweight or obese
- smoking
- drinking too much alcohol
- being physically inactive
- being socially isolated
- depression

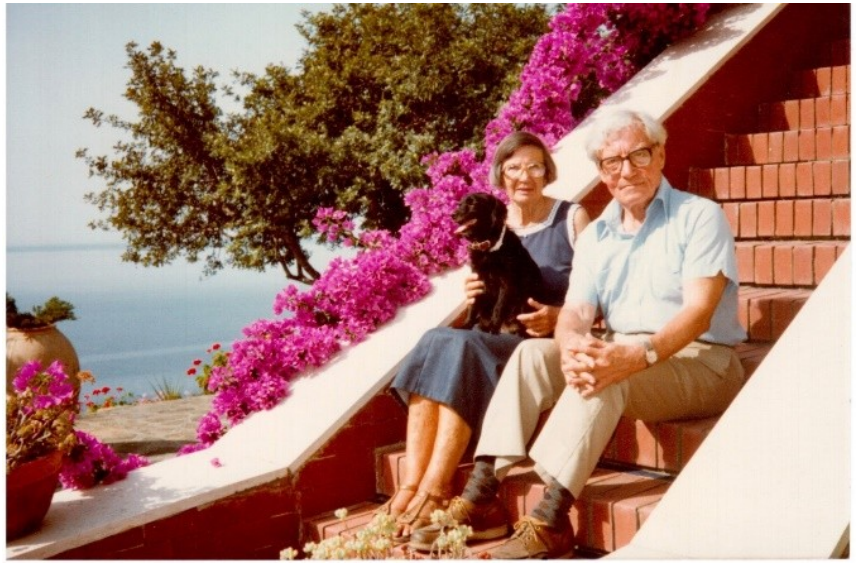
TO MANAGE

- Stay physically active.
- **Eat healthily.**
- Stop smoking and drinking alcohol.
- Get regular check-ups with your doctor.
- Keep up your hobbies and do things that you enjoy.
- Try new ways to keep your mind active.
- Spend time with friends and family and engage in community life.

Source: WHO, 2023. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia

Can diet help prevent cognitive impairment and dementia?

About the diet of the Italians in the Fifties

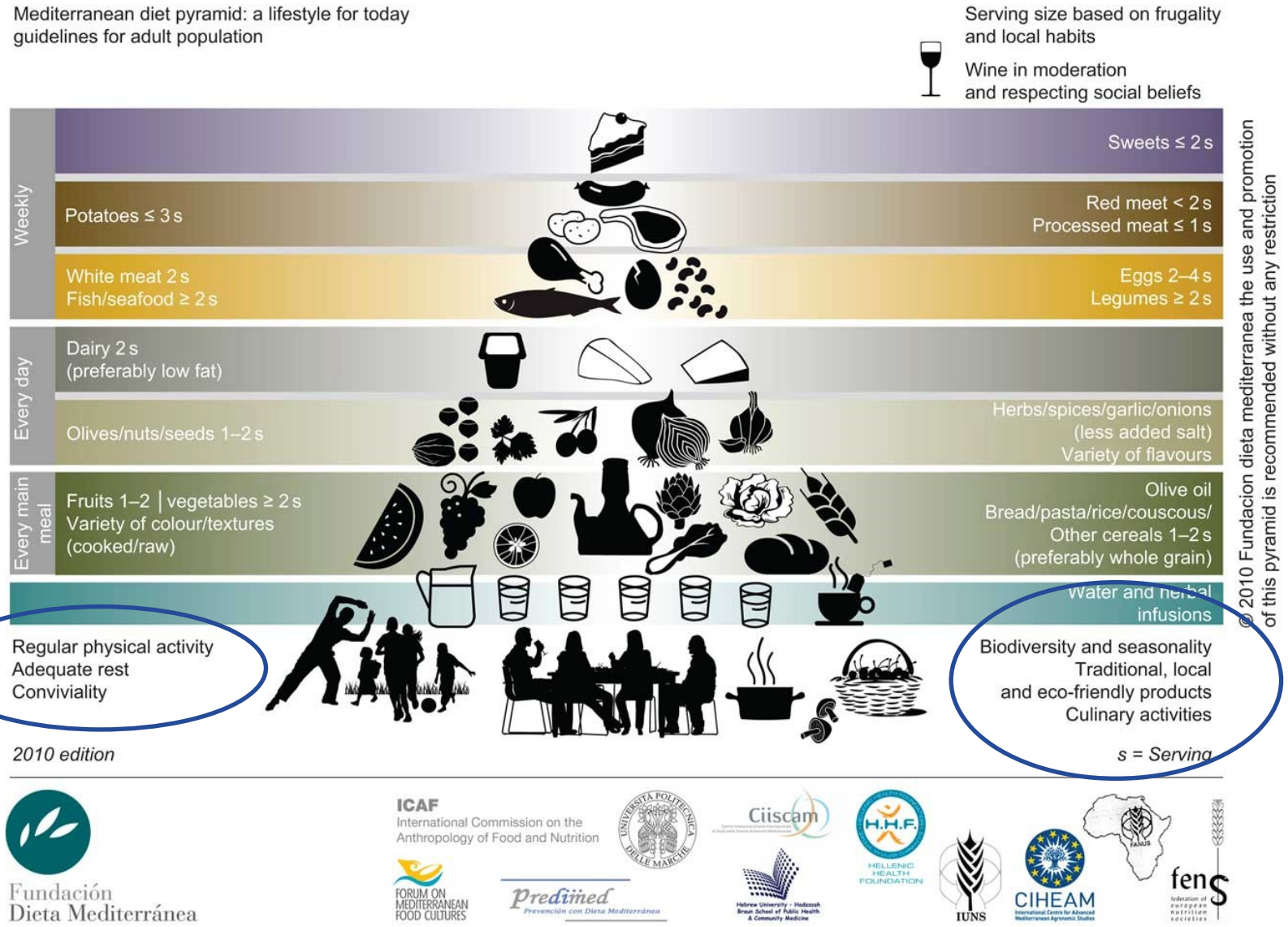


"A hearty dish of beans and short lengths of macaroni (**pasta e fagioli**); lots of bread (never served with any kind of spread); great quantities of **fresh vegetables**; a **modest portion of meat or fish** (perhaps twice a week); **wine**; always **fresh fruits** for dessert".
adapted from: ***Ancel and Margaret Keys****. HOW TO EAT WELL AND STAY WELL: THE MEDITERRANEAN WANew York: Doubleday; 1975.*

"My **concern about diet** as a public health problem **began in the early 1950s in Naples**, where we observed **very low incidences of coronary heart disease** associated with what we later came to call the "good Mediterranean diet".

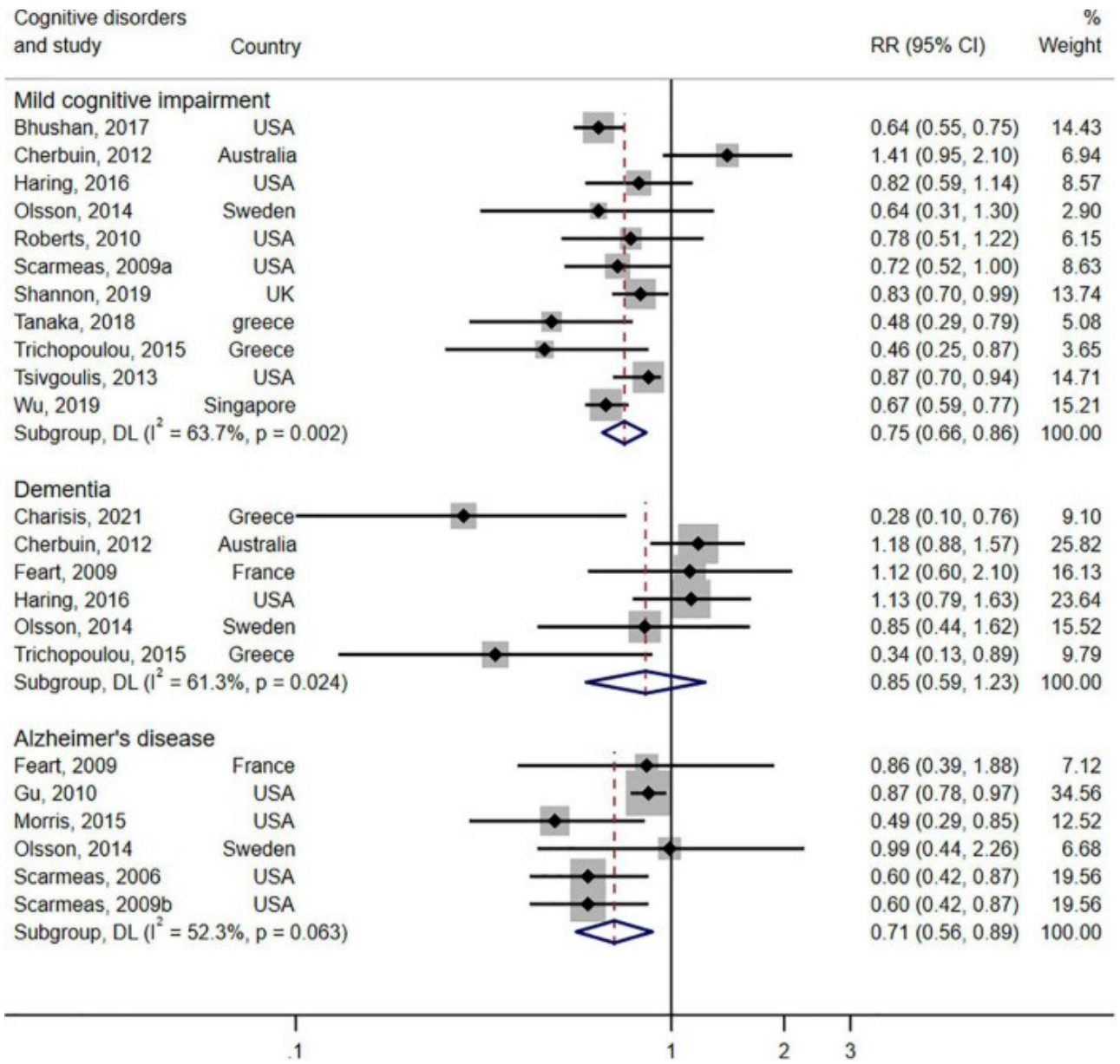
The heart of this diet is **mainly vegetarian**, and **differs from American and northern European diets** in that it is **much lower in meat and dairy products and uses fruit for dessert**. These observations led to our subsequent research in the **Seven Countries Study**, in which we demonstrated that saturated fat is the major dietary villain[…] Our challenge is to **persuade children to tell their parents to eat as Mediterraneans do**" (***Keys A****. Am J Clin Nutr. 1995;61:1321S-1323S*).

A Mediterranean Lifestyle



Biodiversity
Seasonality
Traditional local food
Culinary activities
Conviviality
Adequate rest

Mediterranean Diet and cognitive health: a meta-analysis of prospective studies



Mild cognitive impairment:

RR= 0.75 (95%CI 0.66-0.86) for high vs. low MD

Dementia:

RR= 0.85 (95%CI 0.59-0.23) for high vs. low MD

Alzheimer disease:

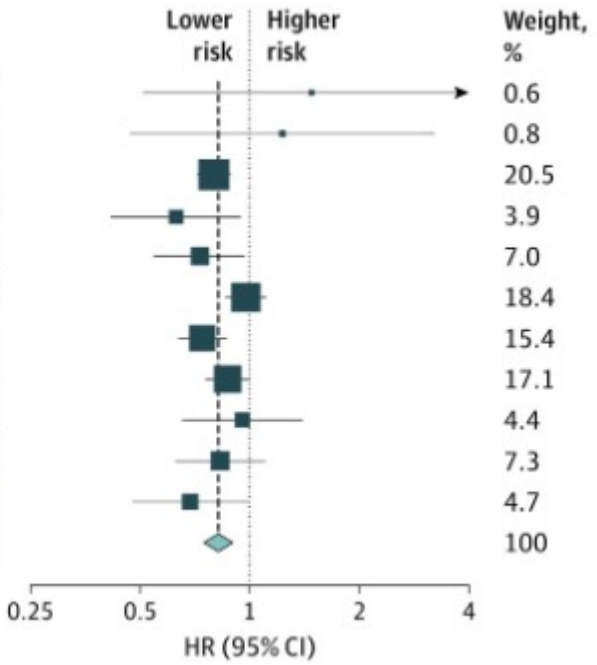
RR= 0.71 (95%CI 0.56-0.89) for high vs. low MD

Fu J et al. Front Nutr. 2022 Jul 28;9:946361.

MIND Diet and dementia risk: a meta-analysis of prospective studies

The MIND diet emphasizes natural plant-based foods, limited intake of animal foods and foods high in saturated fat, and uniquely encourages consumption of berries and green leafy vegetables rich in vitamins and antioxidants

Source	Cohort	No. of cases/ total No. (%)	HR (95% CI)
Vu et al,[26] 2022	CHAP (Black individuals)	109/1503 (7.2)	1.48 (0.51-4.27)
Vu et al,[26] 2022	CHAP (White individuals)	67/946 (7.1)	1.23 (0.47-3.18)
Vu et al,[26] 2022	WHI−MS	951/5308 (17.9)	0.80 (0.72-0.89)
Vu et al,[26] 2022	MAP	222/725 (30.6)	0.63 (0.42-0.92)
Thomas et al,[28] 2022	3C-Bordeaux	356/1412 (25.2)	0.73 (0.55-0.97)
de Crom et al,[21] 2022	RS (baseline I)	1188/5375 (22.1)	0.98 (0.86-1.12)
de Crom et al,[21] 2022	RS (baseline II)	248/2861 (8.7)	0.74 (0.64-0.89)
Zhang et al,[27] 2022	UKB	1363/187 783 (0.7)	0.87 (0.76-0.99)
Present study	WII	220/8358 (2.6)	0.96 (0.66-1.38)
Present study	HRS	338/6758 (5.0)	0.83 (0.63-1.09)
Present study	FOS	217/3020 (7.2)	0.69 (0.48-0.99)
Random-effects model			0.83 (0.76-0.90)
Heterogeneity: $I^2 = 35\%$; $\tau^2 = 0.0064$ ($P = .12$)			



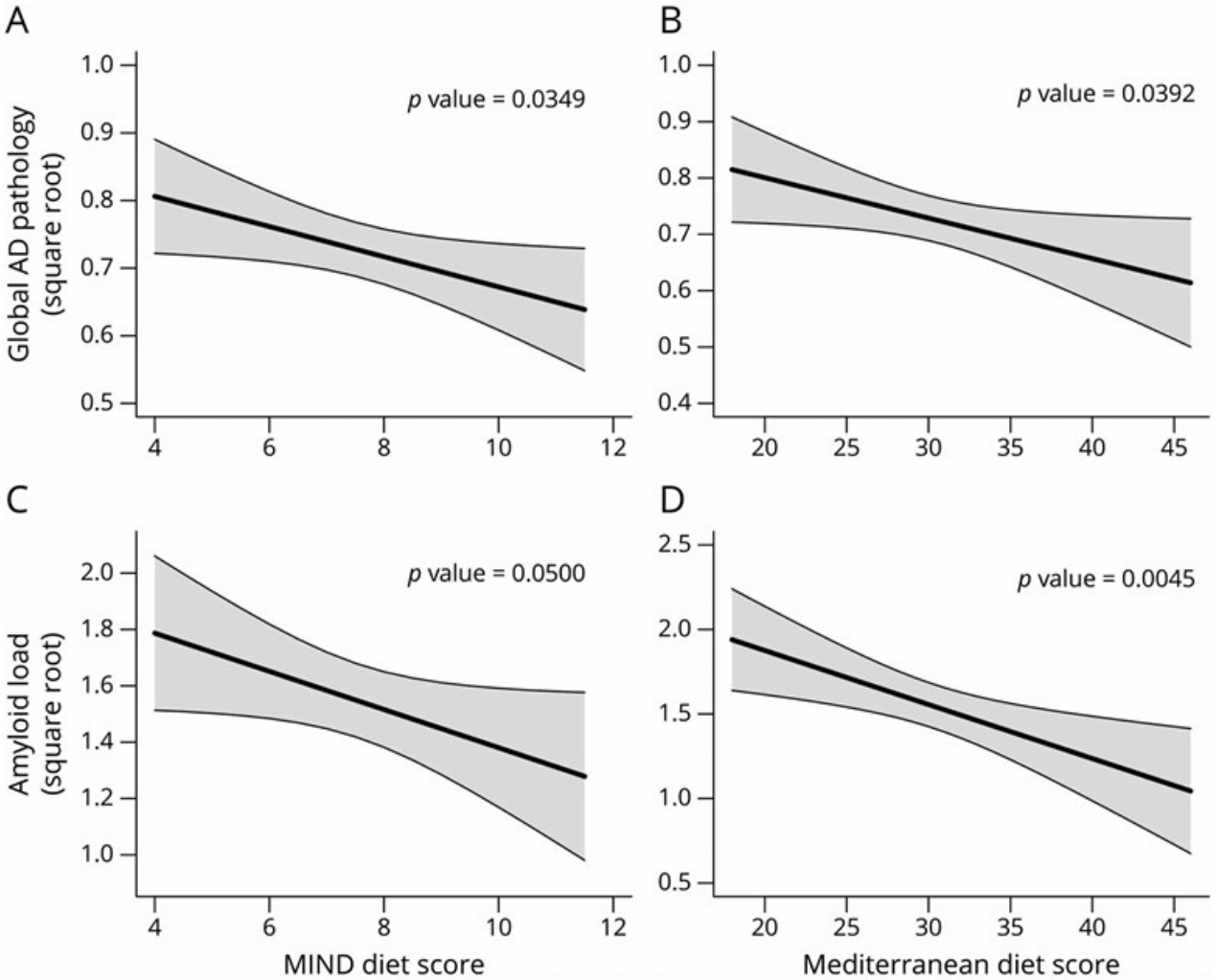
BMC Med. 2023 Mar 14;21:81. doi: 10.1186/s12916-023-02772-3

Mediterranean diet adherence is associated with lower dementia risk, independent of genetic predisposition: findings from the UK Biobank prospective cohort study

Oliver M Shannon [1,#], Janice M Ranson [2,#], Sarah Gregory [3], Helen Macpherson [4], Catherine Milte [4], Marleen Lentjes [5], Angela Mulligan [6], Claire McEvoy [7], Alex Griffiths [8], Jamie Matu [8], Tom R Hill [1], Ashley Adamson [1], Mario Siervo [9], Anne Marie Minihane [10,11], Graciela Muniz-Tererra [3,12], Craig Ritchie [3], John C Mathers [1,✉], David J Llewellyn [2,13,#], Emma Stevenson [1,#]

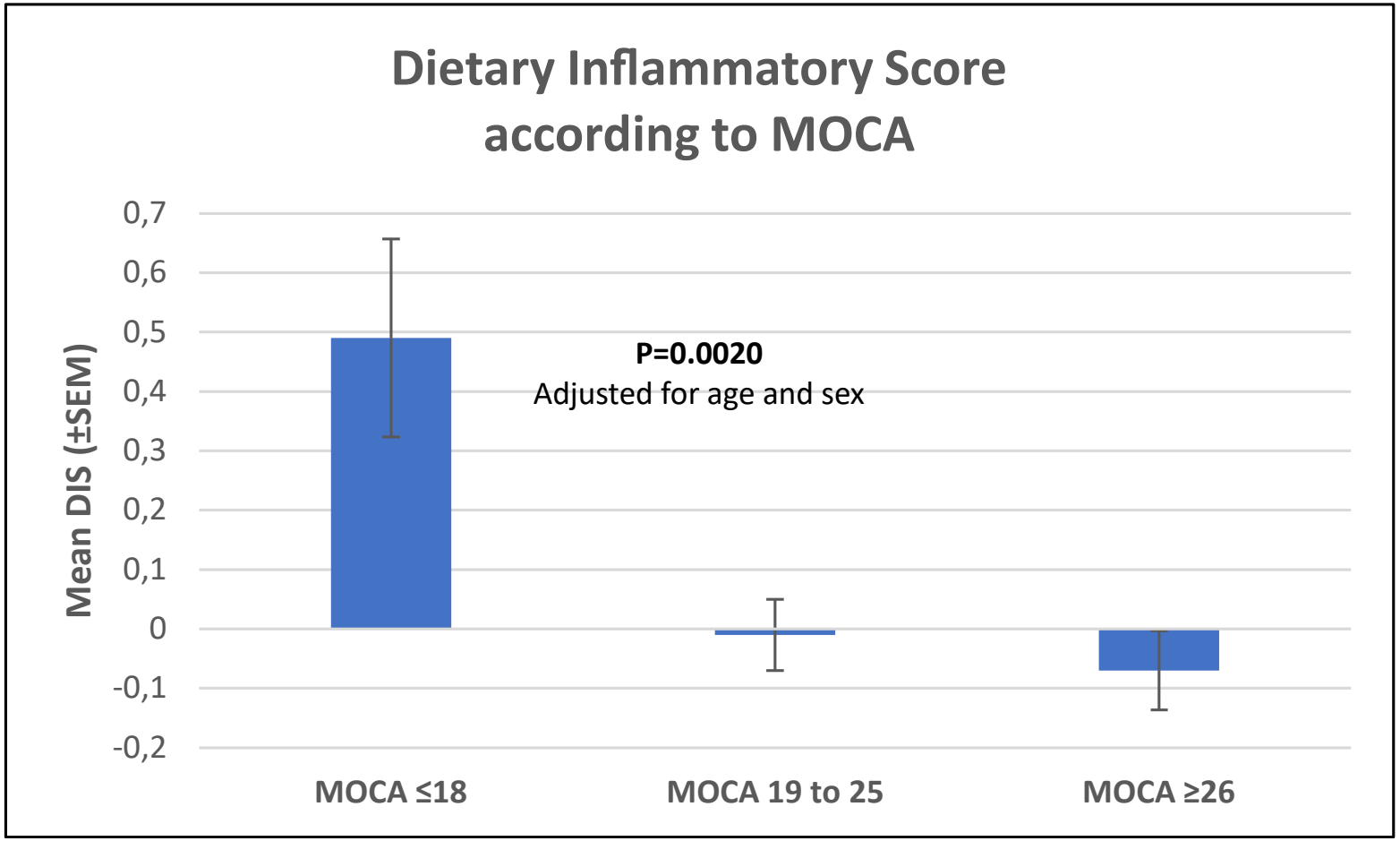
Chen H at al. JAMA Psychiatry. 2023;80:630–638

Association Between MINDDiet and MedDiet with Global AD Pathology and Amyloid Load in Autopsied participants of the Rush Memory and Aging Project



Agarwal P et al. Neurology 2023

Dietary inflammatory score and cognitive performance in the Moli-sani study



Bracone et al., submitted to JAD, 2024

Multinomial Logistic Regression for MoCA categories in Relation to Dietary Inflammatory Score (DIS), in whole population (N=2,474) and according to PHQ-9

	MoCA≥26	MoCA 18 to 26	MoCA ≤18	
	Referent	OR (95% CI)	OR (95% CI)	P for difference
MoCA vs DIS (x 1-SD)				
Whole population	-1-	1.01 (0.92 to 1.10)	1.33 (1.11 to 1.60)	
PHQ-9 <10	-1-	0.97 (0.88 to 1.06)	1.21 (0.99 to 1.47)	0.0014
PHQ-9 ≥10	-1-	1.52 (1.08 to 2.15)	2.36 (1.36 to 4.11)	

SD stands for Standard Deviation and PHQ-9 for Patient Health Questionnaire-9

A PHQ-9 score of ≥10 indicates the presence of mild to severe depressive symptoms

Odds ratios adjusted for age, sex, housing status, total calories intake, history of cardiovascular disease, malignant tumours, diabetic therapy, lipid-lowering therapy, antihypertensive drug use, and drug therapies targeting the central nervous system

Bracone et al., submitted to JAD, 2024

Mediterranean diet improves cognition: the PREDIMED-NAVARRA randomised trial

522 participants at high vascular risk

Table 4 Multivariable-adjusted means after a 6½-year follow-up and differences versus control (95% CIs) in each intervention group

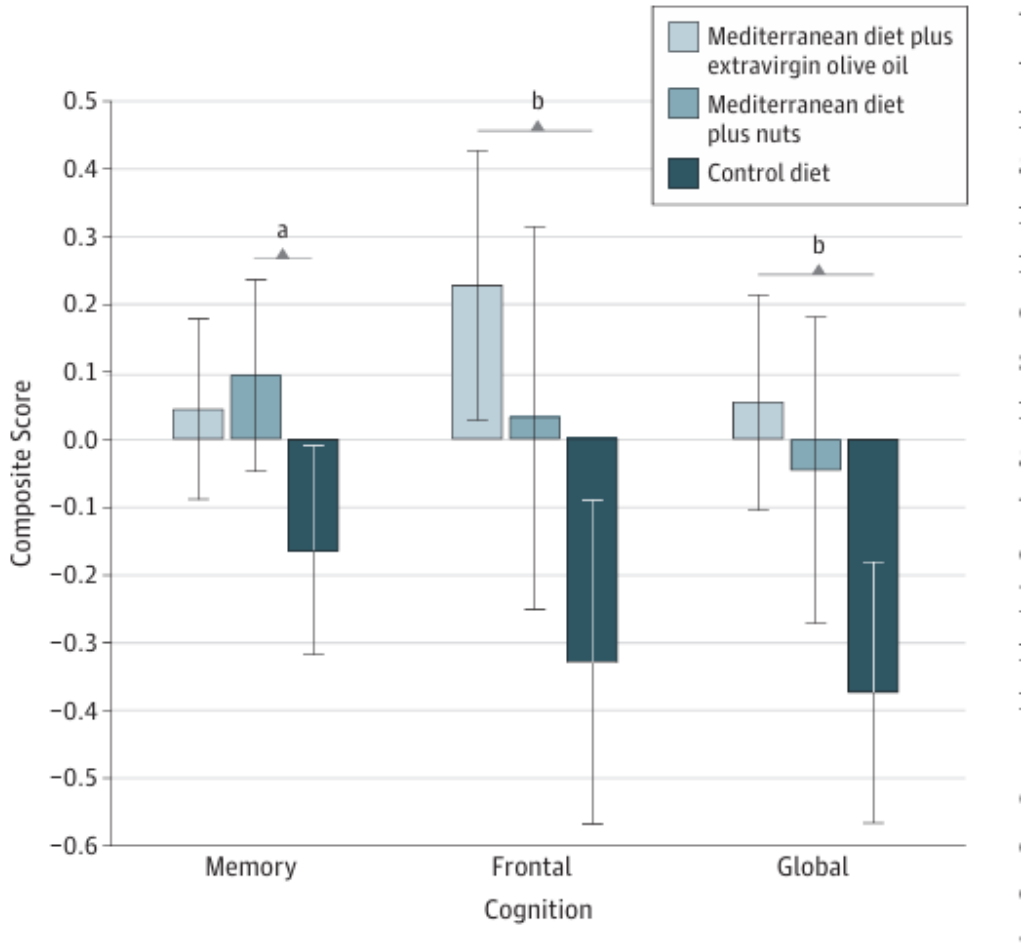
	MedDiet+EVOO (n=224)		MedDiet+Nuts (n=166)		Control (low-fat diet) (n=132)
	Mean (95% CI)	p Value (vs control)	Mean (95% CI)	p Value (vs control)	Mean (95% CI)
MMSE	27.73 (27.27 to 28.19)		27.68 (27.20 to 28.16)		27.11 (26.61 to 27.61)
Adjusted diff. versus control (95% CI)	+0.62 (+0.18 to +1.05)	0.005	+0.57 (+0.11 to +1.03)	0.015	0 (reference)
CDT	5.31 (4.98–5.64)		5.13 (4.78–5.47)		4.80 (4.44–5.16)
Adjusted diff. versus control (95% CI)	+0.51 (+0.20 to +0.82)	0.001	+0.33 (+0.003 to +0.67)	0.048	0 (reference)

General Linear Models. The PREDIMED-NAVARRA trial.
CDT, Clock Drawing Test; EVOO, extra virgin olive oil; MedDiet, Mediterranean diet; MMSE, Mini-Mental State Examination.
Adjusted for sex, age, education, family history of cognitive impairment or dementia, *ApoE4* genotype, hypertension, dyslipidaemia, diabetes, smoking status, alcohol intake, body mass index, physical activity and total energy intake.

An intervention with MedDiet supplemented with either EVOO or mixed nuts was associated with a better global cognitive performance after 6.5 years of follow-up compared with a low-fat control group

Martínez-Lapiscina EH et al. J Neurol Neurosurg Psychiatry. 2013;84:1318-25.

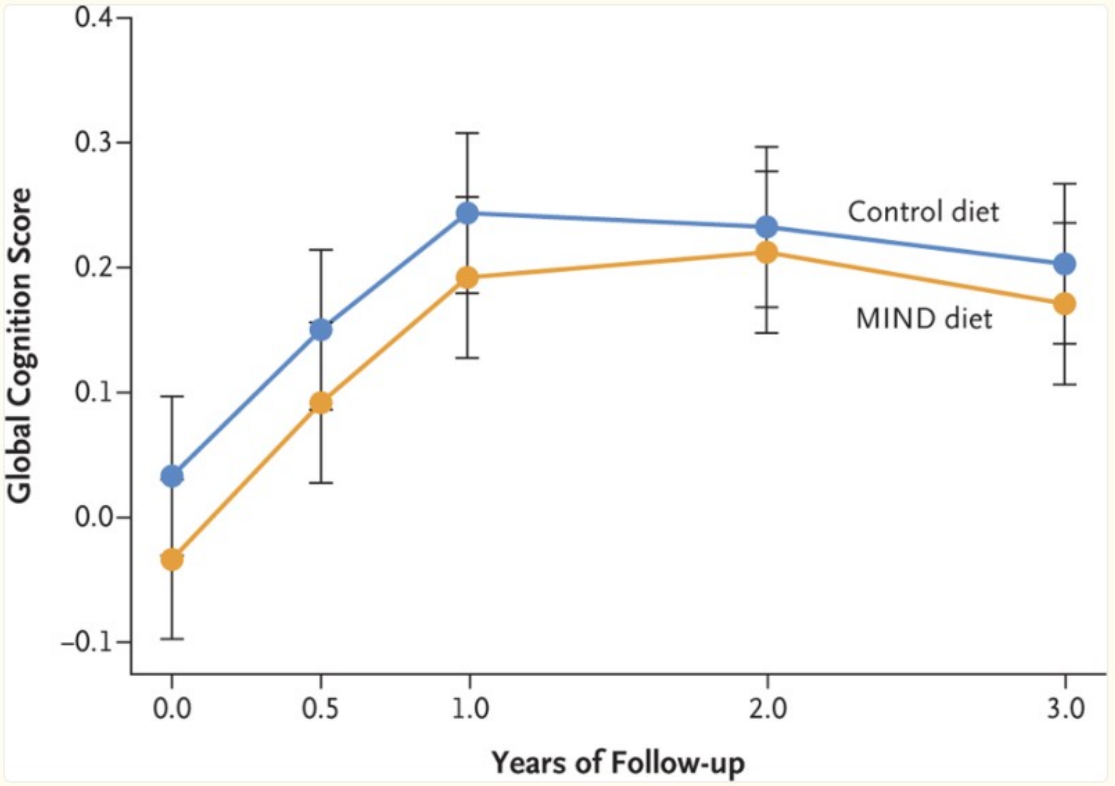
Changes in Cognitive Function Measured With Composites by Intervention Group in the PrediMed Trial



Valls-Pedret et al. JAMA Intern Med. (2015) 175:1094–103

Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons

Figure 2. Changes in the Global Cognition Score during the Trial Period.



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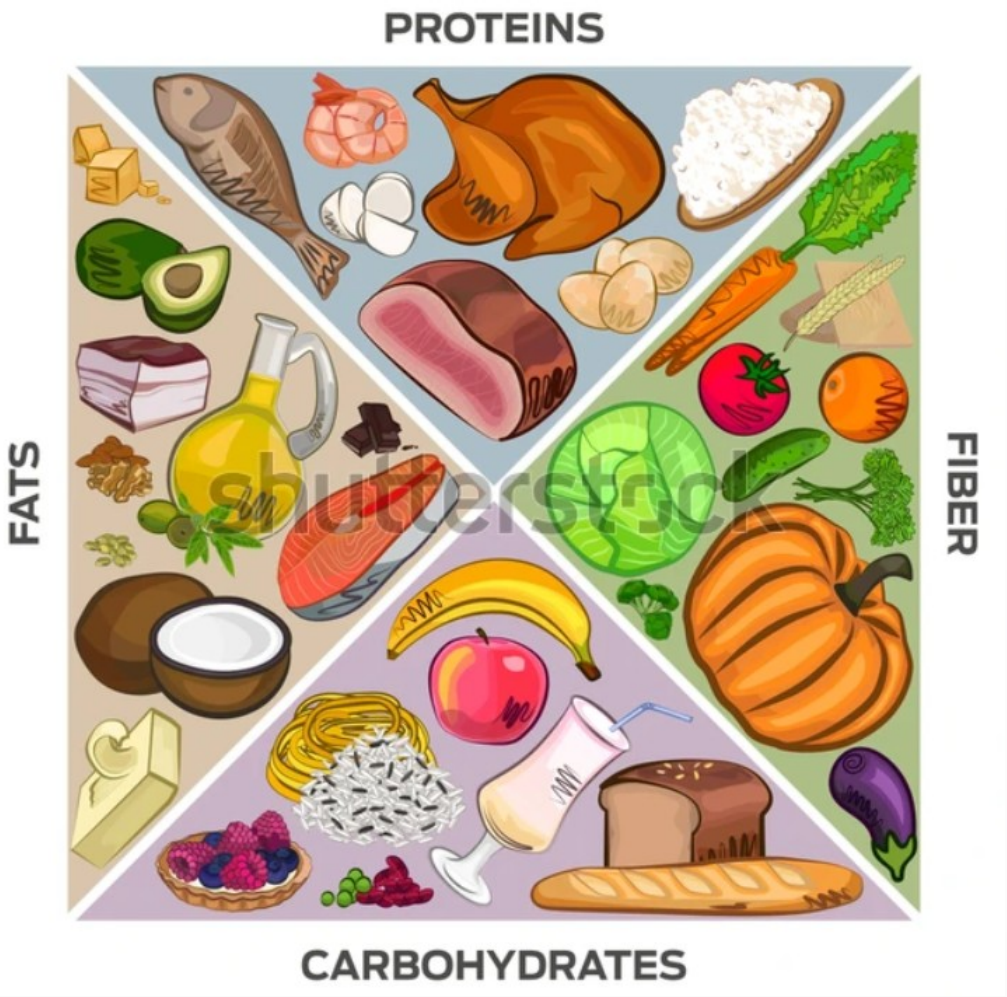
Barnes LL, et al. N Engl J Med. 2023 Aug 17;389(7):602-611.

Beyond the ‘nutrient gate’: the issue of food processing



- For decades, the **effect of diet on health has been almost exclusively considered from a nutrient based perspective,** leading to recommendations of reducing, e.g., sugar, salt and fat

- The **degree of processing** and formulation of foods has been **largely minimized**

- The **potential health effect of food processing and food formulation**, beyond their food ingredients, nutrient composition, and energy content, **is now being widely researched**

The Nova classification

Unprocessed or minimally processed foods	Processed culinary ingredients	Processed foods	Ultra-processed foods
Foods which did not undergo processing or underwent minimal processing technics, such as fractioning, grinding, pasteurization and others.	These are obtained from minimally processed foods and used to season, cook and create culinary dishes.	These are unprocessed or minimally processed foods or culinary dishes which have been added processed culinary ingredients. They are necessarily industrialized.	These are food products derived from foods or parts of foods, being added cosmetic food additives not used in culinary.
			
Legumes, vegetables, fruits, starchy roots and tubers, grains, nuts, beef, eggs, chicken, milk	Salt, sugar, vegetable oils, butter and other fats.	Bottled vegetables or meat in salt solution, fruits in syrup or candied, bread, cheeses, purees or pastes.	Breast milk substitutes, infant formulas, cookies, ice cream, shakes, ready-to-eat meals, soft drinks and other sugary drinks, hamburgers, nuggets.

GROUP 4. Ultra-processed food (UPF)

- The term ultra-processed food (UPF) indicates **industrially manufactured** ready-to-eat or ready-to-heat **formulations made mostly or entirely from substances extracted from foods or derived from food constituents** often containing **added flavours, colours, emulsifiers** and other cosmetic additives, and **little or no food**
- These industrial formulations are **designed to maximize palatability and (over) consumption** through a combination of calorie-dense ingredients and chemical additives
- Examples of typical UPF are **carbonated drinks, processed meat, fruit yogurt, sweet or savoury packaged snacks, ice-cream, chocolate, candies (confectionery), mass-produced packaged breads** and buns, and many others

Monteiro CA et al. Public Health World Nutr 2016;7:28-38
Monteiro CA. et al. Public Health Nutr. 2009;12(5):729-731

UPF intake is on the rise globally

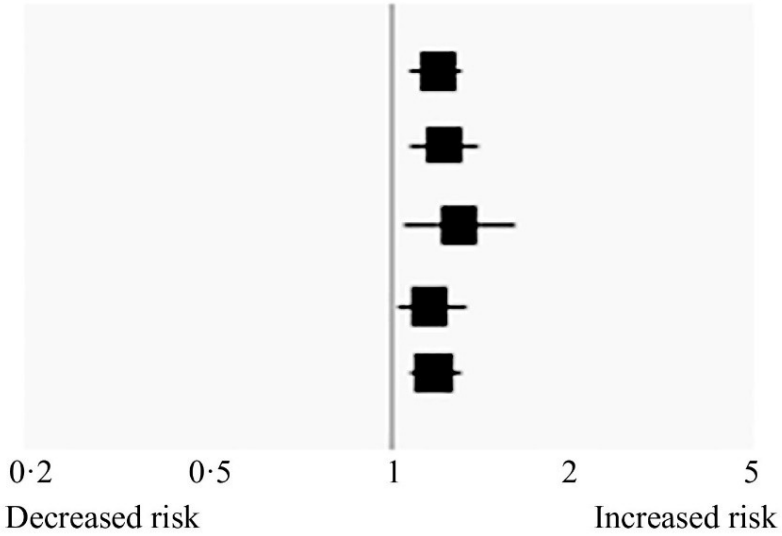
The proportion **of food that is ultra-processed** is

- **60% in the USA and in the UK**
- 50% in Canada
- 42% in Australia
- 32% in Belgium
- 30% in Brasil
- **24% in Spain**
- **13% in Italy (1997)**
- **17% in Italy (INHES 2010-13)**
- 15% in Colombia

Consumption of UPF and health status
A systematic review and meta-analysis

13 prospective cohort studies; 183,491 participants; follow-up 3.5 to 19 years

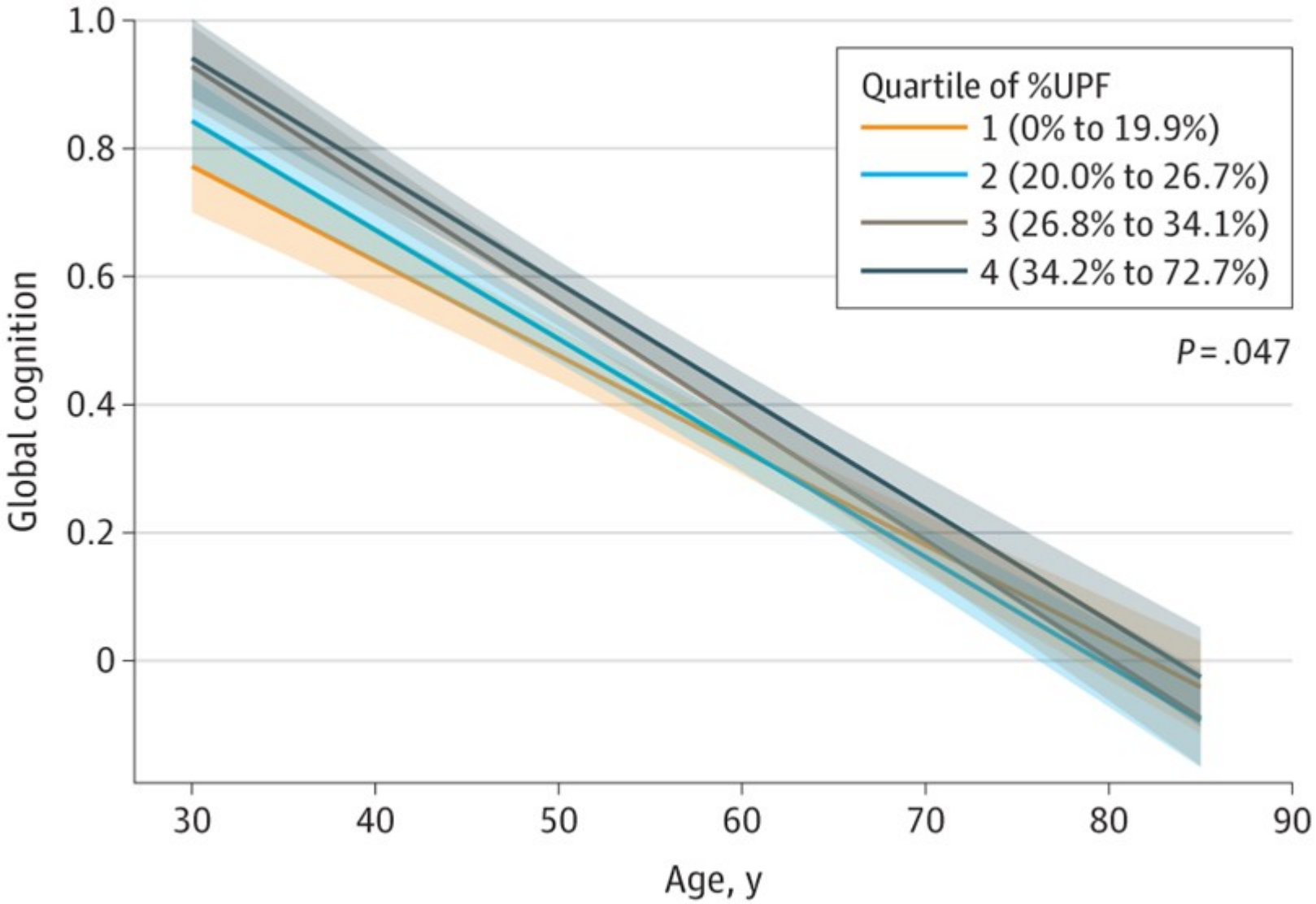
Outcome	No. of studies	*n*/*N*	Risk ratio (random, 95 % CI)	Risk ratio (random, 95 % CI)	*P*	I^2 (%)	P_{het}
All-cause mortality[29,31,33,35,36]	5	4687/111 056	1·25	1·14, 1·37	<0·00001	2	0·40
CVD incidence/mortality[13,35,36]	3	2501/139 867	1·29	1·12, 1·48	0·0003	7	0·34
CV incidence/mortality[13,35]	2	1150/127 969	1·34	1·07, 1·68	0·01	32	0·22
Depression[15,30]	2	2995/41 637	1·20	1·03, 1·40	0·02	42	0·19
Overweight/obesity[27,34]	2	2911/20 278	1·23	1·11, 1·36	<0·00001	0	0·64



Pagliai G, …Bonaccio M, Iacoviello L et al. Br J Nutr. 2021 ;125:308-318.

Do UPFs affect brain health?

Ultra-processed Foods and Cognitive Decline: findings from the ELSA-Brasil



Exposure: UPF consumption

Outcome: Changes in cognitive performance over time evaluated by the immediate and delayed word recall, word recognition, phonemic and semantic verbal fluency tests, and Trail-Making Test B version

Follow-up: 8 years

Results: Participants who reported **consumption of UPF of more than 19.9%** of daily calories had a 28% **faster rate of global cognitive decline compared** with those who reported consumption of UPF up to 19.9% of daily calories

Gomes Gonçalves N et al. JAMA Neurol. 2023;80:142-150.

Ultra-processed Food Consumption and Risk of Dementia in the UK Biobank

- Study sample: 72,083 participants (≥55 y) free from dementia at baseline
- Exposure: UPF intake as per Nova classification
- Outcome: All-cause dementia comprising Alzheimer disease (AD) and vascular dementia
- Follow-up: 10 years
- 87 developed AD and 119 developed vascular dementia

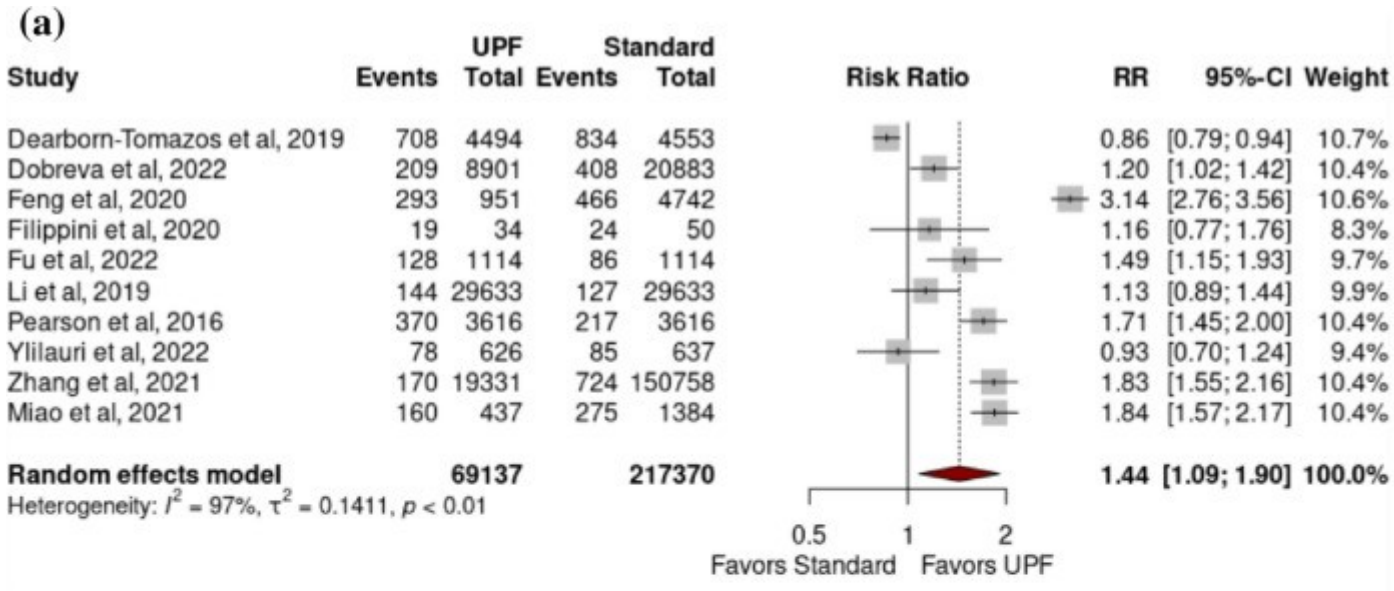
Risk of Alzheimer disease	Risk of vascular dementia
HR= 1.25 (95&CI 1.14-1.37) For 10% increase in UPF	HR= 1.28 (95&CI 1.06-1.55) For 10% increase in UPF

Replacing 10% of UPF weight in diet with an equivalent proportion of unprocessed or minimally processed foods was estimated to be associated with a **19% lower risk of dementia** (HR 0.81; 95% CI 0.74–0.89).

Li H et al, Neurology. 2022;99(10):e1056-e1066.

Ultra-processed Foods and Risk of Dementia: a meta-analysis of observational studies

(a)



Study	UPF Events	UPF Total	Standard Events	Standard Total	RR	95%-CI	Weight
Dearborn-Tomazos et al, 2019	708	4494	834	4553	0.86	[0.79; 0.94]	10.7%
Dobreva et al, 2022	209	8901	408	20883	1.20	[1.02; 1.42]	10.4%
Feng et al, 2020	293	951	466	4742	3.14	[2.76; 3.56]	10.6%
Filippini et al, 2020	19	34	24	50	1.16	[0.77; 1.76]	8.3%
Fu et al, 2022	128	1114	86	1114	1.49	[1.15; 1.93]	9.7%
Li et al, 2019	144	29633	127	29633	1.13	[0.89; 1.44]	9.9%
Pearson et al, 2016	370	3616	217	3616	1.71	[1.45; 2.00]	10.4%
Ylilauri et al, 2022	78	626	85	637	0.93	[0.70; 1.24]	9.4%
Zhang et al, 2021	170	19331	724	150758	1.83	[1.55; 2.16]	10.4%
Miao et al, 2021	160	437	275	1384	1.84	[1.57; 2.17]	10.4%
Random effects model		**69137**		**217370**	**1.44**	**[1.09; 1.90]**	**100.0%**

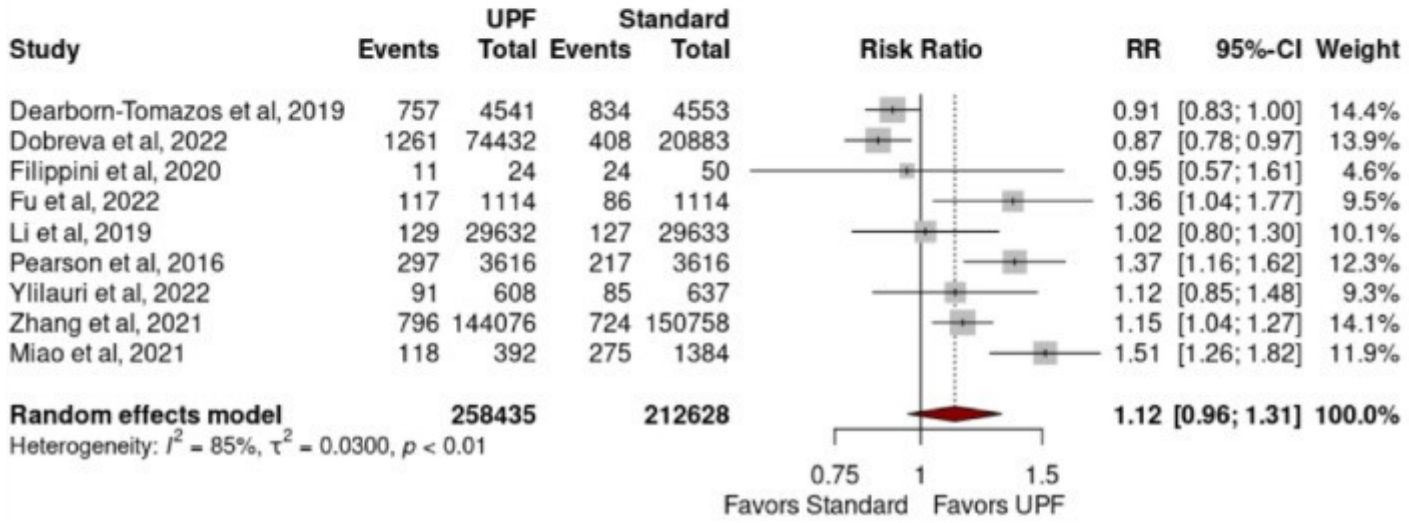
Heterogeneity: $I^2 = 97\%$, $\tau^2 = 0.1411$, $p < 0.01$

All-cause dementia

RR= 1.44 (95%CI 1.09-1.90)

For high vs. low UPFs consumption

(b)



Study	UPF Events	UPF Total	Standard Events	Standard Total	RR	95%-CI	Weight
Dearborn-Tomazos et al, 2019	757	4541	834	4553	0.91	[0.83; 1.00]	14.4%
Dobreva et al, 2022	1261	74432	408	20883	0.87	[0.78; 0.97]	13.9%
Filippini et al, 2020	11	24	24	50	0.95	[0.57; 1.61]	4.6%
Fu et al, 2022	117	1114	86	1114	1.36	[1.04; 1.77]	9.5%
Li et al, 2019	129	29632	127	29633	1.02	[0.80; 1.30]	10.1%
Pearson et al, 2016	297	3616	217	3616	1.37	[1.16; 1.62]	12.3%
Ylilauri et al, 2022	91	608	85	637	1.12	[0.85; 1.48]	9.3%
Zhang et al, 2021	796	144076	724	150758	1.15	[1.04; 1.27]	14.1%
Miao et al, 2021	118	392	275	1384	1.51	[1.26; 1.82]	11.9%
Random effects model		**258435**		**212628**	**1.12**	**[0.96; 1.31]**	**100.0%**

Heterogeneity: $I^2 = 85\%$, $\tau^2 = 0.0300$, $p < 0.01$

All-cause dementia

RR= 1.12 (95%CI 0.96-1.31)

For average vs. low UPFs consumption

Henney AE et al. J Neurol. 2024;271:198-210.

UPFs and multiple health outcomes: an umbrella review of meta-analyses

Lane MM et al. BMJ 2024 Feb 28:384:e077310.

Common mental disorder outcomes → **OR = 1.53; 95%CI 1.43-1.63**

(For high vs. low UPF intake)

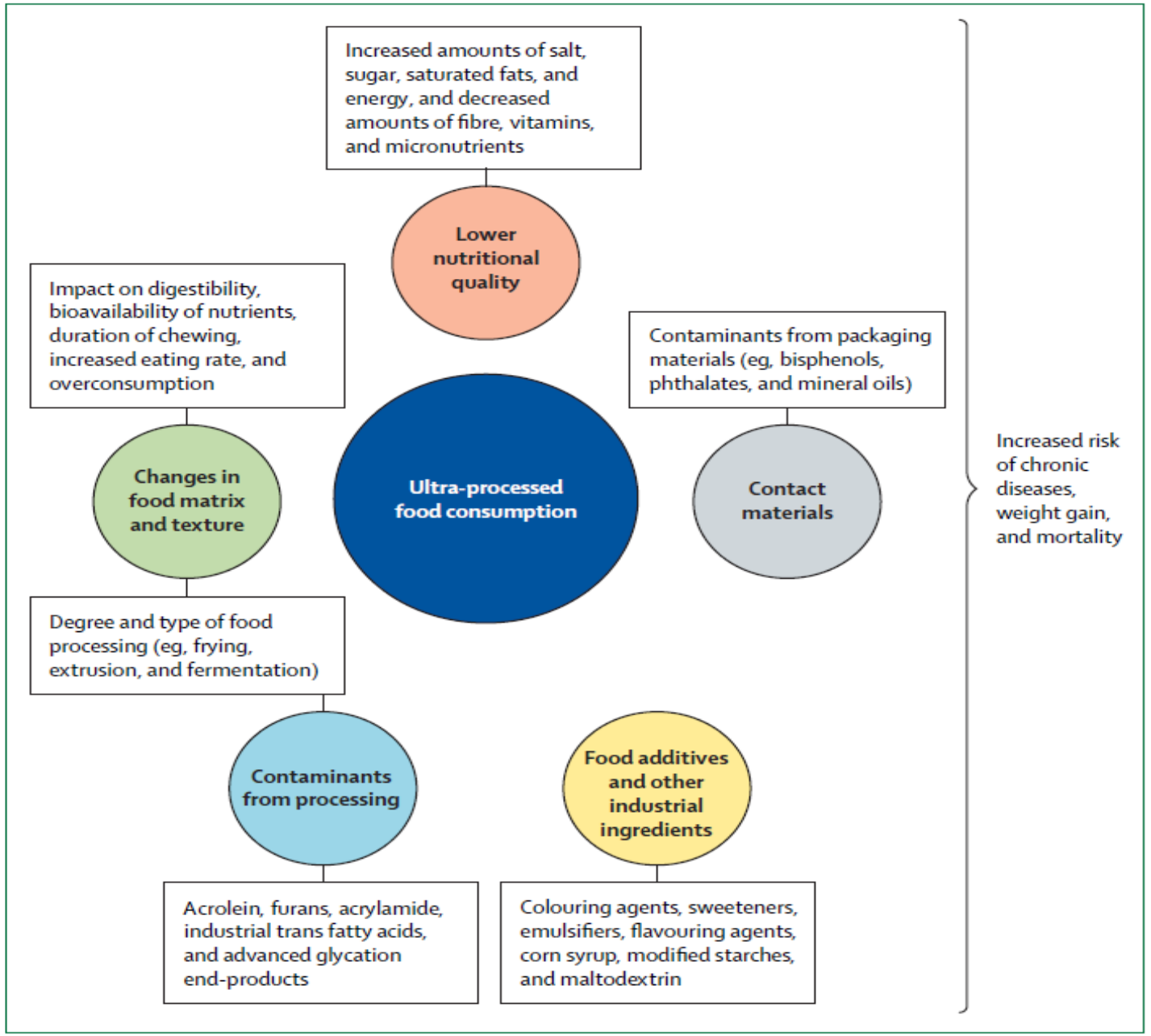
Incident depressive outcomes → **OR = 1.22; 95%CI 1.16-1.28**

Adverse sleep-related outcomes → **OR = 1.41; 95%CI 1.24-1.61**

Anxiety → **OR = 1.48; 95%CI 1.37-1.59**

What are the potential mechanisms linking diet to cognitive health?

Possible mechanisms underlying the associations between UPF and chronic disease



Increased inflammation

Gut dybiosis

Srour B et al. Lancet Gastroenterol Hepatol. 2022:S2468-1253(22)00169-8.

- **Increased levels of circulating proinflammatory cytokines have been associated with cognitive decline**

(Gomes Gonçalves N et al., 2023)

- **Dysbiosis may lead to an inflammatory state that can promote neuroinflammation and contribute to neuropsychiatric conditions**
- **and cognitive decline**

(Hoffman et al., 2023)

- **A traditional Mediterranean Diet possibly leads to the microbiota eubiosis reestablishment and to lower subclinical inflammation**

(Merra G et al., 2020
Bonaccio M et al., 2023)

Conclusions

1. A traditional Mediterranean Diet is reportedly associated with improved cognition and lower risk of dementia and Alzheimer disease

2. Ultra-processed food intake is an emerging risk factor for cognitive health

3. Dietary recommendations to prevent neurocognitive disorders should account for both diet quality and food processing

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