

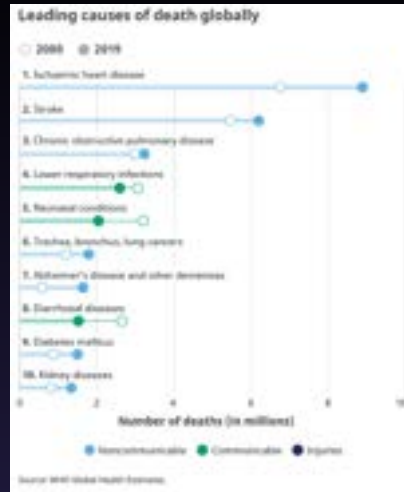
# The future of mental and brain health

System-based and nutrient-based solutions

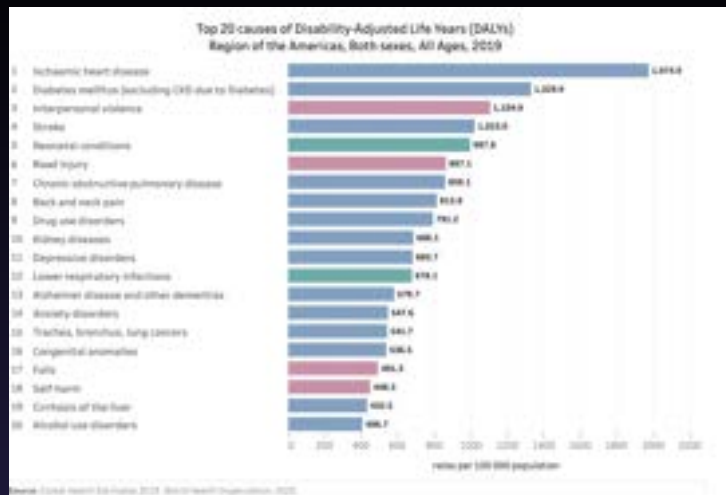
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What are the most important health issues of our day?

## By death (global)



## By disability (US)



What's the main goal, and what's a surrogate?

Surrogates:

- High blood pressure
- High blood sugar
- Extra body weight
- High cholesterol
- Inflammation
- Heart disease, lung disease, cancer?

What matters most is **mental state**

Mental state reflects brain state

How are brain and mental state today?

- Depression = 28% <sup>1</sup>
- Anxiety = 26.9% <sup>1</sup>
- Stress = 36.5% <sup>1</sup>
- Dementia = 55 million <sup>2</sup>

How have things been going recently?

**A hidden pandemic? An umbrella review of global evidence on mental health in the time of COVID-19**

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**A hidden pandemic? An umbrella review of global evidence on mental health in the time of COVID-19**

“This is the first meta-review to synthesise the longitudinal mental health impacts of the pandemic. Findings show that probable depression and anxiety were significantly higher than pre-COVID-19, and provide some evidence that that adolescents, pregnant and postpartum people, and those hospitalised with COVID-19 experienced heightened adverse mental health. ”

Brain health is far from our top priority  
And it shows

Approach to brain health today



Our brain health directly reflects



Lifestyle choices compounded over time

Our choices change our brain biology  
Our brain biology shapes our thoughts, moods, and actions



The quality of our brain outputs mirrors the quality of our brain inputs

## What's shaping our brains?

- Quality/amount of nutrition
- Quality/amount of sleep
- Quality/amount of stress
- Quality/amount of exercise
- Quality/amount of connection to nature, other people
- Exposure to environmental toxins (e.g., air pollution)
- Exposure to infections

## What are the key biological systems governing brain health?

- Vascular
- Neuroplasticity
- Immune (inflammation)
- Hormonal (e.g. cortisol)
- Metabolic (e.g. insulin)
- Neurotransmitters



## What can we do about this?

- **Quality/amount/timing of nutrition**
- Quality/amount of sleep
- Quality/amount of stress
- Quality/amount of exercise
- Quality/amount of connection to nature, other people
- Exposure to environmental toxins (e.g., air pollution)
- Exposure to infections

## Role of nutrients in brain health

### Macro:

- Structural
- Functional

### Micro

- Vascular
- Neuroplasticity
- Immune (inflammation)
- Hormonal (e.g. cortisol)
- Metabolic (e.g. insulin)
- Neurotransmitters

## Nutrients in the best diet for the brain



- Mediterranean/MIND diets best studied for long term brain health outcomes

## Mediterranean/MIND diets

High level:

- Minimally processed foods, especially plant-based
- Rich in polyphenols, unsaturated fats, diversity of foods

Specifics:

- Lots of plants: legumes, vegetables, olive oil, nuts, whole grains (more in MIND)
- Moderate amounts of fish, dairy, and less red meat.

## Key potential dietary elements for brain health

- General micronutrient needs
- Polyphenols
- Omega-3 fatty acids
- Oleic acid/olive oil
- Pre/pro/syn/postbiotics

## Key potential dietary elements for brain health

- General micronutrient needs

ORIGINAL RESEARCH ARTICLE | ARTICLES IN PRESS

### Multivitamin Supplementation Improves Memory in Older Adults: A Randomized Clinical Trial

Lok-Kin Yeung • Daniel M. Abshuler • Melanie Wall • ... Howard D. Sesso • JoAnn E. Manson • Adam M. Brickman  • Show all authors

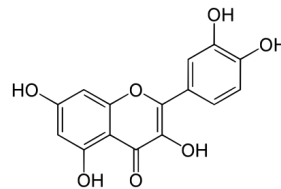
Published: May 24, 2023 • DOI: <https://doi.org/10.1016/j.ajnut.2023.05.011>

## Multivitamin Supplementation Improves Memory in Older Adults: A Randomized Clinical Trial

- “Compared with placebo, participants randomly assigned to multivitamin supplementation had significantly better ModRey immediate recall at 1 y,” estimated to be equivalent to 3.1 yrs of memory change over 3 yr time.”

## Key potential dietary extracts for brain health

### Polyphenols



## Key potential dietary extracts for brain health

### Polyphenols

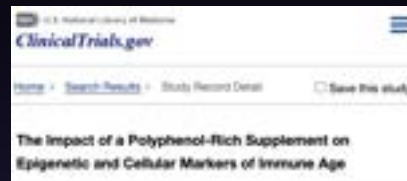
- In a 2020 paper, people who ate more polyphenols had lower rates of developing Alzheimer's dementia (1)
- Consuming polyphenol-rich chocolate has been linked to lower levels of salivary cortisol and lower levels of multiple stress hormones after exposure to stress (2)
- In an interventional trial, people who ate more polyphenols had less depressive symptoms than those eating less (3)

## Key potential dietary extracts for brain health

- Polyphenol mechanisms
  - Neuroplastic
  - Immune
  - Anti-oxidant
  - Metabolic
  - **Epigenetic**

## Key potential dietary extracts for brain health

- Polyphenol mechanisms
  - Neuroplastic
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## Key potential dietary extracts for brain health

- Polyphenol epigenetic mechanisms
  - Polyphenols absorbed direct via gut or after microbiome processing
  - In cell data, polyphenols change methylation/acetylation on genes
  - Some of these genes encode for immune processes

## Polyphenol dosing

- Tempting to max out on one or two
- Data on around 500 mg polyphenols as sweet spot for
  - Mood (1)
  - Inflammation (2)
  - CV health (flavonoids in particular) (3)
  - Improved brain health (4)

## Key potential dietary extracts for brain health

- Omega-3 fatty acids and metabolites

## Key potential dietary extracts for brain health

- Diet rich in omega-3s consistently linked to brain health
- Key omega-3s seem to be DHA and EPA, ~ 2grams a day
- Omega-3s convert to pro-resolving mediators, extra potent inflammatory regulators
- PRMs found naturally in fish oil, can be augmented in post-processing
- \*\* Huge heterogeneity in omega-3 supplement quality!



- 1135 participants without dementia, average age 73
- Evaluated subjective o3 supplement intake and blood markers, development of AD over 6 yrs
- Long-term omega-3 fatty acid supplementers had a 64% reduced risk of AD
- “After incorporating 48 longitudinal studies involving 103,651 participants, a moderate-to-high level of evidence suggested that dietary intake of omega-3 fatty acids could lower risk of all-cause dementia or cognitive decline by ~20%”



## Omega-3 considerations

- Sustainably
- Source
- Surviving molecules

## Pro-resolving mediators

Published: 21 December 2015

**Specialized pro-resolving mediators: endogenous regulators of infection and inflammation**

Maria C. Bassi<sup>1</sup>, Diana Di Loro<sup>1,2</sup>

[Nature Reviews Immunology](#) 16, 61–67 (2016) | [View this article](#)

44k Accesses | 388 Citations | 31 Altmetrics | [Metrics](#)

### Specialized Pro-Resolving Mediators in Neuroinflammation: Overview of Studies and Perspectives of Clinical Applications

by [Marilysandra Valente<sup>1,2\\*</sup>](#), [Marta Dentice<sup>1</sup>](#), [Fabrizio Bellizzi<sup>1</sup>](#), [Paolo Kurtz<sup>1</sup>](#) and [Gian Luigi Di Gilio<sup>1,2\\*</sup>](#)

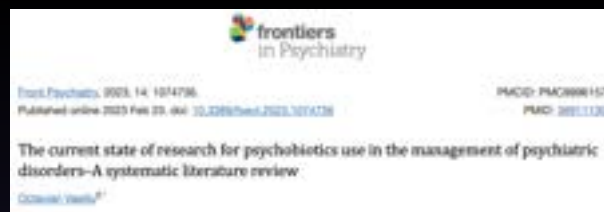
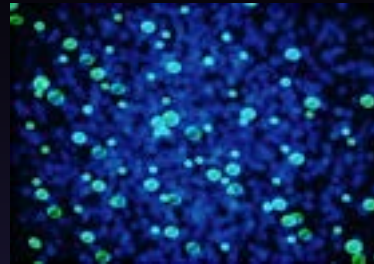
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## And of course...the microbiome

- Psychobiotics
- Oral microbiome + nitric oxide
- Pre/post/synbiotics



- “There have been identified data in favor of probiotics for patients with mood disorders, ADHD, and ASD, and also for the association of probiotics and selenium or synbiotics in patients with neurocognitive disorders.”
- Research quality remains mixed, and preliminary, but idea is that certain bacteria may promote mental health in certain people



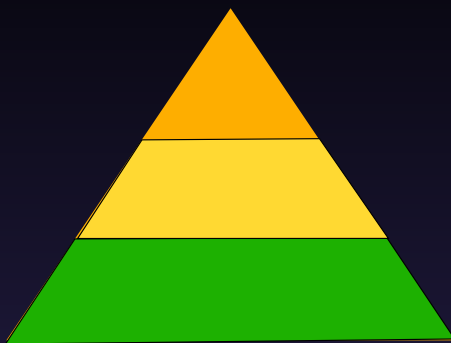
- This was a small pilot randomized clinical trial with about 25 depressed people on antidepressants getting placebo/ multistrain probiotic for 8 weeks
- Found significant improvements in subjective anxiety/ depression scales vs placebo



- "In patients with AD, oral bacteria were detected in brain tissues, and increased levels of pro-inflammatory cytokines were also detected."
- "The presence of bacteria in the brain is related to AD's pathological characteristics, suggesting an etiological oral-brain axis."

- Oral microbiome is part of larger GI tract microbiome
- Health of oral microbiome impacts systemic health through immune system
- Nitric oxide is key to systemic perfusion
- In brain, nitric oxide regulates regional blood flow and connectivity in key memory centers

### Pyramid of brain nutrition



Custom supplementation, custom diets

Key nutrient focus/supplementation

Whole food diet (med may be best)

## The secret sauce



- Human brain health is more than just well-functioning systems
- Human brain/overall health is dependent on **connection**



- Review of 38,614 people
- Being married or in a relationship predicts better cognition
- Living with others predicts cognition
- Weekly community involvement predicts better cognition
- “Good social connections (ie, living with others, weekly community group engagement, interacting weekly with family and friends, and never feeling lonely) are associated with slower cognitive decline.”



- 4,642 American adults age 25–75 surveyed over 10 yrs
- Risk of depression more than doubled in those with poor quality social connection

- You can have all the biological ingredients for a healthy brain, but we don't and can't successfully exist in isolation
- Call a friend, encourage a coworker, get out into nature
- A connected brain is more likely to care about health

Thank You!



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