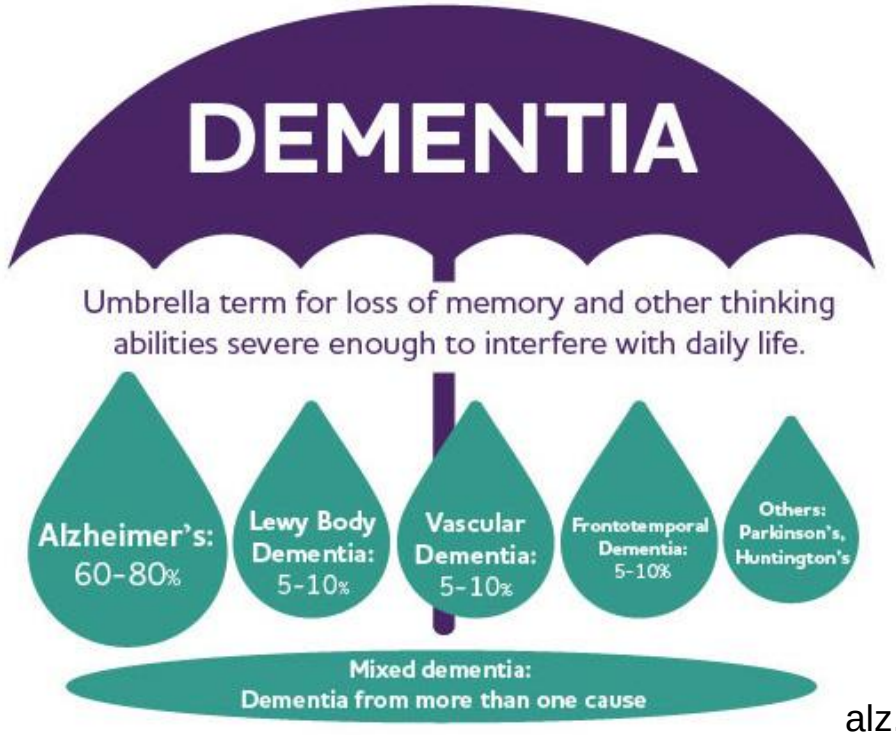
Northwestern Medicine®

Dietary Patterns and Alzheimer's Disease

RCCN: Promoting Healthy Aging Through Nutrition

July 20-21, 2023

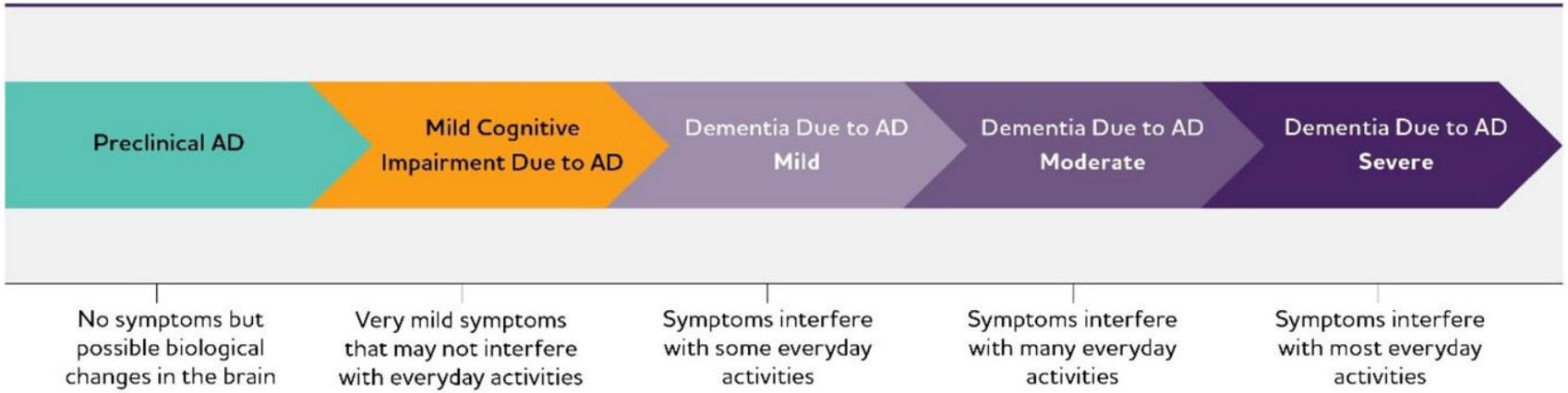
Marilyn Cornelis, PhD



alz.org

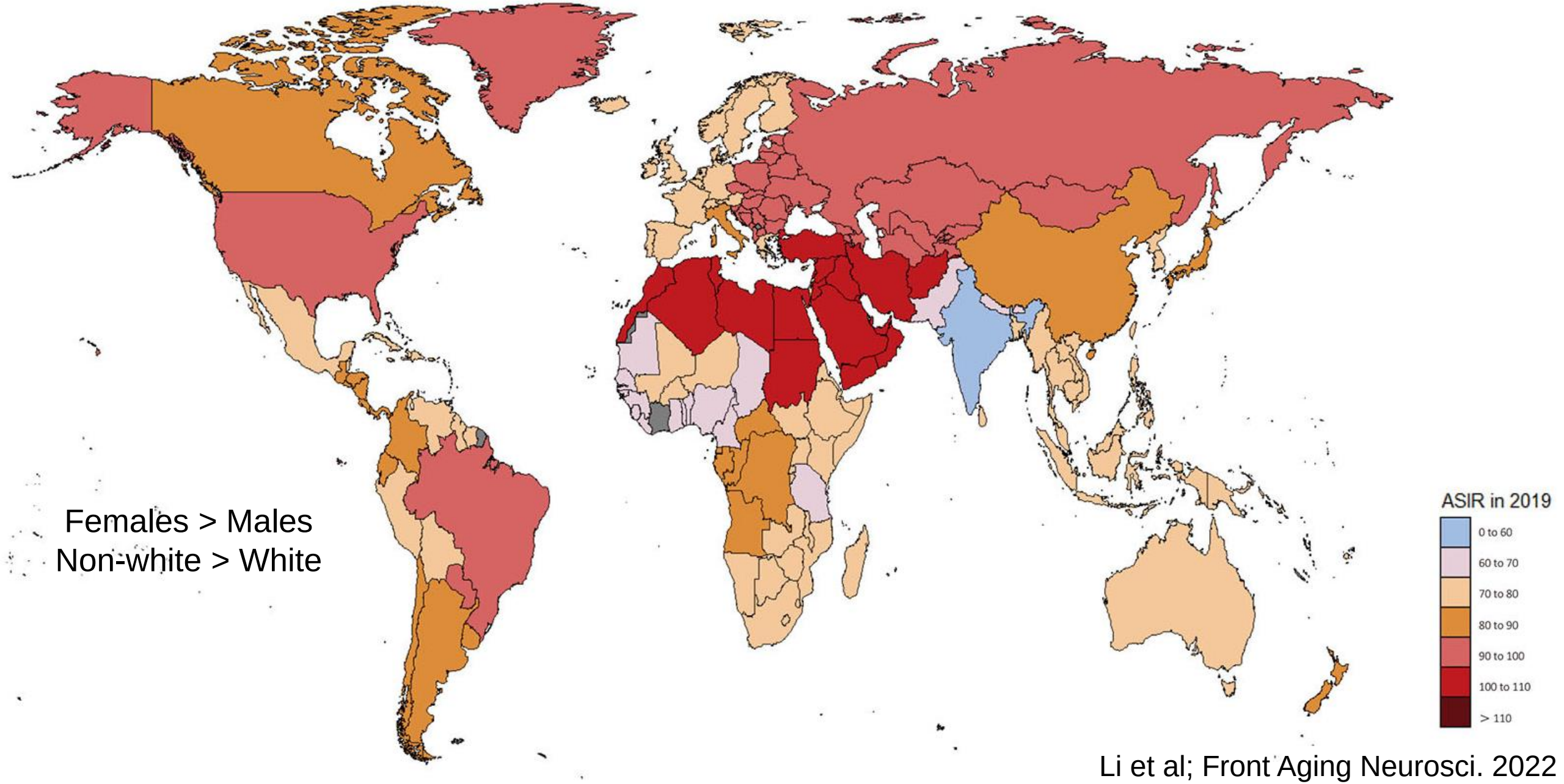
Common causes of dementia

- **Alzheimer's disease**
- Cerebrovascular disease
- Frontotemporal degeneration
- Hippocampal sclerosis
- Lewy body disease
- Mixed pathologies
- Parkinson's Disease



2023 Alzheimer's disease facts and figures. Alzheimers Dement. 2023

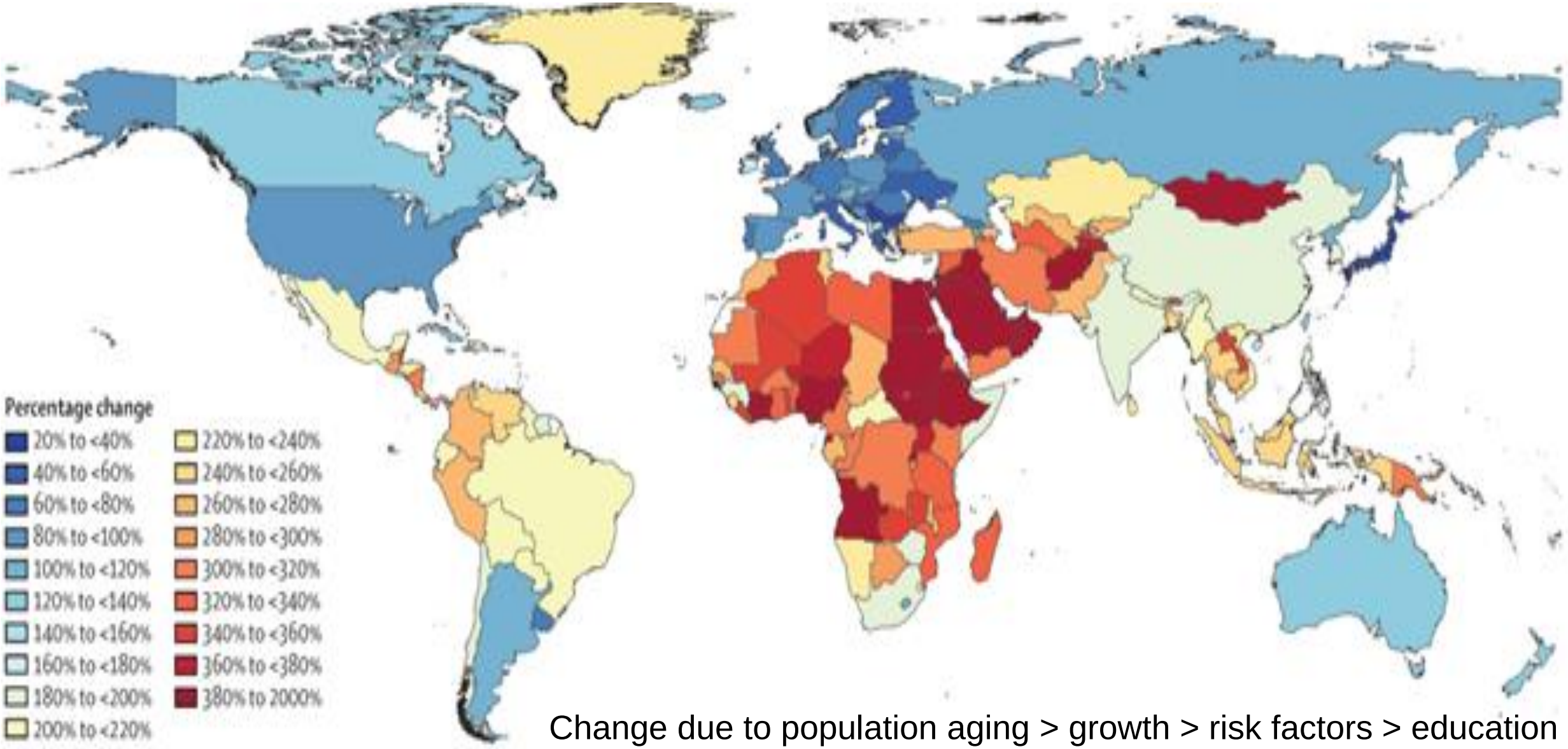
Age-standardized incidence rate (per 100,000) of dementia



Females > Males
Non-white > White

Li et al; Front Aging Neurosci. 2022

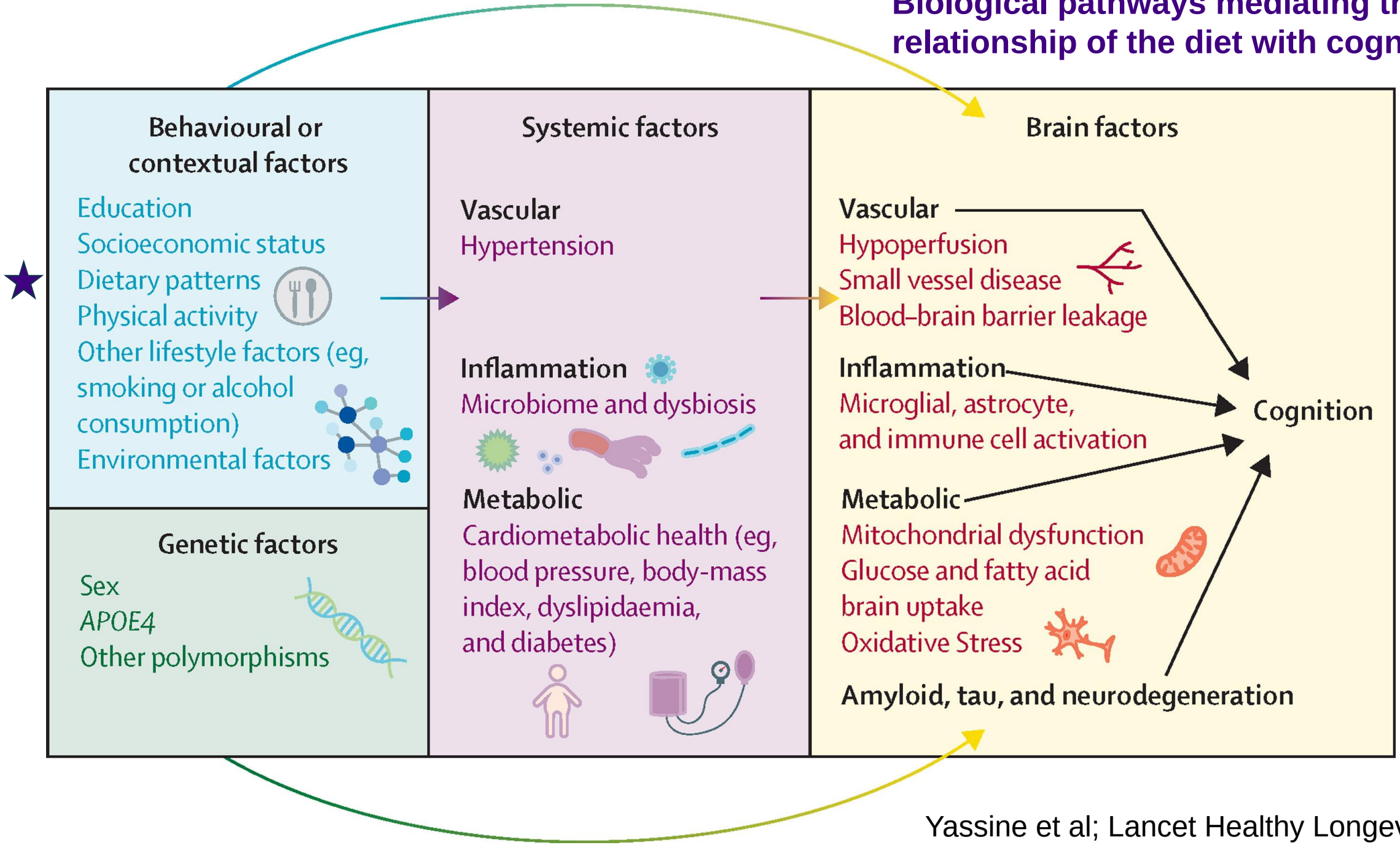
%change between 2019-2050 of all-age prevalence of dementia



Change due to population aging > growth > risk factors > education

GBD 2019 Dementia Forecasting Collaborators. Lancet Public Health. 2022

Biological pathways mediating the relationship of the diet with cognition



Yassine et al; Lancet Healthy Longev; 2022

Single Food/Nutrient Approach










Does not account for synergies between nutrients/food components
Does not reflect real-life setting

Dietary Pattern Approach

1. Evidence-based methods

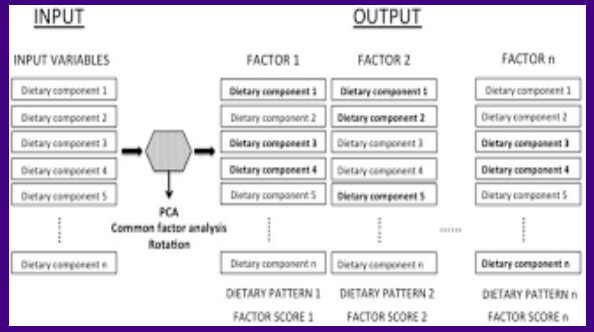
   Apply DPs developed for cardiometabolic health

   Apply DPs developed specifically for dementia

2. Data-driven methods

   Subgroups defined by food preferences/behaviors (environment & genetics)

   Sample/population specific



Mediterranean Dietary Pattern

Diet and overall survival in elderly people

Antonia Trichopoulou, Antigone Kouris-Blazos, Mark L Wahlqvist, Charalambos Gnardellis, Pagona Lagiou, Evangelos Polychronopoulos, Tonia Vassilakou, Loren Lipworth, Dimitrios Trichopoulos

Abstract

***Objective*—To assess the influence of a specific dietary pattern on overall survival.**

***Design*—Cohort study.**

***Setting*—Three rural Greek villages, the data from which were collected as part of an international cross cultural study of food habits in later life.**

***Subjects*—182 elderly residents of the three villages.**

***Main outcome measure*—Overall mortality.**

***Results*—Diet was assessed with a validated extensive semiquantitative questionnaire on food intake. A one unit increase in diet score, devised a priori on the basis of eight component characteristics of the traditional common diet in the Mediterranean region, was associated with a significant 17% reduction in overall mortality (95% confidence interval 1% to 31%).**

***Conclusion*—A diet meeting currently understood health criteria does predict survival among people.**

Table 3—*Rate ratio estimates (95% confidence intervals) derived from Cox's proportional hazards model for diet score as predictor* of survival time*

Predictor variable (category or unit)	P value (two tailed)	Rate ratio* (95% confidence interval)
Age (1 year)	$<10^{-4}$	1·12 (1·06 to 1·17)
Sex (female 0, male 1)	0·87	1·06 (0·55 to 2·03)
Smoking status (non-smoker 0, smoker 1)	0·16	1·67 (0·82 to 3·41)
Diet score (1 unit)	0·04	0·83 (0·69 to 0·99)

*From model including terms for age, sex, smoking status, and total diet score; components of the score were adjusted to 2500 kcal for men and 2000 kcal for women.

Table 4—*Rate ratio estimates (95% confidence intervals) derived from alternative Cox's models with each of eight components* replacing diet score*

Component (category or unit)	P value (two tailed)	Rate ratio† (95% confidence interval)
Vegetable intake (20 g)	0·20	0·97 (0·93 to 1·02)
Legume intake (20 g)	0·13	0·90 (0·78 to 1·03)
Fruit and nut intake (20 g)	0·75	1·01 (0·97 to 1·04)
Cereal intake (20 g)	0·49	1·02 (0·97 to 1·07)
Dairy intake (20 g)	0·01	1·04 (1·01 to 1·07)
Meat intake (20 g)	0·65	1·02 (0·93 to 1·12)
Monounsaturated:saturated fat ratio (1 unit)	0·14	0·60 (0·31 to 1·18)
Ethanol intake (10 g)	0·47	1·07 (0·89 to 1·28)

*Adjusted to 2500 kcal for men and 2000 kcal for women.
†From model including terms for age, sex, and smoking status.

Evolution of Mediterranean Dietary Pattern

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 26, 2003 VOL. 348 NO. 26

Adherence to a Mediterranean Diet and Survival in a Greek Population

Antonia Trichopoulou, M.D., Tina Costacou, Ph.D., Christina Bamia, Ph.D., and Dimitrios Trichopoulos, M.D.

Positive Foods

Vegetables (median)

Legumes (median)

Fruit & nuts (median)

Cereal (median)

* Fish (median) *

MUFA/SFA (median)

Negative Foods

Meat/poultry products (median)

Dairy (median)

Dose-dependent

Ethanol (moderate, g)

> 20 variations of score

Distribution vs specific cut-points

Most model Trichopoulou (Greece) and alternative MedD (US)

Zaragoza-Martí A et al, BMJ Open; 2018
Hutchins-Wiese et al, BJN; 2021

Mediterranean Dietary Pattern & Cognitive Disorders

Journal of *Clinical Medicine* 2021

Alzheimer's Disease, Mild Cognitive Impairment and Mediterranean Diet. A Systematic Review and Dose-Response Meta-Analysis

Frontiers in Nutrition 2022

Association between the mediterranean diet and cognitive health among healthy adults: A systematic review and meta-analysis

Jialei Fu[1], Li-Juan Tan[1], Jung Eun Lee[2] and Sangah Shin[1]*

nutrients 2023

Whole Dietary Patterns, Cognitive Decline and Cognitive Disorders: A Systematic Review of Prospective and Intervention Studies

Rebecca F. Townsend [1], Danielle Logan [1], Roisin F. O'Neill [1], Federica Prinelli [2], Jayne V. Woodside [1,3] and Claire T. McEvoy [1,3,*]

↓ Mild cognitive impairment (MCI) & dementia

Dietary Approaches to Stop Hypertension (DASH) Dietary Pattern

The New England
Journal of Medicine

VOLUME 336 APRIL 17, 1997 NUMBER 16

A CLINICAL TRIAL OF THE EFFECTS OF DIETARY PATTERNS ON BLOOD PRESSURE

LAWRENCE J. APPEL, M.D., M.P.H., THOMAS J. MOORE, M.D., EVA OBARZANEK, PH.D., WILLIAM M. VOLLMER, PH.D., LAURA P. SVETKEY, M.D., M.H.S., FRANK M. SACKS, M.D., GEORGE A. BRAY, M.D., THOMAS M. VOGT, M.D., M.P.H., JEFFREY A. CUTLER, M.D., MARLENE M. WINDHAUSER, PH.D., R.D., PAO-HWA LIN, PH.D., AND NJERI KARANJA, PH.D., FOR THE DASH COLLABORATIVE RESEARCH GROUP*

Food Group	Servings Per Day			Serving Sizes
	1,600 Calories	2,000 Calories	2,600 Calories	
Grains*	6	6–8	10–11	1 slice bread 1 oz dry cereal† ½ cup cooked rice, pasta, or cereal
Vegetables	3–4	4–5	5–6	1 cup raw leafy vegetable ½ cup cut-up raw or cooked vegetable ½ cup vegetable juice
Fruits	4	4–5	5–6	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice
Fat-free or low-fat milk and milk products	2–3	2–3	3	1 cup milk or yogurt 1½ oz cheese
Lean meats, poultry, and fish	3–6	6 or less	6	1 oz cooked meats, poultry, or fish 1 egg‡
Nuts, seeds, and legumes	3 per week	4–5 per week	1	⅓ cup or 1½ oz nuts 2 Tbsp peanut butter 2 Tbsp or ½ oz seeds ½ cup cooked legumes (dry beans and peas)
Fats and oils§	2	2–3	3	1 tsp soft margarine 1 tsp vegetable oil 1 Tbsp mayonnaise 2 Tbsp salad dressing
Sweets and added sugars	0	5 or less per week	≤2	1 Tbsp sugar 1 Tbsp jelly or jam ½ cup sorbet, gelatin 1 cup lemonade

2006

IN BRIEF:

Your Guide To Lowering Your Blood Pressure With DASH

National Heart, Lung, and Blood Institute

Miller et al. AJCN; 2013

Individual components	Standards for maximum score			
	Dixon's DASH index[2]	Mellen's DASH index[3]	Fung's DASH index[4]	Günther's DASH index[5,6]
	Sex-specific (men/women)	Same standards for men and women	Sex-specific	Standards based on sex, age, and activity level
Dietary components for which greater intakes receive higher scores				
Total fruit	≥4 servings/d[7]	—	Fifth quintile	≥4 servings/d[7]
Total vegetables	≥4/≥3 servings/d[7,8]	—	—	≥4 servings/d[7]
Vegetables without potatoes	—	—	Fifth quintile	
Total grains	—	—	—	≥6 servings/d[7]
Whole grains	≥4.7/≥4 servings/d[7,8]	—	Fifth quintile	—
High-fiber grains	—	—	—	≥50% of total grain servings/d[7,9]
Total dairy products	≥2 servings/d[7]	—	—	≥2 servings/d[7]
Low-fat dairy products	—	—	Fifth quintile	≥75% of total dairy servings/d[7,9]
Nuts, seeds, legumes	≥4/≥3 servings/d[7]	—	Fifth quintile	≥4 servings/wk[7]
Protein	—	≥18% of total daily kcal	—	—
Fiber	—	≥14.8 g/1000 kcal per day	—	—
Magnesium	—	≥238 mg/1000 kcal per day	—	—
Calcium	—	≥590 mg/1000 kcal per day	—	—
Potassium	—	≥2238 mg/1000 kcal per day	—	—
Dietary components for which lower intakes receive higher scores				
Meat/meat equivalents	<6 oz (170 g)/d[7]	—	—	—
Meat, poultry, fish, eggs	—	—	—	≤2 servings/d[7]
Red and processed meat	—	—	First quintile	—
Sugar-sweetened beverages	—	—	First quintile	—
Sweets	—	—	—	≤5 servings/wk[7]
Fats, oils	—	—	—	≤3 servings/d[7]
Added sugar	≤3% of total daily kcal	—	—	—
Alcoholic beverages	≤2/≤1 drink/d[7]	—	—	—
Total fat	—	≤27% of total daily kcal	—	—
Saturated fat	≤5% of total daily kcal	≤6% of total daily kcal	—	—
Cholesterol	—	≤71.4 mg/1000 kcal per day	—	—
Sodium	—	≤1143 mg/1000 kcal per day	1st quintile	—
Total score (points)	0–9	0–9	8–40	0–80

DASH Dietary Pattern & Cognitive Disorders

Dietary patterns in middle age: effects on concurrent neurocognition and risk of age-related cognitive decline

Sarah Gauci, Lauren M. Young, Lizanne Arnoldy, Annie-Claude Lassemillante, Andrew Scholey, and Andrew Pipingas

Nutrition Reviews® Vol. 80(5):1129–1159 2021

nutrients 2023

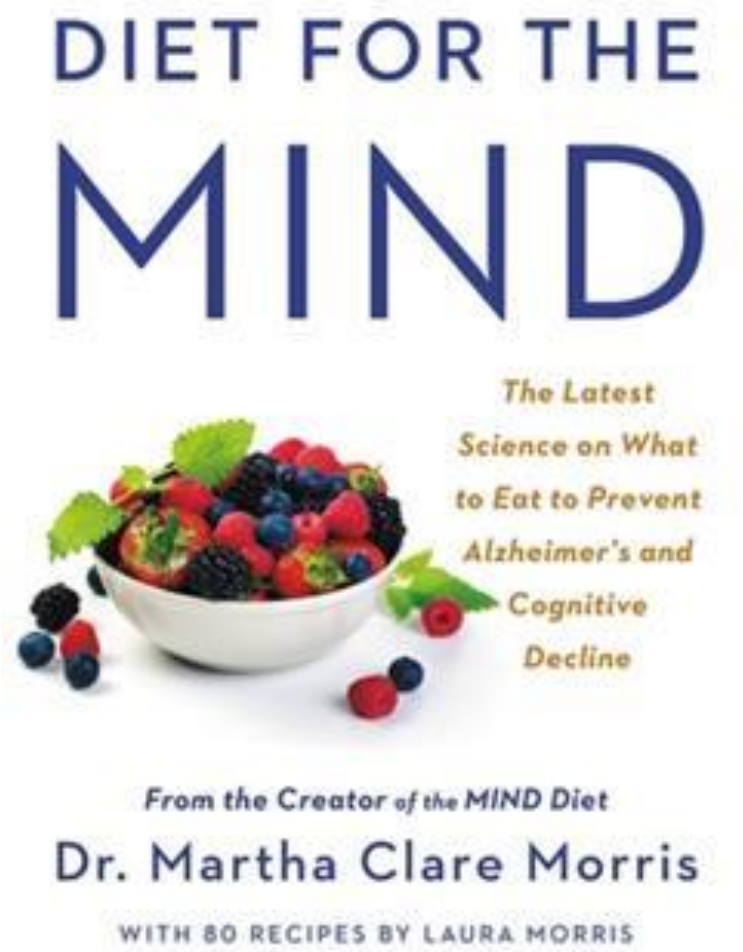
Whole Dietary Patterns, Cognitive Decline and Cognitive Disorders: A Systematic Review of Prospective and Intervention Studies

Rebecca F. Townsend [1], Danielle Logan [1], Roisin F. O'Neill [1], Federica Prinelli [2], Jayne V. Woodside [1,3] and Claire T. McEvoy [1,3,*]

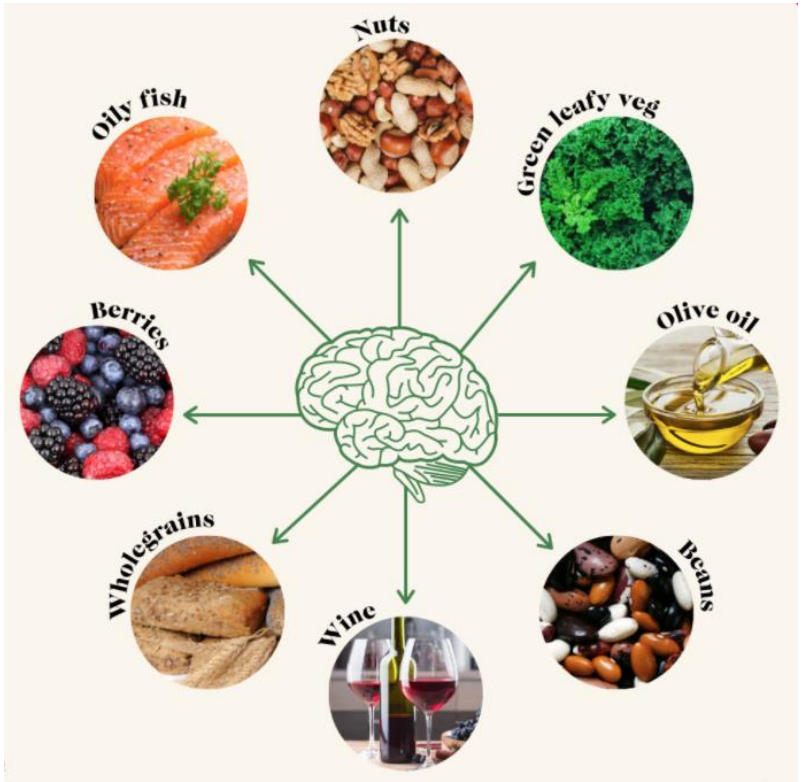
Overall: no/weak support for protection against cognitive disorders

Mediterranean-DASH Diet Intervention for Neurodegenerative Delay (MIND)

Morris et al. Alzheimers Dement. 2015



Rush Memory and Aging Project (n=923, Chicago)
Mean age 81 (range: 58-98)
Mean follow-up 4.5 years



https://www.theguthealthdoctor.com/the-mind-diet

Epstein et al, J Acad Nutr Diet 2012

Panagiotakos et al, Prev Med, 2007

DASH*		MedDiet†		MIND	
DASH components	Max score	Mediterranean diet components	Max score	MIND components	Max score
Total grains ≥7/d	1	Nonrefined Grains >4/d	5	Whole Grains ≥3/d	1
Vegetables ≥4/d	1	Vegetables >4/d	5	Green Leafy ≥6/wk	1
		Potatoes >2/d	5	Other Vegetables ≥1/d	1
Fruits ≥4/d	1	Fruits >3/d	5	Berries ≥2/wk	1
Dairy ≥2/d	1	Full-fat Dairy ≤10/wk	5		
Meat, poultry and fish ≤2/d	1	Red meat ≤1/wk	5	Red Meats and products <4/wk	1
		Fish >6/wk	5	Fish ≥1/wk	1
		Poultry ≤3/wk	5	Poultry ≥2/wk	1
Nuts, seeds & legumes ≥4/wk	1	Legumes, nuts & beans >6/wk	5	Beans >3/wk	1
				Nuts ≥5/wk	1
				Fast/fried food <1/wk	1
Total fat ≤27% of kcal	1				
Saturated fat ≤6% of kcal	1				
		Olive oil ≥1/d	5	Olive Oil primary oil	1
				Butter, margarine <1 T/d	1
				Cheese <1/wk	1
Sweets ≤5/wk	1			Pastries, sweets <5/wk	1
Sodium ≤2400 mg/d	1				
		Alcohol <300 mL/d but >0	5	Alcohol/wine 1/d	1

T1:	Reference	Reference	Reference
T2 HR:	0.98	0.81	**0.65***
T3 HR:	**0.61***	**0.46***	**0.47***

JAMA Psychiatry | Original Investigation

2023

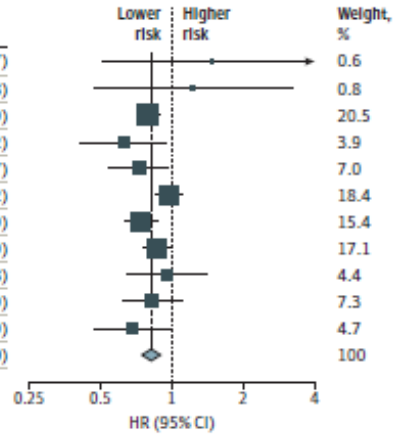
Association of the Mediterranean Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) Diet With the Risk of Dementia

Hui Chen, BS; Klodian Dhana, PhD; Yuhui Huang, BS; Liyan Huang, BS; Yang Tao, MS; Xiaoran Liu, PhD; Debora Melo van Lent, PhD; Yan Zheng, MD, PhD; Alberto Ascherio, MD, DrPH; Walter Willett, MD, DrPH; Changzheng Yuan, ScD

Figure 2. Meta-analysis of Multivariable-Adjusted Hazard Ratio (HR) and 95% CI for Incident Dementia Comparing the Highest vs Lowest Tertile of Mediterranean–Dietary Approaches to Stop Hypertension (DASH) Intervention for Neurodegenerative Delay (MIND) Diet Score

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: $I^2 = 35\%$; $\tau^2 = 0.0064$ ($P = .12$)



↓ All-cause dementia

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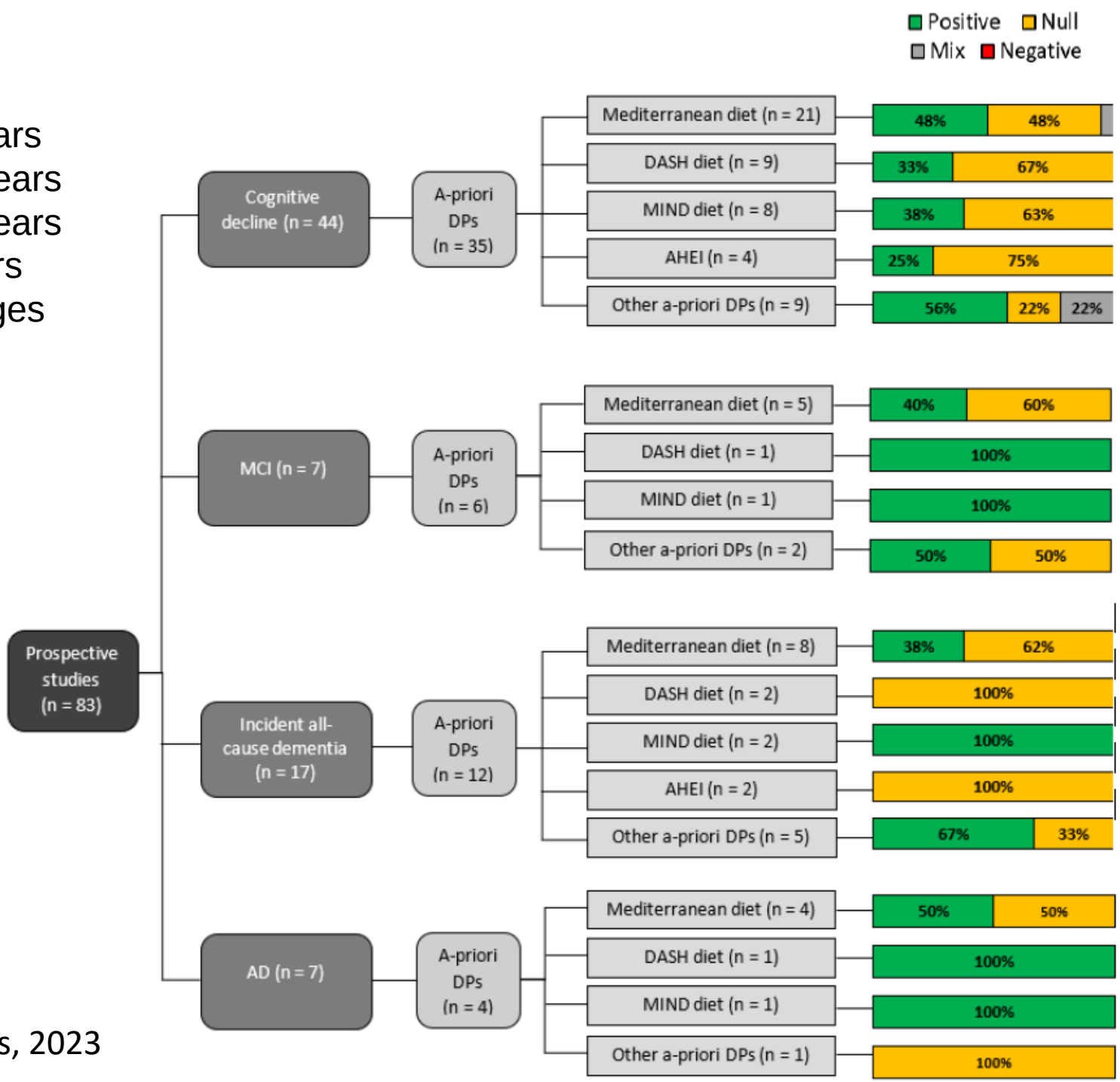
Whole Dietary Patterns, Cognitive Decline and Cognitive Disorders: A Systematic Review of Prospective and Intervention Studies

Rebecca F. Townsend [1], Danielle Logan [1], Roisin F. O'Neill [1], Federica Prinelli [2], Jayne V. Woodside [1,3] and Claire T. McEvoy [1,3,*]

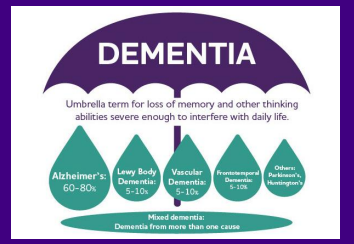
2 studies: 35–50 years
19 studies: 51–64 years
38 studies: 65–74 years
13 studies: 75+ years
11 studies: mixed ages



Townsend et al, Nutrients, 2023

Summarizing the evidence is challenging

- Classic limitations: measurement error, confounding
- Dementia ascertainment (compare to cardiovascular)
  - underlying cause
  - clinical exam vs health records
- Diet scores
  - heterogeneity (meta-analyze?)
  - population/culture specific?



Adherence to MIND Diet, Genetic Susceptibility, and Incident Dementia in Three US Cohorts

Thanh Huyen T. Vu [1,†], Todd Beck [2,†], David A. Bennett [3], Julie A. Schneider [3], Kathleen M. Hayden [4], Aladdin H. Shadyab [5], Kumar B. Rajan [2], Martha Clare Morris [‡] and Marilyn C. Cornelis [1,*]

Nutrients, 2022

Chicago Health and Aging Project (CHAP, n = 2449):	— incident dementia & cognitive decline
Rush Memory and Aging Project (MAP, n = 725)	↓ incident dementia & cognitive decline
Women's Health Initiative Memory Study (WHIMS, n = 5308)	↓ incident (probable) dementia

MIND Dietary Pattern and Its Association with Cognition and Incident Dementia in the UK Biobank

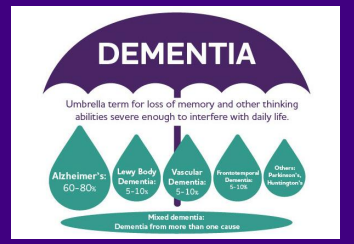
Marilyn C. Cornelis [1,*], Puja Agarwal [2,3], Thomas M. Holland [2,4] and Rob M. van Dam [5]

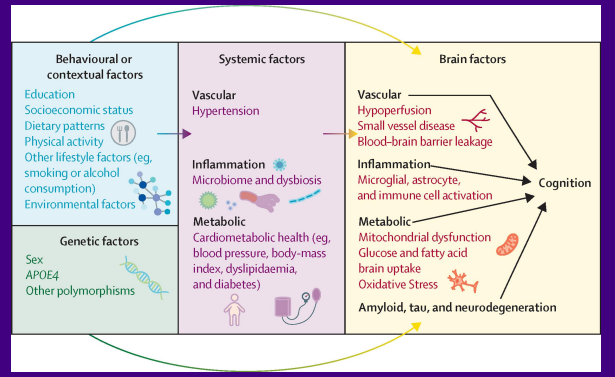
Nutrients, 2022

N=78,663; aged 55+ years
Null overall
↓ Incident dementia among females (HR=0.87 per SD, p=0.008) but not males (1.09, p=0.11) (p=0.008 for interaction).
Similar results for AHEI-2010

Summarizing the evidence is challenging

- Classic limitations: measurement error, confounding
- Dementia ascertainment (compare to cardiovascular)
  - underlying cause
  - clinical exam vs health records
- Diet scores
  - heterogeneity (meta-analyze?)
  - population/culture specific?
- Dementia pathophysiology
  - food/nutrient- pathway specific?
- Diet-dementia temporal relationship





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Marth Clare Morris