Prioritizing Nutrition for the Brain; Affirming National Seafood Nutrition Policy

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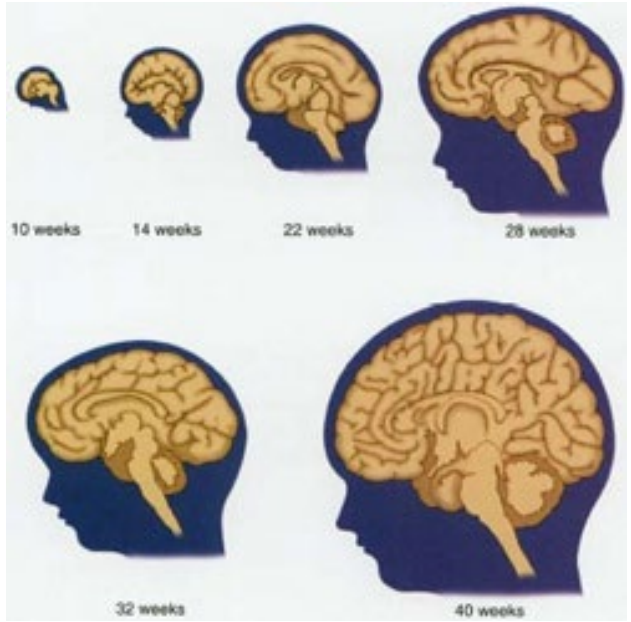
STATE OF THE SCIENCE SYMPOSIUM

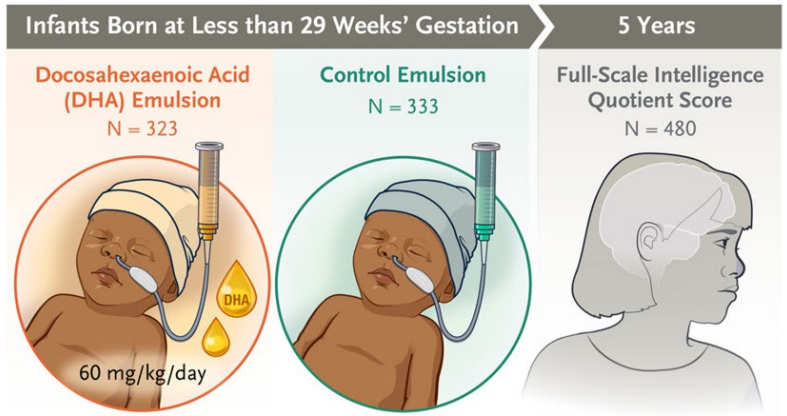
2022: Two RCT nutrient studies showing long term improvement in neurocognitive function

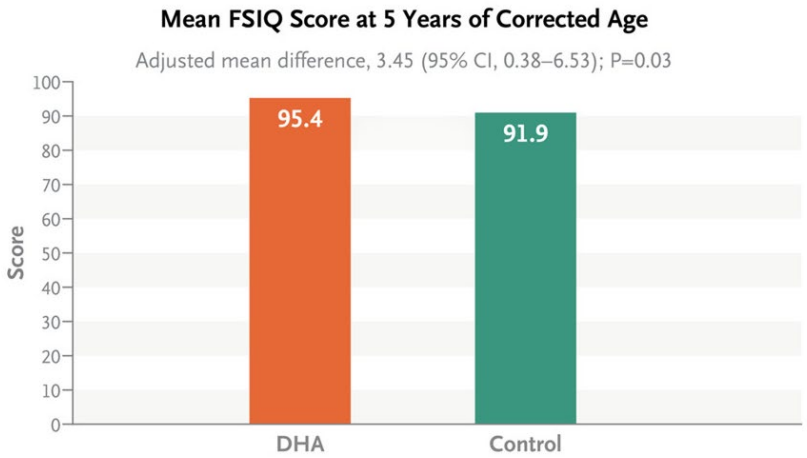
- Gould et al., New England Journal of Medicine.
  - DHA provided to preterm infants caused in +3.5 IQ point increase 5 years later (at age 5)
- Stephenson et al., American Journal of Clinical Nutrition
  - Altered PUFA, including DHA, provided to malnourished toddlers as therapeutic food caused improved neurocognitive performance 6 months later

- Why are these notable studies?
  - Randomized controlled trials (RCTs) with neurocognitive outcomes are rare because of expense and difficulty compared to observational studies (e.g. prospective cohort trials).
  - Long term assessments tax research team and participant resources

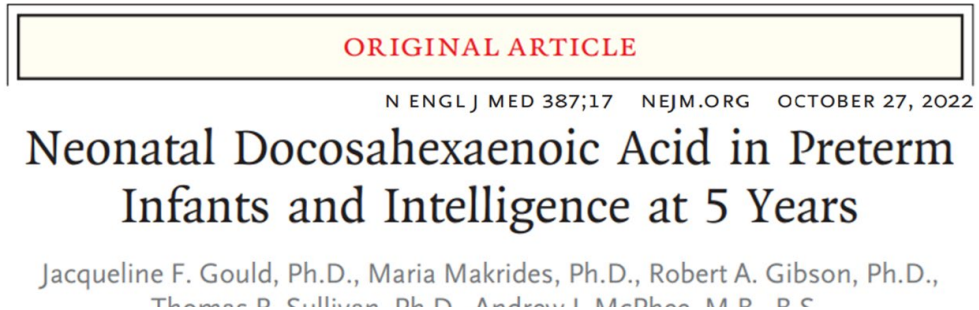


Long term higher IQ at 5 years with omega-3 DHA



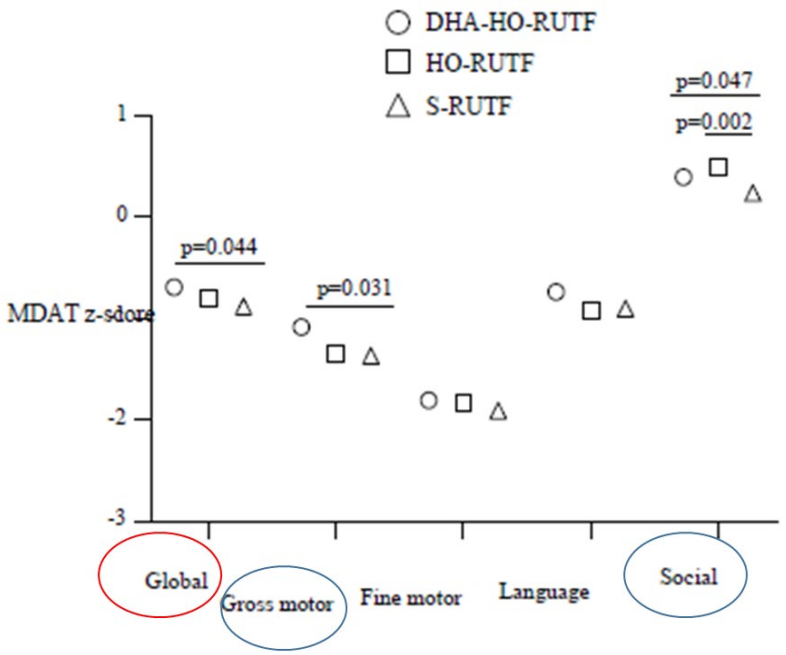


- Very premature infants provided with DHA in the first ~12 weeks of life
  - = last trimester if not premature
- At school age, 5 years old, no intervention
- +3.5 IQ points

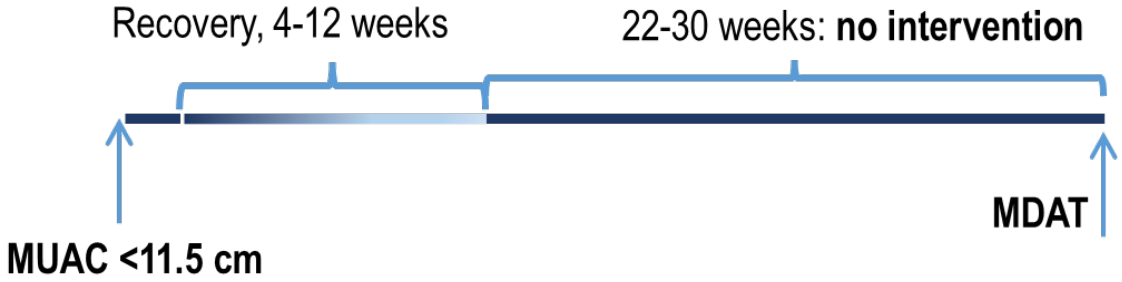


Long term improvement in neurocognitive performance with omega-3 DHA

- Malawi Developmental Assessment Tool (MDAT) better in
  - DHA-HO=hi DHA, low linoleic
  - Six months post-dose



Malawi Developmental Assessment Tool domain



RUTF, per 100 kcal
- **LA <780mg**
- **ALA >110 mg**
- **DHA allowed**

Previously proposed
- LA <1,110mg
- ALA >33mg

Low linoleic acid foods with added DHA given to Malawian children with severe acute malnutrition improve cognition: a randomized, triple-blinded, controlled clinical trial *Am J Clin Nutr* 2022;115:1322–1333

Kevin Stephenson,[1] Meghan Callaghan-Gillespie,[2] Kenneth Maleta,[3] Minyanga Nkhoma,[3] Matthews George,[3] Hui Gyu Park,[4] Reginald Lee,[2] Iona Humphries-Cuff,[5] R J Scott Lacombe,[4] Donna R Wegner,[2] Richard L Canfield,[4] J Thomas Brenna,[4,6] and Mark J Manary[2,3,7]

2022 Malnutrition vs. Brain famine

Prostaglandins, Leukotrienes and Essential Fatty Acids 180 (2022) 102427

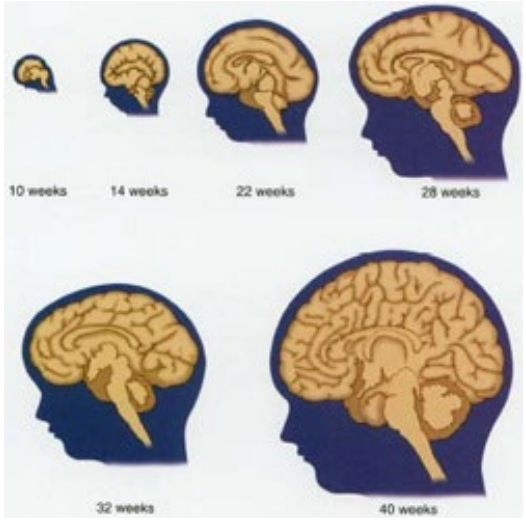
Neurodevelopment, nutrition and genetics. A contemporary retrospective on neurocognitive health on the occasion of the 100th anniversary of the National Institute of Nutrition, Hyderabad, India

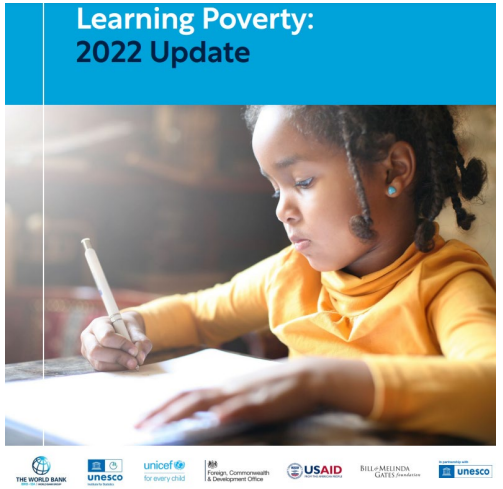
Michael A. Crawford [a], Yiqun Wang [a], David E. Marsh [a], Mark R. Johnson [a], Enitan Ogundipe [a], Ahamed Ibrahim [c], Hemalatha Rajkumar [c], S. Kowsalya [d], Kumar S.D. Kothapalli [b,*], J.T. Brenna [b,*]

- Globally, alleviation of malnutrition focuses on the diseases of adults and, for children, body growth = calories and protein
- **Brain famine** results from shortage of nutrients required for brain development
  - Omega-3, Iodine, Selenium, Zinc, Iron, …
- Brain disorders, seldom listed among Non-Communicable Diseases, tops the global burden of disease
- Enduring balanced supply of brain supportive foods should be a global priority
- *Equity and equality come together in properly nourishing mothers and babies*

Food as Medicine (?)
a subset of *Food for Health*

- Food as Medicine is a slogan that resonates – great
- But, *pregnancy, lactation, infancy and childhood* are not diseases in need of treatment or cures
- Brain development requires specialized nutritional support – not exactly medicine
- Good food is the base requirement for good health
- *Food for Health*
  - *Most importantly, <u>brain health</u>*
- What food?



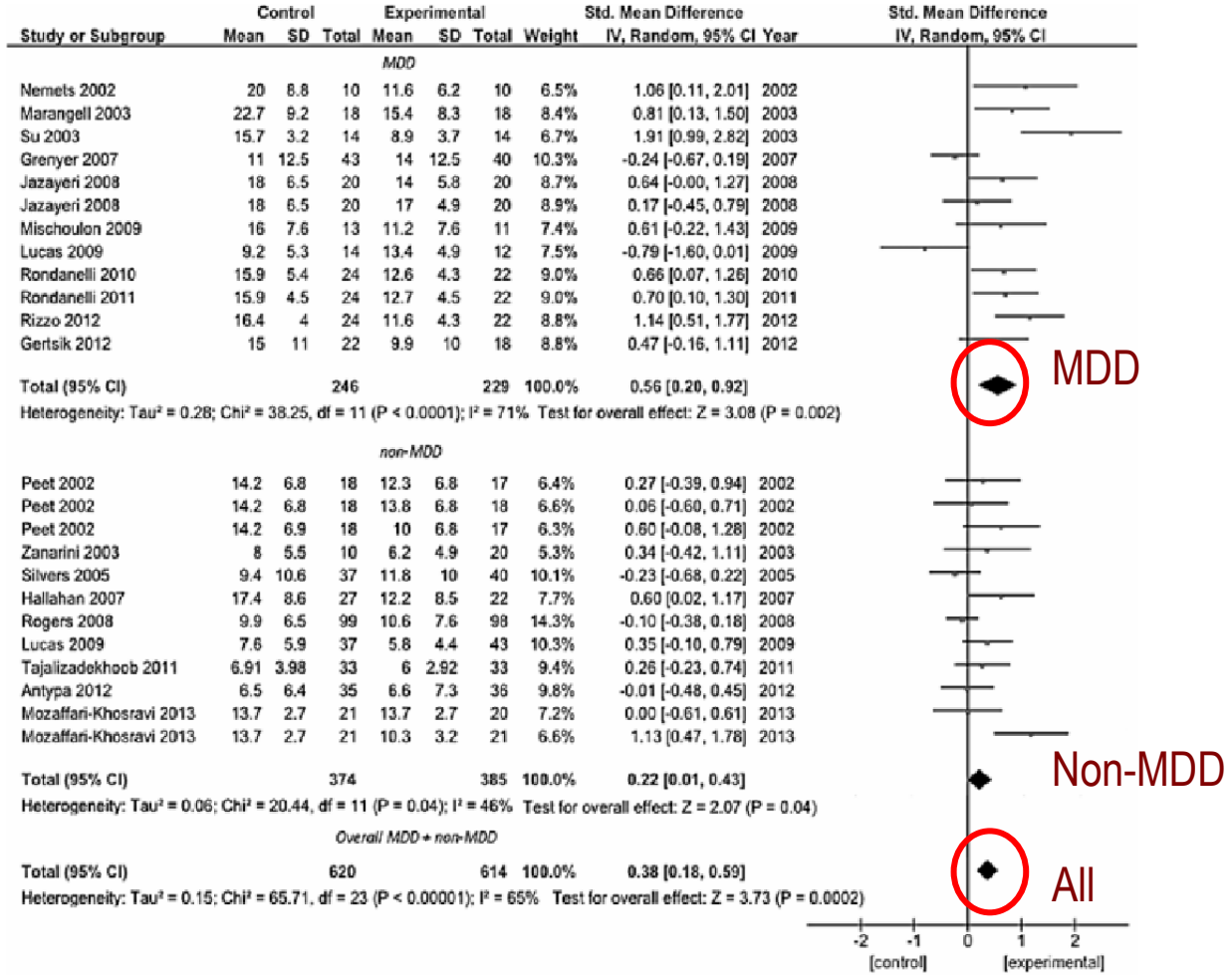


OPEN ACCESS Freely available online PLOS ONE

Role of Omega-3 Fatty Acids in the Treatment of Depressive Disorders: A Comprehensive Meta-Analysis of Randomized Clinical Trials

Giuseppe Grosso[1]*, Andrzej Pajak[2], Stefano Marventano[3], Sabrina Castellano[1], Fabio Galvano[1], Claudio Bucolo[1], Filippo Drago[1], Filippo Caraci[4,5]

1 Department of Clinical and Molecular Biomedicine, Section of Pharmacology and Biochemistry, University of Catania, Catania, Italy, 2 Department of Epidemiology and Population Studies, Jagiellonian University Medical College, Krakow, Poland, 3 Department "G.F. Ingrassia", Section of Hygiene and Public Health, University of Catania, Catania, Italy, 4 Department of Educational Sciences, University of Catania, Catania, Italy, 5 IRCCS Associazione Oasi Maria S.S. – Institute for Research on Mental Retardation and Brain Aging, Troina, Enna, Italy



Omega-3 works Depression & EPA

- Studies using EPA and DHA treatment for depression
- MDD: Studies on diagnosed Major Depressive Disorder
  - Depression assessed by psychiatric health care provider
- Non-MDD
  - Depression assessed by questionnaire
- Both MDD and non-MDD respond to EPA-dominant intake.

Reflection of predominant LA in industrialized country diets?

2025 Dietary Guidelines Advisory Committee Updating 2015 evidence for neurocognition

Scientific Questions

The 2025 Dietary Guidelines Advisory Committee (Committee) is examining a list of prioritized scientific questions, informed by the proposed list of scientific questions identified by HHS and USDA. The Committee divided into subcommittees to conduct its evidence review. Each question is addressed by one subcommittee; however, some topics (like dietary patterns) and populations (like older adults) are addressed in multiple questions and

Subcommittee 1: Dietary Patterns and Specific Dietary Pattern Components Across Life Stages
Systematic Review Questions:
What is the relationship between dietary patterns consumed and risk of cognitive decline, dementia, and Alzheimer's disease?
What is the relationship between dietary patterns consumed and risk of depression?

USDA

Scientific Report of the 2015 Dietary Guidelines Advisory Committee

Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture

DGAC **2015**
Dietary Patterns and Neurological-Psychological Illness

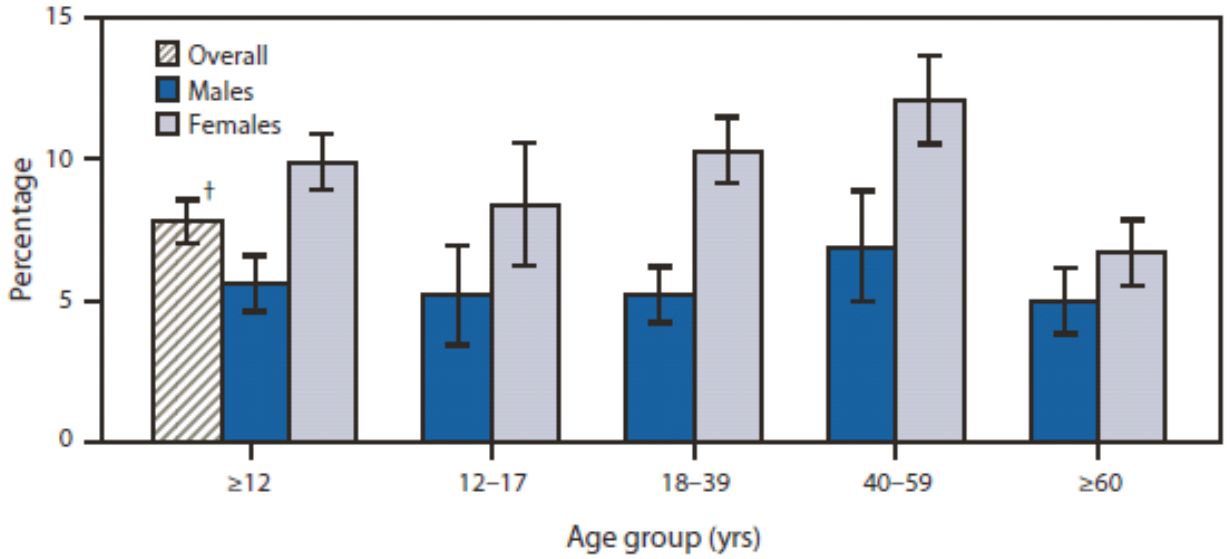
What is the relationship between dietary patterns and depression?

What is the relationship between dietary patterns and age-related cognitive impairment, dementia, and Alzheimer's disease?

NEL Systematic Review

Tom Brenna

U.S. Scope of Depression



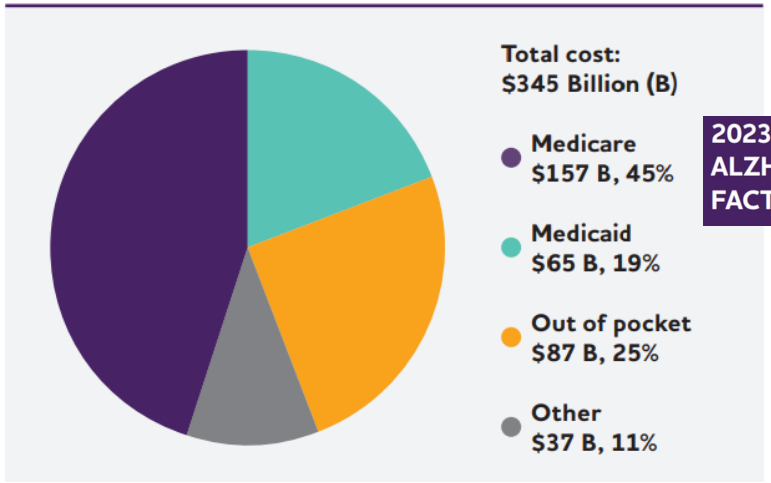
- In any 2-week period, 8% of Americans 12 years of age and older experienced depression
  - **21.3 million Americans**, were depressed according to NHANES screening 2007-2010
- Approximately 80% of persons with depression reported some level of functional impairment because of their depression, and 27% reported serious difficulties in work and home life.

Morbidity and Mortality Weekly Report (MMWR), January 6, 2012 / 60(51);1747
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6051a7.htm?s_cid=mm6051a7_w

Magnitude of age-related cognitive decline (2023)

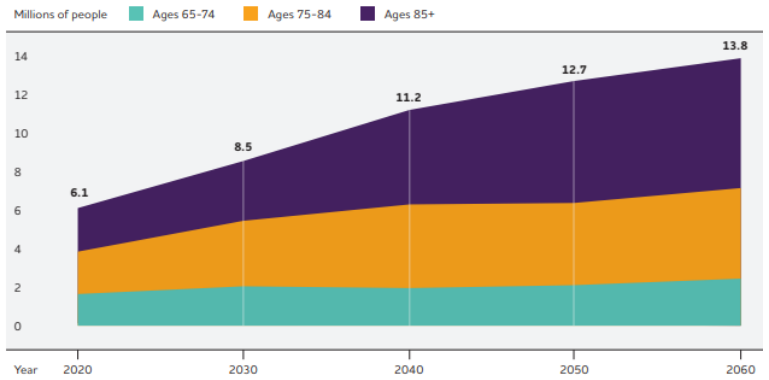
- Estimates and projections from the Alzheimer's Association and Lancet place age-related dementias currently at fractions of $Trillions transitioning to many $ Trillions

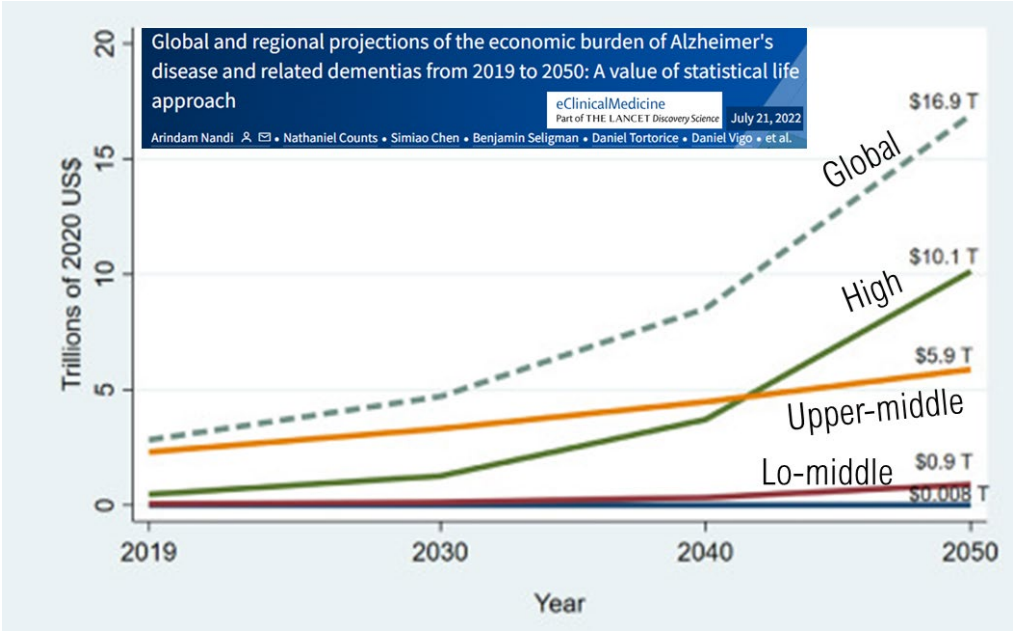
Distribution of Aggregate Costs of Care by Payment Source for Americans Age 65 and Older with Alzheimer's or Other Dementias, 2023*



2023 ALZHEIMER'S ASSOCIATION
ALZHEIMER'S DISEASE FACTS AND FIGURES

Projected Number of People Age 65 and Older (Total and by Age) in the U.S. Population with Alzheimer's Dementia, 2020 to 2060





Analytical Framework: Dietary Patterns and Neurological-Psychological Illness

Target Population

Children and adults (2y+), healthy and at risk for chronic disease

{Literature will be examined by age group, sex, race/ethnicity, and geographic location as appropriate. Age/lifestage groups of interest include children, adolescents, adults, including pregnant, lactating, and peri-postmenopausal women, and older adults}

Key Definitions:

- **Dietary patterns***:* The quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

Intervention/Exposure

Adherence to a dietary pattern (e.g., a priori patterns (indices/scores), data driven patterns (factor or cluster analysis), reduced rank regression, or patterns derived from other methods (DASH, vegetarian))

Comparator

Different levels of adherence to a dietary pattern; Adherence to a different dietary pattern

Potential Confounders

- Total energy intake
- BMI
- Age
- Race/ethnicity
- Sex
- SES
- Smoking
- Alcohol intake
- Physical activity
- Family history

Endpoint Health Outcomes

- Depression
- Dementia/cognitive decline/Alzheimer's Disease

Systematic Review Questions:

- What is the relationship between dietary patterns and risk of depression?
- What is the relationship between dietary patterns and risk of dementia/cognitive decline/Alzheimer's disease?

Dietary Patterns and Depression Description of the Evidence

- Includes 19 articles (17 prospective cohort studies, and 2 analyzed data from RCTs)
  - 2 analyzed data from RCTs that tested/described dietary patterns, 6 used indices/scores, 10 used data-driven methods, 1 used reduced rank regression

- Despite methodological and outcome heterogeneity in this body of evidence, some protective dietary patterns emerged:
  - Patterns emphasizing seafood, vegetables, fruits, and nuts, were generally associated with reduced risk
  - Patterns emphasizing red and processed meats and refined sugar were generally associated with increased risk

Dietary Patterns and Cognitive Impairment, Dementia, Alzheimer's
Description of the Evidence

- Includes 30 articles (28 prospective cohort studies, and 2 analyzed data from RCTs)
  - 2 analyzed data from RCTs that tested/described dietary patterns, 23 used indices/scores, 3 used data-driven methods, 3 used reduced rank regression
- Most (18 of 28) articles found an association between dietary patterns and age-related cognitive impairment, dementia, and/or Alzheimer's disease, and some commonalities emerged:
  - Patterns higher in fruits, vegetables, nuts, legumes, and seafood were generally associated with reduced risk
  - Patterns higher in red and/or processed meats were generally associated with greater risk
  - Relatively few studies reported on refined sugar and added salt, and patterns including these nutrients tended to report greater risk

Question 6: What is the relationship between dietary patterns and risk of neurological and psychological illnesses?

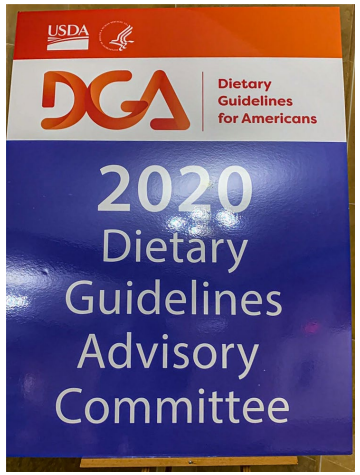
Source of evidence: NEL systematic review

Conclusion

Limited evidence suggests that a dietary pattern containing an array of vegetables, fruits, nuts, legumes and **seafood** consumed during adulthood is associated with lower risk of age-related cognitive impairment, dementia, and/or Alzheimer's disease. Although the number of studies available on dietary patterns and neurodegenerative disease risk is expanding, this body of evidence, which is made up of high-quality observational studies, has appeared only in recent years and is rapidly developing. It employs a wide range of methodology in study design, definition and measurement ascertainment of cognitive outcomes, and dietary pattern assessment. DGAC Grade: Limited

Limited evidence suggests that dietary patterns emphasizing **seafood**, vegetables, fruits, nuts, and legumes are associated with lower risk of depression in men and non-perinatal women. However, the body of evidence is primarily composed of observational studies and employs a range of methodology in study design, definition, and measurement of dietary patterns and ascertainment of depression/depressive signs and symptoms. Studies on dietary patterns in other populations, such as women in the post-partum period, children and adolescents, as well as those in various ethnic and cultural groups, are too limited to draw conclusions. **DGAC Grade: Adults – Limited; Children, adolescents, and women in the post partum period – Grade not assignable**

2015 Dietary Guidelines Advisory Committee Report 207



Conclusions

from (most recent) 2020 DGAC on Pregnancy & Lactation

*…[seafood] consumption during **pregnancy** may be related to…**better cognitive development and language and communication development in children**.*

*…the Committee concurred with existing recommendations that **women who are lactating should continue to consume seafood at the same amounts recommended during pregnancy**.*

[…at least 8 and up to 12 ounces of a variety of seafood per week from choices that are lower in methylmercury and higher in omega-3 fatty acids.]

*…The Committee therefore supports recommendations for **women who are lactating to consume food sources of long-chain polyunsaturated fatty acids, such as fish**.*