"BECOMING AN ALZHEIMER'S PATIENT IS ALMOST ALWAYS A CHOICE. THIS BOOK EXPLAINS WHY."

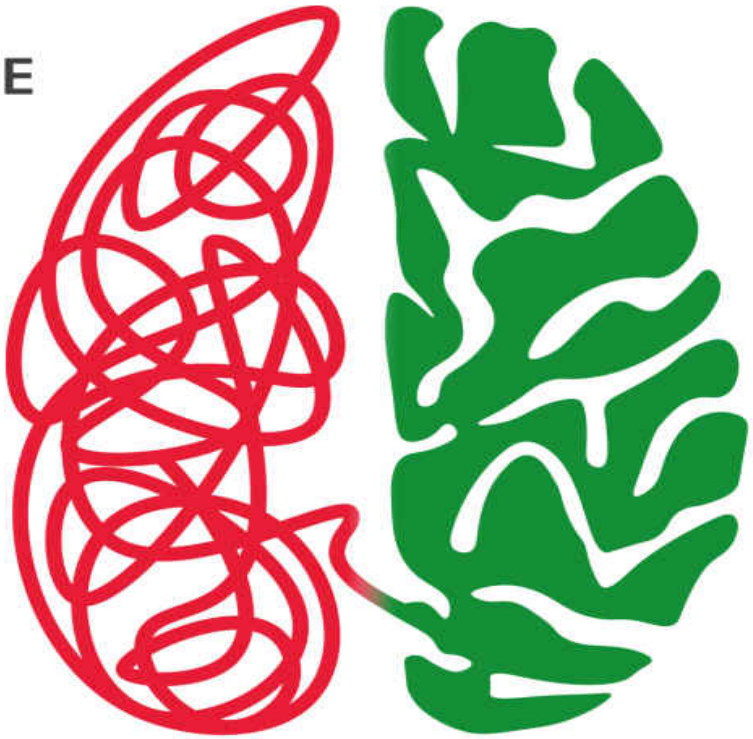
*Dr David Perlmutter, Neurologist & New York Times Best-Selling Author*

# ALZHEIMER'S:

# PREVENTION IS THE CURE

## YOU ARE THE MASTER OF YOUR BRAIN'S FUTURE HEALTH

LEARN HOW TO DEMENTIA-PROOF YOUR DIET AND LIFESTYLE




PATRICK HOLFORD

*Founder of*
FOODFORTHEBRAIN.ORG


TEST YOUR COGNITION ONLINE

**Praise for *Alzheimer's: Prevention is the Cure***

"Patrick Holford has been a leader in the field of dementia prevention for years, and his superbly researched new book should lead to a reduction in the global burden of dementia, something for which there is a great need."

**Dr Dale Bredesen, MD, author of the New York Times bestseller, *The End of Alzheimer's* and *The Ageless Brain***

"The world is facing a devastating onslaught of dementia as populations get older and yet there is little, if any, effort by the authorities to prevent dementia. Instead of wasting resources on trying to develop a treatment, we urgently need to adopt the approach proposed in this book: find the best ways to prevent the disease processes that lead to dementia. The potential benefits are huge both in personal and in economic terms. The book must lead to a change in official policies!"

**Professor Emeritus A. David Smith, University of Oxford**

"It is clear that Patrick Holford has seen through the dogma around drug development for Alzheimer disease and that the emperor has no clothes. More importantly, Alzheimer's prevention is both scientifically plausible and, indeed, actually works in practice. His simple, clear guidelines are not only a realistic way to cut the risk of this dehumanizing disease, they will also cut your risk of diabetes, cancer and hypertension – what are you waiting for?"

**Professor Stephen Cunnane, Université de Sherbrooke, Canada**

"This book succinctly and fearlessly promotes prevention as the way forward in the battle against Alzheimer's disease, and rightly promotes homocysteine lowering B vitamins and omega-3 fatty acids as important keys to such prevention."

**Professor Joshua Miller, Rutgers University, USA**

“This book challenges outdated medical dogma and provides a comprehensive, science-based approach to Alzheimer’s prevention. As the former president of the International Society for Orthomolecular Medicine, I recognize the urgent need to move beyond failed pharmaceutical strategies and embrace evidence-backed interventions such as targeted nutrition and lifestyle optimisation. This book is a beacon of hope for the future of brain health.”

**Dr Atsuo Yanagisawa, President of the Japanese Society for Orthomolecular Medicine**

“Alzheimer’s Disease was once thought to be mysterious and incurable. Recent studies, however, have identified poor nutrition as the most likely driving cause. This opens the door for good nutrition as a secret weapon for both prevention and treatment. But what do we mean by good nutrition? In *Alzheimer’s: Prevention is the Cure*, Patrick Holford carefully summarizes the state-of-the-art evidence for what to eat and what to avoid so we can stay healthy and sharp into our nineties. To infinity and beyond!”

**Richard J Johnson MD, Emeritus Professor of Medicine, University of Colorado**

“Becoming an Alzheimer’s patient is almost always a choice. This book explains why.”

**Dr David Perlmutter MD, neurologist and author of five New York Times best-sellers**

“It is education, rather than medication, that we need and foodforthebrain’s global campaign is something we fully support to help achieve this.”

**Wu Ying Ping, President of the China Health Association**

“We must popularise prevention. Foodforthebrain’s initiative is the way forward. It is something everyone can do right now for themselves.”

**Gao Qiang, former Minister of Health, China.**

“As a clinician with a special interest in saving cognition, I have witnessed the struggles of Alzheimer’s firsthand. This book is a transformative power of food in brain health. With easy to understand scientific background and many practical tips, it not only empowers readers to make healthier choices but also offers hope for a brighter future. A must-read for anyone looking to safeguard their mind, memories and well-being!"

**Dr Sabine Donnai, VIAVI CEO**

“Having discovered raised blood levels of the amino-acid ‘homocysteine’ in patients with Alzheimer’s Disease my research focuses on its relation to dementia and cognition in general. However, as a retired General Practitioner, I recognise the importance of adopting a holistic approach to disease. This book is an excellent primer on the many steps you can take to reduce your own risk of developing dementia.”

**Dr Andrew McCaddon, retired GP**

“Vast sums of money have been spent finding drugs that may help to slow the progress of this dreadful disease. Disappointingly, very little time or money has been spent looking at prevention. This book crystallizes Patrick Holford’s findings from a lifetime spent gathering evidence from across the globe, which shows the difference that can be made by changing the way we live.”

**Dr Rona Tutt OBE, Past President of the National Association of Head Teachers (NAHT) Trustee of the Food for the Brain Foundation.**

“Patrick Holford’s work in nutritional knowledge translation is unrivalled for its potential to impact public health and disease prevention.“

**Andrew Cusciana, International Society for Orthomolecular Medicine (Canada)**

“As an elderly health journalist with a genetically raised risk of Alzheimer’s, it looms large on my radar. This hugely well-informed and hopeful handbook offers a radical new way of cutting your risk. It explains how what we eat and how we live can combine to protect the brain from damage.

Unlike the drug approach, it doesn’t involve a magic bullet, targeted at the contents of our skull. Instead it exploits the fact that the brain has multiple connections with the rest of the body and that keeping our body healthy with nutrition and lifestyle can deliver a healthy brain. As yet you are unlikely to find such a protocol anywhere else.”

**Jerome Burne, award winning medical journalist.**

***Other books by Patrick Holford***

*Balance Your Hormones*

*Boost Your Immune System* (with Jennifer Meek)

*Burn Fat Fast (with Kate Staples)*

*Delicious, Healthy, Sugar-Free* (with Fiona McDonald Joyce)

*Flu Fighters*

*Food is Better Medicine than Drugs* (with Jerome Burne)

*Good Medicine*

*Hidden Food Allergies* (with Dr James Braly)

*How to Quit Without Feeling S**t* (with David Miller and Dr James Braly)

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*Ten Secrets of Healthy Ageing* (with Jerome Burne)

*The 5-Day Diet*

*The 9-Day Liver Detox* (with Fiona McDonald Joyce)

*The Alzheimer's Prevention Plan* (with Shane Heaton and Deborah Colson)

*The Feel Good Factor*

*The Homocysteine Solution* (with Dr James Braly)

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*The Low-GL Diet Cookbook* (with Fiona McDonald Joyce)

*The Low-GL Diet Counter*

*The Optimum Nutrition Bible*

*The Stress Cure* (with Susannah Lawson)

*Upgrade Your Brain*

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FOUNDER OF THE
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This book is not intended as a substitute for medical advice or treatment. Any person with a condition requiring medical attention should consult a qualified medical practitioner or suitable therapist. The recommendations given in this book are solely intended as education and information and should not be taken as medical advice. Neither the author nor the publisher accepts liability for readers who choose to self-prescribe. Do not change your medication without consulting your doctor.

***The truth is always disturbing.***
Old Chinese proverb

# About the Author

## *Patrick Holford, BSc, DipION, FBANT, NTCRP*

Patrick Holford is a leading spokesman on nutrition and mental health and founder of the Food for the Brain Foundation, VitaminC4Covid and the Institute for Optimum Nutrition, an educational charity that offers degree accredited training in nutritional therapy. Originally trained in psychology, Patrick was involved in groundbreaking research showing that multivitamins can increase children's IQ scores – the subject of a *Horizon* television documentary in the 1980s. He was one of the first promoters of the importance of zinc, essential fats, low-GL diets and homocysteine-lowering B vitamins and their importance in mental health and Alzheimer's prevention, working closely with David Smith, Emeritus Professor of Pharmacology at the University of Oxford. He is the founder of the charitable Food for the Brain Foundation and Director of the Alzheimer's is Preventable campaign and Chair of their Scientific Advisory Board and Alzheimer's Prevention Expert Group (APEG).

He is the author of several papers and 48 books, translated into over 30 languages, including *The Optimum Nutrition Bible, Optimum Nutrition for the Mind, Food is Better Medicine than Drugs, the Ten Secrets of Healthy Ageing, The Hybrid Diet* (co-authored with Jerome Burne) and his latest book *Upgrade Your Brain*. He is a retired visiting professor at the University of Teesside and is in the Orthomolecular Medicine Hall of Fame and on the Editorial

Board for the Orthomolecular News Service. He is also an Ambassador for dementia prevention in China. Patrick brings 40 years of research and experience in the field of nutrition.

## ABOUT FOOD FOR THE BRAIN FOUNDATION

The Food for the Brain Foundation (foodforthebrain.org) is an educational and research charity, focusing on dementia prevention. Its free, online, validated Cognitive Function Test, followed by the Dementia Risk Index questionnaire, assesses eight drivers of dementia, including ‘brain fats’, ‘B vitamins’, and ‘low carbs & GL’, thus identifying those who may be eating too many carbs and not enough B vitamins and brain fats, then advising them on what they can do to minimise risk. It also offers the DRIfT 5-in-1 biomarker test, which assesses key nutritional and metabolic factors linked to brain health, enabling early intervention to reduce risk of cognitive decline. *See Resources for a list of country and language specific websites*.

# Contents

Acknowledgements
Guide to Abbreviations and Measures
References and Further Sources of Information
Introduction

**PART 1 – WHAT DOES & DOESN'T CAUSE ALZHEIMER'S**

1. Amyloid ≠ Alzheimer's and the Tauist's Delusion
2. Less than 1% is 'in the Genes' and the ApoE4 exaggeration
3. Alzheimer's is Caused by a Systems Breakdown

**PART 2 – THE 8 PREVENTION DOMAINS**

4. The Four Biological Horsemen of the Brain Apocalypse
5. Brain Fats – Omega-3, Phospholipids, Vitamin D and Cholesterol
6. Methylation, Homocysteine and the Causal Role of B vitamins
7. Omega-3 and B vitamins – the Dynamic Duo
8. How our Sugared Brains are 'Fructed' and How Ketones aid Recovery
9. Anti-age your brain with antioxidants, glutathione and NAC

10. Use it or Lose it – Lifestyle Factors that Protect Your Brain

11. Brain Recovery and Repair – the Sleep, Stress and Hormone Connection

12. Microbes and the Mind

**PART 3 – PREVENTION IN ACTION Your Alzheimer's Prevention Plan**

13. Assessing and Reversing Your Risk with the Cognitive Function Test

14. Your Alzheimer's Prevention Plan - Diet, Supplements & Lifestyle

15. The Global Citizen Science Alzheimer's Prevention Revolution

Recommended Reading

Resources

Index

# Acknowledgements

There are over 30,000 published studies on Alzheimer's prevention. No-one could possibly be on top of it all. My great fortune is that I stand on the shoulders of giants – neuroscientists, doctors, nutritionists and pharmacologists whose life's work has been to go a mile deep into their speciality. I am talking about Professors Helga Refsum, from Oslo University, and David Smith, from Oxford University, who know more about homocysteine and B vitamins in the context of Alzheimer's than anyone. Close second is Dr Andrew McCaddon, a retired GP and homocysteine researcher, and Professor Joshua Miller, from Rutgers University. Then, on the seafood and omega-3 front, Professor William Harris and Dr Simon Dyall lead the field, which was started by Professor Michael Crawford's discovery of its centre point in all brains, and continues, at the age of 94, to keep teaching and supporting me. Also, Dr Fredrik Jernerén, who helped unravel the omega-3-B vitamin co-dependence.Also, the brilliant Dr Malcolm Kendrick who has single-handedly exposed the ongoing myths about cholesterol, an essential brain nutrient, and statins.

Then, there are my 'no sugar daddies', endocrinology Professor Robert Lustig and Professor Rick Johnson, who have unravelled what sugar, and particularly fructose, is doing to our brains. Also, Professor Stephen Cunnane, the king of ketone therapeutics and their role in brain recovery. On the antioxidant front I am most grateful to our brilliant chemist, Dr Konrad Kowalski, who developed our Glutathione Index test and solved the problem of how to measure homocysteine and glutathione accurately and

inexpensively. Thank you, also, to Dr Louise Newson for her help unravelling why hormone deficiencies tip too many women towards dementia; Dr William Grant for being the true expert in everything related to vitamin D, light and sunshine; Associate Professor David Vauzour and Dr Victoria Sampson for enlightening me about microbes and the importance of dental health.

My ‘go to’ neurologist, with a lifetime of experience in the front line, is Professor Peter Garrard. It fails me to understand why Professor Garrard has struggled, for a decade, to find any funding from any government agency or Alzheimer’s charity for the single most important study needed in Alzheimer’s prevention – on the combination of omega-3 and homocysteine lowering B vitamins. We need a philanthropist to break this stranglehold. Perhaps most of all, I am deeply grateful to the brilliant, insightful Dr Tommy Wood, Associate Professor of Neuroscience at the University of Washington, who generously heads our research department at the charity foodforthebrain.org. His expertise in systems-based thinking, as well as the role of an active mind and body, and all the complex interactions that affect our brain, is second to none. Each of these true experts have taught and advised me, as well as checking relevant sections of this book.

My work is part of a movement, a revolution that is unstoppable, that will transform mental health globally, driven by people, not politicians or pharma; headed by our not-for-profit Food for the Brain Foundation and its incredible team, headed by Emma (CEO), Steff and Drew (digital masters), backed up by Kate; the multi-talented Kim (putting the principles into delicious recipes in the Upgrade Your Brain cookapp), who takes care of the thousands of people engaging with our COGNITION transformation project; Cath, managing research; Fran, helping get donations of time and money, Ray and Sarah for making the money work; Dorota, out there upgrading catering offerings

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There are so many more I'd like to thank across the world, from Dr Atsuo in Japan, Junfang, Yaoming and Steven in China, Dr Ilyes Baghli in Algeria, Dr Efrain Olszewer in Brazil and so many others. I am also deeply grateful to the thousands of scientists whose work often goes unnoticed and, for reasons of greed and ignorance, appears to fail to move the dial. Yet, without their dedication, you wouldn't know that Alzheimer's is a preventable disease that almost no-one needs to suffer from. We have to tell as many people as possible how to prevent it.

Wishing you the best of health and happiness.
Patrick

# Guide to Abbreviations and Measures

1 gram (g) = 1,000 milligrams (mg) = 1,000,000 micrograms (mcg or µg). Most vitamins are measured in milligrams or micrograms. Vitamins A, D and E are also measured in International Units (iu) – a measurement designed to standardise the different forms of these vitamins, which have different potencies.

1µg of retinol (µg RE) = 3.3iu of vitamin A (RE = Retinol Equivalents)
1iu RE of beta-carotene = 6mcg of beta-carotene
100iu of vitamin D = 2.5µg (multiply or divide by 4 to convert)
100iu of vitamin E = 67mg
1 pound (lb) = 16 ounces (oz)
2.2lb = 1 kilogram (kg)

**Vitamin D** (25-hydroxyvitamin D) in the blood:
30ng/ml (US measure) = 75nmol/l (UK measure)
So, multiply or divide by 2.5 to convert

**HbA1c** is measured either in % (US measure) with above 6.5% equating with diabetes and 6% with pre-diabetes or in mmol/mol (UK measure) with 48mmol/mol equating with diabetes and 42mmol/mol with pre-diabetes

**mM = mmol/l**, molar concentration, the measure of the concentration of a specific chemical compound per unit of

volume µmol/L = micromole, sometimes written mcmol, per litre.

# References and Further Sources of Information

Both to save paper and to give you access to the actual researcher papers and articles themselves, the numbered references in this book link to this webpage: Foodforthebrain.org/alzheimers-references

Here, you can not only see the reference, but, in most cases, click on the link to the actual paper or article yourself. It also means we can update these references, as more studies come out.

## *Important note*

This book is not intended as a substitute for medical advice or treatment. Any person with a condition requiring medical attention should consult a qualified medical practitioner or suitable therapist. The recommendations given in this book are solely intended as education and information and should not be taken as medical advice. Neither the author nor the publisher accepts liability for readers who choose to self-prescribe. Do not change your medication without consulting your doctor.

# Introduction

There are a few things not in dispute about Alzheimer's. Everyone agrees that Alzheimer's is no way to end one's life. Although risk increases with age, it is not caused by age as such. This is evident from the many 90+ year olds who have no loss of cognitive function.

Fewer than 1% of Alzheimer's cases are caused by genes. At least half of Alzheimer's cases could be eliminated by targeting prevention. This is because the hardest hitting known risk factors are largely under your control – what you eat, supplement and how you live. These facts are not disputed.

Where the science and the medical 'establishment', which includes the pharmaceutical industry, differ is in three areas. The cause, the diagnostic definition and the treatment, as well as the extent to which Alzheimer's can be prevented.

**What causes Alzheimer's?**

Firstly, the cause. The conventional pharmaceutical view, or spin, is the claim that Alzheimer's, which makes up two thirds of dementia cases, is caused by a build up of amyloid plaque. This is wrong. A fact that is an inconvenient truth for the pharmaceutical industry, which has spent an estimated £250 billion to develop an amyloid blood test, then a drug to lower it.

I'm sure the original intentions of big pharma were true – to find a cure - but having spent so much going down the amyloid rabbit hole, it has become an unhealthy obsession that simply isn't supported by the science, but might just

get a financial return if they can fool enough people and control the medical narrative.

The reality is that Alzheimer's, and most other dementias, are a result of a combination of risk factors that affect either the structure of the brain, how it functions, or how we make use of our neural network.

This is not only a completely different way of looking at this disease, known as 'systems-based', but it also describes the process of cognitive decline more accurately. The implication is that there is rarely just one cause of damage to the brain, but many that come together to kill off brain cells.

It also provides many targets for prevention, and we are discovering how they interact. Pollution exposure, for example, is a risk factor but not in those with good B vitamin status.

This doesn't sit well with the 'normal' reductionist model of a randomised-controlled trial, where you change one thing to see it's effects on one outcome, nor the 'blockbuster drug' for all with dementia, ignoring that each person's drivers for cognitive decline are different. In other words, it necessitates a different method of scientific investigation. This is explained in Chapter 3 - 'Alzheimer's is a Systems Breakdown'.

**Defining and Diagnosing Alzheimer's**

You would be diagnosed with Alzheimer's if you have a combination of a decline in memory and thinking skills (cognitive function), along with brain shrinkage in the 'medial 'part of the brain. The two usually decline in parallel. You cannot diagnose Alzheimer's without this kind of brain scan of the medial temporal or hippocampus(al) region.

Very few unfortunate people inherit 'causative' genes – APP, presenilin 1 and 2 – that crank up amyloid accumulation and result in very early-onset Alzheimer's. For

these unfortunate few, the accumulation of amyloid is a major problem. So, the presence of these genes is needed to 'diagnose' gene-caused Alzheimer's. More on this in Chapter 2.

**Predictive Blood Biomarkers**

Alzheimer's cannot be diagnosed on the basis of an amyloid blood test, or one for p-tau, or ones for homocysteine, omega-3, blood sugar, glutathione, vitamin or any other blood test. This list actually contains three different types of measures. Understanding the difference is helpful in understanding how to prevent Alzheimer's.

The first two, amyloid and p-tau, reflect the presence of amyloid deposits and tangled nerves, which are found more often in those with dementia, but can be present in those with no cognitive decline, and can be absent in those with Alzheimer's. So, while their presence does predict higher risk, so too does being older. Neither are causal.

P-tau is perhaps the more interesting, because it causes tangles in nerves in the brain called 'neurofibrilliary tangles'. You can imagine how that would mess up cognition, and it does. Unlike amyloid, the higher your p-tau levels in the brain, the worse is your cognitive function. So, the presence of p-tau isn't exactly a diagnostic proof of pending dementia, but certainly does mean increased risk.

The next two – homocysteine and omega-3 – let's call them biomarkers for now, also predict risk. Homocysteine, explained in Chapter 5, reflects a person's B vitamin status. B vitamins (and other nutrients) are essential for a process called 'methylation', which is totally vital for the brain to work. Raised homocysteine not only increases dementia risk by ten-fold, but also increases risk of microcerebro-vascular disease (tiny blood vessels in the brain) by seventeen times. Think 'mini-strokes' or TIAs (transient ischemic attacks).

While we are on this subject, people often ask, 'what's the difference between Alzheimer's and vascular dementia?'

Vascular dementia is driven by these breaks, blockages, bursts of blood vessels. If the event is big, like a stroke, there's a steep drop towards cognitive decline. If it's small - a mini-stroke or transient ischemic attack (TIA), it's a smaller drop.

Often, when a person's brain is scanned, they find lots of little spots of damage. So, vascular dementia usually progresses, step by step, downhill. Alzheimer's would probably appear more gradually, like walking down a steady slope. Both conditions usually end up in the same place, and looking much the same in scans of that central area of the brain. And since both really have the same causes, often a person is diagnosed with 'mixed' dementia, most often meaning Alzheimer's and vascular dementia. Together, Alzheimer's, vascular and mixed dementias add up to about 90% of all dementia diagnoses.

Now, back to homocysteine. Unlike amyloid, we can say that homocysteine really is causal. The reason this can be confidently asserted is that if you give B vitamins, homocysteine goes down, brain shrinkage reduces, cognitive decline slows down or stops. If homocysteine goes up, and brain shrinkage increases and cognitive function gets worse. This is consistent with a modification of the actual disease process. Chapter 6 makes this clear.

Not everyone has a raised homocysteine, but those who do will be having accelerated brain shrinkage, and B vitamins in the right dosage, well above what you can eat, will slow that down. So, B vitamins won't work for everyone, but will work for those with raised homocysteine, which could be about half of people over 65, but is many more in some countries such as China.

Amyloid, in contrast, is present in some of those with no cognitive decline, and not there in some with Alzheimer's. What's more, drugs which reliably lower amyloid burden have yet to produce any clinically meaningful improvement.

It hasn’t been for lack of trying. For instance, the trials usually involve giant numbers (the smaller the beneficial effects, the bigger the study needs to be to ‘see’ any difference compared to placebo). Then there are the terrible, extremely common and potentially fatal adverse effects. Even the heavily pharmaceutically influenced UK medical watchdog, NICE, have told the National Health Service not to prescribe these drugs because the potential benefits are too small and the risk too high to justify the annual treatment cost of about £50,000. Homocysteine wins hands down over amyloid, and lowering it with B vitamins is a 10p a day cost with no adverse effects. That is the cheering truth for patients.

Let’s take a look at another non-drug preventative treatment. Omega-3 from fish and fish oils. The higher your blood level, the more fish you eat, the more omega-3 you supplement, the lower your risk. So, it too is a modifiable biomarker.

But not all studies that have given omega-3 at various stages of the disease process have worked. On its own, the evidence for omega-3 is not as good as that for homocysteine-lowering B vitamins, given to those with raised homocysteine (above 11mcmol/l), as explained in Chapter 6. However, when both omega-3 status and B vitamin status are good we start to see a major, consistent benefit in slowing down cognitive decline, explained in Chapter 7.

This is because your brain is literally made out of fat – more than half of its dry weight is fat. Neurons (brain cells), which do all the talking to each other, have a membrane made out of fats bound to ‘phospholipids’ (*see Chapter 5 to understand the importance of phospholipids, rich in eggs, and also why cholesterol is an essential brain nutrient, along with vitamin D*), and these two are coupled together to form the active, functional neuronal phospholipid-fatty acid membrane.

But to become linked together they need B vitamins, which gives you one of the recipes for a healthy brain - omega-3, B vitamins and phospholipids - a perfect example of why a system-based way of thinking is needed to tackle the threat of Alzheimer's. It is a fact of biology that the STRUCTURE of the brain and the ability to make new neurons is dependent on these building materials.

Remarkably, this very promising area of research has received no funding from any government agency or Alzheimer's charity, despite a ten-year campaign to raise the funds from UK and EU research agencies, so the evidence for it is not yet fully nailed down. This could be grounds for suspecting that drug company interests are involved, potentially supressing competition. More on this in Chapter 7.

Two other tests I mentioned were blood sugar, or HbA1c, which detects the amount of sugar-damaged red blood cells you've got, and glutathione – a natural antioxidant that repairs cells in the body. That's how diabetes is diagnosed. High HbA1c. The higher your HbA1c, the worse your diabetes and the higher your risk of dementia and Alzheimer's. Similarly, the more sugar or ultra-processed foods you eat, the greater your risk of both brain shrinkage and cognitive decline. Also, having this kind of high sugar diet raises homocysteine considerably. Chapter 8 explains all this and why the fruit sugar fructose is particularly bad. Sugar, or glucose, which is what carbohydrates break down into, is a primary fuel of the brain. It's delivered there by insulin. Too much sugar not only makes HbA1c go up, it also makes insulin not work, known as insulin resistance. Then, you can't deliver the fuel into the brain, creating brain fog and sugar cravings. The brain literally can't FUNCTION properly.

In this chapter, you'll also learn about an alternative brain fuel, ketones, and how a ketogenic diet and keto-friendly nutrients can help restore brain function, especially

when there's a messed up fuel supply as a result of insulin resistance and excess sugar and carbs.

Whenever you burn fuel, be it glucose or ketones, you get exhaust fumes called oxidants. That's why smoking and pollution increase dementia risk, and eating more vegetables, fruits, or supplementing vitamin C reduce risk. How much antioxidant potential you've got is what measuring glutathione is all about. (This is the subject of Chapter 9.) This is also a vital part of the function of the brain.

The last 'biomarker' test I mentioned is vitamin D. The higher your vitamin D level, the lower is your risk, and supplementing vitamin D lessens risk. Those with low vitamin D levels have 19 times more risk of cognitive decline and those with a high level have a quarter of the risk of Alzheimer's.

Is it causal and why would it be? These are questions explored in Chapter 5. Of course, the more time you spend outdoors, the more vitamin D you are likely to make and the more exercise you are likely to take. And the more fish you eat, the higher will be your intake. Vitamin D is especially rich in oily fish. These kinds of overlaps are easily dealt with in a systems-based model, but really mess things up in a reductionist hunt looking for one marker and one treatment, driven by the primary aim to make money.

Now, what happens is, you measure all these five biomarkers – homocysteine, omega-3, HbA1c, glutathione and vitamin D? That's the subject of Chapter 4. This kind of 'index' of risk is going to be gold for any prevention strategy and is the cornerstone of our approach at foodforthebrain.org. The odds are it is going to be a lot more helpful than an amyloid or p-tau test, not least of all because you can actually do something about it.

## Predictive Genes

Apart from the rare causative genes, there are predictive genes which increase risk. The most researched is a gene that makes the fat carrier ApoE. Genes are the instructions to build things and 'apoprotein' transports fats (lipids) and becomes lipoprotein – that's what the L in HDL or LDL cholesterol stands for. Having a variant of the ApoE gene, called ApoE4, increases risk, as explained in Chapter 2, but you'll discover that this increased risk can be eliminated by 'doing the right things'. What these are will be laid out in full in Chapter 14.

**Use It Or Lose It**

Many risk factors affect the UTILISATION of the brain – exercise, social interactions, learning, hearing, vision and so on. All these are explained and explored in Chapter 10. Also, after activity, there needs to be a period of repair, in much the same way that your dog falls asleep after a walk. Sleep, stress and hormones all effect the ability of the brain to recover and explain why women are more at risk. The drop off in oestrogen and progesterone with the menopause cranks up adrenalin, which makes for more anxiety and insomnia. That's the subject of Chapter 11.

**Microbes and the Mind**

Another brain stressor is infection. This can happen by bacteria and other microbes, for example from mould, infecting the brain. There's one, p.gingivalis, that can travel from the mouth to the brain in those with gum disease, and another, a type of herpes virus, that can go from the gut to the brain. These also add to the toxic load in your brain, creating inflammation. This new area of risk is explored in Chapter 12.

By the end of this chapter you'll understand all the factors that lead to cognitive decline and, ultimately, Alzheimer's, and why it really isn't at all difficult to prevent it ever occurring.

**Alzheimer's Treatment – What's Working?**

Let's define an effective treatment as something that either prevents or slows down the rate of cognitive decline in an undiagnosed person, or something you do or give to a person diagnosed with either mild cognitive impairment, dementia or Alzheimer's, that either slows down or stops progression, or perhaps even reverses it .

Another definition of success would be stopping or slowing down the rate of brain shrinkage. To claim that Alzheimer's has been 'cured' or reversed, you'd have to show an increase, that is a reversal in brain shrinkage, especially of the critical medial temporal lobe or hippocampal region. Chapter 13 gives you interesting cases of people who have pulled out all the stops and arrested cognitive decline and brain shrinkage even after a diagnosis.

An example here is homocysteine lowering B vitamins given to those with diagnosed pre-dementia, called Mild Cognitive Impairment (MCI), diagnosed on the basis of a Clinical Dementia Rating scale, abbreviated to CDR. This is what they measure in the big drug trials.

A one-year trial of B vitamins, versus placebo, resulted in no CDR score - in other words a reversal in any symptoms that would diagnose Mild Cognitive Impairment - in a third of those given B vitamins compared to those given placebo, but only in those who started the trial with elevated homocysteine levels. The beneficial effect was greatest in those with sufficient omega-3 status.

Every anti-amyloid drug trial has so far failed to report a single person reversing their Clinical Dementia Rating. At best, they have reported modest slowing down in the rate of decline. So, no-one gets better, but some get worse slightly more slowly. Also, none have shown a significant decrease in the rate of brain shrinkage and the more 'effective' trials have actually shown an increase in the rate of total brain shrinkage.

What you'll find out in Chapter 13 is that the most effective 'treatments' have been systems-based. That is in individuals that have taken actions to reduce more than one risk factor behaviour and improved more than one biomarker. Unsurprisingly, these are 'cases' of people who have done different combinations of things based on their unique areas of risk. This doesn't easily lend itself to that 'randomised controlled trial', changing one thing only and giving everyone the same treatment. But so what?

This idea is a bit like saying how do we treat car breakdowns? Let's try more petrol, or more oil, or fixing a part, or cleaning a spark plug, or more tyre pressure. It's pretty obvious that there are a number of things that could lead a car to breakdowns (So) first you need to diagnose what's causing the problem, then 'treat' it, not just give everyone the same treatment. How you do this in the case of preventing cognitive decline and Alzheimer's is explained in Chapter 13.

What you will discover is that it is highly likely that almost no-one needs to develop this tragic disease, if they are willing to make reasonable changes to their diet and lifestyle, and take some supplements. The reason I say 'almost' is that there is that small percentage of Alzheimer's that is caused by genes. This is explained in Chapter 2.

That doesn't mean that people with these genetically causative types of dementia, that crank up amyloid accumulation, cannot substantially slow down progression. For these people, anti-amyloid drug treatment might actually work, but tragically, there's so few of them – not enough to make money – that remarkably little research is being done to find out.

**Prevention Is The Cure**

Despite all the incontrovertible evidence, I know of no majority Alzheimer's charity that is focussing on non-drug prevention. In the UK, I have been assured by the CEO that

the Alzheimer's Society has delegated 'prevention' to Alzheimer's Research UK, as has Race Against Dementia, and ARUK have told me that they spend considerably less than 5% of all research money on non-drug prevention. Similarly, of the apparent £166 million pledged by UK government, literally none of it filters down into real prevention covering any of the key drivers mentioned in this book.

Given that pharma can fund its own drug trials out of potential profit, and that the majority of the risk for Alzheimer's is preventable through diet, lifestyle and environmental changes, logic would dictate that AT LEAST half of all funds available would go towards non-drug prevention research and promotion.

Are the public, who donate money to charities and pay taxes to governments, aware that promising non-drug treatments are being ignored simply because they don't make someone enough money? Hopefully, some well informed trustees on their boards might blow the whistle and insist more of the funds raised go towards non-drug prevention, which is part of their charitable remit.

Government resources, that is our taxes, are channelled into organisations such as, but not only, the World Dementia Council, to implant and dictate policy to pave the way for more profitable drugs. In the US, the head of the the National Institutes of Ageing, Dr Masliah, who heralded the amyloid breakthrough, based on his research showing high levels in the brain, as 'the golden era of Alzheimer's disease research', then channelled billions of research dollars in that direction. But, according to a major investigation written up in a book, '*Doctored: Fraud, Arrogance, and Tragedy in the Quest to Cure' Alzheimer's',* it turns out he had manipulated photos of brain tissue and other technical images in his research. The National Institutes of Health announced that it

had found that Dr Masliah engaged in research misconduct and that he no longer held his leadership position.[1]

Another advocate of the amyloid hypopthesis is Dr Marc Tessier-Lavigne, the former president of Stanford University. He resigned in 2023 after an intrepid student journalist revealed numerous altered images in the research of his lab, in papers he co-authored. A Stanford University investigation, however, didn't find evidence to conclude that he personally engaged in research misconduct**.** They did note that, at various times when concerns with his papers emerged between 2001 and 2021, 'Dr. Tessier-Lavigne failed to decisively and forthrightly correct mistakes in the scientific record'.[2]

The amyloid agenda is also promoted globally through the World Dementia Council, which hosts meetings around the world. Ironically, I was 'prevented' from attending the World Dementia Council's 2024 annual meeting in London, which focussed on prevention, despite being recommended by leading professors and being the CEO of the UK's leading prevention charity.

The word 'prevention' is being hijacked to mean earlier drugs given, not on the basis of cognitive decline, but some arbitrary yardstick – such as the blood test they'll probably want all over 50 to have to create the pitch for early medication.

This is called 'diagnostic creep' and is how you increase those that can be treated. This was done with statins by lowering the 'normal' cholesterol level until most people over 50 would become eligible for the drug – myself included, despite not having a single indicator of cardiovascular risk.

Risk factors such as homocysteine, probably the only factor that can be said to be causal at this point in time, known to anyone seriously researching Alzheimer's, are intentionally ignored.

A classic example of this was the 2024 update of the Lancet Commission's report on dementia prevention, a highly influential publication that guides, for example, the NHS in the UK.[3] For the third time running it failed to include any mention of either homocysteinelowering B vitamins, or the dozens of published research studies on omega-3, or highlight the critical role of sugar in their report, despite having to hand the necessary papers, which had been sent to them by members of our Alzheimer's Prevention Expert Group (*see Resources*).

The omission of any mention of the evidence regarding homocysteine had been previously highlighted to the authors in their 2017 and 2022 versions. Reports such as these have to be 'peer reviewed' by independent scientists. Yet a study last year found that nearly 60% of the experts who reviewed manuscripts for four prominent medical journals received at least one payment from industry during a recent three-year period and, overall, these reviewers or their institutions received more than $1 billion from companies.[4] This is, quite simply, corruption which is defined as 'having or showing a willingness to act dishonestly in return for money or personal gain'.

One year on, the Lancet has failed to publish and address the letters sent by experts criticising this report. This closing down of any critique is directly against the ethical basis of scientific publication and peer review. The trouble is, so many researchers, leading 'experts' and opinion leaders know that they have to tow the line, focus and exaggerate the effects of amyloid or p-tau in order to get grants, promotions, commissions and consultancies. You just don't bite the hand that feeds you.

It is not a lack of research which is the drag factor in preventing Alzheimer's. It is corruption that lies deep within government agencies, influenced by profiteering industries, and the media, paid to publish puff pieces such as a recent

one in the Telegraph[5] headed ‘Alzheimer’s drugs should be prescribed like statins’, claiming falsely that the ‘amyloid cascade hypothesis’ was proven due to the ‘fact’ of the benefit of the new anti-amyloid drugs. It is for this reason this book, which has been peer reviewed, is self-published, because even the mainstream publishers are really nervous to go against the ‘establishment’ view, so invested in bringing drugs to market despite their danger and ineffectiveness.

**The Alzheimer’s Prevention Revolution**

Marcel Proust said, ‘the real act of discovery is not in finding new lands but seeing with new eyes’. My hope for this book is that you will see how we already know what we need to do to eliminate the risk for Alzheimer’s, or at least postpone that risk past natural lifetime. The solution is about education, not medication. You may lose your hair but there is no need to lose your memories towards the end of your life.

Also, you will discover that the very things that prevent cognitive decline and Alzheimer’s also prevent the other 21st century endemic diseases from diabetes, obesity, heart disease, to arthritis and most cancers. As a result, in the process of reducing your own risk for Alzheimer’s, you will add both years to your life and life to your years.

I do not believe there will ever be a single cure for Alzheimer’s, because there is not a single cause. Like most diseases, it is the ‘perfect storm’ of 21st century diet and lifestyle, that has inevitable consequences. Yet, with new vision, we can change this for ourselves. You are the architect of your brain’s future destiny.

Also, thanks to living in a digital age, we can deliver the same learning and encouragement to make the behaviour changes that prevent this awful disease to billions around the world.

Our goal, at foodforthebrain.org, is to test over 20 million people - a million each from the UK, Germany and Poland, a similar number from the US, Canada, Brazil, Japan, Algeria and 10 million in China, which has the highest prevalence of dementia – on our free on-line Cognitive Function Test and COGNITION questionnaire, translated into many languages. This then calculates a person's Dementia Risk Index based on diet and lifestyle and medical history, as well as offering a home test kit to measure the important biomarkers discussed in this book.

We hope you'll be one of them. The information and results are then anonymised and entered into what will soon be the largest database for prevention research in the world, accessible by researchers. It also means we can find the super-brainers whose cognitive function remains great year on year, and learn from them what they are doing to prevent cognitive decline. All this is funded, charitably, by you and people like you – citizen scientists. Not corporations with vested interests, putting profit before people.

We hope the free test will be shortly available on-line in almost all major languages in the world. We hope you will join us as a Citizen Scientist and advocate, starting with yourself and your immediate family, which is the subject of the last Chapter, Chapter 15.

Wishing you the best of health and happiness, Patrick Holford

PART  1

# What does & doesn’t cause Alzheimer’s

What is Alzheimer’s? To what extent is it caused be genes? What role do amyloid and tau, the targets for new drugs, play?
To what extent can you reduce or even eliminate your risk with changes to your diet, lifestyle and supplementation?
This part shows you.


# Amyloid ≠ Alzheimer’s and the Tauist’s delusion

If you think that Alzheimer’s or dementia is caused by amyloid plaques in the brain, or tangles of nerves (neurofibrillary tangles) associated with p-tau, you have been successfully fooled. But you would not be alone. There is a vast sleight of hand going on that remarkably continues to hijack research into true causes and potential cures for Alzheimer’s, despite a mountain of clear evidence to the contrary.

Let’s start at the beginning. Some people suffer increasingly severe cognitive decline. This affects about one in ten older people. We call this dementia. Some people with dementia, on scanning their brains, have big gaps in the central part of the brain. This is used to diagnose the form of dementia known as Alzheimer’s disease, due to the clear evidence of ‘pathology’ – something wrong in the brain that amounts to the death of significant amounts of brain cells in critical areas.

So, here we have two clear diagnostic criteria. Firstly, a loss of cognitive function, which is what is tested by the

dementia prevention charity, Food for the Brain, with its free, online Cognitive Function Test. Secondly, a loss of actual brain, which is diagnosed by a type of brain scan of the central or medial part of the brain. This scan was first developed based on research at Oxford University, headed by Professor David Smith, who is a member of the Scientific Advisory Board - see foodforthebrain.org/sab.

# What causes Alzheimer's?

So, then the question is: what causes it? There has never been any evidence (and there is still no evidence), that Alzheimer's, except for the very rare early-onset types of Alzheimer's caused by genes, is caused by deposits of amyloid protein or amyloid plaque in the brain. "Over the past 25 years, Alzheimer's research has suffered a litany of ostensible fraud and other misconduct by world-famous researchers and obscure scientists alike, all trying to ascend in a brutally competitive field," claims Charles Piller in the New York Times[6], author of the book, *Doctored: Fraud, Arrogance, and Tragedy in the Quest to Cure Alzheimer's.*

An example of the 'doctoring', reported by Dr Matthew Schrag, professor of neuroscience at Vanderbilt University, in *Science* in 2022, identified as many as 10 papers on the protein that deserve deeper scrutiny.[7] The report also cited other prominent researchers who have had difficulty replicating results of the studies on the specific proteins. The original research has now been withdrawn.

The reality is that about 30% of older people have plaques in their brains without dementia. About 15% of those with dementia don't have amyloid plaques.[8] Having amyloid plaques doesn't cause dementia. Mice whose brains have been molecularly engineered to produce amyloid plaques behave normally. Even a head full of plaques only results in

mild memory problems. Many of us have plaques in our brain and remain completely healthy.

# What started the amyloid excitement?

Less than 1% of diagnoses of Alzheimer's are caused by genes. These account for very early onset cases. The genes are Amyloid Protein Precursor (APP) gene and Presenilin (PS1 and PS2). Now these rare dementias can all plausibly be assumed to be caused by amyloid plaque deposition, and to be potentially curable by its removal. However, being so rare, there is little commercial imperative to find out. There is, however, one study in 2019 that tested two different antiamyloid treatments given to those with this rare early-onset Alzheimer's. Despite both drugs effectively lowering the amyloid burden, there was no clinical improvement, but a slight worsening for one of these treatments compared to placebo. In addition, one in five had brain swelling.[9] That would be reason enough to give up on the amyloid hypothesis.

The big mistake, however, was the leap of faith assuming that therefore ALL Alzheimer's, which makes up two thirds of dementias, were also caused by amyloid accumulation and could be so treated with drugs to lower the amyloid burden.

# What happens if you 'treat' amyloid plaques?

Blocking the enzymes that make amyloid has made people worse, not better, despite lessening the amyloid burden.[10]

Vaccinating animals to remove the plaques doesn't change anything to do with dementia, but it does reduce the amyloid. The anti-amyloid vaccine injections in humans have been equally ineffective (in terms of impacting dementia), despite lowering their amyloid burden.

The pharmaceutical companies running these failed trials have pushed and pushed until they could just about get a 'significant' difference in the rate of degeneration of patients versus placebo on assessment questionnaires – just enough to get a medical licence despite being clinically ineffective. Lecanemab was the first to be licensed in the UK, in 2024. The difference in the lecanemab trial between those on the drug and those on placebo was equivalent to less than half a point (0.45) change on an 18 point Clinical Dementia Rating (CDR) scale.[11] According to a British Medical Journal editorial this decrease "fell well short, representing only around a third of what a minimum clinically important difference might look like."[12]

On another scale, the Alzheimer's Disease Assessment Scale (ADAS), both those on placebo and drug treatment start to decline rapidly after 15 month (*see figure 1 right*). The Alzheimer's Society[13] report this miniscule difference as 'Lecanemab slowed down the speed at which memory and thinking skills got worse by 27%'.

This was the figure reported in the newspapers, ignoring the fact that, in reality, those on the drug just hit the same rock bottom about 3 months later than those on the placebo and the difference is so small that no-one is likely to notice. No-one got better. They all got worse. Quite a few got adverse effects, with brain bleeding and swelling. More than a quarter had adverse reactions. A few died as a consequence. Is three months of 'slightly less worse' worth the suffering of one in four and the death of a few (about one in 500) at vast expense? If such treatment was started before a person was put into care, at best it could mean putting them in a care home three months later. If treatment

were given while in a care home it would mean three months more time in a care home. Either way, at a treatment cost more likely to be in the region of £50,000 per year this is clearly not cost effective for the NHS or any health care provider.

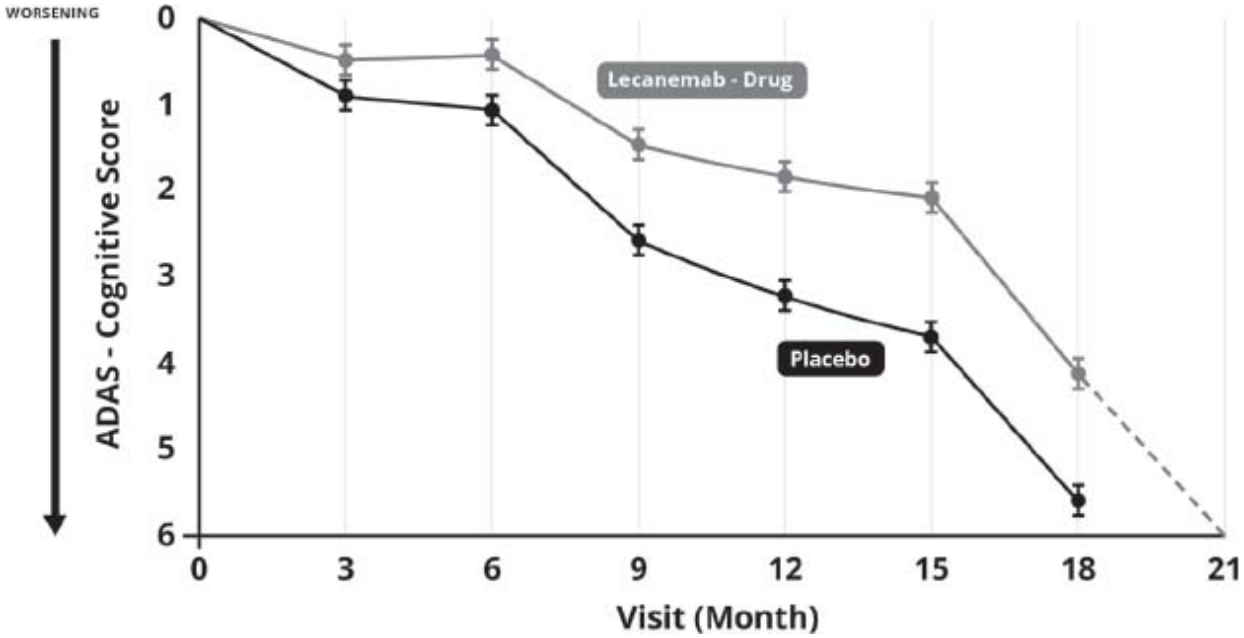



**Fig 1. Worsening of ADAS cognitive score with lecanemab versus placebo**

But still, drug regulatory agencies, paid for by the drug industry, dished out licences because the results were ‘statistically significant’- the result of enrolling as many as 1795 people. Larger trials make small positive results look better.

Even so, the UK watchdog NICE said the evidence wasn’t good enough and recommended the National Health Service not to give anti-amyloid treatment – at about £50,000 a patient per year when you factor in the cost of scans needed to check for bleeding and swelling with each injection and medical costs. Despite this you’ll read newspaper headlines such as ‘Alzheimer’s drugs should be prescribed like statins’,

as appeared in the *Telegraph*[14], interviewing Professor Hardy from UCL.

Please also bear in mind that even these bad results are the best that the drug company, who funded and ran their own drug trial, could conjure up with questionable methodology. The CDR (Clinical Dementia Rating) is essentially a questionnaire completed by a partner/carer and clinician. If you had vested hope that your loved one might improve on an experimental drug, might you answer slightly more positively?

Also, these trials are meant to be ‘double-blind’ i.e., the patient (and carer/partner) doesn’t know if they are injected with a placebo or drug. But when almost a quarter get severe side-effects just how ‘double-blind’ is it? If you got side-effects, assumed you were on the drug, would the hope of improvement bias your answers?

The truth is it is easy to cheat in trials, or at least massage the results in your favour, and there is a strong motive to do so, if it’s your drug, job and profits at stake. That’s why I trust trials done on drugs or vitamins by independent researchers. These don’t exist for the antiamyloid drugs and are unlikely to, due to the vast expense of such trials.

Independent researcher Sarah Ackley wanted to do a meta-analysis for publication in the British Medical Journal of anti-amyloid drug trials. She identified 34 trials suitable for inclusion in her analysis, but was denied access to the data of 20.[15] In other words, a drug company can run a failed trial, ditch it and move on, only revealing those that show an effect. Out of the 14 trials she was allowed to see the data from their meta-analysis concluded: *“Combined results from 14 randomized controlled trials provide evidence that reduction in amyloid levels alone is unlikely to substantially slow cognitive decline within the follow-up period of most typical trials. The results of pooled estimates suggest that use of anti-amyloid drugs is not a viable strategy for the*

*prevention or treatment of Alzheimer's disease and that other potential targets may merit more attention."*

Pharmacology Professor David Smith from the University of Oxford responded to the *British Medical Journal*[16] saying *"Scientists should seriously question the validity of the basic amyloid hypothesis, as was pointed out more than 10 years ago in relation to earlier trials.*[17] *These findings should direct our attention to the prevention of Alzheimer's disease by slowing down the disease process, for which there are many possible approaches. The study also raises an ethical question: is it justifiable to ask patients to undergo yet more trials of anti-amyloid treatments? Moreover, we should all question the morality of the drug companies that declined to give these researchers access to data for 20 of the 34 trials they wanted to study."*

In scientific terms, the poor results of the clinical trials, despite lowering amyloid burden, added to the already existing mountain of evidence, that amyloid deposits don't cause Alzheimer's; lowering it doesn't stop the disease process, doesn't improve cognitive powers in any meaningful way and doesn't slow down brain shrinkage. In fact, if anything, it accelerates the main physical measure of brain shrinkage. In the anti-amyloid trial for donanemab, those on the amyloid treatment had considerably more whole brain shrinkage – greater than 20% more than those on the placebo (see graph below).[18] You would think that the whole field would get the message by now; stop funding this dead end and explore other avenues. But there is a lot of investment in the 'amyloid cascade hypothesis' that no-one wants to give up. It's become an unhealthy obsession.

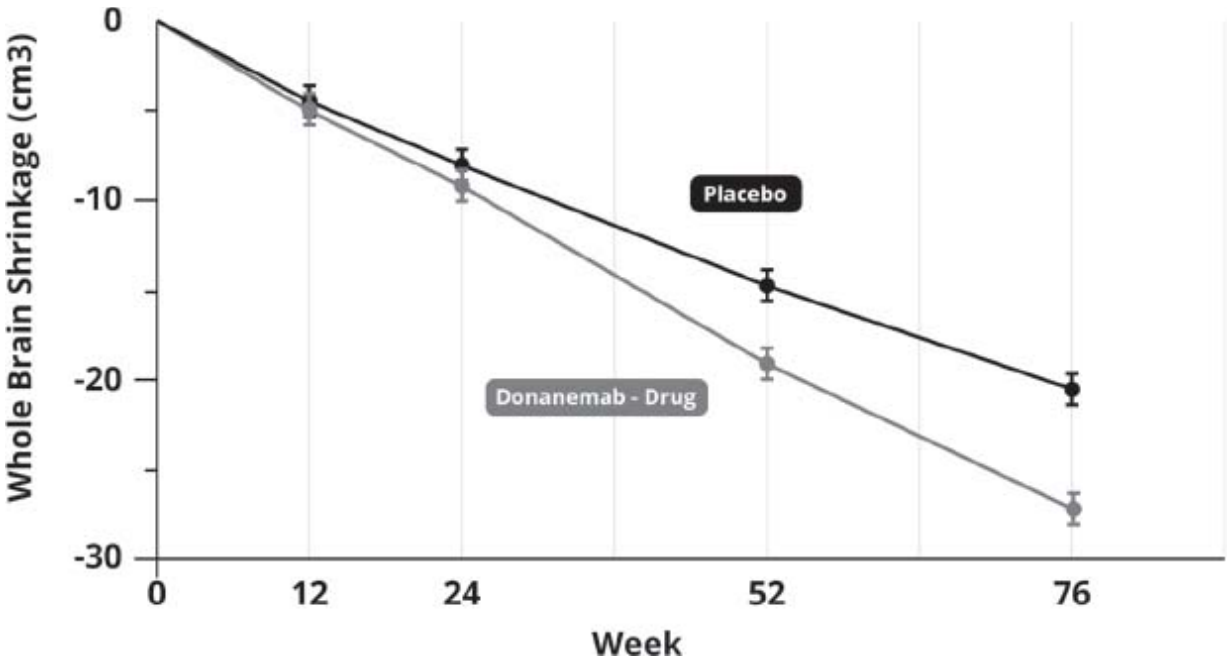



**Figure 2 – Brain shrinkage with donanemab versus placebo**

In the US, the Alzheimer's Association and in the UK the Alzheimer's Society and Alzheimer's Research UK, have all supported this line of research and continue to do so. The Alzheimer's Society, having part funded original research into amyloid with Professor Hardy, consider this their greatest contribution to the field, 'revolutionising dementia research'.[19] The trouble is, it's a dead end.

In 2024, there were 164 clinical trials registered assessing 127 drugs, many of which are based on amyloid and p-tau.[20] With several million 'eligible' patients, pharma is not going to give up.

# Why aren't other avenues being explored?

It’s partly to do with money. No-one can get research money if they’re not looking at amyloid (or p-tau – more on this in a minute).

In the UK, the Medical Research Council continues to pour good money after bad by making another £20 million available for drug trials.[21] That’s taxpayers’ money backing the wrong horse, despite a lousy track record. In the US, the National Institutes of Health and the National Institutes of Aging spend vast sums pushing in this fruitless direction. Big pharma spends twice as much as the government agencies and the charities, both of which are funded by the taxpayers, probably around $150 billion so far. So, perhaps $250 billion has been spent getting almost nowhere. Sure, we know a lot more about amyloid and p-tau, but are no closer to a ‘cure’.

I remember when, at the G8 Summit in 2013 in London**,** pharmafunded scientists said, *Within ten years we’ll have a cure*. Listening to the BBC Radio 4’s *Inside Health* programme on ‘What’s next for Alzheimer’s’[22] in November last year, they said the same thing. How can you claim you’ll have a cure when you don’t even know the cause? I predict we’ll be in the same place in ten years if the Alzheimer’s industry doesn’t move on from amyloid and p-tau.

But it gets worse. Despite nothing but evidence to the contrary, based on the completely false notion that ‘Alzheimer’s IS amyloid’, we are being told an amyloid blood test is around the corner. This will tell us nothing useful. It won’t tell us who has Alzheimer’s or who is at risk. So why take the test?

The case for developing a test was made by Professor Hardy in the Telegraph. “My dream is you go the doctor at age 60, have a test, just as you would do for cholesterol. So, it finds you’re at high risk for Alzheimer’s disease, let’s put you on anti-amyloid drugs. Scientifically not difficult.” This may be his pipe dream but, as you have read, no treatment has yet shown a clinically significant effect. A Cognitive Function Test is a better (and free) predictor than an amyloid

test, antiamyloid drugs don’t work and are dangerous. Also, statins don’t work nearly as well as we were led to believe. But the two-step dance of a test that feeds a prescription to healthy people certainly made a lot of money. Over $1 trillion. Statements like this are about sales not science. At best, not that there is evidence to support this, he says that it could mean going from diagnosis to nursing home in seven years instead of five years. In other words, no-one gets better or stays the same. They would just get worse more slowly.

All this is laid out beautifully in a book by Karl Herrup, Professor of Neurobiology and Investigator at the Alzheimer’s Disease Research Centre at the University of Pittsburgh, called *How NOT to study a disease – The Story of Alzheimer’s*. If you are questioning what I am saying, please read this book. You can find it in the online bookstore at foodforthebrain.org in the books section.

The medical-pharmaceutical industry is so desperate to find a treatment and make money that it just can’t give up. It reminds me of the story of Mullah Nasrudin, who was looking at the illuminated ground under a lamp post. A passer-by asked, ‘What are you looking for?’ The Mullah said, ‘I dropped a coin.’ The passer-by replied, ‘Did you drop it around here?’ The Mullah said, ‘No, but it’s the only place I can see’.

It’s akin to a campaign to ‘cure’ lemmings when the only cure is for them not to jump off the cliff in the first place. Why spend all that money researching how to give lemmings the medical attention and hospital care as they approach death, when there is a far simpler and less expensive way to help them not need it. Prevention.


Fig. 1 'Waiting for a cure'


Fig. 2 Prevention

A person with dementia will cost the state and family around £100,000[23]. We can help someone substantially reduce their

risk by joining Food for the Brain's COGNITION programme with a small annual donation. So, for everyone we save from dementia, we could help thousands more.

But let's be clear. It is true that having lots of amyloid in your brain can increase the PROBABILITY of getting Alzheimer's in the future, in much the way that being older also increases the probability of getting Alzheimer's. But it doesn't cause it. So 'curing' amyloid won't cure the disease.

The same thing is happening with another 'marker' in the brain called p-tau, which is associated with having more tangled nerves. Tau is a normal protein that becomes an abnormal, toxic protein called p-tau. The 'p' stands for phosphorus or 'phosphorylated' because there's an enzyme that adds on the 'p' and another that takes it away. Much like amyloid, having more p-tau increases the PROBABILITY of Alzheimer's, but does it cause it? Many people have raised levels of p-tau (we all have some) with no problems at all. However, unlike amyloid, there is a threshold such that if you have a lot of p-tau, which means a lot of tangled nerves, this does correlate with the degree of cognitive impairment.

By using the same sleight of hand, £10 million has been put up by the Bill Gates Foundation and people funding Alzheimer's Research UK, to find the blood test for p-tau (I think they've already decided on one called p-tau 217), despite questionable evidence that p-tau causes Alzheimer's and may just be an artefact of the disease process. In a similar way, tooth decay caused by nutrition and lifestyle deficiencies, such as too much sugar and not brushing your teeth.

No doubt, those with raised p-tau 217 will be told they have 'pre-clinical dementia', despite no evidence that they do. Of course, if they had a p-tau lowering drug that actually worked, as in reducing dementia risk, that might be excusable, but they don't. Those that have blocked the enzymes that cause the accumulation of p-tau have failed. A more relevant question is what causes p-tau to go up? In

other words, go to the root of the problem. However, this sleight of hand may be used to sell drugs that don't work, much like 'cholesterol' has been used to sell statins.

My cholesterol is slightly high – I have no disease, no risk factors for heart disease and there is no evidence that lowering my cholesterol will lower my future risk, but still my doctor wants to prescribe me statins. Why? Because GPs are given a calculator called QRisk where you pop in age and cholesterol level and it says 'prescribe statins'. In any case – two thirds of heart attacks are predicted by high homocysteine – not cholesterol.

# The P-Tau Delusion

With the failure of amyloid drugs to commercialise much emphasis is being put on p-tau inhibitor drugs. So far there are no good clinical results with several horses in the race.

The only thing I know that *does* lower p-tau is lowering homocysteine with B vitamins. Homocysteine, a toxic amino acid also found in those with Alzheimer's and dementia, promotes the enzyme that makes p-tau and blocks the enzyme that clears it from your brain[24], as the diagram overleaf shows.

However, homocysteine, unlike amyloid, is actually causal. That is, lowering homocysteine with B vitamins, stops the accelerated brain shrinkage, stops the cognitive decline and memory loss. That is consistent with a disease-modifying treatment and possibly the only thing, which from the current evidence, could be said to be causal. It is possible that some of its benefit is in lowering p-tau. There's not enough research yet to say more than that at this point in time.

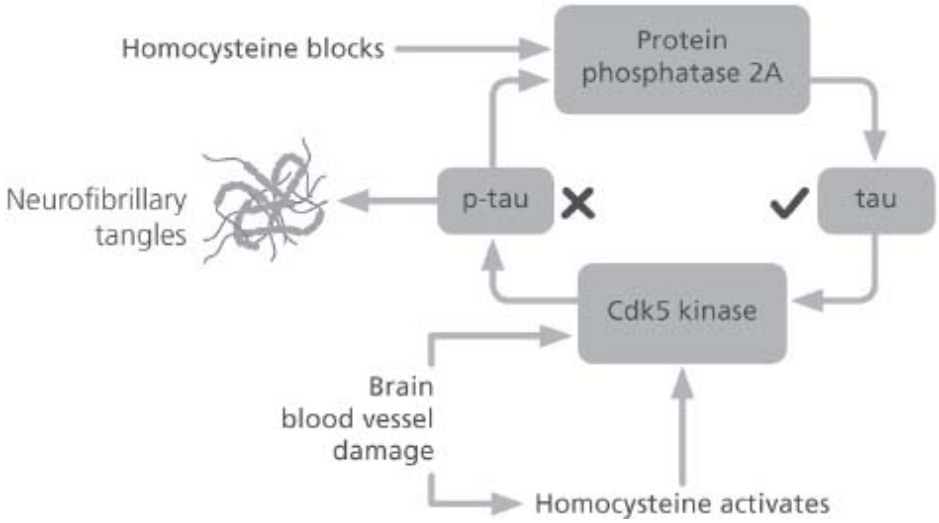



**Figure 3 – How lowering homocysteine inhibits p-tau formation.**

Of course, the 'tauists' know this and most of the drugs being developed try to do what lowering homocysteine does. Building on a few discoveries that 'methylene blue'[25], a methylated colouring, interfered with the formation of p-tau, and that the amino acid cysteine is involved in tau accumulation[26], drugs such as HMTM (Hydromethylthionine mesylate) exploit this bit of chemistry. Lack of B vitamins messes up methylation and homocysteine accumulates, leading to more p-tau formation. (Homocysteine is made from the amino acid methionine, which can also be turned into the amino acid cysteine, then glutathione – *see Chapter 6*). It is unlikely these drugs will have a substantial clinically significant effect, and much less so than lowering homocysteine. No doubt they will have adverse effects to factor in. But it won't stop the drive to get such tau accumulation- inhibitor (TAI) drugs to market. Of course, it would be easier to just lower homocysteine with inexpensive and safe B vitamins, but these cannot be patented and hence cannot generate the profit pharma companies are looking for.

If treatment was really being driven by science, everyone would already be shouting about homocysteine lowering B vitamins *(see Chapter* 6). One senior representative of a pharma company told Professor David Smith, whose research on homocysteine is par excellence, that homocysteine lowering B vitamins would be a 'multi-billion blockbuster drug if it could be patented'. But therein lies the problem.

That doesn't mean there won't be other causes. Not everyone who develops Alzheimer's has high homocysteine levels. There are other natural processes and compounds that can become damaging if they get out of balance. For instance, oxidants and inflammation protect against injury and infection but can damage mitochondria - the so called 'energy' factories inside every brain - if levels get too high. The effects of insulin resistance and damaged glucose control are similar.

Diabetes and dementia are strongly linked, the first doubling the risk of the second.[27] In truth, both homocysteine, which is a measure of a vital process called methylation, oxidation, insulin resistance and inflammation all affect the mitochondria. One clue for inflammation being involved relates to the finding that those with rheumatoid arthritis using heavy duty anti-inflammatory drugs have less risk for Alzheimer's.[28]

These are some of the fruitful avenues that have been explored and show real promise. But they have all largely been ignored because of the unhealthy obsession by Pharma, the Alzheimer's societies and government funding bodies on amyloid and tau.
They will be explored in subsequent chapters.

In Food for the Brain's model of dementia, glycation, oxidation, methylation and the vital role of brain fats, which actually build the brain, are central. I call them the 'four horsemen of the mental health apocalypse'. The discovery that the homocysteine lowering B vitamins and omega-3 are co-dependent and together, dramatically slow brain

shrinkage and improve cognitive function much better than any amyloid or p-tau treatment to date, is of major importance. Yet, this has been largely ignored by the blinkered Alzheimer's establishment.

So, next time you are asked to donate to Alzheimer's charities ask them if any of the money is being spent on amyloid or p-tau. If it is, I'd suggest politely declining. If instead they are funding research into oxidation, inflammation, homocysteine, insulin or mitochondrial function, then that's a much better sign that your money is being put to good use.

# Is Alzheimer's prevention the cure?

However, just focusing on one of these avenues may be misguided. It is based on the current paradigm of medical research – find the thing that is causing the disease, then 'cure' that. This assumes there is one cause and therefore one treatment. Of course, this is what you need for a drug to make money.

Let's take homocysteine as an example. Not everyone who develops dementia or Alzheimer's has high homocysteine. According to research at the US National Institutes of Health, it accounts for 22% of the risk.[29] Those who do have high homocysteine will reliably develop dementia and lowering it reliably reduces their cognitive decline. So, high homocysteine is a CAUSE, but not the only cause. Insulin resistance leads to diabetes and increases the risk for dementia. So, insulin resistance, driven by too much sugar and refined carbohydrates, is probably a cause, but not the only one. There isn't enough evidence yet to declare 'cause', but the evidence that exists certainly points that way.

There is a different way of thinking and researching called ‘systems-based’ science. Much like the straw that breaks the camel’s back, this approach presumes there are a number of conditions, not just one, that can result in a disease such as Alzheimer’s or dementia. After all, a stroke or head injury can be a cause of cognitive decline, even if you don’t have high homocysteine or blood sugar problems. (It could be that a potential causal mechanism that ties these together is cerebrovascular dysfunction – disturbed blood supply to the brain. High homocysteine, by the way, increases risk of this by 17-fold[30]).

In my book *Upgrade Your Brain*, which gives all the referenced studies for statements made here, I argue that every known risk factor or biomarker for cognitive decline, dementia or Alzheimer’s affects either the structure, the function or the utilisation of the neuronal network and that it is combinations of these that crank up risk and ultimately brain pathology.

It’s like saying five critical things have to work for your car to move forward and not crash. Tyre pressure good, brakes working, enough gas, oil to lubricate the engine and water to cool it. If any one of these is completely broken, the car stops or crashes. If two are not working well, such as low oil and low water, the car grinds to a halt. If the brakes aren’t working, you crash.

We tend to think this way in nutrition and lifestyle medicine. It’s the combination of insults such as high sugar intake, too many fried foods, lack of vegetables, too much alcohol and smoking, that breaks the camel’s back. That heart attack is the ‘perfect storm’ of several underlying factors.

This systems-based approach isn’t popular in science and very few funders ever put up money to fund this kind of research. Usually, a funder wants to fund one stream of research, possibly a clinical trial of one approach, in the belief that this one factor is the key and a great discovery

will be made. The reality is that it is usually combinations of factors that drive risk, with the manifestation of the disease itself being the ‘broken back’. Pollution, for example, is a risk factor for dementia … but not in those with good vitamin B6, folate or B12 status[31], which are the three B vitamins needed for methylation, indicated by lower homocysteine. Methylation is a major mechanism in the body, used to detoxify pollutants and toxins.

This is where Food for the Brain’s approach is unique. By collecting data from people like you who have both taken the Cognitive Function Test and completed the COGNITION questionnaire, and keep doing so, we can look at what drives cognitive function up and down. In other words, what ‘breaks the camel’s back’ or alternatively, makes it ‘strong’. This kind of complex systems-based science has become possible due to big data gathering (such as we are doing), advances in complex statistics, computer power and programming AI algorithms. Our Head of Science, Associate Professor Tommy Wood, is an expert in this kind of approach to neuroscience.

It is, I believe, the future and why we will probably find no single primary cause for Alzheimer’s, and certainly not amyloid or p-tau, but combinations of diet and lifestyle and other factors that create the tipping point that leads to dementia. Then, we will have the means to prevent this tipping point from ever being reached. In other words, we may discover that prevention is the cure.


# Less than 1% is ‘in the Genes’ and the ApoE4 Exaggeration

Genes are at the heart of the discovery of Alzheimer’s but, in fact, play a very small part. When Alois Alzheimer first identified the phenomenon of early onset dementia which was named Alzheimer’s in 1910, it was based on the autopsy of the brain of a patient called Auguste, in which there were deposits of a ‘peculiar waxy substance’, now known to be amyloid plaques.

Amyloid is a protein. About half the dry weight of your body is made up of proteins, including enzymes, hormones, muscles, skin, bone and so on. Proteins are themselves made from amino acids in much the same way words are made from letters. There are 22 amino acids, although there are only 9 essential amino acids from which we can make the 22 amino acids we need to build proteins (This is a bit like being able to turn an E into an I and an L). Some neurotransmitters, such as serotonin, are made from single amino acids (and called mono-amines). So, amino acids are

the building blocks of life, and we get them from eating food containing protein, which is then digested down into amino acids and effectively reassembled into body parts. How does our clever biology do this manufacturing of proteins? That's what genes are all about.

Genes contain a 4-letter code (computers programme in 1s and 0s, a 2 number code). Within the strands of DNA, which are like rungs on a ladder of the chromosome, there are four substances, called nucleotides - adenine (A), cytosine (C), guanine (G) and thymine (T). Each strand has two of them, for example, AT or CG. This code gets copied into every new cell, providing the instructions to assemble amino acids together into proteins. Amyloid happens to be 40 amino acids in a particular configuration.

The big breakthrough came in 1984 when it was discovered that amyloid proteins are also found in the brains of those with Down's Syndrome. Then, with the evolution of the ability to 'read' genes, the hunt was on to find the gene mutation that was responsible for making all this amyloid, or actually a precursor protein that then produced amyloid.

The gene was discovered and named Amyloid Precursor Protein gene, or APP for short. The troublesome APP mutation is very rare. As of 2023 there were 500 individuals, who may account for considerably less than 10% of cases of early-onset Alzheimer's[32].

A child with a parent who has this gene mutation has a 50% chance of developing it. If both parents have it, it is inevitable that amyloid will accumulate and they'll get dementia usually in their fifties. If a person free of this gene were to marry someone with it, their children would have a 50% risk. So, it is what is called a causative gene. Then, two other causative genes were discovered, called Presenilin 1 and 2. The three causative genes (APP, Presenilin1 and 2 – collectively called Dominantly Inherited Alzheimer's Network DIAN) account for considerably less than 1% of all Alzheimer's diagnoses[33]. While most go downhill rapidly

there some unexplained cases where, despite having these genes, and accumulating amyloid, good cognitive function is maintained.[34]

Now, while the original emergence of Alzheimer's were these very early-onset cases, today, Alzheimer's is the diagnosis given to anyone with shrinkage of the central area of the brain and accounts for two thirds of diagnoses, the vast majority occurring after the age of 65.

# Predictive genes such as ApoE4 and MTHFR

While these causative genes are very rare, you can inherit variations of genes that, statistically, increase your risk under certain circumstances, but do not cause it.

There are something like 76 other genes[35] which appear to confer a very small additional risk. Taken together, some statistical models even suggest that 75-85% of the risk can be explained by combining these into a polygenic risk score.[36] Not everyone agrees with this.

Before going on its worth contextualising the role of non-causative genes, which provide the instructions for proteins. Think of them like dimmer switches. Whether the genes are activated (called 'expressed') or not depends on the circumstances or conditions they are in. Darwin highlighted these two categories most eloquently when he said, in *Origins of Species*, that there were two driving forces – the conditions of existence and natural selection. But, in all his writings, he said 'conditions of existence' were more important. Let's take the example of badgers and foxes. If you urbanise the environment, foxes do well (natural selection), badgers do badly. If you ruralise, back come the badgers. There's a really important message in this analogy,

which we can understand by considering a highly predictive gene, ApoE.

# The ApoE4 exaggeration

The single greatest, most researched and best-known predictive gene is a variation of a gene that makes a protein, called apoprotein. Apoprotein carries fats in the bloodstream. Fats are called lipids and when the apoprotein ‘trailer’ is loaded with lipids it's called a ‘lipoprotein’. You will have heard of Low-Density-Lipoprotein (LDL) and High-Density-Lipoprotein (HDL), often wrongly oversimplified as ‘good’ and ‘bad’ cholesterol. The cholesterol is the fat on the apoprotein trailer. We all have a pair of genes with the instructions to make apoprotein, but that genetic instruction is slightly different in some people, which is called a ‘variant’. A particular variant, ApoE4, is found in about one in five people and about 2-3% have a pair of these ApoE4 genes.

If you have this gene, your risk for developing Alzheimer’s roughly doubles on average compared to someone who doesn’t. With two copies, it roughly quadruples.

This raises an important point about the way medical research is reported, that is worth knowing about if you are taking responsibility for your own health. Relative risk tells you the difference in the way two groups reacted to things like having a gene or getting a drug. What it doesn't tell you is your absolute risk of responding to the drug or having the gene. Without that, it’s difficult to make an informed decision.

Let’s say a treatment has been found in a RCT to reduce the risk of developing a disease by 50%. Sounds impressive. Let me have it now! But it could be that the absolute risk of you developing the disease is only 2%. Then your 50% reduction actually means that your risk only drops by 1%.

The absolute risk for Alzheimer's from having the ApoE4 gene is considered to be 4 to 6%.[37]

Even this sounds like bad news but please remember this is a prediction not a destiny set in stone. ApoE4 is not a causative gene which means, like the badger and fox, it only kicks in under certain 'conditions'. Think of these risks above as occurring in the 'normal' conditions of the normal bad diet called the SAD diet (standard American diet) and lifestyle that is the equivalent of 'urbanisation' in our example. That's what most people eat and it's from them this risk is established. So, under the normal, bad circumstances that we've created in the 21st century, the presence of ApoE4 becomes the straw that breaks the unhealthy camel's back. How this happens is largely to do with accumulating too much cholesterol and LDL[38] and the promotion of inflammation. The inflammation, in turn, leads to more amyloid plaque. Ironically, the anti-amyloid drug lecanemab is associated with more bleeding and swelling[39], which are potential causes of death, in those with ApoE4, so those with ApoE4 are advised against taking this drug and probably other antiamyloid drugs.

But what happens if you change the conditions of your life and diet, such as those that lessen inflammation and lower LDL cholesterol?

After all, genes exert their effect across your biology, and that biology changes depending on what you eat and how you live. Even if you have a gene variant such as ApoE4 it is more like a dimmer switch and can be 'over-expressed' or 'down-regulated', turned up or dimmed down. That is why some with the gene develop Alzheimer's and others don't.

# Dimming down ApoE4

The ApoE4 gene is downregulated by eating a low-glycaemic load (GL) diet, low in sugar, or a more ketogenic diet with specific Mediterranean-style food choices, including fatty fish, cruciferous vegetables, olive oil, low alcohol consumption. Six supplemental nutrients have reasonably good evidence of down-regulating ApoE4.

These are omega-3 DHA, B vitamins (B2, B6, B12 and folate) vitamins D3 and K2, quercetin (found in red onions) and resveratrol.[40] This approach to modifying the effects of the genes we inherit with personalised nutrition is a fundamental tenet of orthomolecular medicine, sometimes called personalised, precision or optimum nutrition. Could changing these things eliminate the increased risk of ApoE4?

Before I answer that it's worth knowing a bit about the fundamental design of studies that create the headlines we read in newspapers, saying that this or that increases your risk of dementia.

Now, most thorough studies testing things that might help reduce the risk of Alzheimer's – better diet, more exercise, cognitive stimulation, omega-3s, homocysteine lowering B vitamins - will have one group taking the 'treatment', and a placebo or control group who aren't. Other studies are 'observational', where they look back at those, for example, who smoke or who don't to see what percentage go on to develop Alzheimer's.

That is, they don't actually change anything, but look at people who do or don't eat fish, or exercise, to see what that does to their risk of developing Alzheimer's. In both 'intervention' and 'observational' studies, the researchers also look at the differences in key attributes between the two group. So they are comparable – similar age spread, similar percentage of men and women, similar number of smokers, for example, but also whether the participants do or don't have the ApoE4 variant. This is how they eliminate 'bias' between the two groups. Let's take a look at what happens

in some of these studies where they measured ApoE4, and to what extent having ApoE4 makes a difference.

A good example of this is a study, published in the British Medical Journal, involving 29,072 people in China, 20% of whom had the ApoE4 gene.[41] Each had their diet and lifestyle assessed for 10 years.

It found that whether or not a person had ApoE4 made no difference to the positive reduction in risk achievable by simple diet and lifestyle changes. “These results provide an optimistic outlook, as they suggest that although genetic risk is not modifiable, a combination of more healthy lifestyle factors are associated with a slower rate of memory decline, regardless of the genetic risk,” wrote the study authors.

Another study – the FINGER trial – followed a group who improved their diet, exercise, cognitive training, and cardiovascular risk for 2 years compared to those who didn’t. The changes worked to decrease risk and slow down decline in cognitive function. But most interestingly, having the ApoE4 gene made no difference to the outcome.[42]

Think of these healthier people with a better diet and lifestyle as ‘healthy, strong camels’. No longer was the mere presence of ApoE4 able to break their back.

# B vitamins modify methylation genes linked to dementia

Several Alzheimer’s predicting genes affect a process called methylation. Healthy methylation depends on adequate B vitamin intake, primarily B6, B12 and folate, as you’ll see in Chapter 6. Much like ApoE4, inheriting a variant of a key methylation gene that makes an enzyme called MTHFR increases risk for Alzheimer’s by about a third.[43] This gene provides the instructions to make an enzyme – methyl-tetra-

hydrofolate-reductase – that is vital for methylation, a process that is central to keeping your brain healthy. The variant of this gene called MTHFR 677TT, makes you less good at methylation so your level of brain damaging homocysteine rises. Having a raised homocysteine level increases risk for dementia by ten-fold and cerebrovascular (blood vessels) dysfunction by 17-fold.[44] About one in three people have this gene variant.

It's all about that total load. Let's take an example of choline, which makes a brain essential phospholipid. Since methylation is also needed to assemble these phospholipids, which are brain essentials found in eggs and fish, having a poor diet deficient in phospholipids creates more methylation demand, and consequently, greater need for B vitamins.

But if you make defective methylation enzymes due to the presence of the MTHFR 677TT gene, this is a classic example of a change in the conditions (lack of phospholipids) putting more 'stress' on the camel's back, and then the presence of MTHFR 677TT gene variant becomes that 'last straw'. As you'll learn in Chapter 5, having more choline in your diet halves a person's future risk of cognitive impairment and Alzheimer's.[45]

But what happens if you improve the conditions by giving B vitamins to improve methylation? We will go into these studies in detail in Chapter 6, but here's an example. In a placebo-controlled study of older people with mild cognitive impairment, about a third had the MTHFR677TT variant that increases Alzheimer's risk.

Half were supplemented with B vitamins, and half given a placebo. The B vitamin supplement almost arrested further memory decline and slowed the rate of brain shrinkage by 52%[46], reducing shrinkage of the Alzheimer's areas of the brain by 9-fold.[47]

Was there any difference between those with or without the risky gene variant MTHFR677TT? It made no difference to

the beneficial effect of the B vitamins. I've yet to find a study giving adequate amounts of homocysteine lowering B vitamins, where the presence of MTHFR677TT made any difference to the benefit derived from the B vitamins. It's another example of why healthy camels don't get broken backs from inheriting 'predictive' genes. I think of these genes like weak torchlights, which you can see in the darkness of a bad diet and lifestyle. But once you shine the light of optimum nutrition, you can't even see the torchlight.

# The merit of gene testing to personalise your prevention

Too often genes are blamed as drivers of disease when (with the exception of rare causative genes) the primary drivers are what you put in your mouth or how you live your life - both factors under our control. Over-emphasizing the importance of genes encourages people not to take responsibility for improving diet and lifestyle and taking charge of their own disease prevention.

There is merit, however, in testing your gene polymorphisms, Apoe4 and MTHFR 677TT are examples, because they can show you whether you will specifically benefit more from B vitamins and specific forms of folate, choline and omega-3, along with lower fat, less alcohol and reduced carb intake. Gene testing can therefore fine-tune your prevention approach.

Gene testing should also test for other gene variants, shown in the table below, together with their prevalence. Those who have inherited that gene variant from both parents are 'homozygous'. Each gene variant will put more stress on a part of your biochemistry, which is supported by specific nutrients. For example, those who have the ApoE4

gene need the support of the nutrient choline and benefit from a high antioxidant and anti-inflammatory diet.

| Gene | Prevalence* | Nutrition Support | Notes |
|---|---|---|---|
| MTHFR C677T | 34% (44% hetz, 12% homz) | Folate, B2 (co-factor). Consider methyl folate, Zn, B12 | Major impact but can be fully compensated by nutrients - folate and B2 |
| DHFR -19del | 33% (33% hetz, 16% homz) | ***Limit*** folic acid. Food folates or methyl folate | More common in European populations |
| MTR 2756A>G | 19% (30% hetz, 4% homz) | Consider methyl B12, Zn | High homocysteine (inhibits recycling) |
| BHMT R239Q | 30% (41% hetz, 9% homz) | Zn, betaine, choline | High homocysteine (inhibits recycling) |
| APOE | 25% hetz, 2-3% homz | Choline. Anti-inflammatory. Antioxidant | APOE4 is higher in N. Europe. Lower in Asia. Biggest single genetic risk factor for late onset Alzheimer's |
| BDNF | 19% (30% hetz, 4% homz) | Exercise, Vitamin D, B3 | |
| GSTM1 (Null) | 50% (50:50) | Glutathione, Vit E, C etc | Gene is present or absent. |
| KLOTHO F352V | 14% (23% hetz, 24% homz) | Avoid UPFs (excess phosphorous or phophates) | Hetz variant is protective. Homz in detrimental |
| APP V7171 | 0.0001% (0.001% hetz, 0% homz) | Highly penetrant - i.e. causal | Pathogenic - i.e. causal but rare |
| PSEN1 M146L | Below statistical | Highly penetrant - i.e. causal | Pathogenic - i.e. causal but rare |
| PSEN2 N141 | Too low to present | Highly penetrant - i.e. causal. Inflammatory | Pathogenic - i.e. causal but rare. Early onset Alzheimer's |

***Prevalence - first number is the frequency of the risk allele. Hetz - heterozygous frequency. Homz - homozygous frequency.**

I often recommend such testing in those with cognitive problems and especially in those who struggle, for example, to bring down their homocysteine or cholesterol level. Gene testing can reveal the weakest links in their biochemistry, the logjams so to speak, and which set of circumstances are

needed to get their brain’s chemistry singing the right tune. If you’d like to explore this option see *‘Gene Testing’* in *Resources* on page 192.


# Alzheimer’s is Caused by a Systems Breakdown

Now we know that neither amyloid nor p-tau nor genes (for 99% of people) cause Alzheimer’s, what does? At one level the answer has to be ‘many things’. The list below shows the many known risk factors but there are likely to be many more.

There are detailed research papers published on each of these and, of course, most are under our control to a considerable extent. But, somehow, prevention gets minimised or side-lined in the quest for a cure, which always seems to be ‘within ten years’. An example of this is the 2024 Lancet Commission report on dementia prevention, the third since 2017, which ignores many of the hardest hitters with the most evidence and biggest effect, that are easy to change. By doing so they vastly underestimate the percentage of dementia cases that could be prevented at 45%. It may well be double this. We will unpick the omissions in the Lancet Commission in Chapter 5, 6 and 8.

I propose that every known risk factor or biomarker for cognitive decline, dementia or Alzheimer's affects either the structure, the function or the utilisation of the neuronal network, and that it is combinations of these that crank up risk and ultimately brain pathology.

Although one thing, such as massive alcohol intake, or a brain injury, or stroke, or chronic deficiency of omega-3 or B12, could bring on dementia and Alzheimer's, for the majority it is a combination of factors – a 'perfect storm'. It isn't just 'use it or lose it'.

We've seen super smart people slip into Alzheimer's. Nor is it just something like lack of omega-3. Japan, which has one of the highest intakes of seafood, also has a considerable amount of Alzheimer's. Nor is it just a result of brain damage such as stroke or head injury.

In the chart below you see how almost all these risk factors fit well into the 'structure', 'function', 'utilisation' model.

Air pollution
Alcohol
Antacid use (PPIs)
Antioxidant intake
Anxiety
B vitamins
Cardiovascular disease
Cataracts and visual loss
Cholesterol
Choline
Cognitive activity
Exercise
Education
Dental health
Depression
Diabetes
Fructose intake

Genes
Glucose imbalance
Gum disease
Gut health
Head trauma
Hearing
Herpes
High blood pressure
Homocysteine
Hormones
Inactivity
Inflammation
Insulin resistance
Loneliness
Menopause
Metformin
Mould
Muscle mass
Obesity
Omega-3
Phospholipids
Polyphenol intake
Seafood
Sleep
Sleeping pills
Smoking
Social isolation
Stress
Stroke and TIAs
Sunlight
Vitamins C, D and E

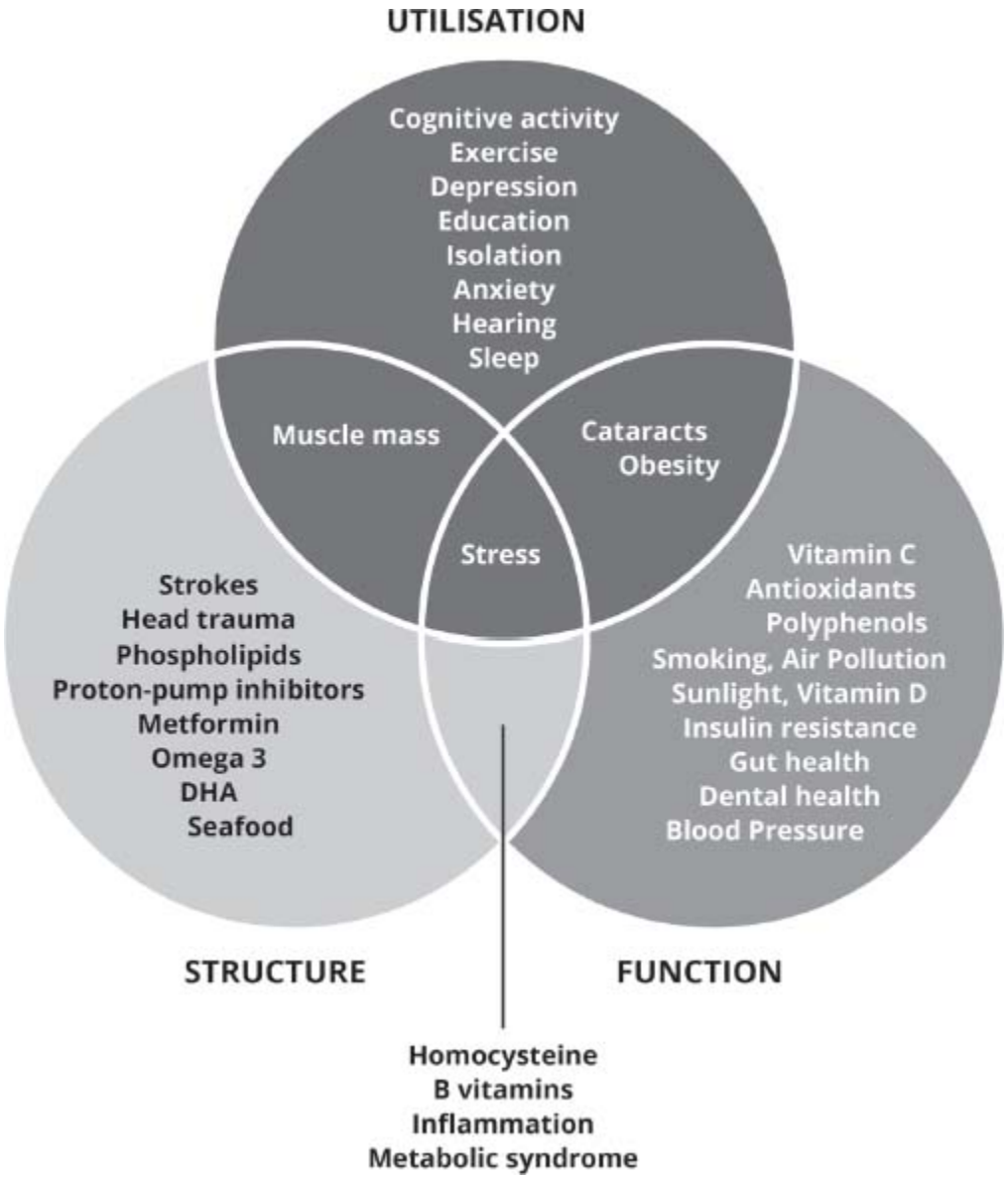



**Figure 4 – Structure, Function and Utilisation model of risk factors for cognitive decline**

Much like our examples of how nutrients are synergistic – for example, omega-3 fats don't reduce risk if you're B vitamin deficient, which is the subject of Chapter 7 – so too are risk factors. Pollution is a risk factor, but only in those low in B vitamins.[48] Poor sleep is a risk factor, but not so much in those who exercise.[49] There are many such examples which is why studies that just look at one thing, without

understanding the interactions, are going to under-estimate the power of prevention.

We can get a bit more nuanced about this ‘systems-based’ approach to cognitive decline and Alzheimer’s by recognising what it doesn’t cover. Women, for example, have a higher risk after the menopause. Lower oestrogen and progesterone levels seem to play a part. Also, we hear about miracle memory medicines, for example the fungus Lion’s Mane. In much the same way that Alzheimer’s cannot be caused by a deficiency of drugs, nor can it be just a deficiency of Lion’s Mane, or simply a result of low oestrogen or progesterone, since most women do not develop Alzheimer’s despite being post-menopausal and men also suffer. So, what are these hormones and mushrooms doing? In the model below, developed by our head of research, associate professor Tommy Wood at the University of Washington together with neuroscientist Dr Josh Turknett, you’ll see the addition of factors that stimulate repair, regeneration, growth and plasticity of the brain. This is what hormones and certain mushrooms do, as I’ll explain in Chapter 11. This is also why sleep and reducing stress is so important.

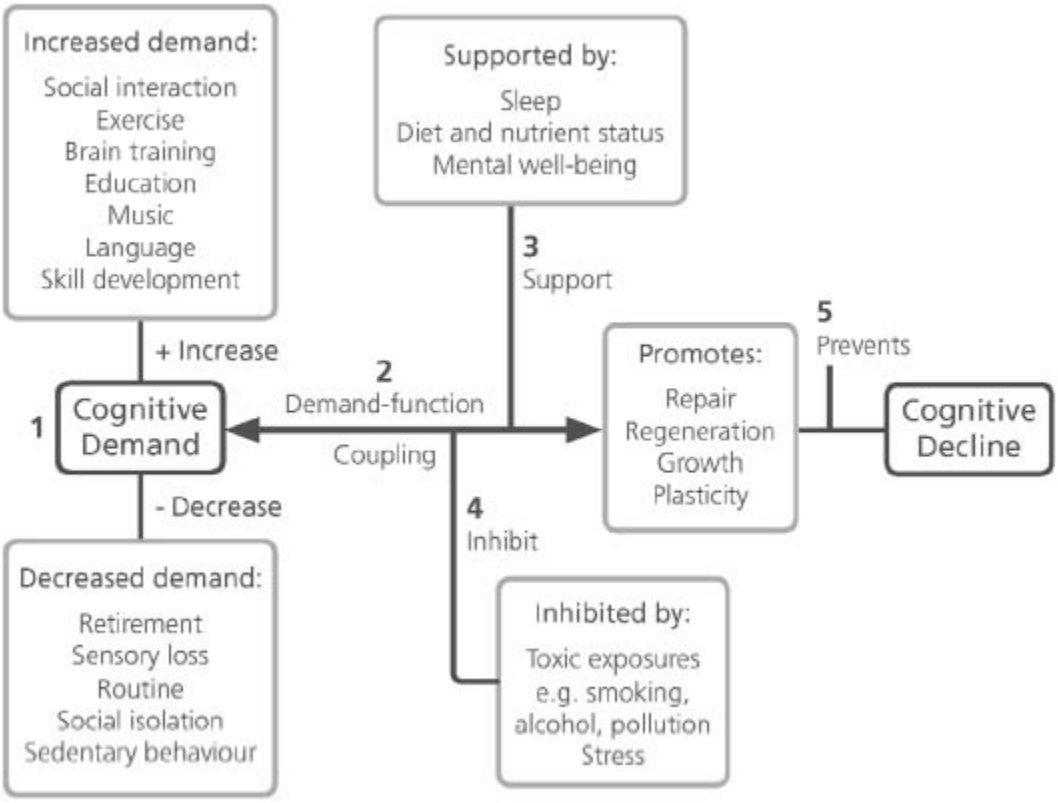



**Figure 5 – The Demand Coupling Model;** *used with permission of Drs Tommy Wood and Josh Turknett*

This 'systems-based' model of cognitive decline is the subject of our recent paper[50], co-authored by members of Food for the Brain's Alzheimer's Prevention Expert Group (*see foodforthebrain.org/apeg*). It is more than a theory. It is much closer to what actually happens in your brain and body, a step closer to reality than the linear 'one cause, one cure' reductionist model that those wanting to make big bucks out of block-buster drugs depend on. In Part 2, you'll learn more about how your diet and lifestyle impact the structure, function and utilisation of the brain. This shift to systems-based thinking demands, not only a whole new approach to Alzheimer's prevention, but also a whole new approach to scientific investigation itself.

# Systems-based science vs reductionist randomised controlled trials

Let’s start with the status quo. The randomised double-blind placebo-controlled trial (RCT), where one group gets one thing and the other a placebo, and neither researcher nor participant know (double-blind), is considered the ‘gold standard’ of research. So, there’s one thing changed and one health-related measure at the start and the finish. But what about all those ‘confounding variables’ like Apoe4, smoking, homocysteine, diet, exercise and so on? Researchers trying to control for these things by making sure both the treatment group and the placebo group are ‘equal’ – same % of smokers, Apoe4, homocysteine levels and so on. It is, of course, impossible to control for ‘everything’ but they do the best they can. Most studies will exclude certain people, perhaps those with diabetes or other mental illness, and stick to a certain age-group. Also, if it’s an ‘intervention’ trial, how long is it? One month, one year? The average RCT costs $7 million. A longer one, like these anti-amyloid treatment trials, with more than 1,700 people studied over 18 months, is likely to cost considerably more than £100 million. Up to 2021, the total spend on anti-amyloid or p-tau drug trials was estimated at over $42 billion[51], but, in truth, probably cost double this all told. Since then, the big trials have been published, so the cost will have more than doubled.

Please note that the smaller the benefit, the more people you have to test for longer to start to see a small but statistically significant effect. Take the example of Lecanemab, the anti-amyloid drug. The main trial involved 1,795 people given drug or placebo for 18 months at a cost of almost certainly in the hundreds of millions of dollars.

On an 18 point Clinical Dementia Rating scale, those on placebo got 1.66 points worse and those on the drug got 1.21 points worse.[52] So, the drug made people just under half a point less worse than they would have been without it. The result was only statistically significant because it was so big.

An effective treatment could have shown up as beneficial with many fewer people and in a shorter time frame. A study giving homocysteinelowering B vitamins, at a fraction of the cost, with no downsides, to 266 people reported that 33% ended the one-year trial with no Clinical Dementia Rating at all. Why do we not hear about this?[53]

The reality is that drug companies design trials to get a result – they will not waste this amount of money on a potential failure. They run and design the trial, control the data, manipulate the PR and make sure they get what they need to push their drug forward. If a trial doesn't work they don't publish it, nor disclose the data.

As we saw with the anti-amyloid trials, independent researcher Sarah Ackley, writing for the British Medical Journal, was denied access to the data of 20 out of 34 trials.[54] In other words, a drug company can run a failed trial, ditch it and move on, only revealing those that show an effect. Even in those they publish they can still hide the data so others can't really check their statistics. Why would they hide certain data and disclose others? It's pretty obvious. Out of the 14 trials she was allowed to see the data from their meta-analysis concluded, "the use of anti-amyloid drugs is not a viable strategy for the prevention or treatment of Alzheimer's disease and that other potential targets may merit more attention." The only protection we have is from the supposedly independent 'peer reviewers' that each trial must submit their trial to for their critique. Yet a study last year [55] found that nearly 60% of the experts who reviewed manuscripts for four prominent medical

journals received at least one payment from industry during a recent three-year period, exceeding, in total, $1 billion from the companies whose products were on trial.

Personally, I only trust drug trials carried out by independent researchers, not the makers of the drug, published in open-source journals, not those indirectly funded by pharma or agencies funded by pharma. There are no such trials run on the anti-amyloid or tau Alzheimer's drugs.

Please understand that no-one researching nutrition or lifestyle factors, such as vitamins, exercise, hormones, hearing loss, sleep, stress, seafood, pollution or smoking, could ever raise the millions needed to do this so-called Gold Standard research.

The system is rigged towards man-made, patentable, profitable drugs. Even the regulator, who gives the drug a licence is largely paid by the drug industry. In the UK, for example, the Medicines & Health products Regulatory Agency (MHRA) – the drug watchdog, which gives out licences to sell, received £20 million from just five big pharma companies[56]. 86% of its funding is from the industry it controls[57]. The US Food and Drug Administration (FDA) is said to receive 75% of its funding from big pharma.[58]

# Alzheimer's doesn't have one cause

Now, if Alzheimer's is multi-factorial how would you not only discover what's causing it, bearing in mind that that will be different for each individual, but also then 'treat' or advise those individuals? This is what has been made possible by the new era of 'big data' and the explosion of digital processing capacity.

At foodforthebrain.org we aim to get data on millions of people. Already we've gathered (anonymous) data from close to half a million tests. This year we hope to test up to 18 million people in China alone and hope to reach 20 million all over the world. How? It's simple. Anyone can go to foodforthebrain.org (.cn in China or .jp in Japan) and do three things:

1. Take the Cognitive Function Test. This is a validated measure of your cognitive function right now. It'll take you 15 or so minutes. Every six months we'll invite you back so we can track your cognitive function changes over time.
2. Complete the COGNITION questionnaire. This 140-question questionnaire follows the Cognitive Function Test. It's very comprehensive and covers many aspects of nutrition, lifestyle and medical history. All this is free. It then works out your future Dementia Risk Index and tells you how to reduce your future risk.
3. Take the DRIfT pin prick blood test. This costs a little, a donation to help fund our research, and involves pricking your finger and putting a few drops of blood onto a card that is sent to you in a home test kit. It measures the main biomarkers for glucose balance, brain fats (omega-3 and vitamin D), homocysteine for B vitamin status and a Glutathione Index, which is a measure of your antioxidant status.

So, now you imagine you've got a giant spreadsheet of (anonymised) data on millions of real people, each different and unique, some improving diet and lifestyle behaviours, some not, some supplementing nutrients, some not, each recording their cognitive function over time, not just at the beginning of a trial or the end. Thanks to vast computer

processing speed, advances in artificial intelligence, we can then see what patterns of diet and lifestyle behaviours correlate with best cognitive function over time and which correlate with worsening cognition. So, then we'll be able to tell you what the 'average' perfect diet and lifestyle is, and what are the worst combos of factors you really want to avoid. The blood tests also help to actually 'bio-hack' you. To look inside and see what is happening to your biology.

By comparing the levels of these five key biomarkers we can work out a DRIfT index, with the lowest score correlating with the best cognitive function as a predictor of future dementia risk. This means we can then look at which nutrition and lifestyle changes most effectively push the dial of your biology towards health. This is called Citizen Science, because you provide the data and also see the results of the analyses, to help and encourage you to make the most impactful changes. No-one is hiding or manipulating data to get a licence to make money. The research database is open to researchers wanting to do studies on various aspects of prevention.

# Personalised prevention is the way forward

Even as good as all this is, no-one is 'average'. For sure, following a combination of well evidenced prevention changes, such as those tested in the FINGER trial, is highly likely to help most, but what if you could 'personalise' and go close up on your key driving risk factors and really focus on minimising them?

Also, in the DRIfT blood test, one person may have perfect glucose control (shown by their HbA1c level), but raised homocysteine, perhaps due to B12 malabsorption.

Another may be fine for homocysteine, but have low vitamin D or omega-3. To make this real, my wife Gaby and I, eating the same food, having more or less the same lifestyle, and taking more or less the same supplements, took the test. Gaby's homocysteine level was 15mcmol/l – above 10 is cause for concern, because this is in the brain-shrinking zone. Mine was 7, so I'm OK. We were both taking a multivitamin providing 10mcg of B12 and eat B12-rich foods – eggs, fish, meat, dairy (none for me as I'm allergic). So, Gaby is a B12 malabsorber, or lacking in folate, and now supplements 500mcg a day of B12 and 400mcg of methyl folate. Her homocysteine is now 8, so she's OK. B12 and folate deficiency is remarkably common, as you'll find out in Chapter 6. In the UK, last year, it resulted in 3,500 hospital admissions, which was a fourfold increase from previous decades.

# COGNITION personalises your prevention and coaches you to do it.

By now you might be thinking, "I'd like someone to tell me exactly what to do and how to do it." You can. It's called COGNITION. It's a personalised programme we've been building for the past five years, where you are shown what is most contributing to your future risk (from the free, online COGNITION questionnaire that works out your Dementia Risk Index). Then, you choose what you want to work on changing and it sends you emails, text reminders, things to watch, read, listen to and do, and supports you through zoom and chat groups. There's even a cookery app that designs recipes according to your personalised needs, and a community of people to support you, ask questions and

share ideas with. Then, as you retake the Cognitive Function Test and the questionnaire, it feeds back how you're doing and keeps encouraging you in the right direction. All of this is available for just a small annual donation.

If you're willing to pay towards the research, you'll be sent the 5-in-1 DRIfT blood test kit and further advised what diet to follow, what lifestyle changes to make and which supplements to take. It will even send you your personalised supplements to optimise any blood biomarkers and then retest those not optimised (that is those not in the 'green' zones).

This whole journey is reiterative, guiding you through the 8 domains of prevention shown below, until each is 'in the green' based on your nutrition and lifestyle information, and each blood biomarker is 'in the green' based on your blood tests. Whether it takes you three months, six months, a year or 2 to get there, the end result is you will have dementia-proofed your diet and your lifestyle, and have every reason to expect you'll never develop Alzheimer's disease.


**Figure 6 – The 8 domains of Alzheimer's prevention.**

You've now become a Citizen Scientist. Imagine millions of people like you enrolling and making changes all over the world. This is the prevention revolution driven not by money but by research. In Chapter 15, you'll see dozens of cases of people who have transformed and regained their mental health.

# Warning – the side-effects may seriously improve your health

But there are side-effects. Just about every change that helps protect you from Alzheimer's also reduces risk of other disease, including arthritis, diabetes, cancer, heart disease, high blood pressure, stroke and weight gain, as well

as other neurological and psychological diseases, such as Parkinson’s, depression, insomnia, anxiety and ADHD.

In contrast, drugs have ‘black box’ warnings listing all sorts of adverse effects. The anti-amyloid drugs have the danger of brain bleeding and swelling. A dozen people, so far, have died in drug trials. The risk of death is perhaps one in 500. As a nutritional therapist, my insurance policy, in case I injure you and you sue me, gives me £2 million legal funds. It costs £50 a year, but only half of that is actually the insurance. The rest is admin and profit. That’s how dangerous this prevention approach is. Also, cost wise, the estimate of the annual cost for anti-amyloid treatment, which didn’t make anyone actually better, just more slowly less worse, is circa £50,000. While the estimated cost of the COGNITION prevention approach, with repeat blood tests and supplements, is in the region of £500 a year or £1.40 or under $2 a day. Less than a coffee.

# Can Alzheimer’s be reversed?

By now you’re thinking that, maybe you can prevent Alzheimer’s, but can it be reversed in a person who has been diagnosed, if only in the early stages? All that the drugs appear to offer is getting worse slightly less quickly. How late in the journey through cognitive decline into ‘mild cognitive impairment’(MCI), and then late stage Alzheimer’s, can diet and lifestyle actions really make a difference?

To be able to claim ‘reversal’ there are two conditions that would need to be satisfied. First, cognitive function must improve to the point where the Clinical Dementia Rating is ideally zero, which means no longer diagnosable as dementia. The second criteria would be to show, at least, a cessation of any further shrinkage of that central area of the

brain, the medial temporal lobe or hippocampus, and ideally a reversal of some of the shrinkage and perhaps an increase in whole brain volume. This is hard to imagine, but not impossible, since when brain cells have died, we are talking about actually making new neurons, which is a subject I go into in Chapter 11 talking about neuro-regeneration.

Since the presence of amyloid deposits and p-tau, indicating neurofibrillary tangles, tend to accumulate in the Alzheimer's disease process, a reduction in these would also be an indicator of a reversal, but only in the presence of cognitive improvement, as some people with Alzheimer's have low amyloid, and some with high amyloid have no significant cognitive decline. We can consider these downstream pathologies.

In the US, there are two groups working in this direction with a personalised multi-factorial approach. One headed by Dr Dale Bredesen, a member of our Alzheimer's Prevention Expert Group, and the other by Dr Richard Isaacson, Associate Professor at the UMMG Department of neurology at the Miller School of Medicine at the University of Miami. Both have clinics in the US where individuals receive a progressive, personalised prevention intervention based on comprehensive blood test of biomarkers, some of which are discussed in the next chapter.

The case of Simon Nicholls, reported by CNN news last year[59], diagnosed with early stage Alzheimer's, who then joined Dr Richard Isaacson's prevention trial, is particularly telling.

Genetically, Nicholls had drawn a short straw with two copies of the ApoE4 gene, one from each parent. This is not only a risk factor for Alzheimer's, but also heart disease. Just about everyone in his family had had heart attacks and he was heading for one with atherosclerosis. He also had vascular damage in his brain, with areas of white lesion

damage. His mother had also died at age 70 with Alzheimer's.

In January 2023 he joined Dr Isaacson's clinical trial targeting prevention and underwent comprehensive blood tests, including homocysteine, amyloid and tau. His amyloid burden test called Amyloid Probability Score (APS) was 75. "Anything over 58 is positive for amyloid in the brain," Isaacson said. "The results backed up the amyloid PET scan Simon had taken in 2019, where I could see the plaque in his brain." Both his homocysteine and p-tau levels were high. He had decreased hippocampal thickness. His cognitive function showed significant impairment. All this is consistent with early-stage Alzheimer's.

Dr Isaacson then recommended the same kind of nutrition and lifestyle changes recommended in this book and by Food for the Brain. The lifestyle changes included increasing exercise, reducing stress and optimizing sleep. He dramatically increased his exercise and changed his diet, avoiding sugar, artificial sweeteners, alcohol and ultra-processed foods, eating a more plant-based, Mediterranean style diet. In nine weeks he lost 21 pounds, most of it fat, and had put on muscle. He was also recommended to take supplements. "We optimized Simon's omega-3 fatty acid levels, which is especially important for people with APOE4, as they need more omega-3. We also added B complex vitamins to control elevated homocysteine in his blood," Isaacson said. He also took medication prescribed by his doctor and cardiologist.

By October, and then confirmed in December, his blood tests showed Nicholls was negative for both amyloid and tau. His homocysteine had also normalised. By March, a year on, his amyloid score (APS) had dropped from 75 to 25. 25 and below is classified as low risk. The test suggested that his brain amyloid might be normal, with no distinguishable signs of the disease. To confirm this, Isaacson repeated the brain scan that had shown shrinkage

of the hippocampus. The brain volume scans showed that the hippocampus had actually grown in volume in Nicholls' brain since he started making these changes 10 months previously. Is this a case of Alzheimer's reversal? Despite this amazing turnaround, Isaacson remains cautious. After all, he said, this is one person, and similar findings have not been replicated in a larger, more controlled sample and published in a peer-reviewed journal. "I don't believe in the term 'reverse', because I don't know what will happen if the person stops doing the intervention," Isaacson said. "I also don't know if the brain might normalize for a short period of time and then, five years later, catch up. Until I have more data, I don't think that reverse is the right word."


# THE 8 PREVENTION DOMAINS

Discover the most evidence-based steps you can take to dementia-proof your diet and lifestyle. The foods to eat, the supplements to take and the lifestyle habits to hard-wire.


# The Four Biological Horsemen of the Brain Apocalypse

Few people realise that a catastrophic decline in mental health has occurred over the past 50 years. A major 2024 study, published in Lancet Neurology, concludes "Nervous system diseases – [including dementia] are the leading cause of Disability Adjusted Life Years (DALYs) and Years of Life Lost, affecting 3.4 billion people (43% of world's population)."[60]. 'Brain health conditions have become a global health emergency,' according to the Federation of European Neuroscience Societies last year[61].

The lifetime cost of Alzheimer's in 2022 was estimated to be 1.2 trillion across the EU, which is half the UK's total GDP! In China, with almost 300 million people over age 60, 14 million have dementia, representing a quarter of the global number of cases. If this situation continues, it's predicted that by 2050, the cost of treatment will be $1.8 trillion a year. The China Alzheimer's Report[62] concludes: "Therefore,

improving the prevention and treatment of Alzheimer's disease under the government's leadership is urgent."

Note that prevention is put first over treatment. The cost of dementia exceeds that of all diseases, including cancer and heart disease combined. At the other end of the scale there are worrying trends of falling IQ at a rate of about 7% a generation, increasing diagnoses of ADHD and autism with four in ten teenagers now reporting persistent feelings of sadness or hopelessness and almost a quarter (22%) contemplating suicide[63].

If nothing changes, by 2080, suicide may well become the leading cause of death in those under 24. Also, more than a third of children will have severe neurodevelopmental impairment, defined as significantly below the norm for IQ. That's the conclusion of Professor Michael Crawford, who discovered that omega-3 DHA was essential for brain function.

Alarmingly, brain size, deduced from cranial capacity of skulls, has shrunk by a staggering 20% over a mere 30,000 years. It took over six million years for brain size to increase from that of a chimpanzee (350cc) to a peak of 1,600 to 1,700 cc with Cro Magnon man thirty thousand years ago. Today, brain size averages 1,350cc[64]. There is no question that our mental abilities are declining with the constant increase in rates of ADHD, autism, depression, anxiety, insomnia, schizophrenia, dementia and Alzheimer's, as well as other degenerative neurological diseases, such as Parkinson's and strokes.

# The big question is: why?

I'm proposing that there are four main biological drivers of this decline, which I'm calling the four horsemen of the

mental health apocalypse: a lack of brain fats, messed up methylation, loss of glucose control and excessive oxidation. The simplest way to understand the central role these play in both brain and mental health, before we dive into the details in the following chapters, is to consider in more detail the STRUCTURE, FUNCTION and UTILISATION of the neural network.

The brain is made of two types of cells – neurons and glial cells. Each of us has something like 86 billion neurons and about the same number of 'support' cells, called *glial cells*,[65] which help supply the neurons with fuel. The neurons 'talk' to each other with chemical messengers called neurotransmitters, sending signals through their cell walls or neuronal membrane.

The membrane is made of phospholipids, a combination of phospholipids and fatty acids, primarily omega-3 DHA and arachidonic acid, an omega-6 fat. The binding of these two together is dependent on a process called methylation, which needs sufficient vitamin B12, B6 and folate.

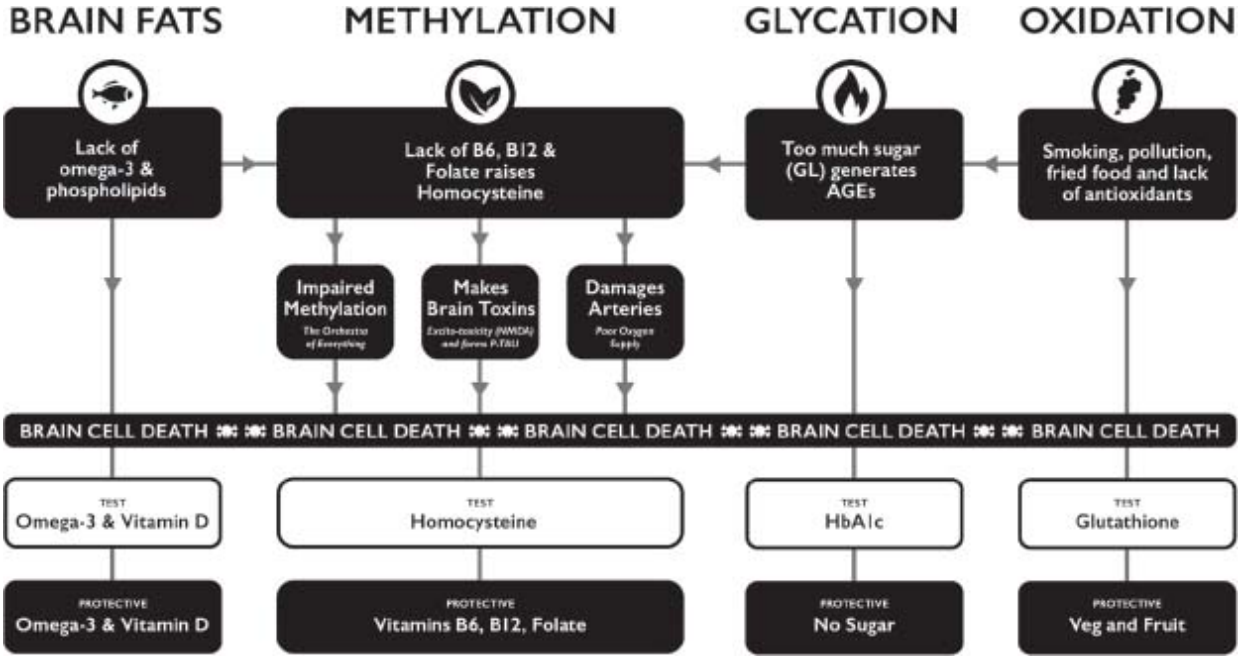



**Figure 7 – The four horsemen of the mental health apocalypse**

The omega-3 fats, phospholipids and B12 are rich in marine food, with plant food providing omega-6, folate and some B6. Logically, the human brain could not have formed without a rich supply of both marine and plant food. These nutrients are essential to maintain the structure of these critical brain cell membranes

Neurons are fuelled by either glucose or ketones, the energy packets produced when you are on a low carbohydrate diet. The glucose depends on the hormone insulin to be delivered into neurons. Excess carbs and sugar lead to insulin resistance and messed up fuel delivery to the brain. This causes brain fog, inability to concentrate and think straight and, ultimately, dementia and Alzheimer's. Fructose, now added to so many foods, is a particular problem. Ketogenic diets can aid brain recovery. All this is discussed in detail in Chapter 8.

Any generation of energy, including a thought, results in exhaust fumes called oxidants. Those membranes, and the fatty acids within them, literally change shape through oxidation and have to be reset, which is why we have to sleep. It's when our brains get cleaned up and rebooted so to speak.

Increased oxidation is a major contender for mechanisms leading to Alzheimer's. With oxidation comes inflammation, another strong contender. This is discussed in detail in Chapter 9 and explains why a high intake of vegetables, fruit, polyphenols – compounds found in plants that are strong antioxidants, vitamin C and E - reduce risk, while smoking and pollution increase it, as does a lack of sleep.

To get all these nutrients flowing into and through the brain you need good circulation. That's where exercise – both resistance and aerobic – come in. Mental and physical activity give your brain a good workout. So does listening to conversation, music and vision. Sight loss and hearing loss decrease that neuronal stimulation. All this 'utilisation' is the subject of Chapter 10.

The figure below, taken from our recent paper, 'A systems-based unified model of age-related cognitive decline and its prevention'[66], shows how a plethora of diet and lifestyle changes converge on these three critical aspects of brain health.

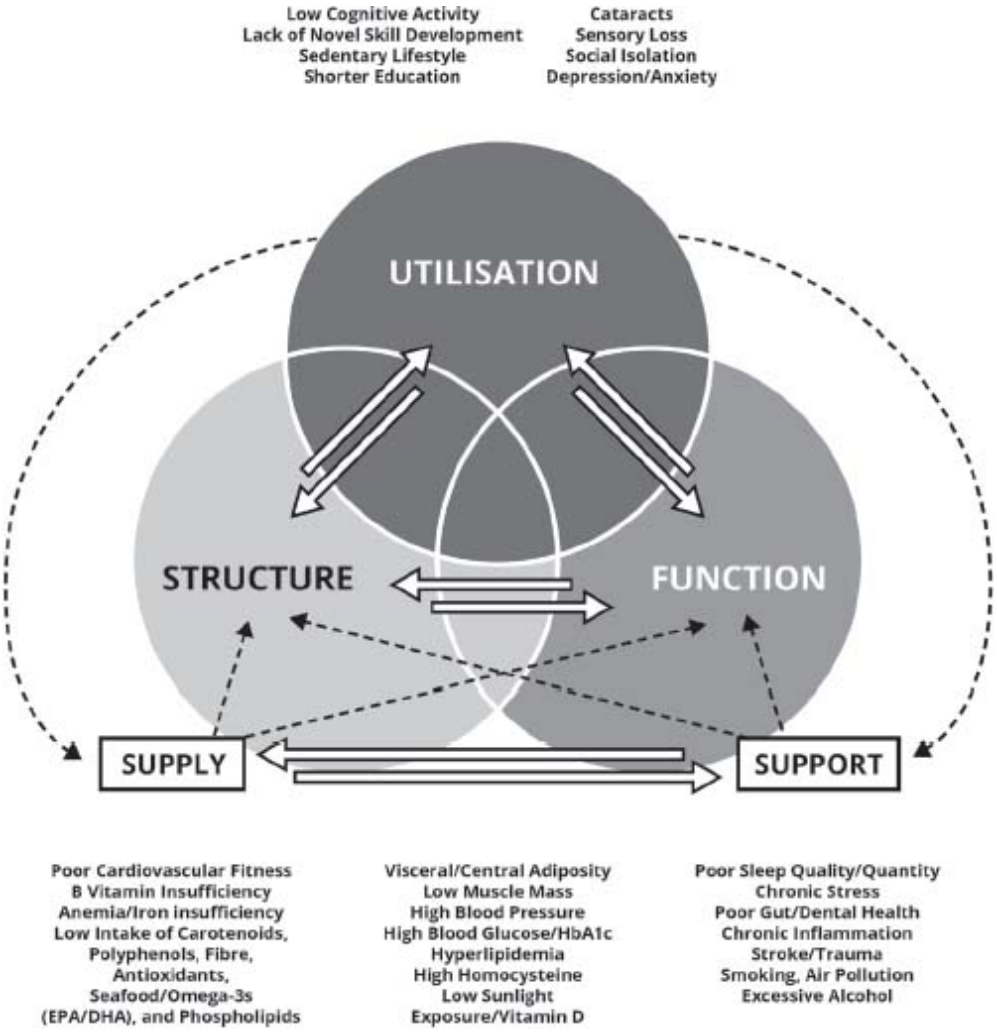



**Figure 8 - Simplified schematic representation of the systems-based model and associated risk factors**

*The proposed system describes cognition as the output from three main interacting variables - utilization, structure, and function. Each variable influences the others and is affected by categories of environmental risk factors that have specific mechanistic effects on those aspects of the system. As an*

*example, increased utilization of cognitive resources increases supply of oxygen, metabolic substrate, and nutrients via neurovascular coupling. Increased utilization also drives downstream support processes (e.g., during sleep).*

# Are you Drifting towards dementia?

How would you know if your biology is in good shape in regard to these four horsemen - a lack of brain fats, messed up methylation, loss of glucose control and excessive oxidation? Of course, you can assess your dietary intake and lifestyle, which is what foodforthebrain's COGNITION questionnaire does, calculating your Dementia Risk Index (DRI).

But even better is to measure your biology itself. There are five main blood biomarkers that do this:

- Omega-3 index – this is the key brain fat
- Vitamin D – an essential fat-based brain hormone
- Homocysteine – an indicator of critical B vitamin status.
- Glutathione – the best measure of antioxidant/oxidant status
- HbA1c – the best measure of glucose balance

Professor Peter Garrard, Director of the Dementia Research Group at St George's, University of London, says "It is vital that functional biomarkers such as homocysteine and omega-3 are measured in this research because these can be changed with nutritional interventions and are associated with reducing risk."


Foodforthebrain.org's 'citizen science' research is encouraging thousands of people to test all these with a test kit called DRIfT (Dementia Risk Index functional Test). They provide a home test kit that involves a single pin prick of blood dripping a small number of blood spots onto a card, which is sent back to the laboratory. They are using this to research DRIfT's ability to predict cognitive function, but also help guide the individual to make diet changes to reduce future risk.

"By tracking a person's blood sugar, vitamin B, D and omega-3 status against changes in cognitive function over time, in addition to lifestyle factors, such as sleep and physical activity, we can learn what really helps prevent cognitive decline." says Dr Wood, the principal investigator for the research. The chapters which follow provide more details on why these individual tests are the most appropriate biomarkers for assessing cognitive function and protecting against Alzheimer's.

These four risk factors, measured in the DRIfT test, are thought to account for over half the modifiable risk for Alzheimer's disease and dementia.[67] But also having an active lifestyle, both physically, socially and intellectually, sleeping well, controlling your stress levels and having a

healthy gut, along with good dental hygiene, further reduce risk substantially. These, combined, make up the eight prevention domains we assess at foodforthebrain.org and advise individuals, like you, what simple diet, supplement and lifestyle changes will help dementia-proof you.


**Figure 9 – The 8 domains of Alzheimer's prevention.**

The following chapters explain each of these domains of Alzheimer's prevention.

# Cognitive decline starts from age 18 and so should prevention

Our research on over 300,000 people shows a steady decrease in cognitive function from at least the age of 18

(*see figure 10*). We are currently testing children from the age of 7. This is quite extraordinary since the validated Cognitive Function Test was originally developed to pick up the early changes in cognition that are used to diagnose cognitive impairment and dementia. Yet, we are seeing that these subtle, measurable functions are steadily decreasing from at least age 18 in most people. This implies that these 'four horsemen' are kicking in very early, almost certainly driving the escalation in ADHD and autism, but also our steady decline in intelligence, mood stability and ability to cope with stress.

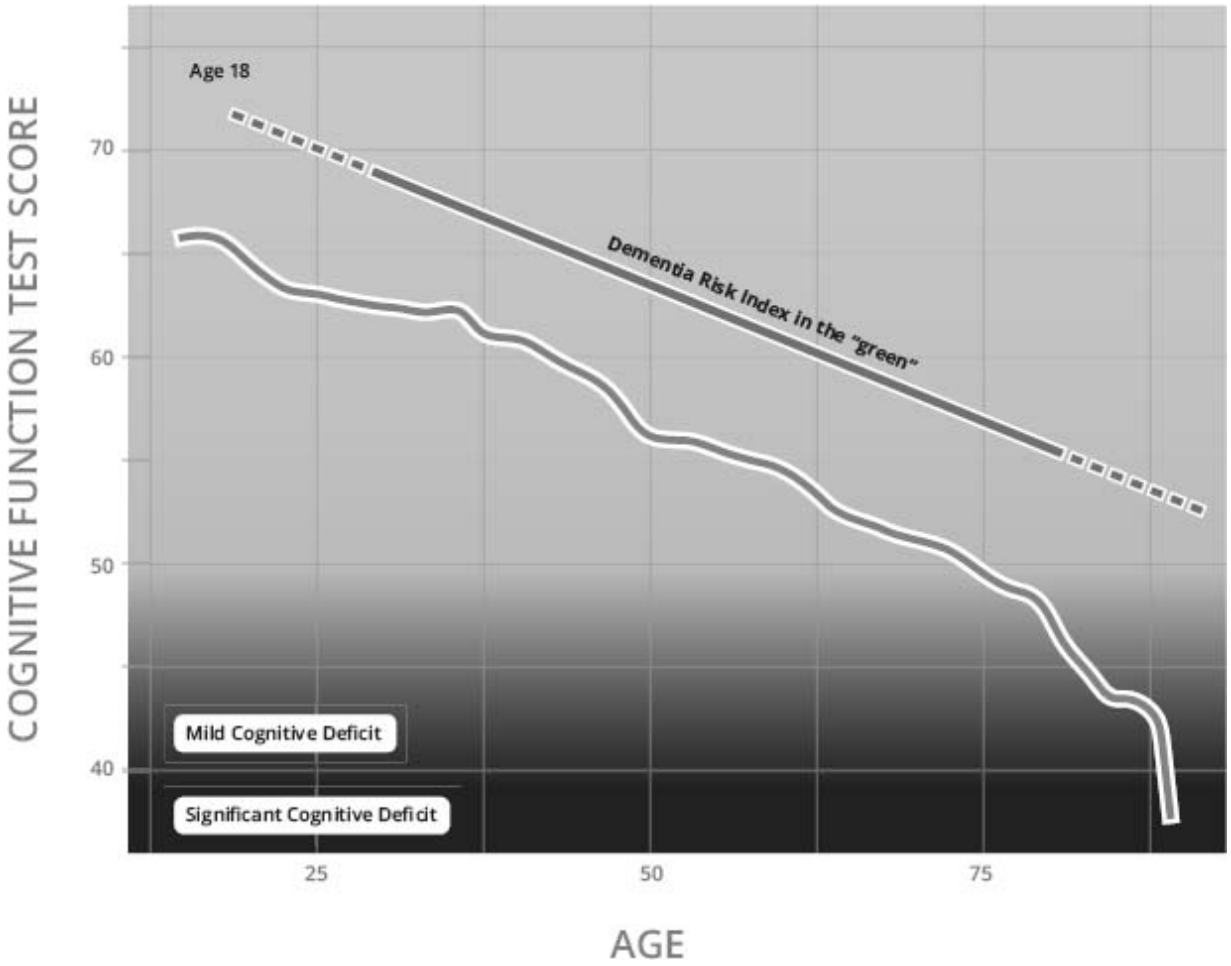



**Figure 10 – Cognitive Function Test score by age.**

What you will also see in the figure (left) is that those who are doing the right things to reduce risk, with a dementia

Risk Index of below 25%, defined as ‘in the green’, are extremely unlikely to develop a level of cognitive deficit, that equates to dementia, during their life. This is calculated from the COGNITION diet and lifestyle questionnaire that you complete alongside the Cognitive Function Test at foodforthebrain.org. In other words, they have dementia-proofed themselves. How? By reducing their risk across these eight domains.

The following chapters explain each of these domains of Alzheimer’s prevention.


# Brain Fats – Omega-3, Phospholipids and Vitamin D

The dry weight of your brain is two thirds fat. The main types of fat are omega-3 DHA, phospholipids such as phosphatidyl choline, and cholesterol. Vitamin D is also important, but not structurally, so the amount you need is very small. Eggs and marine food provide all these essential brain nutrients.

Each of them, when deficient, crank up dementia risk considerably. The better your omega-3 and choline status, the better your cognition, the ‘denser’ your brain - which is good news.

In fact, there is simply no explanation as to how us humans evolved over 6.5 million years - with brain size steadily growing up to 1,700 grams for Homo sapiens, while a chimp’s or gorilla’s brain stayed under 400g, a quarter of the size - without marine foods. A high marine food diet simply has to be the change that allowed Homo sapiens to evolve in the first place. This is the ‘waterside ape’ or ‘Homo

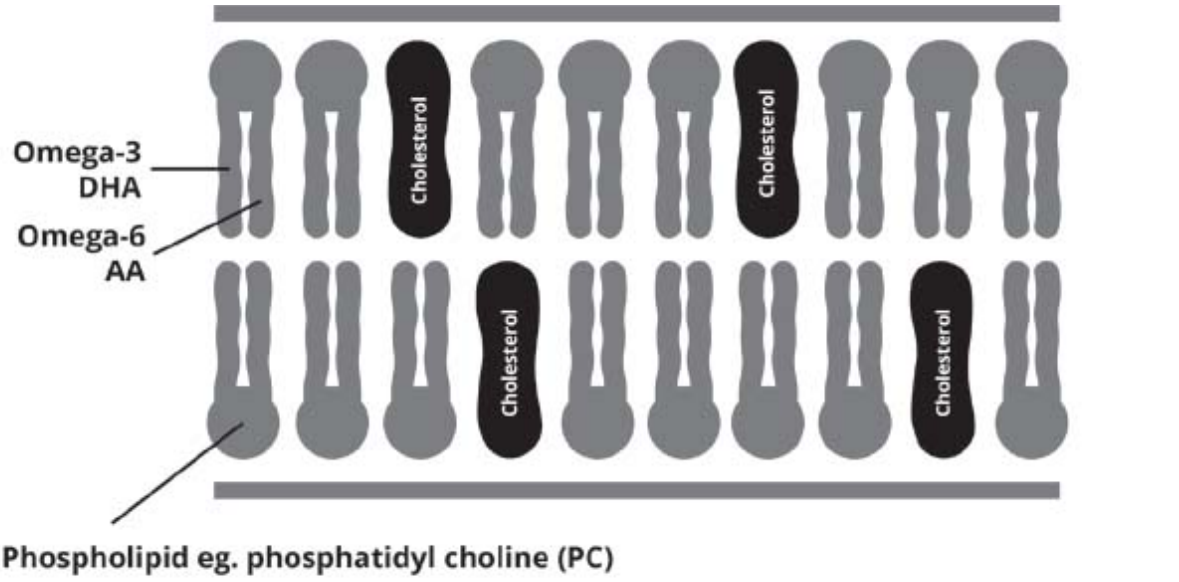
aquatic theory', which I discussed in full in my book *Upgrade Your Brain,* and is also explained in Professor Michael Crawford and David Marsh's book *The Shrinking Brain*.

Our brains are shrinking. Today, average brain size is 1,335 grams – 20% less than that 20,000 years ago. That is also what Alzheimer's is. A shrinking brain. So, it is completely illogical to not investigate the major structural components of the brain - which are decreasing in our diet - and their association with Alzheimer's, and what happens if you increase intake, consistent with the diet our waterside ancestors would have eaten.

# Brain Fats – Omega 3 and Phosphatidyl Choline

The diagram below shows you the essential structure of a neuronal membrane. It is fatty acids, the squiggly bit, attached to phospholipids, the blob, which make this waterproof membrane that can pass messages along into the brain. As we shall see in the next Chapter, those phospholipids get 'married' to the fatty acid by a priest called 'methylation'[68] which depends on B vitamins.

There are two main fatty acids – omega-3 DHA and arachidonic acid (AA), which is an omega-6 fat made from another omega-6 fat called linoleic acid, which is found in plant oils. AA also comes from egg yolk and meat.



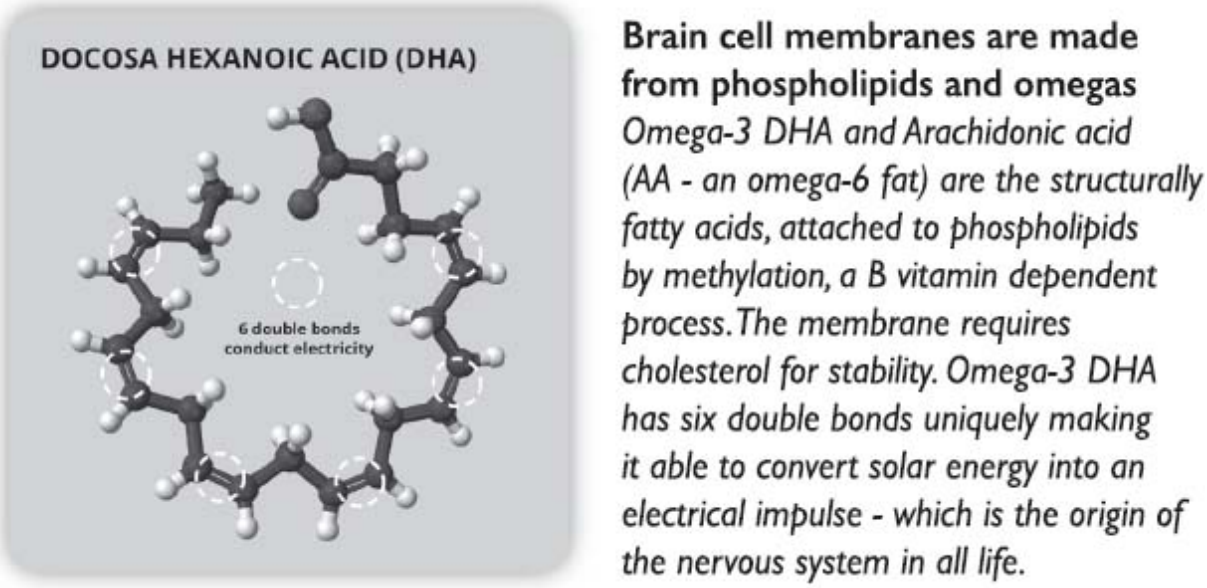




**Figure 11 – Brain cell membranes are made from phospholipids and omegas, dependent B vitamins**

There are quite a few types of phospholipids, but a main one is called phosphatidyl choline (PC), which is abundant in eggs and fish. Omega-3 DHA is mainly found in oily fish (salmon, herring, sardines), but also other marine food. Caviar is a very rich source of omega-3. So, the primary form

of DHA in the brain is PC-DHA – that is phosphatidyl choline attached to omega-3 DHA.

Let's take a look at the evidence relating to omega-3, which is ignored at the highest level of so-called expert advice. For instance, the Lancet Commission[69] - a group of 27 experts which is the 'go to' for government and NHS policy - when updating their report in 2024 on targets for dementia prevention, simply dismissed evidence for omega-3.

In a hidden away section of this 57 page report, under the banner 'Potential risk factors considered with insufficient evidence' (i.e., "not enough consistent evidence exists to meet our high bar for inclusion as modifiable risk factors"), is this one sentence regarding omega-3:

*A French study (n=1279; mean age at baseline of 74·3 years [SD 4·9]; follow-up of 17 years) reported that increased concentrations of omega-3 index in plasma were associated with a decreased risk of dementia [13% less risk] and less decline in medial temporal lobe volume.*[70]

In layman's terms this means that this 2020 study of 1279 people found that those with good omega-3 blood levels had less brain shrinkage and 13% less risk for dementia over a 17-year period. That's a clear win for this decent, long observational study.

Now, let's read the letter to the Lancet from our group of Omega-3 experts – Professor William Harris, founder and director of the Fatty Acid Research Institute, Dr Simon Dyall, the UK's leading expert and our Head of Research at foodforthebrain.org, Dr Tommy Wood, associate professor of neuroscience at the University of Washington.

# *Letter to the Editor of Lancet*

*The Report by Livingston et al. cited only one observational study linking higher blood levels of omega-3 fatty acids with risk for dementia (Thomas 2022), which concluded there was "compelling evidence for a relationship between long-chain omega-3 fatty acids levels and lower risks for dementia."*[71]

*Essentially, the same conclusions were reached by several other similar studies between 2006 and 2024 (e.g.,)*[72] *plus Sala-Vila 2023, Loong 2023, Schaefer 2006, Samieri 2008, Ammann 2017, Melo van Lent 2021 and He 2023 among others.*

*A 2019 review of observational and randomized clinical trials concluded that omega-3 fatty acids were "safe and well tolerated", representing "a valuable and biologically plausible tool in the management of neurodegenerative diseases in their early stages"*[73]*. The vast majority of adults in the Western world have suboptimal blood omega-3 fatty acid levels (Schuchardt, 2024). Correcting this deficit would not only reduce risk for dementia, but also cardiovascular and other inflammation-related diseases.*

*Importantly, the discovery that the cognitive benefits of omega-3s and homocysteine lowering B vitamins are co-dependent by the VITACOG, B-Proof, OmegaAD, and MAPT trials highlights the fact that some neutral omega-3 studies may have been a consequence of this nutrient interplay (i.e., that the omega-3s work in individuals with low (healthy) but not high homocysteine levels). Increased consumption of marine omega-3 fatty acids is safe, simple, cheap and effective tool in the fight to forestall the development of Alzheimer's dementia. Why were these nutrients and the studies supporting their efficacy ignored in the Lancet Commission report?*

So, how did the Lancet ‘experts’ manage to refer to only one study, and an observational one at that, when there are bigger, better, more recent studies that have hit the headlines over the past couple of years? Also, please note, the Lancet limits letters to referring to a maximum of five studies despite the fact that there are many, many more. (Chapter 7 unwraps the omega-3 B vitamin co-dependence they mention, which you will see is a game changer for dementia prevention.)

Anyone in science knows that there is a free access ‘National Library of Medicine’ (called Pubmed - https://pubmed.ncbi.nlm.nih. gov). Only approved, peer-reviewed studies are allowed. Anyone can go there and search for research. If you do and put in ‘omega-3 + dementia’ you’ll find 878 results. Try it. If you add in ‘clinical trial’ you’ll find 189 results. Why can you do it and the Lancet Commission’s “experts” can’t?

The point is, the only way to avoid including omega-3 in one’s list of prevention steps, is to show only one study, then claim that there is insufficient data to do a ‘meta-analysis’. However, the Lancet researchers could find one ‘observational’ study in 2020 involving 1279 people, so why couldn’t they find many others including more recent, placebo-controlled clinical trials, as well as meta-analyses. This failure is remarkably close to scientific fraud. It is, at least, extremely bad science.

One example of a study they definitely should have found, and should have known about, involving an analysis of data from over a quarter of a million people in the UK Biobank, was published in 2023[74] and reported that “the total omega-3 status was inversely related to the risk of Alzheimer’s [13% decreased risk] and all-cause dementia [21% reduced risk]. Thus, - the largest study to date on this topic, confirmed the favourable relationships between DHA and risk for dementia. We also found evidence that non-DHA omega-3 may be beneficial.” Why did the Lancet

Commission choose an older study with fewer people in it rather than this?

Another they should have found, published in 2023 in a leading nutrition journal, The American Journal of Clinical Nutrition[75] - which everyone in nutrition research reads - involved 1135 people in their seventies, without dementia, and tracked them for 6.5 years. Those taking fish oils supplements reduced their risk of developing Alzheimer's by 64%.

The authors then pooled the results of 48 studies involving over 100,000 people and found 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 about 20%, especially for docosahexaenoic acid (DHA) intake."

This study alone has done exactly what the Lancet Commission did to other risk factors – pool the results of, in this case 48 studies, to get a risk reduction percentage. How the Lancet Commission experts could fail to see this mountain of evidence and just cite one study, when already I've shown you over 50 studies showing more evidence of more risk reduction than ANY of the 14 risk factors highlighted in the report with the simplest of actions – eat oily fish and take fish oil supplements.

# Omega-3 increases brain volume and Omega-3 Index predicts it

From the letters above it is clear that more omega-3 means less risk for Alzheimer's and dementia. This is true whether the measure is supplementation, dietary intake or blood levels.

That’s pretty conclusive but let’s go closer up into both the best measure of omega-3 status and its relationship with brain shrinkage, indicated by brain volume.

The best yardstick of your omega-3 status is the level of omega-3 in your blood, or actually the red blood cell membranes, which are similar to neuronal cell membranes. This can be easily measured with a home-test kit using a technique called dry bloodspot analysis, which gives you your ‘omega-3 index’.

This is the amount of omega-3 EPA and DHA found in red blood cell membranes expressed as a percent of all the fats in the membrane. This is what we measure in the DRIfT home test kit at foodforthebrain.org. Above 8% is optimal. Below 4% is bad (classified as red), while 4–6% is at some risk (orange), and 6–8% is adequate but not optimal (yellow). The average American and UK citizen score around 5%. In Japan, where they eat a lot of seafood, many people will score 10%. Vegans, deployed US soldiers and some criminals average 3.5%. You will probably have to take in 1.5 grams of omega-3 (from a combination of oily fish and omega-3 supplements) a day to average above 8%, but we are all different. The only way to know is to measure your level (*see Resources*).

That’s what psychologists at the Linda Loma University in California did for a group of older people, publishing their results in the journal *Brain Sciences*.[76] They found that the higher a person’s omega-3 index was in their blood, the more white matter there was in their brain, and the better they performed in cognitive tests that predicted less risk of dementia.

A recent placebo-controlled study gave 102 people either 1.65g of omega-3 (975mg of EPA and 650mg of DHA) or a soybean oil placebo for three years and measured the extent of white matter lesions, effectively brain damage.

Those on the supplements had less additional white matter lesions than those on the placebo but the results

weren’t quite “statistically significant.”[77] However, in those positive for ApoE4, the results were significant. Remember how those with the ApoE4 gene variant are less good at handling fats? This study is one of many pieces of evidence showing that ApoE4 carriers need more omega-3. This was reported in Newsweek[78] as ‘‘Remarkable’: Supplement May Slow Breakdown in High-Risk Alzheimer’s Cases" reporting that “fish oil supplements caused a “remarkable” reduction in the breakdown of brain nerve cells in individuals with a gene linked to Alzheimer’s disease.”

Most of these studies were in people already showing cognitive decline. What about healthy older people? Dr Veronica Witte and colleagues from the Department of Neurology at the Medical University in Berlin decided to find out by giving 65 healthy 50–75-year-olds 2.2g a day of omega-3 in fish oil supplements for 26 weeks and seeing what happened to their brains. Not only did they get some significant cognitive improvements, with better memory and more flexible thinking and ability to focus, but their brains also got a physical upgrade, with an increase in grey-matter volume and more white-matter integrity, which indicates better wiring. In just six weeks you could see evidence of a brain upgrade! Also, the higher their blood levels of omega-3, the greater the improvements.

# Choline and phospholipids

Phospholipids are not widely known, but they are undoubtedly a brain essential, as omega-3 fats or arachidonic acid must be attached to them to work in the brain, as the figure on page 49 illustrates. There are a number of kinds of phospholipids, all starting with ‘phosphatidyl’. These are:

Phosphatidyl choline (PC)

Phosphatidyl serine (PS)
Phosphatidyl inositol (PI)
Phosphatidyl ethanolamine (PE)

They then get attached to an omega-3 fat, for example DHA, to build that brain-cell membrane. So that's:

**Phosphatidyl + choline + DHA = PC-DHA**

The more PC-DHA you have, the lower your risk of Alzheimer's, and the less you have, the greater your risk. Those with Alzheimer's have 2.5 times less in their blood and 20% less grey matter (brain volume).[80]

Phosphatidyl choline (PC) is also the raw material for the brain to make one of its most important neurotransmitters, acetylcholine. The first generation of drugs such as Donezepil (Aricept) for dementia were based on helping to protect acetylcholine and stop it breaking down. The phosphatidyl part is easy to make; it's the other part, choline, serine, etc., that we have to eat. How much you eat makes all the difference.

A study of 125,000 people followed over 12 years, from the UK Biobank data and published in the American Journal of Clinical Nutrition[81], found a direct relationship between dietary intake of choline, with a steady decrease in risk as a person's dietary choline levels increased up to around 400mg a day. Risk for Alzheimer's and dementia were also lowest at this level of intake. Choline is rich in eggs, fish and meat.

Choline, in the form of phosphatidyl choline, is found in lecithin capsules and granules, which are a popular vegan health food product. Two 'high PC' lecithin 1,200mg capsules a day gives 250mg of phosphatidyl choline (PC) which is the form that choline is used in the body. This is what I recommend for optimal brain protection (*see Resources*), as well as eating eggs.

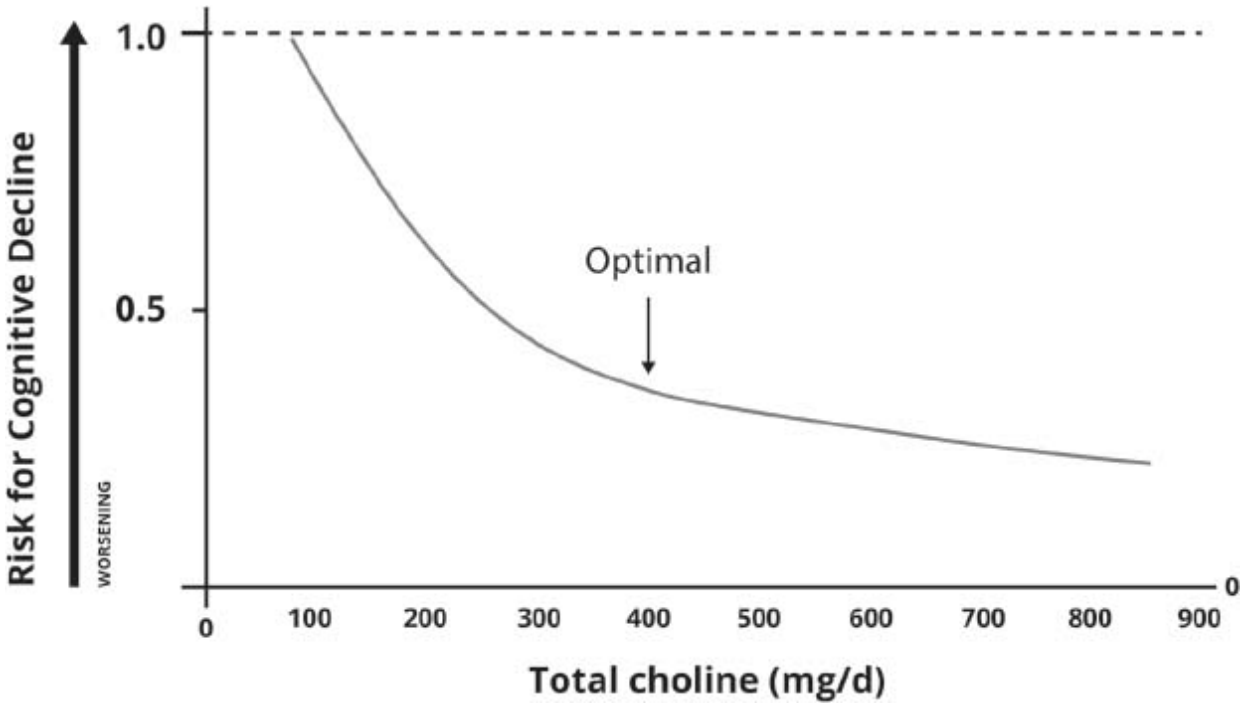



**Figure 12 – Choline intake and risk of cognitive decline.**
*Source: Niu Y et al, The American Journal of Clinical Nutri on, 2024*

An egg provides around 120mg, a 50g beef or salmon steak around 50mg. Cow's milk has a little, but just a fraction of that found in human milk. Beef liver is the richest source. Eggs are by far the best source. Plant based sources include soya, quinoa and other nuts, seeds and beans, also broccoli. 50g of almonds or broccoli gives about 25mg.

Long-term studies looking at dementia risk in relation to egg consumption show that eating eggs - both more than one and more than 2 a week - was associated with both halving risk of being diagnosed with Alzheimer's, and much lower risk of Alzheimer's pathology in the brain. Why? The researchers concluded that 39% of the total effect of egg intake on Alzheimer's dementia was mediated through dietary choline. Eggs also contain other important brain nutrients, including vitamin B12, vitamin D and cholesterol.[82]

# Optimal vitamin D and UV exposure cuts Alzheimer's risk by a third

Vitamin D is an all-rounder as far as your brain and mental health is concerned, and it's worth ensuring your level is optimal, both for brain and body. It helps neurotransmission and has an anti-inflammatory and neuroprotective effect on the brain by reducing inflammation and the oxidative stress,[83] both of which are drivers of cognitive decline.

Vitamin D deficiency increases the risk of Alzheimer's.[84] In a study in France involving 912 elderly patients followed for 12 years, a total of 177 dementia cases occurred. Those with low vitamin D levels had a nearly three-fold increased risk of Alzheimer's.[85] Supplementing 800iu (20mcg) a day for 12 months has also been shown to improve cognitive function.[86]

Supplements may also help ward off dementia, according to a recent large-scale study involving over 12,000 dementia-free 70+-year-olds in the USA.[87] More than a third (37%) took supplements of vitamin D, and those who did had a 40% lower incidence of dementia. Professor Zahinoor Ismail, of the University of Calgary and University of Exeter, who led the research, said, 'Overall, we found evidence to suggest that earlier supplementation might be particularly beneficial, before the onset of cognitive decline.'

You want to get your blood level above 75nmol/l (30 ng/ml), which usually means supplementing 3,000iu in winter and perhaps up to 1,000iu in summer, depending on your sun exposure.

Talking of sun exposure, the more UV exposure you get the lower your risk. That's what an analysis of UV exposure across 204 countries concludes.[88] Countries with low UV

exposure, including the UK, have a dementia incidence of about 200 in 100,000, while high UV countries closer to the Equator have an incidence of 50 in a 100,000. This relationship was as significant as age. While sunlight makes vitamin D in the skin, both sunlight and vitamin D[89] also crank up serotonin production in the brain. This supports a comprehensive study looking at 'time spent outdoors' and dementia, showing that very little time outdoors is strongly related to higher risk for dementia.[90] The lowest risk occurred at 1.5 h/day on average, 2 hours per day in summer, and 1 hour per day in winter. Most vitamin D is made in the skin in the first 30 minutes.

It's close to impossible to do 'intervention' studies in these kinds of environmental and lifestyle areas as it is with smoking[91] and air pollution[92]. Imagine the ethics of designing a study where 1,000 people have to smoke 20 cigarettes a day and 1,000 either don't smoke or have a placebo cigarette or vape. Yet, based on similar observational studies shown above for vitamin D, 'everyone' has smoking and air pollution down as a risk factor - and something to target to minimise risk. (It is not, however, easy for an individual to change their air pollution exposure).

The Lancet Commission, for example, has both smoking and air pollution as a modifiable risk factors, but completely ignores vitamin D (and UV exposure), despite the observational studies showing raising vitamin D levels is associated with a bigger risk reduction than stopping smoking or reducing air pollution, as well as clear evidence of supplementation reducing risk. Which is easier? Supplementing a vitamin D capsule or stopping smoking or reducing air pollution?

Also, it is easy to test a person's vitamin D level and advise them accordingly. This is why vitamin D is included in the DRIfT home test kit analysis to both assess risk and advise a person what to do.

The richest dietary source of vitamin D is oily fish. Eating more oily fish, supplementing and getting outdoors, exposing skin to UV are clear and important messages for reducing Alzheimer's and dementia risk.

# Low cholesterol increases risk, as does very high cholesterol

A quarter of all the cholesterol in the body is in the brain, with low cholesterol (below 4mmol/l) being a major risk factor for dementia.[93] In a study that looked at commonly measured biomarkers to identify who might be at risk of dementia, having a high homocysteine level (i.e., low B-vitamin status) and a low cholesterol best predicted risk.[94] A major cause of very low cholesterol, below 4 mmol/l, is the inappropriate prescription of cholesterol-lowering statins. The majority of statin trials have failed to show a reduced risk of cognitive decline in dementia.[95]

Earlier we spoke about the ApoE4 gene variation. The ApoE gene makes apo-lipoprotein, which carries cholesterol from the brain's blood supply into those neuronal membranes, building the brain. Those with ApoE4 are *less good* at transporting cholesterol. So, the reason ApoE4 seems to increase risk of brain degeneration is precisely because cholesterol isn't being delivered into neurons.

High cholesterol, however, is also statistically associated with increased risk for dementia.[96] The increased risk of 14% for all cause dementia in those with 'high cholesterol' is not so massive in this study of 17 studies involving just over 1 million people. This is what the Lancet Commission relied on to make their 'anti-cholesterol' case. This study of studies actually showed two studies where LDL was not a risk factor, and one was. However, they weighted the studies such that

they got a significant 8% increase in risk. The definition of 'high cholesterol' varied in studies from 6.2 to 6.5mmol/l (240 to 250 mg/ dL). This level of evidence is so much weaker than that for omega-3, as an example. Yet from this study, high cholesterol is elevated to being the number one preventable risk factor for dementia. This is not realistic and will no doubt feed prescriptions for ineffective statin prescriptions which, for some, may do more harm than good.

But do bear in mind that people with an unhealthy diet high in sugar and carbs, will tend to have a higher total cholesterol level. This point is made in the Lancet Commission's report:

*"In a Danish cohort study of 94,184 people, followed up from a mean age of 58 years, people who did not adhere to dietary guidelines (i.e., eat at least three weekly servings of all of fruit, vegetables, and fish; rarely drink sugar-sweetened drinks; rarely eat prepared meat like sausages or have takeaways) were more likely to have high LDL cholesterol.*[97]*"*

Therefore, it is possible, indeed very likely that it is not the cholesterol, but the things that tend to raise it, that are increasing the risk (*See Chapter 8*). As you will see, the Lancet Commission also ignored sugar as a driver of dementia which is another major failing of this report.

The reason why there was hope for statins helping dementia in the first place was that 'vascular dementia', meaning damaged and narrowed blood supply, hence nutrient supply to the brain, accounted for almost a fifth of dementia. But it is not 'excess cholesterol' that is driving either vascular dementia or Alzheimer's, or indeed heart disease (for more on this, see my book *Say No to Heart Disease* or Dr Malcolm Kendrick's books *The Cholesterol Con* or *The Clot Thickens*, or listen to my podcast with him on podbean.patrickholford).

For some readers the idea that cholesterol is not the béte noir, and statins not the solution for heart disease, will seem like heresy. That sentiment is why Dr Malcolm Kendrick was accused by the Daily Mail of being a ‘statin denier’ and thereby potentially killing people as a consequence of this ‘misinformation’.[98] He sued the Mail and won on every single point of science so they had to pay out several million pounds and make an apology. The evidence for statins helping reduce cardiovascular risk is flimsy. The only independent trial, not funded by the makers, found that they did not.[99] Yet, the inclusion of ‘high cholesterol’ as accounting for 7% of the preventable risk for dementia in the Lancet Commission’s report will no doubt have the effect of encouraging doctors to prescribe cholesterol-lowering statins despite, as the Lancet Commission report says, ‘A Cochrane review of RCTs of statins given in later life found no effect on either dementia risk (one study) or cognitive outcomes (two studies).[100]

In the world of nutritional therapy, we do not consider that having slightly raised cholesterol (up to 6.5mmol/l) is a problem if you eat a low-sugar/carb diet, thus have low levels of blood glucose or blood fats called triglycerides. We are more interested in your ‘good’ HDL cholesterol level being high. In another study, having a high HDL level in midlife predicted a significantly lower future risk of dementia.[101] Low HDL, not high cholesterol, is a key indicator of metabolic syndrome, which describes a pattern of biological changes that lie behind most metabolic diseases such as diabetes heart disease and obesity.

High blood pressure is similar to high cholesterol. While it is robustly associated with increasing risk of Alzheimer’s it may also just be a consequence of a bad diet and lifestyle. Lowering it with medication is questionable. One study found that you’d have to treat a thousand people with intensive blood pressure lowering pills to bring their blood pressure

down to a healthy 120/80 to save one from mild cognitive impairment. But over 300 would have a serious adverse event, which is defined as death or hospitalisation.[102]

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# In summary,

**Get your omega-3 index above 8%.** You can measure your omega-3 index with a home test kit. Psychologists at the Linda Loma University in California did this for a group of older people, publishing their results in the journal Brain Sciences.[103] They found that the higher a person's omega-3 index was, the more white matter there was in their brain and the better they performed in cognitive tests that predicted less risk of dementia. Omega-3 index is part of the DRIfT home test kit from foodforthebrain.org/drift

**Eat oily fish three times a week or SMASH it.** S for salmon, M for mackerel, A for anchovies, S for sardines and H for herrings or kippers. Caviar has the highest known levels of omega-3 DHA which literally builds your brain. Even having one serving a week almost halves risk for Alzheimer's.[104, 105]

**Supplement omega-3 fish oils.** Aim for any supplement that provides 500mg of omega-3 DHA. This means two capsules a day. If you're vegan, supplement algal omega-3 DHA.

**Eat an egg and/or nuts and seeds every day** – preferably free range and organic.
Eating just two eggs a week halves future risk of Alzheimer's.[106]
Most of the benefit from eggs is that they are high in

choline.
I also supplement two ‘high phosphatidyl choline (hi PC) lecithin’ capsules any day I’m not eating eggs.
The best seeds are chia, flax, hemp and pumpkin.
The best nuts are walnuts, pecans, and macadamia nuts, but all nuts are a good source of protein and minerals.

**Exercise outdoors and supplement vitamin D.**
Cognitive decline is 19 times more likely if you have a low blood level of vitamin D. Alzheimer’s disease is 4 times less likely if your level is high. Those who supplement vitamin D have a third less risk. In the winter months, up to March supplement at least 1,000iu up to 3,000iu. A vitamin D test is part of the DRIfT test at foodforthebrain.org/drift

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**Check out the brain fat friendly recipes** in our Upgrade Your Brain Cookapp, listed in Chapter 14.


# Methylation, Homocysteine and the Causal Role of B vitamins

Alzheimer's is all about losing connections. Biological connection is what methylation is all about. Methylation is a process that turns one thing into something else, switches genes on and off, detoxifies and micro-tunes metabolism at a rate of something like a billion reactions every few seconds.

Let me give you three examples. If the fire alarm rings, within seconds you're pumping with adrenalin. How? The precursor to adrenalin, dopamine, gets transformed by methylation into adrenalin. Genes, you've heard, are like dimmer switches. They can be turned on (expressed) and turned off (suppressed). This 'switching' is done by methylation. A tiny thing called a methyl group (1 carbon and three hydrogen atoms - $CH_3$) is tagged onto a gene to do this.

In the last chapter we learnt about choline, which can be made in the body. This requires methylation. Insulin and

thousands of other members of your biological orchestra require methylation. Marrying that phospholipid to omega-3 to make a neuronal membrane also does too.

Methylation depends on the presence of B vitamins, primarily vitamin B6, B12 and folate. No B vitamins, no methylation, everything breaks down and a toxic amino acid called homocysteine goes up. When homocysteine levels in the blood go up, it damages blood vesselsin both your body and brain.

Raised homocysteine predicts over 100 diseases (*shown over*) and mainly, but not only, diseases of arteries and neuronal membranes. Multiple sclerosis, where the 'insulating' sheath around nerves breaks down, is an example. Parkinson's, in which the ability to make dopamine is messed up, is another. Neural tube defects, formerly called spina bifida, is another. That's why folate is recommended in pregnancy.

Let's cut to the chase: homocysteine is THE ONLY modifiable factor with enough evidence to be described as causal for Alzheimer's. If it goes up, risk goes up and memory gets worse; if it goes down, risk goes down and memory gets better.

If a person is given B vitamins to lower homocysteine, blood levels go down, memory and measures of cognitive function improve or stop declining, and brain shrinkage is arrested or considerably slowed down. Lowering homocysteine modifies the disease process. The evidence for this, in randomised placebo-controlled trials, backed up with advanced brain scans, is undeniable.

I will go into this, but let's start off with an example. In trials where people are either given anti-amyloid treatment, homocysteine lowering B vitamins, or placebo, anti-amyloid treatment INCREASED the rate of brain shrinkage by about 20%, while homocysteine-lowering B vitamins, REDUCED the rate of brain shrinkage by up to 73%. (68% on average, but higher in those with sufficient omega-3). On the same

measure of cognitive function - the Clinical Dementia Rating (CDR), which is an 18 point scale that you'd want at zero, meaning no clinical dementia - the homocysteine-lowering B vitamins were not only three times more effective, but also 30% of those getting them ended the year with no CDR score at all, while not a single person on anti-amyloid treatment achieved this.

This evidence is undeniable. Yet, it is denied. How? Why? Homocysteine-lowering B vitamins are inexpensive, non-toxic but, (perhaps tellingly) non-patentable. In 2012, the headline in the Daily Mail was "The 10p a day vitamin supplement that tackles dementia: So why is the drug industry spending billions?"

This statement was made by former Vice Dean of Oxford University's medical school, pharmacology Professor David Smith, arguably the world's leading authority on homocysteine and Alzheimer's prevention, thirteen years ago.

It is time we woke up to the fact that Alzheimer's is a preventable disease, not an inevitable part of ageing", said Professor Smith. He had been approached by a representative of a major pharmaceutical company who told him, 'this would be a blockbuster drug, generating billions of dollars, *if* it could be patented'.

That's the 'why' of this outrageous denial. Frankly, I consider it as serious as the denial of the dangers of thalidomide, because literally millions have developed dementia and Alzheimer's directly because of raised homocysteine, so simply corrected with a B vitamin supplement.

In the last 13 years the evidence for homocysteine-lowering B vitamins as a major breakthrough in Alzheimer's prevention has just got stronger and stronger. If you go to the National Library of Science (pubmed.ncbi. nlm.nih.gov) and put in 'homocysteine,' you'll find 30,000 studies. If you search on homocysteine + dementia, you'll find 1,275.

The first two papers, which means the most read, are authored by Professor David Smith and colleagues. The first one, entitled *'Homocysteine – from disease biomarker to disease prevention'*, lists the 100 diseases that homocysteine predicts, and which lowering homocysteine reduces the risk for and, in most cases, helps to reverse or relieve the symptoms of these conditions (some conditions are irreversible). These are shown below. Almost all neurological and mental health conditions are listed here.

# Plasma total homocysteine as a disease biomarker

| Cardiovascular diseases | |
|---|---|
| Myocardial infarction | Atrial fibrillation |
| Severity of coronary artery disease | Cerebral small vessel disease |
| Hypertension | Cerebral microbleeds |
| Restenosis of coronary arteries and adverse outcomes after angioplasty | Disruption of blood-brain-barrier |
| Stroke | Endothelial mediated dilatation – impaired Vascular complications of diabetes |
| Stroke mortality | Raynaud's syndrome |
| Silent brain infarct | Takayasu arteritis |
| Carotid plaque area, stenosis, intima-media thickness | Thromboangiitis obliterans (Buerger's disease) |
| Intracerebral arterial stenosis | Moyamoya disease |
| Peripheral vascular disease | Behçet disease |
| Venous thrombosis | Erectile dysfunction |
| Arterial aneurysm | |
| Arterial stiffness | |

| Other syndromes | |
|---|---|
| Mortality | Sclerosis |
| Frailty | Sickle-cell disease |
| Cancer | Burning mouth syndrome |
| Metabolic syndrome | Atrophic glossitis |
| Obesity | Quality of life in centenarians |
| Bone disease, osteoporosis | Obstructive sleep apnea |
| Inflammatory bowel disease, Crohn's | Hypothyroidism |
| Non-alcoholic fatty liver disease | Telomere shortening |
| Renal insufficiency, chronic kidney disease | Systemic lupus erythematosus (SLE) |
| Chronic obstructive pulmonary disease | Dermatomyositis |
| Alcohol abuse | Inflammatory response |
| Psoriasis | Periodontal disease |
| Vitiligo | Hearing loss |
| | Gout |
| | Blood lead concentration |

| Maternal Homocysteine | |
|---|---|
| Pregnancy complications | – orofacial clefts |
| Outcomes in child | – renal function |
| – small for gestational age, fetal growth | – child cognition |
| – neural tube defects | – child behaviour |
| – congenital heart disease | – schizophrenia |
| | – autism spectrum disorder |

| Central nervous system diseases | |
|---|---|
| Incident Alzheimer's disease/dementia | Alzheimer brain pathology (P-tau) |
| Vascular dementia, vascular cognitive impairment | Multiple sclerosis |
| Post-stroke cognitive impairment | Cognitive decline in Parkinson's disease |
| Cognitive decline after concussion | Depression |
| Cognition in children | Bipolar disorder |
| Cognition in elderly | Schizophrenia |
| Initiation of cognitive decline in ageing | Amyotrophic lateral sclerosis/Motor Neuron Disease |
| Conversion from cognitive impairment to dementia | Multiple System Atrophy |
| Cognitive decline in dementia | Impaired motor development in infant |
| Atrophy of brain tissue/gray matter | Early neurological deterioration after stroke |
| Atrophy of brain white matter | Glasgow coma scale |
| White matter damage | Migraine |
| | Autism spectrum disorder |

*The table lists diseases and syndromes for which there are reports of association with raised total homocysteine. Reproduced with the permission of the authors Professors David Smith and Helga Refsum from the paper* Smith AD,

Refsum H. Homocysteine - from disease biomarker to disease prevention. *J Intern Med*. 2021 Oct;290(4):826-854. doi: 10.1111/joim.13279. Epub 2021 Apr 6. PMID: 33660358. © *2021 The Association for the Publication of the Journal of Internal Medicine 3 Journal of Internal Medicine.*

The second paper listed in Pubmed is entitled *'Homocysteine and Dementia: An International Consensus Statement'*. It says, *"elevated plasma total homocysteine is a modifiable risk factor for development of cognitive decline, dementia, and Alzheimer's disease in older persons.*

*In a variety of clinical studies, the relative risk of dementia in elderly people for moderately raised homocysteine (within the normal range) ranges from 1.15 to 2.5, and the Population Attributable risk ranges from 4.3 to 31%. [e.g., up to 31% of your risk for Alzheimer's is attributed to high homocysteine]. Intervention trials in elderly patients with cognitive impairment show that homocysteine-lowering treatment with B vitamins markedly slows the rate of whole and regional brain atrophy and also slows cognitive decline.*

*The findings are consistent with moderately raised plasma total homocysteine (>11 mcmol/L), which is common in the elderly, being one of the causes of age-related cognitive decline and dementia.*

*Thus, the public health significance of raised homocysteine in the elderly should not be underestimated, since it is easy, inexpensive, and safe to treat with B vitamins. Further trials are needed to see whether B vitamin treatment will slow, or prevent, conversion to dementia in people at risk of cognitive decline or dementia."*

I remember, at the G8 summit on dementia prevention, in 2013 in London, a similar statement was made by a consortium of 113 of the world's leading dementia prevention experts, it concluded:

*"We estimate that about half of Alzheimer's disease cases worldwide might be attributable to known risk factors. Taking*

*immediate action on the known risk factors could perhaps prevent up to one-fifth of predicted new cases by 2025. There is already sufficient evidence to justify immediate action. We call upon the Health Ministers of the G8 countries to greatly increase government funding for research on the prevention of dementia."*

And so, what was the response to this advice from the world's leading prevention experts in the UK? Every single application to do research on homocysteine and B vitamins, by two of the UK's most respected NHS neurologists, Professor Peter Garrard and Professor David Smith, has been rejected.

What's more, the charity that helped fund the first trial showing the remarkable benefit of B vitamins, Alzheimer's Research UK (ARUK), whose charitable remit includes *'the promotion of research into the causal mechanisms of neuro-degenerative diseases with the aim of treating or preventing them',* spends just 4.36% of their over £50 million annual income on non-drug prevention.[107]

The response to the call by the Alzheimer's Society, whose annual income exceeds £100 million, has been even worse. Its charitable remit is *'to disseminate the results of such research for the public benefit into the cause and possible cures whether partial or complete, and the possible prevention of the said disease'*.

However the society has told me that it doesn't fund prevention research and have delegated that to ARUK. The UK government pledged £166 million a year for dementia research, yet none of this money is available for B vitamins and homocysteine research.

I'm spelling this out because any intelligent person can guess 'why' homocysteine is being blanked – there's no money to be made on B vitamins. But worse, they have to compete with the anti-amyloid treatment that big pharma just can't let go of - having spent 100's of billions of dollars getting virtually nowhere of importance.

But now you can start to understand ‘how’ this denial is maintained. It’s two-pronged. Firstly, block funding for further research. Secondly, deny its existence. That brings us nicely to the Lancet Commission omission. A good place to start is the letter submitted to the Lancet by a group of world experts, including Professor David Smith:

# *The Lancet ‘Omission’: Why are homocysteine and B vitamins missing from the Lancet Commission’s Report on Dementia Prevention, Intervention, and Care?*

Joshua W. Miller [1], Andrew McCaddon [2], Jintai Yu [3], Babak Hooshmond [4], A. David Smith [5]

1. Dept. of Nutritional Sciences, Rutgers University, New Brunswick, NJ, USA
2. Faculty of Social and Life Sciences, Wrexham University, Wrexham, UK.
3. Dept. of Neurology and National Center for Neurological Disorders, Huashan Hospital, State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science, Shanghai Medical College, Fudan University, Shanghai, China
4. Aging Research Center, Karolinska Institute, Stockholm, Sweden
5. Dept. of Pharmacology, University of Oxford, Oxford, UK

*“The Lancet Commission’s latest update on dementia is timely and important. We wish to point out a glaring omission from the report. Homocysteine is a sulphur amino acid product of methionine metabolism. It predominantly reflects the status of three B vitamins: folate, and vitamins B12 and B6. A consensus statement of international experts concluded that a raised blood level of homocysteine (hyperhomocysteinemia) is a modifiable risk factor for the development of cognitive decline and dementia, including Alzheimer’s disease, in older persons[108].*

*The relative risk of dementia for moderately raised homocysteine ranges from 1.15 to 2.5, and between 4 and 31% of dementia might be caused by raised homocysteine. Homocysteine-lowering treatment with inexpensive and safe B vitamins markedly slows brain shrinkage and cognitive decline in elderly individuals with cognitive impairment[109]. Notably, the effect of homocysteine on dementia risk is strongest when omega-3 status is inadequate, suggesting a synergistic effect[110].*

*Unfortunately, despite such robust scientific evidence, determination of homocysteine levels in individuals presenting with memory impairment is not routinely undertaken. Prevalence of hyperhomocysteinemia in older American adults is greater than 10%[111].*

*Health economic analysis shows that homocysteine screening, followed by treatment with B vitamins, would be highly cost-effective in older adults presenting with cognitive impairment. It is therefore disappointing that the Lancet Commission fails to recognize hyperhomocysteinemia as an important, modifiable risk factor for age- related cognitive decline and dementia. We look forward to the Commission correcting this omission.”*

You might wonder if perhaps the Lancet Commission experts just didn't know about homocysteine? That would be strange, because a 2024 review in the Journal of Prevention of Alzheimer's Disease which you'd imagine a dementia prevention expert would read, since it is the leading journal in their field - listed reducing homocysteine among the top five evidence-based actions[112].

Also, the biggest, most comprehensive meta-analysis of 396 studies on Alzheimer's prevention not only listed hyperhomocysteinemia (high homocysteine) as 'Class 1' evidence, but also stated that *'Homocysteine-lowering treatment seems the most promising intervention for Alzheimer's disease prevention'.* This paper, by one of China's leading Alzheimer's prevention experts, neurology Professor Dr JinTai Yu, is the fifth most read research paper in Alzheimer's prevention. Professor Yu, the Executive Vice Director of the Institute of Neurology at Fudan University in Shanghai, is both a member of our Scientific Advisory Board and co-author of the Lancet letter.

Also, a US National Institutes of Health review attributes almost a quarter (22%) of the risk of Alzheimer's to raised homocysteine, and a further 22% to lack of seafood and omega-3 fish oils.[113] You'd really have to have your head deeply buried in the sand to miss all this, if your expertise was dementia prevention.

But it gets worse. This is the third version of this report. The first was in 2017, after which the lead author Professor Gill Livingston was sent all the scientific papers by Professor David Smith; the second was in 2020 and, suspecting another report was due both myself and Professor David Smith, resent the papers and Professor Livingston acknowledged receipt in an interview with a journalist. From correspondence with the other experts/authors it is not clear if this evidence was shared with them, although some were aware of the homocysteine research. One argument could be that they lacked the resources to do a thorough meta-

analysis to calculate the percentage of risk reduction that could be achieved by lowering homocysteine. But the papers above have already done this for them.

Telling was her response when interviewed by award-winning medical journalist Jerome Burne. She said *“There are claims that high levels of the amino acid homocysteine can be the result of a vitamin deficiency and that it raises the risk of Alzheimer’s. But high homocysteine only affects a small number of people and there are no trials that show that lowering it has any benefit.”*

Both these statements are simply untrue and we know Professor Livingston had been sent the evidence to show this. The only older people unlikely to benefit from B vitamins are those who don’t have raised homocysteine.

The Lancet have rejected this letter, which shut down ‘peer review’ - a crucial step in establishing research has been properly done. What should happen is that journals publish letters, the author replies so their medical and scientific ‘peers’ can decide how valid the critique is.

This was just another example of how knowledge about homocysteine is kept out of sight. Not only is discussion in journals blocked and money for research withheld, but the authorities are so desperate to keep homocysteine off the table that anyone who understands the topic may be physically barred from scientific meetings.

Last year the highly influential World Dementia Council had a session focussed on prevention. Meetings of the Council target policy makers in health services and government. Various professors had asked the council to admit me, as CEO of the UK’s leading dementia prevention charity. I was denied admission on the grounds there were not enough seats. I went along anyway and saw there were 40 empty seats indicating ‘no shows’.

Prevention has come to mean blocking amyloid - because that is what could be profitable. Shamefully the charities agree. The World Dementia Council is funded by the

Alzheimer's Society, the Gates Foundation and the Alzheimer's Drug Discovery Foundation, which is funded by the pharmaceutical industry.

# How many have raised homocysteine?

In a study of almost 8,000 people in China in 2020, the average level in men was 12.5 and in women was 9.1.[114] In a study of men in Korea over age 18, 40% had a homocysteine level over 11.[115] This means something like one in two men were already in the 'brain-shrinking' zone.

A US study found approximately 40% over the age of 60 had a level above 11.[116] High homocysteine is probably less common in the US, where flour is fortified with folic acid, than the UK. All we know is that two in five adults over 61 in the UK have insufficient B12 to prevent accelerated brain shrinkage.[117] And in Ireland, the figure is 3 in 5 over 50.[118] Lack of B12 means raised homocysteine. It is realistic to assume that over a third of older people have a homocysteine level over 11. That's a lot of unnecessary but costly confusion and misery.

# How B vitamins lower homocysteine

So, how does homocysteine do so much damage and why do B vitamins prevent this. There are two ways – by messing up processes in the brain and by damaging blood vessels. An example of these two avenues of attack is a recent study that reported that having a high homocysteine level

increased risk of cognitive impairment 10-fold and risk of cerebrovascular dysfunction (think stroke and TIAs) by 17-fold[119].

Homocysteine is part of a chain of biochemical reactions running constantly in the brain. It is involved in methylation, the master conductor of the brain's orchestra, which also turns genes on and off and is dependent on what's in our diet, especially folate and vitamin B12. It is also dependent on us eating protein which provides the nutrient methionine, an amino acid, from which the body can make a compound known as S-adenosyl-methionine (SAMe) which does all the vital methylation at a rate of billions of reactions every minute.

Same also has a number of other useful properties such as being an anti-depressant and a pain killer. This multitasking means that our drug regulation system can't handle it properly.

In fact, it's so effective as an anti-depressant and pain killer that it has been banned in the UK and EU.

Hold on, how does that happen? Drug regulations classify substances as either a 'food' or a 'medicine'. A medicine is defined as something that treats, prevents or cures a disease. This means it has to apply for and be awarded a medical licence which require expensive studies. But like B vitamins this runs straight into the 'profitability' problem. Being a natural compound, it can't be patented, so it's not worth applying for a licence to sell it. So, it just fell down the crevasse between 'food' and 'medicine' in the UK, although you can buy in the USA.

Fortunately, regulation can't interfere with methionine making SAMe, which does all that methylation, providing we have enough B6, B12 and folate. There's also some need for vitamin B2 and B3 and a pathway in the liver that needs zinc and TMG (tri-methyl glycine) see Figure 13 over page.

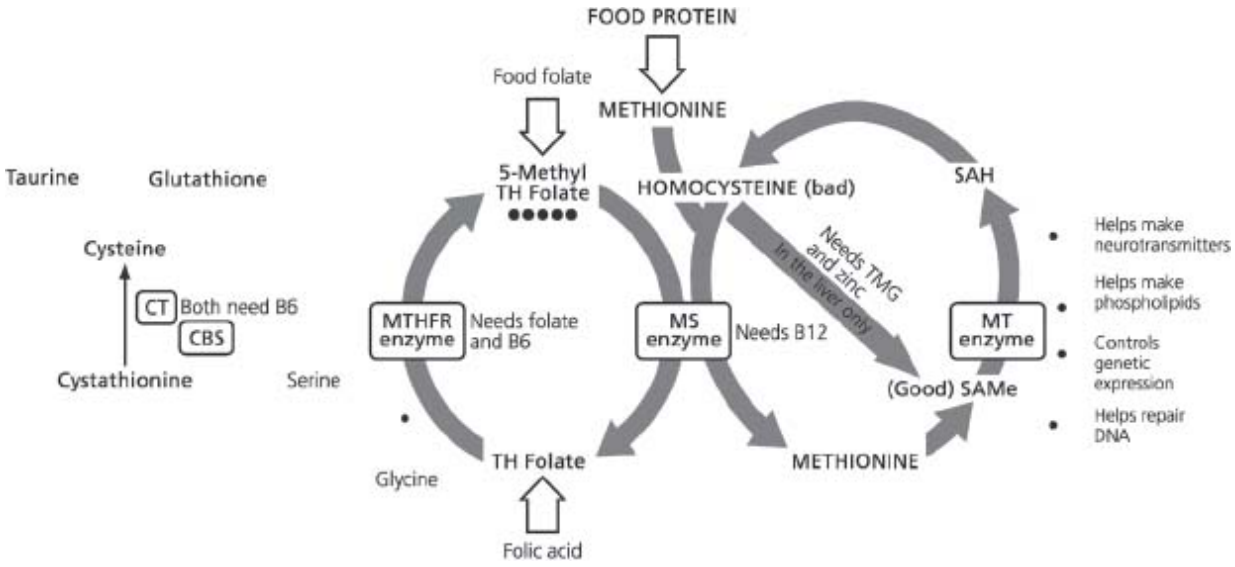


Figure 13 – How B vitamins turn toxic homocysteine into SAMe

If you have enough of all these nutrients, homocysteine can be transformed into something beneficial - a key antioxidant, 'glutathione' which is discussed further in Chapter 9. So, providing some glutathione, or its precursor cysteine (n-acetyl cysteine or NAC) helps 'shunt' homocysteine to SAMe to do all that wonderful methylation.

This is why most homocysteine lowering formulas contain vitamin B6, B12, folate, zinc, TMG and either NAC or glutathione. There are perhaps also some advantages in using methyl-B12 and methylfolate. *See Resources regarding supplements for further details and a list of the best homocysteine-lowering formulas*.

# If Homocysteine goes up memory gets worse and vice versa

The journey towards proving causation has three phases. First, you must establish a strong association between, in this case, low homocysteine and low risk, and high homocysteine and high risk. Second, you look for a plausible mechanism to explain this. Then, you run placebo-controlled trials to show that the 'intervention' - that is B vitamins in this case - both lower homocysteine and have a positive effect on both cognitive function and brain shrinkage.

The association between homocysteine, memory decline, dementia and Alzheimer's risk is beyond doubt. That study above, where high homocysteine predicts a ten-fold increased risk for cognitive decline, is an example. Other studies all show the same thing. Also, when it goes up, memory goes down, and when it goes down, memory gets better.[120] To a considerable extent the same thing applies to one's B12 and folate status. Higher blood levels of B12 and/or folate equate to better cognitive function and less risk for Alzheimer's.

The evidence for B12 is the strongest, although not as strong as homocysteine itself. Some might argue that all homocysteine is just a 'surrogate' test for B12 deficiency. This is partly true, but if you have adequate B12 and a lack of folate, up goes homocysteine and vice versa. There are also many things known to increase Alzheimer's risk that also are associated with raised homocysteine – smoking, stress, sugar (fructose), lack of exercise, zinc deficiency, inflammation to name a few.

# Measuring your B12 status

Vitamin B12 is quite unique in that it can't be absorbed until it is transformed in the stomach by a secretion called 'intrinsic factor'. This is inhibited by antacid drugs that block stomach secretions, called proton-pump inhibitors or PPIs.

These drugs reliably lower blood B12 levels and increase risk for dementia. These drugs, which usually end in '…azole', lower B12 levels and raise homocysteine. The latest review of all studies concludes: 'Our review showed significant changes in diagnostic biomarkers of vitamin B12 status in long-term PPI users, including elevated homocysteine and methylmalonic acid (MMA) concentration levels defining cellular vitamin B12 deficiency.'[121] In terms of future dementia risk, those taking PPI antacids for more than 4.4 years have a 30% increased risk.[122]

B12 deficiency, which is remarkably common, is a major cause of high homocysteine, but it is not the only cause. Last year, in the UK there were also 38,140 courses of treatment involving people with vitamin B12 deficiency anaemia (called pernicious anaemia) and 3,490 hospital admissions due to vitamin B12 or folate deficiency anaemia, which is a fourfold increase in the past 20 years.[123] Many people with pernicious anaemia need vitamin B12 injections, since they have a problem absorbing oral B12 in supplements (*see Resources regarding the Pernicious Anaemia Society*). This is both a function of bad diet and over-medication. Diabetes and anti-hypertensive diuretic medication also lower B12 levels, the former by interfering with absorption, the latter by promoting excretion.[124]

So, dietary assessment of B12 intake is not enough. It's in animal products – meat, fish, eggs, milk. But how do you know you're absorbing it well enough? You have to measure blood levels. The best test for determining your B12 status is called holo-transcobalamin (HTC). Next best is methylmalonic acid (MMA), then serum B12. Serum B12 is the standard test used by doctors. It's more readily available but not nearly as accurate as HTC, but gives a good starting-point. The problem, however, is that the reference range in the UK is wrong.

The UK reference range of above 180pg/ml being sufficient is out of date and in need of revision,[125] along with the US lower level of 200pg/ml. In Germany and Japan, anything below 500pg/ml is considered deficient. Accelerated brain shrinkage due to a lack of B12 does happen with B12 levels below 500pg/ml. The amount of B12 you need is whatever both normalizes your homocysteine level and your blood B12 level. Bear in mind that if your homocysteine is raised, it is likely you are either not getting enough B12, folate or B6. So, it's worth measuring homocysteine as proof that you have a methylation problem, then supplementing a homocysteine-lowering B vitamin formula with all these in it to cover all bases.

A strong association between high homocysteine, low B12 and folate and Alzheimer's risk is well established.

# How homocysteine probably causes Alzheimer's and cognitive decline

Why could homocysteine, which tells you that you have a problem with methylation, actually cause cognitive decline and also crank up Alzheimer's risk? There are several potential mechanisms:

- Homocysteine directly raises both p-tau, promoting those neurofibrillary tangles, and amyloid protein, which, as we have seen, are the hallmarks of Alzheimer's.[126]
- Homocysteine is both a direct toxin to neurons and raises NMDA, another nerve toxin.
- Homocysteine damages blood vessels, which often results in mini-strokes (TIA's) seen as patches of brain

damage.
- Methylation helps make choline and also attach those phospholipids to the omegas, which is the main structural component of neuronal membranes.
- It helps make glutathione which then protects your brain from oxidation.
- Without SAMe all sorts of things go wrong – genes, DNA repair, neurotransmitter production, insulin production and so on.

That's why homocysteine is so totally central to health. Possibly even the single best measure of your health resilience, since nearly everything associated with worsening is associated with raised homocysteine. That is why the sub-title to my book, *The Homocysteine Solution*, first written in 2003, is 'the biggest health breakthrough of the century'. It remains so. I know of no other biomarker that predicts risk for over 100 diseases.

I do not understand why Professors David Smith, from the University of Oxford, and Helga Refsum, from the University of Oslo, who first put homocysteine on the map for dementia, have not received a Nobel Prize. They have published well over 100 landmark research papers of the highest order for medical science. Unless it is just that the solution is so simple and inexpensive. But let's start at the beginning.

# Lowering homocysteine slows down or stops cognitive decline and brain shrinkage

Fifteen years ago, Professor David Smith and his colleagues from the University of Oxford, decided to investigate whether

B vitamins could prevent Alzheimer's from ever developing in the first place. He had a hunch it might, and if it did, that would be an important lifesaving discovery.

So, in 2010, he and a few colleagues gave high doses of B vitamins (folic acid 800mcg, B12 500mcg and B6 20mg) for two years to half a group of 270 people with age-related memory decline; while a placebo tablet was given to the other half.[127]

He also tested their homocysteine levels and ran an MRI brain scan at the start and the end of the trial to identify the characteristic brain damage that is a critical diagnostic indicator for Alzheimer's. In addition, he assessed their cognitive function on various tests, including the Clinical Dementia Rating, at the beginning, after a year and at the end of the 24–month placebo-controlled trial.

This is exactly the same kind of trial design and measures currently used in the anti-amyloid research, except that most of the amyloid trials are shorter - 18 months rather than 2 years.

The results strongly suggested that homocysteine was a cause of cognitive decline that leads to Alzheimer's and that B vitamins were, very possibly, a safe, cheap and effective treatment. This is precisely the kind of major breakthrough that scientists dream of and get awards for. Other findings from the trial were that the B vitamins only have a beneficial effect in patients with high homocysteine.

Among older people with no memory loss, the total brain size normally shrinks at about 0.5% a year. If you've got mild cognitive impairment, this increases to 1%, and in those with Alzheimer's the brain is normally shrinking at 2.5% a year. In this trial, those who took the placebo suffered more brain shrinkage the higher their homocysteine level was. When the level was above 13mcmol/l their brains shrank at the rate of 1.52% per year. But shrinkage in those with homocysteine below 9.5mcmol/l was only 0.71 %.

The effect of giving the B vitamins was remarkable, providing homocysteine levels were above 13mcmol/l. Shrinkage more than halved, compared with the placebo – a drop of 53% (see Figure 14 below), down to almost normal levels for healthy ageing. Also, on more detailed brain scans, those on the B vitamins had almost nine times less shrinkage in the Alzheimer's-related areas[128], as shown right.

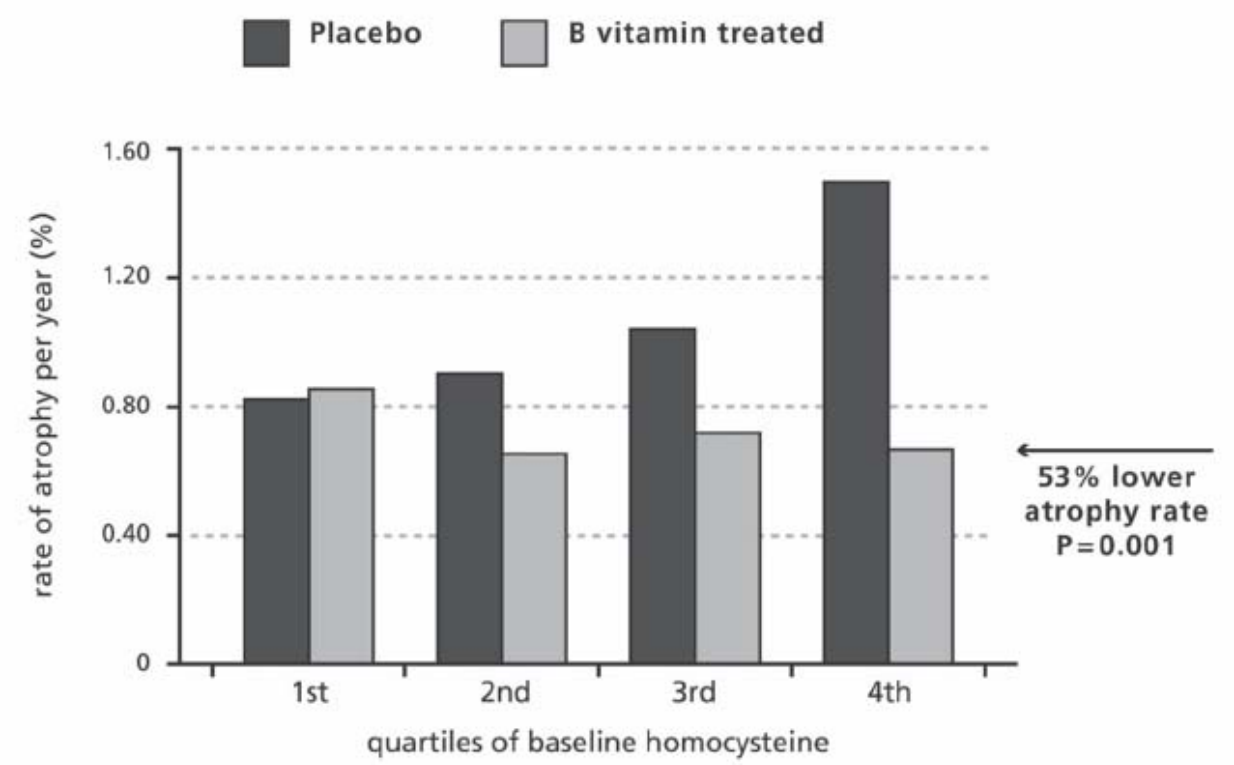


**Figure 14 – The effect of B vitamins on the rate of brain shrinkage** *Adapted from results of the trial of A. D. Smith, et al., Public Library of Science ONE, 2010, used with permission.*

The second part of this research, which looked at whether the vitamins also improved mental performance, found a similar pattern. On the placebo, mental function got worse the higher the homocysteine, but for those participants who were given the vitamins, their mental performance stayed the same. The difference in cognitive decline between

placebo and treatment was significant for those with a homocysteine level of over 11mcmol/l.

Since a shrinking brain and declining cognition is what shows up in people who go on to develop Alzheimer's disease, these results provide the strongest evidence yet that keeping your homocysteine low will protect you from both age-related memory decline and Alzheimer's disease.

This combination of high dose B12, folic acid and B6 has proven particularly effective. In one study, when people with dementia were treated with it for two years their increase in homocysteine was only a quarter of those in the placebo group.[130]

In addition to lowering homocysteine, there are lots of studies showing the benefits of B12 on the various mechanisms through which it protects the brain. One of the latest reviews concludes:

'Clinical studies showed homogenously that vitamin B12 in combination with further representatives of the B-vitamin family, or alone, have beneficial effects on cognitive function, inflammation and brain atrophy in elderly adults without cognitive decline or in mild cognitive impairment patients.'

Studies dealing with patients suffering from Alzheimer's disease found reduced vitamin B12 plasma levels compared to healthy controls. Moreover, supplementation of B vitamins was reported to improve cognitive functions in numerous (randomized) clinical trials.[131]

Folate supplementation is also effective. A study by Jane Durga from Holland's Wageningen University gave people over 50 years old, without memory loss but with slightly raised homocysteine (greater than 13 mcmol/l), a supplement of 800mcg of folic acid a day or a placebo.[132] Three years later, on memory tests, the supplement users had scores comparable to people 5.5 years younger.

So the B vitamin-homocysteine story is a casebook example of careful and imaginative research, transforming

treatment in a field that previously could offer little hope of effective treatment.

If medicine was based on the evidence, everyone with cognitive decline would be recommended to have their homocysteine level tested, which is what we offer at foodforthebrain.org or, at least, supplement B12 500mcg daily.

I've been campaigning for this for over a decade, yet still in the UK, a GP is not allowed to prescribe B12 for cognitive decline and virtually none measure homocysteine. Even if they want to, it's not easy for them to get it done. We do it on an inexpensive test kit at foodforthebrain.org (*see Resources*).

Bear in mind that this high dose is in no way dangerous, but is also not necessary for those with normal homocysteine levels. For them, 10mcg of B12 a day is probably enough. This is what I supplement daily. However, so many people over 60 do have high homocysteine, quite possibly because of poor vitamin B12 absorption, and consequently need higher amounts. Your optimal intake is simply whatever brings your homocysteine below 10mcmol/l, and ideally closer to 7mcmol/l. Also, today we prefer to give methyl-folate, not folic acid, as it is more effective[133] and has a better safety profile at high doses.

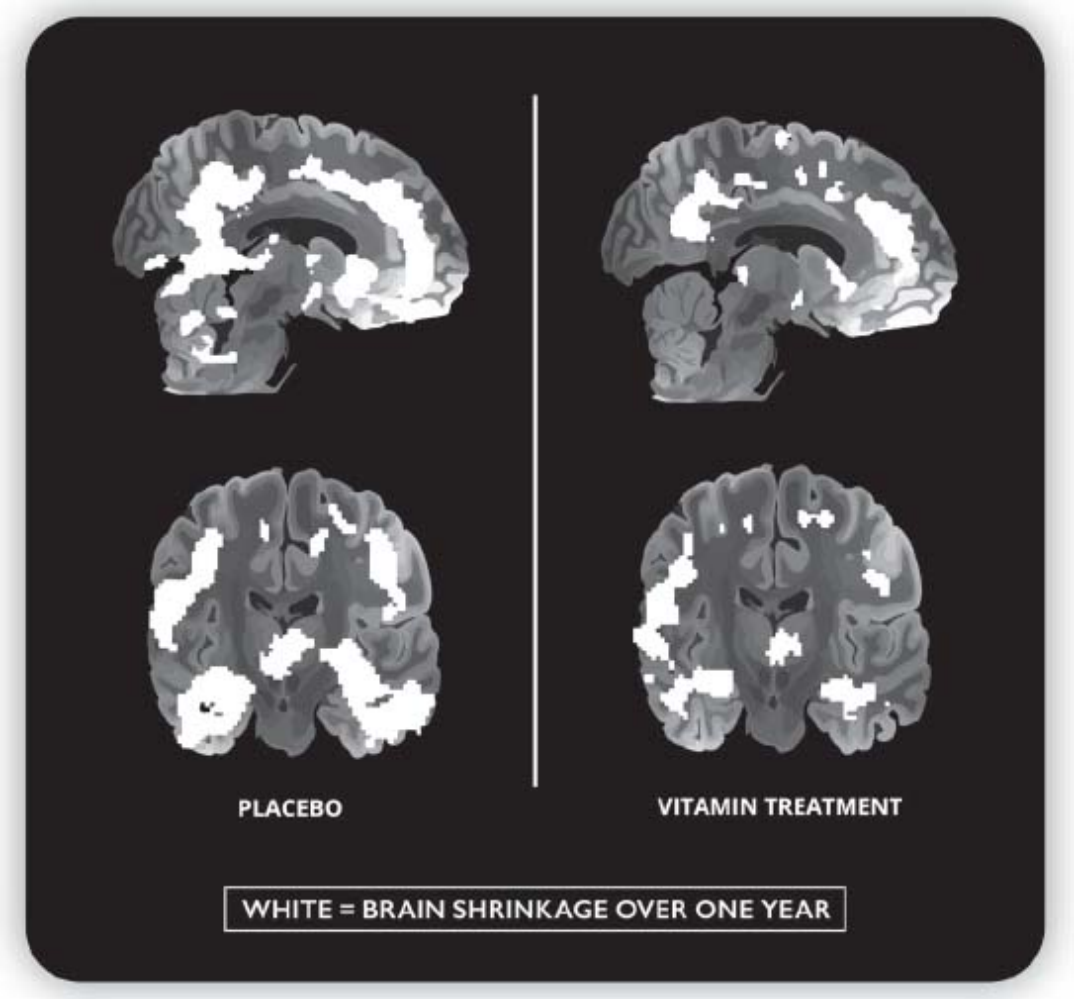


Figure 15 – Brain shrinkage in those with pre-dementia (MCI) on placebo or B vitamins in a year

# The belittling of the B vitamin homocysteine approach

Also, please note that the way pharma-friendly interests have tried to belittle homocysteine lowering B vitamins, is to design and fund trials giving B vitamins, versus placebo, to people who aren’t deficient, or don’t have raised homocysteine, with no cognitive decline, then declare that B

vitamins don’t have any more effect on cognition than placebo.

It’s like giving pain killers to people with no pain and saying they don’t reduce pain.

A classic example of this is a meta-analysis of studies of people with no cognitive decline, hence no room for improvement, concluding that B vitamins don’t work[134]. This was done by a posse of researchers called ‘B-Vitamin Treatment Trialists’ Collaboration’ which looked impressive with some big names, who are well known to have received payment in the millions of pounds, from pharma.

This became the most widely quoted rebuttal to the homocysteine/B vitamin breakthrough a decade ago, declaring ‘Homocysteine lowering by using B vitamins had no significant effect on cognitive function’.

On closer inspection, in a critique by Dr Andrew McCaddon from the University of Wrexham and Professor Joshua Miller from the University of Rutgers, “careful examination of the trials in the meta-analysis indicates that no conclusion can be made regarding the effects of homocysteine-lowering on cognitive decline, since the trials typically did not include individuals who were experiencing such decline.”[135] In Professor Miller’s words, “You can’t prevent something that isn’t happening.”

This was clearly a hatchet job to stop the competition, and had the effect of drying up research funding, just as the amyloid bonanza was in full swing back in 2014.

A more recent 2020 assessment, of 396 studies in total, of people with cognitive decline concluded, ‘Homocysteine-lowering treatment seems the most promising intervention for Alzheimer’s disease prevention.’[136]

# Aspirin and statins interfere with the benefit of B vitamins to lower homocysteine

Although not the subject of this book, raised homocysteine and lack of B12 and/or folate, increase risk for both heart attack and especially strokes quite considerably. This is hardly surprising, since homocysteine directly damages blood vessels and increases risk of cerebrovascular damage by 17 times if a person's homocysteine is raised.

This effect, however, is not seen in all trials. Why this is so may be to do with the drugs people are often on in trials involving those with cardiovascular disease, namely aspirin and statins. A recent re-analysis combining data from two previous trials examined this by looking at the cognitive benefit of those given B vitamins who were or weren't also taking aspirin. Their conclusion was 'In older people with MCI, B vitamins had significantly favourable effects on global cognitive functioning and whole brain atrophy rate in those who were not taking aspirin, but not in aspirin users.'[137]

A similar thing might be going on with statins. In the relation to stroke risk, not cognition, two meta-analyses found that in those who either lowered their homocysteine level by 20% or more or took B vitamins for 3 years or more, the overall risk of stroke was 23% to 29% less.[138] However, in those trials where a high proportion of the trial's participants took statins, there was no benefit; however in trials where under 80% took statins, there was a 23% reduction in stroke risk.[139]

There are two possible ways to explain this drug-nutrient interaction. Maybe the drugs had delivered all the benefit there was to be had and the B vitamins had no room for delivering improvement. Or, there might be something inherent in aspirin and/or in statins that interferes with the

potentially beneficial effect of vitamins. The truth is, we don’t know yet why this happens, just that it does.

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## In summary,

- Eat a serving a day of both greens and either beans, lentils, nuts or seeds. These are all high in the B vitamin folate, as well as vitamin B6.
- Test your blood homocysteine level with a home test kit and supplement B vitamins, if needed.
- A level above 10mcmol/l, which is extremely common in people over 60, is strongly associated with accelerated brain shrinkage and increases risk of Alzheimer’s ten-fold. Homocysteine is easily lowered by supplementing vitamin B6, B12 and folate, but the amounts needed are much higher if your homocysteine level is high. I recommend everyone to supplement 10mcg of B12, which is what you’ll find in a good multivitamin, but if your homocysteine is raised you’ll need 500mcg a day to lower it. It’s completely safe so there’s no harm in taking this much.
- The Homocysteine test is available separately and is part of the pin prick DRIfT test from foodforthebrain.org/tests

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**Check out the B vitamin friendly recipes** in our Upgrade Your Brain Cookapp, listed in Chapter 14.


# Omega-3 and B vitamins – the Dynamic Duo

In the last chapter we learned that giving the right dose of B vitamins to those with raised homocysteine (above 11mcmol/l) and cognitive impairment produced 53% less brain shrinkage and nine times less shrinkage of the areas of the brain affected by Alzheimer's, stopping or slowing cognitive decline considerably in those with mild cognitive impairment.

In the chapter before you learned that upping your omega-3 status could reduce future risk of dementia by about a third (studies show between 13 to 64% with the most comprehensive review showing about 20%).

But I'd be only telling you part of the story if I said that all trials of B vitamins and omega-3 fish oils have worked.

## *Failed trials of B vitamins and omega-3 – why?*

You might also be wondering why homocysteine and B vitamins are rarely mentioned as a major driver of cognitive decline, dementia and Alzheimer's.

This is because studies that have given B vitamins to people without high homocysteine levels (above 11mcmol/l) haven't made a significant difference to cognitive function, even if they might further lower a person's homocysteine. These studies are like giving pain killers to people not in pain and reporting no difference.

The most widely reported study like this by Dr Paul Aisen[140], was published in the Journal of the American Medical Association, giving Alzheimer's patients with an average homocysteine level of 9mcmol/l B6, B12 and folate versus placebo for 18 months. The B vitamins did lower homocysteine, by 2 points, to 7mcmol/l, but didn't produce a change in an assessment measuring the scale of Alzheimer's. Also, it is likely that any treatment, including B vitamins, may be less likely to show benefit the further along a disease process a person is. It is also notable that the lead author was disclosed as 'a consultant to the following pharmaceutical companies involved in the development of potential treatments for Alzheimer's disease'. More than a dozen pharma companies are listed. These companies would certainly favour such a trial being done and widely publicised.

Then, if you pool together lots of trials of B vitamins, at variable and potentially ineffective doses, that have not selected people with high homocysteine, and failed to produce a beneficial effect on cognition, you can produce a meta-analysis that shows that vitamins don't work.

This is what Professor Anne Rutjes and colleagues did in what, on the face of it, looks like a thorough investigation of B and other vitamins and mineral supplements, as a highly regarded Cochrane Review.[141] The front page conclusion read, 'We did not find evidence that any vitamin or mineral supplementation strategy for cognitively healthy adults in

mid or late life has a meaningful effect on cognitive decline or dementia'. This then generates newspaper headlines that supplementing vitamins is a waste of money.

Very few people will read through this 151 page report which correctly states: "Particularly for B vitamins, bias may arise from pooling studies which differed in participants (e.g., with or without elevated homocysteine at baseline) and interventions (various constituents and doses). This 'broad brush' approach may disguise effects."

However, the B-PROOF trial in Holland gave people with homocysteine above 12 a supplement containing 400mcg folic acid and 500mcg vitamin B12 or a placebo tablet.[142] So, that's the right selection of people and the right dose of B vitamins. Two years later, homocysteine had dropped by 5 points in the B-vitamin group, but cognition, as measured by a rather basic memory test called MMSE, had decreased by 0.1 points in the B-vitamin group and 0.3 points in the placebo group. This benefit wasn't significant. The authors concluded, at best, B vitamins 'may slightly slow the rate of decline of global cognition'.

It's a similar story for omega-3. Studies with too low omega-3 levels, or given too late in the disease process, usually haven't worked. But one study in Sweden, called OmegAD,[143] gave either a placebo or a hefty 2.3 grams of omega-3, providing 1.7g of DHA, which is certainly in the optimal range, and those given the high-dose omega-3 didn't fare better. The 179 participants had mild to moderate Alzheimer's, so perhaps it was too late in the disease process?

Or maybe one cannot work properly without the other? This would make sense since we know those B vitamins are the priest that helps marry the omega fat bride to the phospholipid groom. No priest, or no bride or no groom, no marriage.

Consider vision, light and glasses as an analogy, to make the point. In people with poor vision, having a pair of glasses

help bring things into focus. Increasing light helps. If you have glasses but are in the dark, you still can't see. And if you have plenty of light but no glasses, still your vision is blurry. So, you need both light and glasses to reverse poor vision.

Perhaps that's how it is works with omega-3 and B vitamins, wondered Professor David Smith and his colleague Dr Fredrik Jernerén. Could the results of their landmark B-vitamin trial have been better in those with higher omega-3 levels versus low levels? It was too late to give omega-3, but they could go back to the original blood samples taken at the start of the trial and measure the omega-3 status of the participants.

They split the group into thirds and found that the B-vitamin treatment didn't work at all in the third with the lowest omega-3 status, but in the group with the highest omega-3 DHA, the results were remarkable. The reduction in brain shrinkage wasn't the average of 53% seen in their first study, but 73% less in those with homocysteine above 11mcmol/l![144] That brought the rate of brain shrinkage down to that which normally occurs in older people with no memory problems at all! (Compare this to the most recent anti-amyloid drug treatment, donanemab, where the rate of whole brain shrinkage *increased* by over 20%. A study of several anti-amyloid trials reported an average 9% increase in the rate of brain shrinkage).

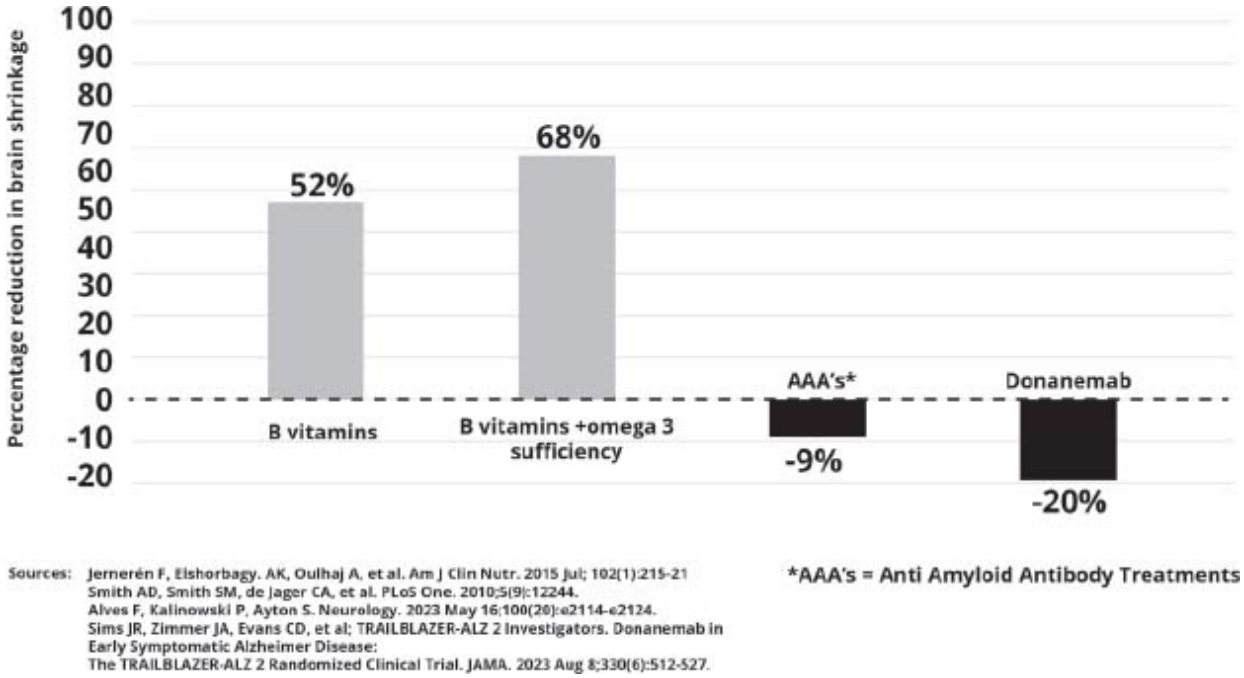



Figure 16 – Reduction in brain shrinkage with B vitamins and omega-3 versus AAAs collectively and donanemab

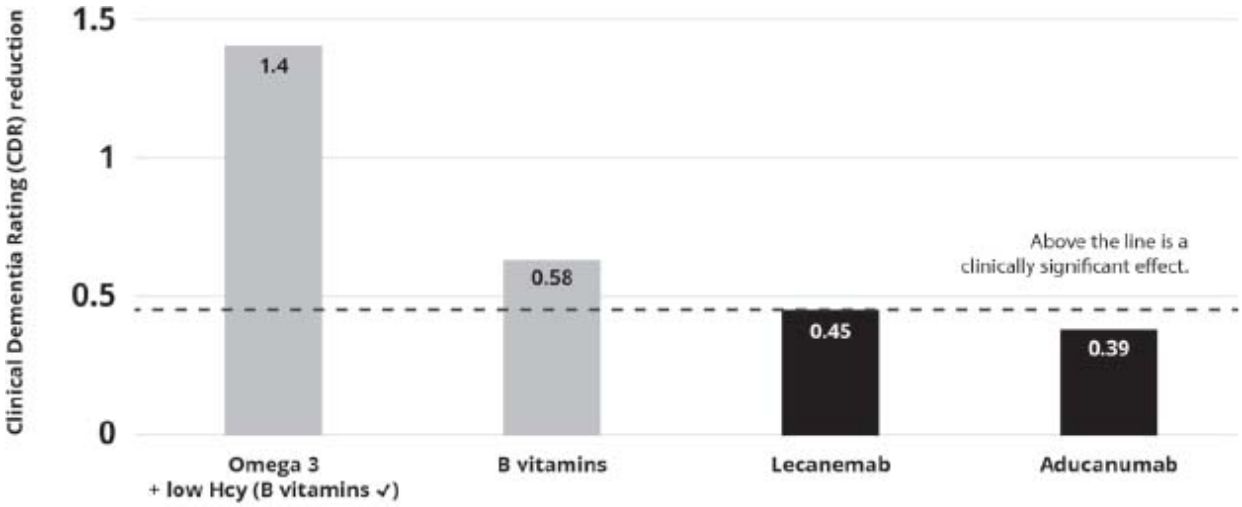
The figure above shows the difference between the B vitamin and omega-3 approach versus anti-amyloid medication.

The same thing happened to their cognition: those with low omega-3 status had no benefit from the B-vitamin treatment, while those with higher omega-3 levels had a remarkable improvement, with virtually no further memory loss.

That got the B-PROOF trial researchers in Holland wondering if their well-designed trial, intending to see if a good dose of B6, B12 and folic acid could be protective, had failed because of a lack of omega-3. So, they went back to their original blood samples and measured the omega-3 DHA status of the participants. They found exactly the same thing – those with the lowest omega-3 levels had no memory benefits from the B vitamins, while those in the top third for omega-3 DHA had a massive benefit which was statistically significant so, once again, showing that the homocysteine-

lowering B vitamins, which should work by improving methylation in those with raised homocysteine, don't work if you haven't got enough omega-3 DHA to build a healthy brain.[145]

Then in Sweden, the failed OmegAD trial researchers teamed up with the Oxford researchers to reanalyse their results, wondering if the B-vitamin status of their participants, who had Alzheimer's, might have been the reason for their lack of result. So, they went back to their original blood samples, this time splitting the group into those with a homocysteine score below 11.7, meaning better B-vitamin status, those with a homocysteine score above 15.7 and those in between.[146] They found a massive benefit in terms of cognitive improvement in those with the lower homocysteine levels given the omega-3 supplement. The benefit in those given omega-3 with a homocysteine below 11.7 was several times greater than that of any anti-amyloid treatment.




Sources: Jerneren F et al Journal of Alzheimer's Disease 69 (2019) 189–197 189
Oulhaj A, Jernerén F, Refsum H, et al. J Alzheimers Dis. 2016;50(2):547-57; Van Dyke C N Engl J Med 2023 Jan 5;388(1):9-21; Tampi RR, Forester BP, Agronin M. Drugs Context. 2021 Oct 4;10:2021-7-3; Jerneren F, Cederholm T, Refsum H, et al. J Alzheimers Dis. 2019;69(1): 189-197.

Figure 17 – The reduction in the Clinical Dementia Rating (CDR) with omega-3 DHA, B vitamins and anti-amyloid medication

Meanwhile, a study in China gave people with mild cognitive impairment either folic acid or DHA supplements, or both, or a placebo.[147] Only the combination of B vitamins and omega-3 DHA produced a highly significant improvement in cognitive function.

Also, the B vitamin and omega-3 status of diabetics may make all the difference to whether or not they develop the extremely common cognitive decline associated with diabetes. A study looking at omega-3 and homocysteine levels in diabetics found that 'insufficient levels of n-3 PUFA, along with elevated serum homocysteine, significantly increase the risk of developing diabetic cardiovascular disease (DCD)'. Just being low in omega-3 or B vitamins, as illustrated by a high homocysteine, wasn't nearly as damaging as being low in both omega-3 and B vitamins. The researchers followed up this discovery in a study with mice that showed that treatment with a combination of fish oil, folate, and vitamin B12 improved cognitive impairment, once again confirming this important nutrient synergy.[148]

Give a builder a hammer. Do you get a house? No. Give a builder a bag of nails. Do you get a house? No. Give a builder some planks of wood. Do you get a house? No. Give a builder a hammer, a bag of nails and some planks of wood and you get a house. This analogy is pretty much what's going on in your brain. The wood is omega-3, the nail is the phospholipid and the hammer is the methylating B vitamins. You need both enough omega-3 DHA and enough phospholipids providing choline (to make phosphatidyl choline), as well as good methylation, meaning a low homocysteine level, which is a result of B-vitamin supply, bearing in mind that some people need a much higher intake of B12 due to poor absorption.

# We need a definitive trial on omega-3 plus B vitamins

If the case for both omega-3 and homocysteine-lowering B vitamins wasn't already strong enough to put them centre stage in the prevention of Alzheimer's, the discovery that omega-3 doesn't work in those with high homocysteine, and homocysteine lowering B vitamins don't work in those with insufficient omega-3 – that they are co-dependent – means we have vastly under-estimated their benefit when both are provided at optimal levels.

The discovery of the co-dependence of B vitamins and omega-3 in protecting memory begs for a trial combining the two. This trial was ready to run seven years ago, designed by one of the UK's leading neurologists, Professor Peter Garrard at the University of London's Neuroscience Research Section. It's large enough and long enough to definitely answer the question as to whether giving B vitamins and omega-3 to those with mild cognitive impairment will prevent them from developing Alzheimer's. But no one will fund it.

While the cost of developing Alzheimer's drugs has been estimated at $42.5 billion by 2021[149], and by now will be several fold more with the recent large-scale trials each costing in the hundreds of millions, both European and British governments and research agencies have so far refused to fund any study on B vitamins and omega-3. Meanwhile in the UK, a Department of Health and Social Care spokesperson has said, 'We are working hard to find a cure for dementia, doubling research funding to £160 million a year by 2024–25'.[150]

I went to the launch of the Geller Dementia Commission, a project to transform the way we deal with dementia in the UK. Given that even the most conservative estimate of how much could be prevented hovers around 50%, I asked the CEO of the Alzheimer's Society whether half their money for

research could be ring-fenced for prevention. She agreed it made sense. I asked her how much she had to spend. She said £6 million.

Also, on the top table, was Professor Peter Garrard. He confirmed that such a B vitamin and omega-3 trial was arguably the single most important prevention trial badly needed. I asked him how much it would cost to do it impeccably, long enough and large enough to confirm if the combo of B vitamins and omega-3 could stop those with mild cognitive impairment progressing to Alzheimer's. He said £3 million.

I went back to Kate Lee, CEO of the Alzheimer's Society and said that's a win-win – spend half of what you've got to do the most important, highest potential impact prevention study. She told me that they don't fund prevention studies. So, in the UK alone, we have two leading Alzheimer's charities raising and spending over £30 million a year on research, but virtually none goes into real, non-drug prevention – and none into the most promising, evidence-based preventative: B vitamins and omega-3.

In the UK, Europe and the US, there is a complete blind spot when it comes to non-drug prevention, as the Lancet Commission omissions makes clear.

Supplementing B vitamins and omega-3 might cost you £100 a year. The cost of the latest amyloid drug is £20,700, plus all the necessary medical costs and scans to check for the common adverse effects of brain swelling and bleeding.

This approach, if rolled out, would cost billions of pounds. The B-vitamin and omega-3 approach would save billions of pounds. We asked Oxford University's health economist, Apostolos Tsiachristas, who is Associate Professor in Health Economics at the University of Oxford, how much could be saved if doctors simply tested homocysteine in those over 60 and prescribed inexpensive B vitamins. '[This] is predicted to be a highly cost-effective policy that could save costs to the UK economy of approximately £60 million per year,' he said.

It was also estimated it would promote healthy longevity, adding 14 years to life expectancy.[151]
Is it any wonder healthcare is failing?

# Could omega-3 and homocysteine-lowering B vitamins eliminate half of all Alzheimer's risk?

A risk factor is assessed for its impact using a measure called the population attributable risk (PAR). Professor May Beydoun at the US National Institutes of Health did this for both raised homocysteine (lack of B vitamins) and low intake of seafood or omega-3. For Alzheimer's, the attributable risk for each of these was 22% – that's 44% combined.[152] It's not quite fair to add these two together, though, because there is overlap – someone could have both risk factors. It would be more reasonable to say that these two, easily resolved risk factors, might account for a third of all risk of Alzheimer's. But now we know that B vitamins and omega-3 are co-dependent, which means that the beneficial effect of B vitamins has been vastly underestimated because omega-3 status wasn't taken into account, and similarly, the effect of omega-3 has been vastly underestimated by not factoring in B-vitamin status.

Even the best 'meta-analysis' of all risk factors for Alzheimer's, looking at 396 studies in total, which put homocysteine-lowering B vitamins at the top of the promising approaches, didn't factor in omega-3 and what we now know about the dynamic duo of omega-3 plus B vitamins.

The take-home message is to make sure you have both sufficient omega-3 and B vitamins in your diet and supplement programme.

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# In summary

**Test both your homocysteine and omega-3 index**, with the aim to bring the omega-3 index in above 8%; and your homocysteine level, with the goal of being below 10 and close to below 8 mcmol/l. Then, both improve your diet and supplement accordingly.

**For folate, eat greens, beans, lentils, nuts and seeds.** Also supplement 200mcg. If your homocysteine is high, increase this to 400mcg and take methyl-folate rather than folic acid.

**For B12, eat fish, eggs, meat or milk.** Supplement 10mcg in a multivitamin. If your homocysteine is raised, you'll need 500mcg a day.

B6 is in all these foods above. Most decent multis will give you 20mg, which is probably enough.

**Eat oily fish three times a week.** SMASH it (salmon, mackerel, anchovies, sardines, herrings or kippers). Fresh tuna - not the canned stuff - is also a rich source, as are oysters, fish roe, taramasalata and, of course, caviar

**Also supplement omega-3, aiming for an omega-3** supplement that provides 500mg of DHA, 750mg of EPA. You can get vegan omega-3 DHA, derived from algae, if you're that way inclined.

**I both eat seafood and supplement.** My omega-3 index is 10%, about that of many people in Japan. If you eat a lot of seafood, you might not need to supplement - and if you supplement daily with sufficient amounts of omega-3 DHA and EPA, you might not need to eat seafood. But this approach is less desirable since there are so many other important brain-essential nutrients in seafood such as phosphatidyl choline.

**Your best foods for phospholipids**, and especially phosphatidyl choline (PC), are eggs and marine food. The best supplemental source of phosphatidyl choline is lecithin. You can get 'hi-PC' lecithin which has the most. Two 1200mg capsules will give you a significant amount. If you are not eating seafood or eggs I'd certainly recommend this, especially if you're trying to recover your cognitive function. Choline itself can be supplemented. The optimal level appears to be around 400mg a day, but that includes what you eat. Phosphatidyl choline is better since it is in the form your brain uses and needs. It can also convert this to other phospholipids however, there is some merit in also supplementing phosphatidyl serine (PS) directly.

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**Check out the brain fat and B vitamin friendly recipes** in our Upgrade Your Brain Cookapp, listed in Chapter 14.


# How our Sugared Brains are ‘Fructed’ and How Ketones Aid Recovery

Are our brains being fructed? The fruit sugar ‘fructose’ isn’t generally considered a food that’s best avoided. After all, it comes from fruit.

Yet a radical new theory, developed by Richard Johnson, Professor of Nephrology at the University of Colorado, explains how it can trigger various damaging changes in our metabolism that make us more likely to develop chronic conditions such as diabetes and obesity, as well as Alzheimer’s.

It ties together many of the associations that clearly show that obesity, diabetes and blood sugar related biomarkers (glucose, HbA1c, insulin resistance) predict Alzheimer’s and also increase sugar cravings - which are associated with brain fog and memory loss.

Professor Johnson, a member of our Alzheimer’s Prevention Expert Group (*see Resources*), has produced

what is effectively a biochemical wiring diagram of the connections fructose turns on and off, that are making an increasing number of people sick.[153] Not only has modern man's sugar consumption gone up thirty fold in the last 200 years, but the kind of sugar we eat has radically changed shifting towards more fructose with the introduction of 'high fructose corn syrup' since the 1990's.

Fructose makes up half of white sugar - the other half being glucose - and most of fructose corn syrup, which is the main sweetener in fizzy drinks and ultra-processed foods, as well as being the main sugar in fruit.

The brain and the body know what to do with glucose. It is the main fuel for the brain's neurons, followed by ketones (*see page 100*). Neurons cannot burn fructose for energy.

# Fructose promotes brain fog, fatigue, weight gain, diabetes and fatty liver

In the liver the amount of fat stored from eating fructose increases, driving fatty liver disease, while the cell's mitochondria, which create the body's and brain's energy molecule ATP, become less productive. Also, blood pressure goes up. The result is that you get fatter, with more brain fog and fatigue and feel less inclined to exercise. Fructose, and too much sugar overall, is a major promoter of diabetes.

Meanwhile, an anti-ageing process called autophagy - that would normally clear away used up and damaged mitochondria, the cell's energy factories, to make room for new ones - is disabled. When fructose gets into the brain, it is one of the factors causing the brain to form clumps of amyloid protein.[154]

How on earth does fructose carry out such a blitz on our bodies? Why would the body run a program that was potentially so lethal? “It would be wrong to think of fructose as some sort of major toxin, although it becomes neurotoxic in excess,” says Professor Johnson. “Instead, its remarkable range of effects are part of an ancient set of biological programs, which we call the ‘Survival Switch’, that work to prepare animals for hibernation, storing supplies in preparation for times of famine.” This is why fat storage increases and energy drops off, producing brain fog. The trouble is, we in the 21st century western world, never run out of food or fructose. We don’t hibernate in the winter. We just keep eating.

Fructose has to be converted to glucose to provide clean energy to the brain. But excess can also be easily turned into fat in the liver for storage. An important study in 2019 showed that, while glucose in the liver stimulates the mitochondria to produce energy, fructose slows that down with the consequence of making more fat and less energy.[155]

“The most important takeaway of this study is that high fructose in the diet is bad,” commented Dr. Ronald Kahn from the Joslin Diabetes Center. “It’s not bad because it’s more calories, but because it has effects on liver metabolism to make it worse at burning fat. As a result, adding fructose to the diet makes the liver store more fat, and this is bad for the liver and bad for whole body metabolism.” A study in Nature journal shows that high fructose decreases physical activity, increases fat storage and doesn’t give the brain the same energy boost that glucose does[156], putting people into ‘couch potato’ mode.

Fructose, more than glucose, cranks up inflammation in the brain and increases anxiety by depressing the brain’s adrenalin ‘off switch’, GABA. It also promotes insulin resistance. Insulin is the hormone that transports glucose,

the main fuel of the brain, into neurons. So, ironically, insulin insensitivity or resistance means that the consequence of continuously eating too much sugar, and especially fructose, is glucose starvation in the brain. This causes ‘brain fog’ and, ultimately, neuronal cell death and Alzheimer’s.

# High sugar, fructose diets, diabetes and dementia – the evidence is substantial

Back in 2004, researchers at Columbia University stated that people with high insulin levels – the principal hallmark of metabolic dysfunction – were twice as likely to develop dementia as those with healthy levels. Moreover, those with the highest insulin levels had the worst memories.[157] The same year, an Italian study also established a link between heightened insulin levels and declining mental function.[158]

Fructose is half of sugar and the main sugar in high fructose corn syrup which is the main sweetener in ultra-processed foods. These foods also increase Alzheimer’s and dementia risk.[159] All this sugar raises blood glucose, which then damages red blood cells - which is why the single best measure for diagnosing loss of blood sugar control and diabetes is counting up the percentage of sugar damaged, or glycosylated, red blood cells.

This is called HbA1c, sometimes called glycated haemoglobin, and is what we measure at foodforthebrain.org.

Keeping blood glucose levels in the low-normal range is reflected by a low glycosylated haemoglobin (HbA1c) which is associated with reduced risk for dementia in several

studies.[160] A recent study of 374,021 older men with diabetes found that keeping the level of HbA1c stable over three years cut risk of dementia by a third.[161]

Having type 2 diabetes almost doubles risk for dementia.[162] Diabetes is also associated with more rapid brain shrinkage.[163] Even people in the upper normal range of blood glucose have increased brain atrophy, impaired cognition and increased risk of dementia.[164]

For instance, one trial measured HbA1c and glucose levels in several thousand elderly people over the course of almost seven years.[165] In that time, over a quarter of the participants developed dementia, and the rising glucose levels were associated with an 18% increased risk of dementia in those without diabetes and 40% in those with, or who developed, diabetes.

Similarly, a Puerto Rican study found that people who consumed large amounts of sugar doubled their risk of suffering poor cognitive function,[166] while another US study discovered a strong correlation between blood sugar level and memory loss.[167] Two studies – one in Ireland[168] and the other in the United States[169] established a link between high dietary glycaemic load (GL) and cognitive decline. Indeed, both of these reports suggested that high GL is even more predictive of the pathological changes associated with Alzheimer's than either high carb or high sugar intake. A high GL diet is also associated with more amyloid plaque[170] and cognitive decline, especially in those with the ApoE4 gene.[171] A long-term study found evidence that brain shrinkage and impaired cognition is more common among people with high blood glucose levels, even within 'non-diabetic' limits.[172]

Childhood obesity - or plumper babies - increase future risk of dementia by 20%. Adult obesity, as measured by body mass index, more than doubles the risk of

dementia.[173] More fat and less fat-free mass distribution on arms is particularly predictive, which is consistent with the ‘fat switch’ turned on, which is what a high fructose diet does.

# Fructose raises homocysteine – B vitamins and omega-3 protects diabetic’s brains

High fructose and insulin resistance also raise homocysteine levels, as does high triglycerides, which are the fats in the blood created from too much sugar and fructose. (Triglyceride level is more important than cholesterol for determining heart disease risk – you want it below 1mmol/l (89mg%).). All these – high glucose, triglycerides, homocysteine and insulin resistance - are the diagnostic hallmarks of ‘metabolic syndrome’: that systems-based pattern of changes that lie behindobesity,diabetes,heartdisease,cancer,arthritisandAlzheimer’s. In animal studies a high fructose diet raised homocysteine by 72% in five weeks.[174]

As we saw on page 86, having a low omega-3 and B vitamin status, shown by a raised homocysteine, massively increases the risk of someone with diabetes becoming cognitively impaired, while optimising omega-3 and B vitamin status, protects their brain.[175]

These two studies illustrate why it is so vital to consider the interactions between risk factors, and why our four horsemen - disturbed glucose balance, lack of omega-3, homocysteine-lowering B vitamins and antioxidants - is highly likely to be the ‘perfect storm’ that tips many people into Alzheimer’s.

# Sugar - The Lancet omission

With this veritable mountain of evidence, you'd imagine that cutting down on sugar would be up there in the top tips for reducing Alzheimer's risk, for example, in that 2024 Lancet Commission report. But no, the report says: "Eating a diet high in fruit and vegetables and low in ultra-processed foods is good for many health conditions and affects the dementia risk factors of obesity, diabetes, and hypertension, but insufficient evidence exists to say that this diet is directly useful for dementia prevention."

That omission inspired a letter from our group of experts on sugar metabolism. It reads as follows:

*To the Editor,*

*The authors present a comprehensive epidemiological-based review of risk factors for Alzheimer's disease (AD). However, epidemiology can be misleading if the underlying pathophysiology is not considered. For example, the observation that obesity, gout, and diabetes are risk factors for AD at midlife but not at time of diagnosis is likely due to the marked weight loss that commonly presages diagnosis of dementia, similar to that seen in subjects with end-stage renal disease. Diet, which drives these conditions, follows these same confounding rules.*

*Recent studies argue that fructose generated and metabolized in the brain may account for the majority of cases of AD. Fructose is a risk factor that can explain development of AD from inception to end-stage*[176]*. Endogenous production of fructose is largely driven by diet (sugar, refined carbohydrates, ultraprocessed foods, salt, red meats, and alcohol). Hyperglycemia also increases brain fructose production*[177]*. Humans with AD show 5-fold higher intracerebral fructose levels as well as higher metabolites of*

*the polyol pathway (which generates fructose) than age-matched control[178]. Fructose metabolism stimulates foraging as a survival response, but when chronically activated in animals causes CNS insulin resistance, mitochondrial dysfunction, ATP depletion, neuronal loss, and amyloid plaque and tau protein deposition, similar to AD[179]*

*The mechanism is mediated by fructokinase and resultant uric acid inhibition of mitochondria in microglia, a finding supported by animal data, metabolomics, and Mendelian studies.[180]*

*An essential strategy for preventing AD is to follow a healthy diet low in added sugars and refined carbohydrates.*

Richard J Johnson[1], Robert Lustig MD MSL[2], David Perlmutter[3]

1. Department of Medicine, University of Colorado, Aurora, CO, USA;
2. Department of Pediatrics, University of California, San Francisco, CA, USA;
3. University of Miami Miller School of Medicine, Miami, FL, USA

The letter was rejected. It had not only shown the direct association of fructose, sugar, refined and ultraprocessed foods and dementia, but also the several mechanisms which include the depletion of fuel supply (insulin resistance), the depletion of brain energy (ATP), omessed up energy production (mitochondrial dysfunction), loss of brain cells (neuronal loss) and increase in amyloid and p-tau. This is not an easy area to do randomised controlled trials in, especially since they’d have to run for several years.

Even diabetes, as a preventable risk factor, is delegated to contribute 2% of the risk. If you ask AI in a Google search, you’ll get a figure of 60% increased risk if diabetic.

As for B vitamins and omega-3, the association between sugar, dementia and Alzheimer's is beyond doubt. The mechanisms are becoming increasingly clear – a veritable onslaught on the brain from all fronts. Randomised placebo-controlled trials will never be done because they are impossible and unethical. Yet, somehow, the observational evidence of association for vision and hearing loss and air pollution, is deemed acceptable - while the evidence for sugar is not. Why?

Is it the influence of big food? Is it due to the medical blindspot about nutrition? These are impossible questions to answer, but certainly big food lobbies exert their influence by funding studies and influencing or appointing scientists employed by governments, medical and health services to make decisions.

"The fact is, humanity has gone from consuming around 2 kilos a year of sugar - before refined sugar was invented and popularised - to over 70 kilos per person per year with a big jump in the 1980's towards fructose, as corn sugar became cheaper than cane. Our metabolism, honed over millions of years, just can't cope and both brain and body suffer", says Johnson[181].

Is it credible that what you eat has absolutely no modifiable impact on dementia? That is the take home message from the Lancet Commission report. That's a terrible message, and explains why rates of diet-related disease - including obesity, diabetes, heart disease, cancer and dementia - are rocketing, along with healthcare costs.

Of course, they'll argue that the quality of the evidence for diet isn't good enough, or that it's not easily measured. But with almost 7,000 studies published in peer-reviewed journals on nutrition and dementia - and only 531 on air pollution (to which they assign a 3% risk contribution), and 1,263 on hearing loss (to which they ascribe a 7% risk contribution) - it makes you question whether this Lancet

research is truly credible. Diet is more complex to research than hearing loss but, as Albert Einstein said ‘Not everything that matters can be measured and not everything that can be measured matters.’

# Eat your fruit, don’t drink it

None of this means that we should avoid fruits, which contain only a small amount of fructose that comes with beneficial fibre that feeds our vital gut bacteria, plus various nutrients. Not so for fruit juice, devoid in fibre. A glass of orange juice is the equivalent of three oranges, but without the fibre. So, eat your fruit, don’t drink it.

But is does explain why too much blood glucose - from regularly eating generous amounts of sugar-laden foods and carbohydrates - is so damaging. The liver turns the excess glucose into fructose with all its knock-on effects. Other foods that can accelerate fructose production are alcohol and salt.

This rise in fructose makes it all too easy to start piling on the pounds, regardless of how many calories you have cut, or how much further you are running. It’s a connection that very few nutritionists or GPs are aware of.

A sign of the widespread damage that Survival Switch can cause is that low ATP shows up in the brains of people in such disorders such as obesity, diabetes, fatty liver disease and Alzheimer’s. Understanding this points to new ways to cut the risks of these chronic disorders.

# Stabilising HbA1c cuts dementia risk by a third

A simple, but very effective one, is to run a blood test – HbA1c – the gold standard test GPs use to screen for diabetes. A recent study of 374,021 older men with diabetes found that keeping the level of HbA1c stable over three years cut risk of dementia by a third[182]. Similar benefits have been found with patients with pre-diabetes. But far lower levels of HbA1c than those used to diagnose diabetes are associated with the first signs of brain shrinkage, which is the hallmark of cognitive decline even in teenagers.

In this case, levels above 36mmol/mol (5.4%) are associated with brain shrinkage and cognitive decline[183], while above 42mmol/mol (6%) is classified as pre-diabetes and above 48mmol/mol (6.5%) as diabetic. The youngest non-genetic dementia diagnosis is that of a 19-year-old man in China.[184] A low HbA1c is good and is a proxy for insulin sensitivity, which has been associated with a reduced risk of dementia in several studies.[185]

# Switching to ketones for brain energy

When the glucose ‘engine’ starts to malfunction, as often happens with diabetics and those with memory decline, ketones, manufactured in the liver from fat, are a terrific alternative source of energy for the brain.

Under these circumstances, the brain often derives a fifth of its energy from ketones. ‘Fuelling cells’ called astrocytes, which help prep the ketones, are even positioned next to the neurons. Ketones may even be a preferred fuel, especially for those with age-related memory decline.

You don’t have to generate ketones for the brain to work optimally, even though it might help. Normally, the brain uses about a quarter (22%) of the total energy we take in

from food. We can get all that from glucose. However, if there are ketones in our system, the brain will use them in preference.

## *C8 oil – the fuel for ketone production*

Ketones are primarily made in the liver from medium chain triglycerides (MCTs). The backbone of a fat molecule is a chain of carbon atoms. A MCT is between 6 and 12 carbon atoms long. In contrast, olive oil is a long-chain fat, with 14 carbon atoms. Coconut, palm and olive oil are sources of MCTs. However, recent research has proven that almost all ketones are made from a sub-fraction of these fats called C8 (short for carbon 8, or caprylic acid triglyceride, an 8-carbon-chain fat).[186] Coconut oil is only 7% C8, while most MCT oil, which you can buy in a health-food store, is 12% C8. You're better off getting pure C8 oil, which is also available in health-food stores and online (*see Resources*), if you want to supply your brain with ketones. C10 is the next best, but it's not nearly so good for making ketones.

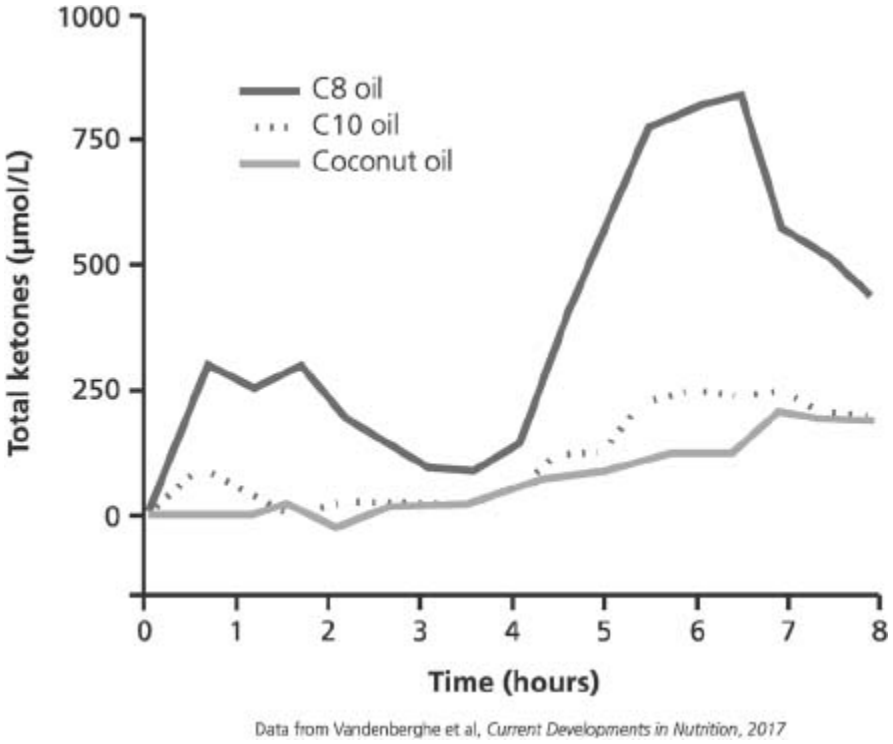


**Figure 18 – Ketone levels resulting from C8 oil, C10 oil or coconut oil**

Two breakthrough studies in Canada, by Dr Melanie Fortier and Professor Stephen Cunnane from Sherbrooke University, have established that C8 oil can be extremely helpful as an energy source for those with cognitive decline. Cunnane's research team gave people with either Alzheimer's[187] or pre-dementia[188] two tablespoons of MCT oil (30g of C8 and C10) or a placebo and measured their cognitive abilities, as well as how much energy their brains made. They kept making the same amount of energy from glucose, but had a 230% increase in energy made from ketones. As they started making more energy, certain areas in their brains lit up. These related to functions such as memory and language, and on tests, these improved.

'Measures of episodic memory, language, executive function, and processing speed improved on the C8 versus

baseline. Increased brain ketone uptake was positively related to several cognitive measures,' reported Cunnane.

Professor Cunnane is another member of our Scientific Advisory Board at Food for the Brain and holds the chair in ketotherapeutics at the university. His research has shown that Alzheimer's patients start to suffer glucose deficiency in certain regions of the brain, even before they start to experience any symptoms. There may be various reasons for this, but the most likely candidate is insulin resistance, which makes it more difficult for the fuel to make its way into the neurons. This makes sense, as diabetics are three times more likely to develop Alzheimer's than non-diabetics.

'We know from our scanning research that the glucose deficit is not due to damage to the neurons, but to insufficient amounts being available as fuel,' explains Cunnane. 'It's safe to treat this deficiency with ketones.'

On the other hand, if the condition remains untreated, the fuel-deprived neurons suffer the sort of damage that ultimately leads to Alzheimer's. 'Burning ketones can also increase the number and output of the cell's energy factories, mitochondria, damaged by fructose,' says Professor Robert Lustig of the University of California, author of the best-selling book Metabolical. He is also a member of the charity's Alzheimer's Prevention Expert Group *(see Resources)*.

Meanwhile, in New Zealand, neurologists decided to test the effects on 26 people diagnosed with Alzheimer's by putting them onto a low-carb ketogenic diet for 12 weeks, or a healthy low-fat but not ketogenic diet as the 'control', with each participant following both diets.[189] On the ketogenic diet, there were improvements in their daily function and quality of life measures, which is quite remarkable at this late stage of the disease process.

# Mind the brain energy gap with ketones

‘People with cognitive decline have an energy gap,’ says Cunnane. ‘Probably due to insulin resistance, they are not able to make use of glucose. Providing a food source, C8 oil, from which the body can readily make ketones, fills that energy gap, brain cells come back to life and memory and brain function improve as a result. It reminds me of those announcements on the London Underground: “Mind the gap.”’

Practically, as in his studies, that means having a couple of tablespoons of C8 oil. The energy effect lasts for a few hours, so this might be best administered by taking a teaspoon two or three times a day, then building up to 2 teaspoons three times a day. It’s a pleasant, creamy taste. A few people get gastrointestinal upset from these oils, which is mitigated by emulsifying - for example, having the oil in a smoothie, or having it with a meal, or building up the dose slowly over time.

Some people have C8 oil with their coffee, as advocated by lowcarb enthusiast David Asprey, apparently inspired by the Tibetans’ yak-butter tea. He invented bullet-proof coffee, adding grass-fed butter and two tablespoons of MCT oil to coffee.

My hybrid latte (*recipe below*) combines carb-free almond milk, almond butter and two tablespoons of C8 oil, plus a teaspoon of unsweetened cacao and half a teaspoon of cinnamon.

This approach also naturally promotes the enzyme GLP-1, targeted by the weight loss drugs Ozempic and Wegovy, but without the side-effects or rebound weight gain.


**Figure 19 – How to make a Hybrid Latté**

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# In summary,

- **Avoid sugar and don’t eat junk food.** Avoid the white stuff – flour, sugar, rice and especially ultra-processed foods. Fructose and high fructose corn syrup,

which is widely used as a sweetener, are particularly bad for the brain.

- **Eat your fruit, don't drink it.** Nature never provides fructose without fibre. Stay away from fruit juices, as they contain no fibre but lots of sugar. A glass of orange juice is three oranges worth of juice, but no fibre. Fibre fills you up.
- **Limit your intake of bread, pasta and potatoes.** If you eat more than 100 to 150g a day of grains or potatoes, which is one or two servings max, your risk for dementia goes up.
- **Limit alcohol to a glass of wine a day or equivalent.** Alcohol consumption, especially red wine, may reduce risk in moderation, but there's a narrow window of benefit. Abstinence increases risk, as does having more than 14 units of alcohol a week, which is equivalent to a medium glass of wine every day, according to a study in the British Medical Journal.[190]
- **Add C8 oil to your coffee.** The brain can run on either glucose or ketones, made in the liver from a 'medium chain triglyceride' called C8 oil. Two tablespoons of a C8 rich oil, from coconut oil, improves cognitive abilities, helping provide the brain with energy.[191]
- **Measure your sugar status** with an HBA1c blood test, with the goal to be below 5.4 %, ideally around or below 5%. (See page 193 for more on testing.)
- **Follow a low GL diet** (45GLs to lose weight, 65GLs to maintain it). My *Low GL Diet Cookbook* and the Upgrade Your Brain Cookapp (*see page 160*) support you in eating low GL.
- **Giving your brain a break from carbohydrates** and going ketogenic for a while helps repair it. My book *The Hybrid Diet* explains how to do this. You can go one step further and follow a 5-day fasting-mimicking diet

aimed to get you into autophagy, to clean up damaged mitochondria and replace them. Doing this once a quarter or going ketogenic once a month or following an 18:6 diet, where you don't eat between dinner at 6 or 7pm and lunch at 12 or 1pm, with a Hybrid Latté in the morning, a couple of days a week are all potentially helpful for brain recovery. Dr Georgia Ede's book, *Change Your Diet Change Your Mind,* explains why and how.

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**Check out the low GL, low carb and also keto-friendly recipes** in our Upgrade Your Brain Cookapp, listed in Chapter 14.


# Anti-age your Brain with Antioxidants, Glutathione and NAC

Your brain consumes more energy than any other organ. This combustion creates exhaust – oxidants - that age your brain. That's part of how the brain FUNCTIONS. These oxidants also make skin wrinkly, joints stiff and literally create inflexibility in the brain that leads to cognitive decline. But we also are exposed to oxidants from the outside, our environment - in burnt fumes, that is pollution, and cigarette smoke, in addition to deep fried, burnt and crispy foods.

That is why smoking increases risk of Alzheimer's just as much as having low B-vitamin or omega-3 status, according to the US National Institute of Health's analysis.[192] Smoking is something a person can easily change. Air pollution, for many, is not. It is measured in the amount of particulate matter (PM), and people living in polluted cities are exposed to more. A study of women living in cities in the USA found that those exceeding the 'safe' levels (greater than 12 µg/

$m^3$) had ‘increased the risks of global cognitive decline and all-cause dementia respectively by 81 and 92%’.’[193]

# Vitamin B and C protect against pollution and smoking

While you may not be able to change where you live, can you mitigate the effects of pollution? The answer is yes, in two ways. First, by increasing your intake of antioxidants and also by improving your B-vitamin status.The body detoxifies many toxins, including toxic metals from lead to mercury, by methylation, which is dependent on B vitamins. It also detoxifies many pollutants, especially those in polluted air and smoking, by glutathione conjugation, which is dependent on your intake of antioxidants, including glutathione, NAC, vitamin C and also the active form of CoenzymeQ10, ubiquinol. I explain how to increase your intake of these nutrients on page 115. A similar study to the one above found that residing in locations with PM exposure above the safe level was associated with a higher risk of dementia, but only among people with lower intakes of the homocysteine-lowering B vitamins.[194] ‘Vitamin C in the diet or taken as supplements might help,’ concludes another.[195]

This is why smokers need at least twice as much vitamin C as nonsmokers, just to have basic vitamin C levels in their blood. Men do worse than women. Even with an intake of 200mg a day, they don’t achieve this basic blood level, which is already two to three times the recommended dietary intake and what you’d get in four oranges.[196] It is certainly wise for any smoker to supplement vitamin C, perhaps adding 50mg per cigarette – 500mg if you smoke 10 a day, although there is a good case for everyone to supplement 1,000mg a day, or 2,000mg a day if over 50.

The dangers from both smoking and air pollution isn't simply a result of oxidation, a simple explanation of which is the browning that happens to an apple if you cut it in half and expose to air, much like the rusting of metal. Although pollution is measured by 'particulate matter' thus the 'dirtier' the air the more particles in it, it is the chemical nature of pollution and smoking that underlies their danger. The most dangerous group of compounds contained either in tobacco smoke or car exhaust are polycyclic aromatic hydrocarbons (PAHs), particularly benzo[a]pyrene. In the case of these molecules, the role of glutathione, discussed in detail on page 110, which is not only related to free radicals, becomes central.

Benzo[a]pyrene is not directly reactive - it becomes a potent carcinogen which can bind to DNA and cause mutations only after being metabolized by our organism. Glutathione then grabs onto these carcinogens and helps excrete then from the body. This is one of the reasons we measure a person's glutathione status (*see page 112*) which, if used up and thus depleted, also indicates they are unable to detoxify pollution. Hence smokers have a lower level which increases on quitting or smoking less.[197]

# Increasing intake of antioxidants in diet and supplements reduces risk for Alzheimer's

Those with diets high in antioxidant foods, meaning plenty of variable colours of vegetables and fruit, literally halve their risk for dementia compared to those with low intakes, according to a study of 2,716 people aged over 60.[198] Plants

also contain polyphenols and flavanols, as does red wine and dark chocolate.

| | Lowest GL | Antioxidant | Polyphenol |
|---|---|---|---|
| Olives | *** | *** | *** |
| Blueberries | *** | *** | *** |
| Kale | *** | ** | *** |
| Blackcurrants | ** | *** | ** |
| Strawberries | *** | *** | ** |
| Broccoli | *** | ** | *** |
| Artichokes | *** | ** | *** |
| Cabbage (red) | *** | *** | ** |
| Asparagus | *** | ** | ** |
| Onions (red) | ** | * | *** |
| Avocado | *** | ** | ** |
| Apples | ** | ** | ** |
| Beetroot | * | * | *** |
| Cherries | ** | ** | ** |

There's another good measure, called ORAC (oxygen radical absorption capacity). A shot of pure Montmorency cherry concentrate (Cherry Active – *see Resources*) has an ORAC score of 8,300 ORACS which is equivalent to 103 carrots!

Red wine, chocolate and tea are rich in a polyphenol called epicatechin. Jeremy Spencer, a scientific advisor to Food for the Brain, who is Professor of Nutritional Biochemistry and Medicine at the University of Reading, has shown that polyphenol-rich plants improve blood flow in specific regions of the brain that improve attention, decision-making, impulse control and emotion, improving overall 'executive' function.[199] What's more, the level of flavanols you have in your bloodstream predicts your memory. In the COSMOS study, the biggest impact of increasing flavanols

was seen in those in the lowest third for dietary intake - specifically seeing improvement in aspects of memory that link to the hippocampus, that central area of the brain that degenerates in Alzheimer's.[200] More recent studies giving cocoa, a rich source of flavanols, have shown improved cognition, possibly by improving circulation.[201] This has been confirmed by a big COSMOS trial involving over 20,000 people given a cacao extract supplement rich in flavanols, versus a placebo, for five years.[202]

The optimal intake for brain protection is five to six servings of fruit and veg a day. Half a plate of a main meal counts as two. A handful of berries would count as one. So, if half your plate for two main meals is vegetables, and you have some berries with your breakfast, and another piece of fresh fruit, or perhaps some broccoli heads or tenderstem, or carrots dipped in hummus as a snack, or half an avocado with some high-polyphenol olive oil, you've had six servings. I often have a sugar-free hot chocolate with a dessertspoon of cacao.

# Vitamin C and E supplements cut risk by 40%

Also, critical antioxidants such as vitamin C and vitamin E, if supplemented together, reduced the risk of developing Alzheimer's by 40%. Taking either cut risk by a quarter in a study of 4,740 elderly residents of Cache County, Utah.[203]

A study of all studies to date demonstrated that 'either a high vitamin E or high vitamin C intake showed a trend of attenuating [dementia] risk by about 26%', according to China's leading Alzheimer's prevention expert Professor Jin-Tai Yu of Fudan University in Shanghai. This study shows that

these nutrients are ‘grade 1’ top level dementia prevention factors.[204]

# How glutathione and vitamin C reload each other

Vitamin C, which is water based and protects you against smoke and pollution, and vitamin E, which is fat based, and protects you from burnt and fried fats, including sunburn, are both in the bloodstream outside of cells. Once the Vitamin C has been used by the body, it is ‘spent’ or ‘oxidised’. This oxidised vitamin C is reloaded, in other words, returned to its useful, active antioxidant state, by glutathione. Spent (oxidised) vitamin E is reloaded by Co-enzymeQ10, which is why these nutrients are often included together in antioxidant supplements. The most active, or ‘reduced’ form of CoQ, is called Ubiquinol. It’s another player in this ‘pass the parcel’ dance.

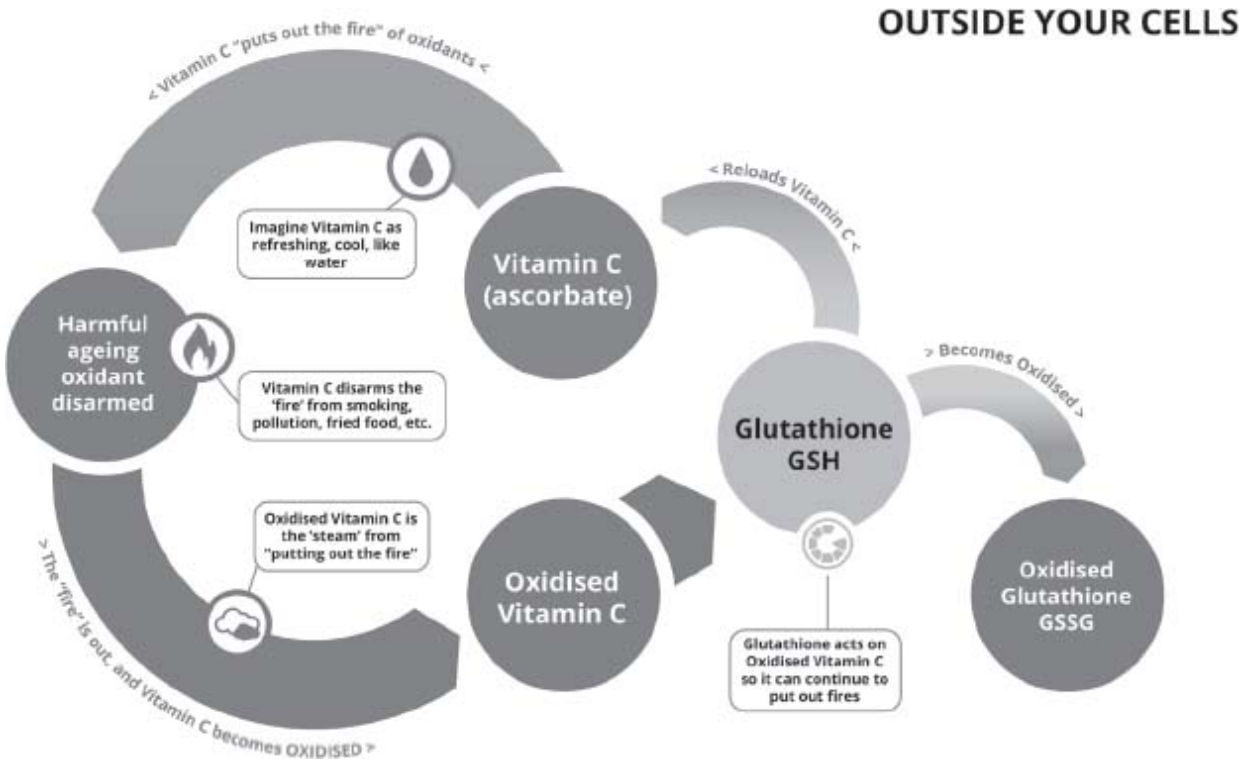


Figure 20 – The Vitamin C – glutathione cycle in disarming harmful oxidants

Inside cells, especially brain cells, glutathione is the most potent antioxidant of all – the master antioxidant.

Every second there are hundreds of thousands of metabolic ‘fires’ going on inside the energy factories in our brain cells. Think of glutathione as the water in the fire engine. It gets rapidly used up, keeping your brain protected. The ‘spent’ or oxidised glutathione, much like steam, then has to be cooled to reload the fire engine. This is done by vitamin C and an enzyme called Glutathione Reductase, returning glutathione back to its fully loaded active antioxidant form. It does this with the help of NADPH, derived from niacin, and Coenzyme Q10 (ubiquinone), creating the most potent form of ‘reduced’ CoQ called Ubiquinol. How glutathione and vitamin C recycle each other is one of the hottest discoveries in brain anti-ageing.[205]

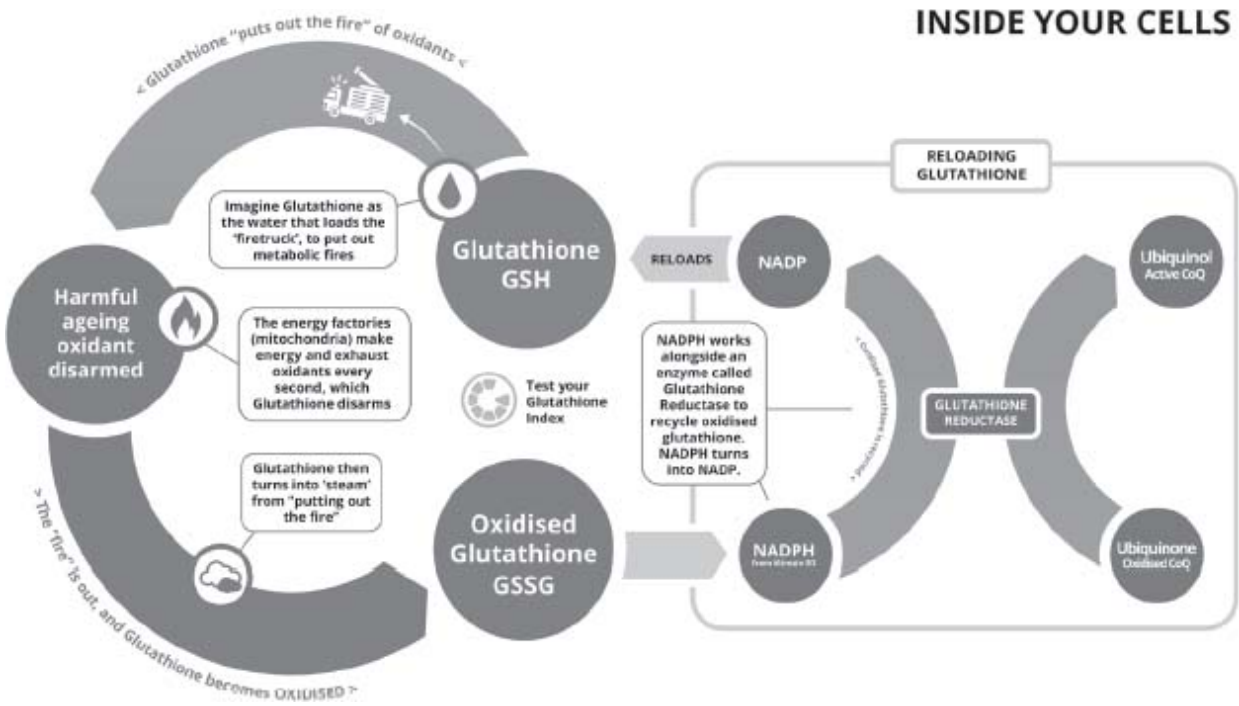


Figure 21 – Glutathione cycle inside cells, recycled by NADPH and Co-enzyme Q

# Glutathione predicts dementia risk

In patients with dementia, the activity of the enzyme Glutathione Reductase (GR), that reloads glutathione back to its active form, reduces. These GR levels alone are therefore a fairly good biomarker of dementia.[206] In general, it can be said that the glutathione metabolism (recycling) loop in those with dementia 'spins' much slower than in healthy patients; hence, they have accelerated brain ageing.

Our brain scientists at foodforthebrain.org have discovered that the ratio between the fully loaded Glutathione and the spent Glutathione, called the Glutathione Index, is the best indicator of ones' true glutathione antioxidant potential. This is what we measure at

foodforthebrain.org, both as a standalone test and in our 5-in-1 DRIfT test.

Those with dementia have a lower potential to dynamically fight free radicals and will have a worse GSH/GSSG, which we call the Glutathione Index.[207] The worse the ratio, the worse a person's cognitive function is likely to be. It's a bit like having a direct measure of how fast your brain is ageing. Patients with dementia have a reduction in glutathione and its ability to be recycled.[208] This ratio, the Glutathione Index, is a biomarker for many diseases, including both type 1 and 2 diabetes[209], liver cirrhosis[210], multiple sclerosis[211] and Alzheimer's disease[212]," says Dr Konrad Kowalski, the analytic chemist in the brain team who has developed this test for foodforthebrain.org. "It's too early to know the perfect number, but it is looking like a Glutathione Index of 500 means your brain can roll with the punches, while below 200 a person definitely needs to be both changing their diet and supplementing antioxidants. Having a way to measure brain ageing with a home test kit from a pin prick of blood, means we can realistically see what the impact of specific diet changes and antioxidant supplements might be."

Since the Glutathione Index is a recent improvement in testing glutathione and antioxidant status, it is too early to have direct evidence of its effects, if raised, on reducing risk for Alzheimer's and cognitive decline. But it is certainly likely to help protect the brain from oxidative damage.

# N-Acetyl Cysteine – the precursor for Glutathione

Nutritional therapists have been measuring red cell glutathione and supplementing either glutathione or its

precursor N-Acetyl-Cysteine (NAC) for decades. However, glutathione supplementation has poor bioavailability[213], largely because it is so rapidly oxidised to GSSG, as it disarms free radicals. In other words, it gets used up quickly doing good work. N-Acetyl Cysteine (NAC), a precursor of glutathione, is therefore often used instead and has been shown to successfully raise plasma glutathione levels, for example, in those with schizophrenia.[214] Anthocyanidins, found in red/blue berries, also recycle glutathione, thus sparing it and effectively more than doubling its effect if supplemented together.[215] Glutathione supplementation, 500mg a day, has been shown to lower and stabilise HbA1c - that most important marker of blood sugar control.[216]

NAC has plenty of evidence to support its use as a promoter of glutathione and mental health, thus reducing the brain's oxidative stress. The latest 2022 review states: "N-acetyl-L-cysteine (NAC) is a compound of increasing interest in the treatment of psychiatric disorders. Primarily through its antioxidant, anti-inflammatory, and glutamate modulation activity, NAC has been investigated in the treatment of neurodevelopmental disorders, schizophrenia spectrum disorders, bipolar-related disorders, depressive disorders, anxiety disorders, obsessive compulsive-related disorders, substance-use disorders, neurocognitive disorders, and chronic pain. Currently NAC has the most evidence of having a beneficial effect as an adjuvant agent in the negative symptoms of schizophrenia, severe autism, depression, and obsessive compulsive and related disorders."[217] It is highly likely to be beneficial in protecting against cognitive decline, dementia and Alzheimer's, and has been shown to do so in animal studies, but well-designed human trials are lacking. NAC is so medically effective that it has been classified a medicine, hence not a food, and is no longer available over the counter in the US.

# The Glutathione – Homocysteine Connection

The figure on page 115 shows that the homocysteine made from methionine in protein can be shunted left towards making glutathione. You'll see that in the step before this cysteine is made. That is why NAC is a precursor for glutathione. You'll also notice that vitamin B6 is required, as well as folate, B12 and B2 for the MTHFR enzyme. B2 (Riboflavin) is especially important in those with the MTHFR677TT polymorphism[218]. You don't need much. Even 10mg of B2 a day is sufficient.

The best way to ensure your production of glutathione is optimal is to test both your homocysteine and glutathione level. If homocysteine is above 10 and glutathione low, below 500, then you need to supplement the appropriate amounts of folate, B12 and B6 explained in Chapter 6. If both your homocysteine is low and your glutathione level is high (in the green on the foodforthebrain.org test) then you have optimised your ability to produce glutathione.

# Magnesium is glutathione's best friend

The often deficient mineral magnesium, best known for reducing cardiovascular disease risk and lowering blood pressure, is vital for glutathione synthesis. Magnesium is required for the gamma-glutamyl transpeptidase (GGT) enzyme, which is key to making glutathione and also increases the activity of glutathione peroxidase (GPx), which speeds up the process of glutathione neutralizing those dangerous oxidants. Thus, magnesium acts as a potent antioxidant and an anti-inflammatory and pushes up your

Glutathione Index (GSH/GSSG)[219]. It is also an anti-depressant and helps calm down hyperactivity and anxiety, thus is good for sleep. A comprehensive meta-analysis of all studies on magnesium and dementia shows that the higher one's magnesium plasma level, up to .085mmol/l, the lower is a person's risk for Alzheimer's. Also, those who supplement magnesium have about half the risk.[220]

Magnesium is commonly low in our diet since most people don't eat anything like enough vegetables, nuts and seeds. One in five people are deficient in it. Most people eat about 270mg, but need closer to 500mg. Eating a diet rich in vegetables, nuts and seeds can get your intake up to 500mg but, much like omega-3, our ancestors would have been eating twice as much as we do today. A small handful or heaped tablespoon of chia or pumpkin seeds (28g or 1 ounce) will give you in excess of 100mg. A similar amount of almonds, peanuts or cashews will give you 80mg. A serving of oats, brown rice, potato or beans, black beans being the best, delivers about 50mg. The best vegetables for magnesium are greens, especially spinach, kale, chard, green beans and peas in that order. A decent serving – think half a plate – can easily deliver 100mg.

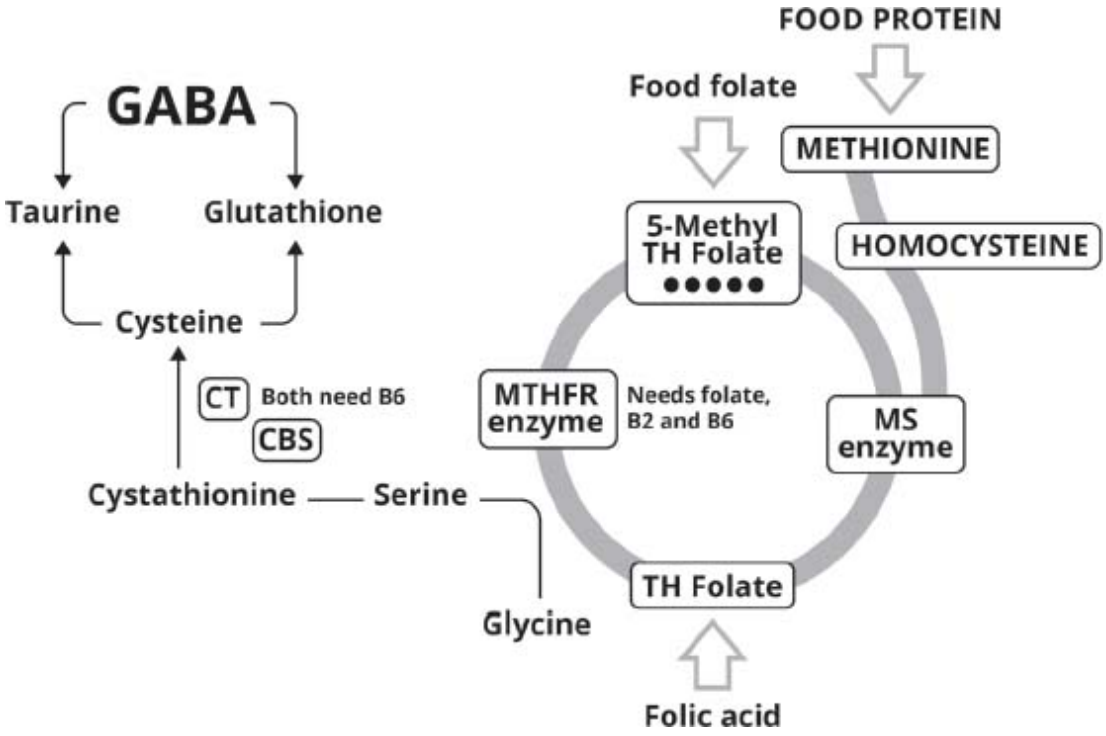


Figure 22 – How homocysteine can be transformed into glutathione, dependent on vitamin B2, B6 and folate

My recommendation is to both eat magnesium rich foods and also supplement at least 100mg a day and increase this to 300mg a day if you have any cardiovascular or mental health concerns from memory to mood.

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# In summary,

- **Eat lots of fresh fruit and veg.** The more you eat, the better, though the benefits start to plateau at 500g a day, which is about five to six servings. Those in the top third of greens consumption had substantially less Alzheimer's-related pathology than those in the lowest third.[221] **Berries** are particularly protective, especially *blueberries* and *strawberries*.[222]

- **Eat a small handful of nuts and seeds every day.** These are rich sources of magnesium and other antioxidants including vitamin E. Walnuts, pecans, macadamia nuts, chia, flax and pumpkin seeds are richest in omega-3.
- **Drink Tea.** The more you drink, the better, as confirmed by a recent study from Singapore.[223] However, other studies are conflicting.[224] My view is to drink tea, green over black, in preference to coffee, and limit your intake of coffee to one or two cups a day to avoid raising homocysteine.
- **Eat dark (70%+) chocolate.** The benefit peaks at 10g, or about 3 pieces. More recent studies on cocoa, a rich source of flavanols, have shown improved cognition, possibly by improving circulation.[225]
- **Supplement vitamin C and E.** I'd suggest 500 to 1,000mg of vitamin C twice a day and 50 to 100mg of vitamin E.
- **Supplement glutathione or NAC**, especially if your homocysteine level is raised. Some homocysteine targeted formulas will contain this. Aim for 400 to 750mg a day. If taking glutathione it becomes more effective if you also supplement or eat anthocyanidins in blue/red berries. You may find it in antioxidant formulas as well
- **Supplement magnesium.** Choose multivitamin and mineral supplements that give you at least 100mg of magnesium.
  Take up to 300mg for optimal protection.
- **Don't smoke and limit pollution.** Don't exercise by busy roads and spend too much time in traffic. City dwellers and smokers need more vitamin C.

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**Check out the antioxidant and polyphenol rich recipes** in our Upgrade Your Brain Cookapp, listed in Chapter 14.


# Use it or Lose it – Lifestyle Factors that Protect Your Brain

Now you've learned how to nourish, build and fuel your brain, and mop up oxidant exhaust fumes. So, we've covered STRUCTURE and FUNCTION. The only reason for so doing is to use your neural network for thinking, feeling, perceiving, learning and moving. Every single thought, perception and movement engages your neural network (neurons are nerves and exist throughout the body). This is UTILISATION.

That is why the more physically, socially, intellectually active you are the better.

Taxi drivers are a case in point. In a study of London cabbies who passed or failed 'the knowledge' exam - memorising the 25,000 streets in London - those who passed actually had more grey matter, and specifically in that central hippocampus area most associated with

cognitive resilience.[226] Think of the brain as a muscle. They had built more brain muscle.

Also, taxi drivers and ambulance drivers - who may or may not be physically fit (after all, they spend a lot of time sitting and driving) - have the lowest risk of Alzheimer's mortality of all occupations in this study of over 8 million people. They literally had a quarter of the risk of dying from Alzheimer's in this British Medical Journal trial.[227]

# The best activity for your brain is at the edge of failure

Even though the 'failed' taxi drivers did worse, it is really good to challenge yourself, learning new things at that edge of failure. The worse you start off, the more you learn.

Every indicator that you can think of – leaving school early, having a lower educational standard,[228] or retiring early[229] – has been associated with increasing risk of cognitive decline. Retiring after the age of 66 equates to two thirds less risk compared to those retiring at 60 to 64, shows research in Sweden.

When Professor May Beydoun, at the US National Institutes of Health, did a comprehensive study of the biggest risk factors for developing Alzheimer's, she attributed 24% of risk to educational status (you'll recall that omega-3/seafood accounted for 22%, homocysteine-lowering B vitamins also 22%, physical activity was 32% and smoking was 31%).[230] So, utilization of the brain, reflected in educational and physical activity, is a big part of keeping your brain healthy.

Associate Professor Tommy Wood from the University of Washington, a neuroscientist who trains Formula 1 racing drivers, likes the edge of failure to engage the brain. A

fascinating study looked at the brains of musicians.[231] While both professional and amateur musicians' brains looked younger than those of non-musicians of the same age, the benefit was greatest in amateur musicians. The researchers suggested that playing music was more of a cognitive stimulus for amateurs – it was harder, so they got more benefit. The cocktail of hormones released as we try, fail, repeat and learn provides the ideal environment for the brain to grow and adapt.

He recommends picking an activity that's truly challenging. 'Cognitive demand requires failure, so pick something you'll be bad at initially. What's cognitively challenging is personal, but learning a new language is better than sudoku, building model airplanes is probably better than reading the news, and playing chess is definitely better than scrolling through Instagram. As you get better, add challenge to keep stimulating your brain.'

Speaking two languages is not only associated with less risk of cognitive decline but, according to one study, 'the neuroprotective effects of lifelong bilingualism act both against neurodegenerative processes and through the modulation of brain networks' connectivity.'[232]

Also, the effects of concentrated learning last a long time. A study of people in their 60s and 70s who engaged in a three-month course of either Spanish, Photography, iPad drawing or music composition not only improved their cognitive function quite significantly at the end of the course, but that improved cognition continued to increase when measured one year later.[233]

# Vision and hearing loss

The Lancet Commission's list of 14 factors driving dementia - ignoring anything nutritional - includes lack of education,

social isolation, visual loss and hearing loss, - all of which effect the ‘utilisation’ of the brain. The last two are the new kids on the block. This follows growing evidence, and interventions, that helping to reduce hearing loss with hearing aids, or improving vision with cataract surgery, reduces or slows down risk of getting dementia.

This is good news and encourages screening early for both, and acting accordingly. But one obvious question isn’t being asked. Why do some people develop cataracts and others don’t?

Let’s start with the eye. Eye cells are like brain cells. The brain is an extension of the eye, and those light receptors that turn the photon energy in light into what you see are packed full of vitamin A (retinol) and omega-3 DHA, and are bombarded with oxidants from light, and therefore needs a constant supply of antioxidants (*see Chapter 9*). The more vitamin C you consume, the less is your risk of cataracts, says a meta-analysis of 30 studies.[234] Another study shows that vitamin C supplementation delays onset of cataracts by two years in those having an eye treatment.[235] Another finds much lower levels of omega-3 DHA and omega-6 AA, the two fatty acids that every single neuron depends upon, in those who develop cataracts.[236] And, of course, diabetes and visual problems go hand in hand, with 40% of diabetics having vision loss. Sugar damages the eye.

The most recent review on eye health and antioxidants concludes: ‘While high concentration of carotenoids such as lutein and zeaxanthin decrease the risk of developing age-related macular disease, anthocyanins and vitamins play a role in the treatment and prevention of other ophthalmic diseases: saffron extract reduced intraocular pressure in glaucoma patients; bilberry extract prevented impairments in lenses and retina, as well as alleviate symptoms of dry eye disease; high concentration of beta-carotene may reduce the risk of developing cataract.’[237]

In my view, the biggest lack of vision is the medical profession's blind spot of looking underneath risk factors and almost completely ignoring nutrition. Something must be making some people lose their vision and hearing, and others not. Given that lack of omega-3 and antioxidants both increase risk for cognitive decline, dementia and Alzheimer's, as well as cataracts, could the link between cataracts and increased risk not be partly a function of omega-3 and antioxidant deficiency? However, the fact that things improve after cataract surgery implies that seeing more helps to an extent.

The same myopic vision occurs with hearing loss. It's the big new prevention factor in the Lancet Commission, accounting for a whopping 7% out of the 45% potentially modifiable risk factors. But what realistically can you do about it? The latest and greatest 3 year study, assigning 3,000 people to either a hearing intervention (audiological counselling and provision of hearing aids) or a 'control' intervention where they had sessions with a health educator, to rule out the bias of just getting more attention, reported that 'the hearing intervention, did not reduce 3-year cognitive decline'.[238] They did find some benefit in those with pre-existing cognitive problems. In other words, if you're struggling to think straight and you can't hear properly, improving your hearing can help cognition.

This is certainly not a game changer for Alzheimer's prevention, nor addresses what causes hearing loss. Unsurprisingly, hearing loss risk is strongly linked to inflammation. Omega-3 fats are potent antiinflammatories. The higher a person's omega-3 intake, the lower is their future risk of hearing loss.[239] Sugar also cranks up inflammation, which also leads to more mucus production in the ear canal. Diabetics have twice the incidence of hearing loss compared to those without diabetes, and those with prediabetes have a 30% higher rate of hearing loss.[240]

So, both hearing loss and vision loss could simply be the consequences (much like amyloid and p-tau accumulation) of an underlying sub-optimum nutrition, and it may just be this lack of the right nutritional intake, and excess of sugar and carbs, that drives both these declines in sensory perception.

The next kid on the block is decrease in smell. I suspect that various technologies will be developed relating to stimulating hearing, vision and smell, without considering the true underlying causes of sensory decline. As Marcel Proust said, “The real voyage of discovery consists, not in seeking new landscapes, but in having new eyes.” You have to be looking at underlying causes to be able to prevent anything.

# Be social

The other ‘confounding variable’ with hearing loss, particularly, is its impact on one’s ability to socialise. If you can’t hear, you can’t converse - and life is one rich conversation. A lack of meaningful social interaction is also a major driver of both low mood and cognitive decline later in life.[241] As water is to fish, social interaction is to humans. We are social beings and we need that exchange with others. So, whatever you can do to meet new people, engage in conversations, join groups - perhaps learning new skills - has to be a step in the right direction.

# Music and dance is a winning combination

Music is a potent brain stimulator in so many ways. Good, rhythmic music literally gets your body moving, so you now have two levels of stimulation – brain and body. It's called 'embodied cognition'. Neurons start firing, so the combo - especially if you do start jiggling - is a real brain workout. Singing aloud adds another dimension. It can also bring old memories back to life and ignite feelings associated with that time when you were listening to this music. This can be really helpful for people with dementia, and can also help in recovering speech after a stroke. Neuroscientist Daniel Levitin explores how music can help heal us in his book *Music as Medicine: How we can harness its therapeutic power*. It's full of good research, summarised in a new *Scientists* article[242] which makes all this much more than a 'nice idea'. But no definitive trial yet exists to show that those who do listen to music, and dance along, have a lower dementia risk.

# Your brain is a muscle – and muscle building helps

That Lancet Commission assigns a mere 2% of risk to physical activity – that's a fraction of that they assigned to hearing loss at 7%. Meanwhile, the comprehensive study at the highly respected US National Institutes of Health that I referred to earlier assigns 32% of Alzheimer's risk to a lack of physical activity, making it the single greatest predictor of the risk of cognitive decline. That's quite a difference!

The brain works hard in exercise, especially if it involves complex movements and learning - such as learning to dance, or doing different movements in a yoga or *t'ai chi* class, or running or walking on uneven surfaces. The brain is processing a lot of information, triggering patterns of muscle

movement and keeping you in balance. You want a bit of both movement and balance. Just working out on a fixed machine or walking on a flat, straight, tarmac path is not nearly as challenging as hill-walking up an uneven path, cycling, surfing, skateboarding or anything where your body is micro-adjusting to keep you in balance.

If you're in a challenging environment, for example hill-walking, or learning something new, your brain is not only getting more exercise, it is positively growing and making new connections. One study of retired people assigned to walk briskly for 40 minutes three times a week showed increased hippocampal brain volume.[243] Another showed benefits from doing one or two sessions of resistance or strength training twice a week.[244]

There may be more benefit to building muscle, which is what resistance training does, than just the stimulation of the exercise. After all, just doing one repetitive exercise might not appear so mentally challenging. Yet, of all the measures relating to how fit or fat you are – your weight, body mass index (calculated from your bodyweight and height), fat mass or muscle mass – it is your muscle mass, or how much muscle you have compared to fat, that best predicts both your brain volume and risk of cognitive decline in later years. Less fat and more muscle is what you want. One big study from the UK Biobank data found that those with a lower fat-to-muscle ratio (FMR) in their legs had around 40% less risk of dementia later in life.[245] Muscle uses energy and 'soaks up' glucose. This helps keep your blood sugar stable and prevent insulin resistance. Often, as people age, they gain weight but swear they aren't eating any more than they used to. This is often simply because they've lost muscle mass. If you don't use it, you lose it.

If you can find an activity that engages both mind and body and is not too repetitive, all the better. As an example, I've taken up paragliding, and qualified at the age of 65. I

had to pass an exam on meteorology, aerodynamics and air law, and failed first time, but now have to think about these things before and during flight. Then, there's the exercise of carrying an 11kg pack up a mountain, and the balance and strength and adjustments my brain is having to make to keep the canopy stable, even before take-off. This may not be your thing, but it shows how one constantly challenging activity can tick so many brain boxes. It is good to learn new sports for this very reason.

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# In summary,

- **Get active for 20 minutes** … and build and maintain muscle. Spend at least 20 minutes doing activities, such as walking, gardening, housework or repairing things – anything that gets you moving. Don't limit yourself to 'exercise' – anything that gives you a faster heart rate and engages different sets of muscles is good.[246] Muscle mass best predicts both your brain volume and risk of cognitive decline in later years.
- **Get balancing.** The brain works hard in exercise, especially if it involves complex movements and learning, such as learning to dance, or doing different movements in a yoga or t'ai chi class, or running or walking on uneven surfaces. The brain is processing a lot of information, triggering patterns of muscle movement and keeping you in balance.
- **Read, watch or listen to stimulating content.** A simple yardstick is to ask, 'Am I learning anything? Am I using my mind?' Reading books or listening to podcasts can be great ways to stimulate your mind, depending entirely on what you engage with.
- **Be social.** Aim to spend two hours a week or at least a day a week spending time with other people in a social

(not work) setting – groups, friends, family, etc.

- **Test your brain in the morning.** Do Sudoko, the crossword or Wordle or something similar – check out this link www.nytimes.com/games/wordle/index.html. You may prefer an app - two that have high ratings are Brain HQ and Lumosity.
- **Learn something new and challenging.** Learning a new language, sport or musical instrument are all good - anything that you keep practising. The worse you are, the better.

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# Brain Recovery and Repair – the Sleep, Stress and Hormone Connection

The last part of our model of cognitive decline, shown on page 28, relates to the daily requirement to recover the brain after a day's worth of activity. It is literally why we have to sleep. It is a total essential, no less important than water, air or food. The analogy is a bit like backing up or resetting your computer, but that doesn't quite do it.

By understanding how we see, you can get the measure of it. When a light photon hits a receptor on the eye, it literally changes the shape of an omega-3 DHA molecule - from a horseshoe (*see Figure 11 on page 49*) to a chair shape - and sets up a chain reaction along the neural network. Imagine billions of these 'shape' changes of different orientations. This is the computer code of our mind that we then interpret as 'blue', 'Peter', 'cloud', and so on. This is the hypothesis of Professor Michael Crawford, published in a journal in 2023,[247] entitled '*Docosahexaenoic*

*Acid Explains the Unexplained in Visual Transduction*', at the age of 93! It's quantum physics and optimum nutrition combined.

All these shape changes are, in essence, oxidation. So, those essential fatty acids are being oxidised in the process of all communication in the brain, be it thinking, feeling, seeing or hearing. That's why the brain and sensory systems are so exquisitely dependent on antioxidants. All those DHA molecules have to be 'reset' or returned to their stable state. That is what's happening while you sleep.

# Is Melatonin the next Vitamin D?

The brain also pumps out an extremely potent antioxidant, melatonin. 'There is credible evidence to suggest that melatonin should be classified as a mitochondria-targeted antioxidant, 'says one review. Is Melatonin the next vitamin D? That's the title of a major scientific review which goes on to show that melatonin also protects neurons from amyloid accumulation.[249] In a small pilot study of elderly patients with a mild cognitive deficit, the ability to remember previously learned items improved, and depression decreased with melatonin.[250] A more extensive, longer-term study found that patients with mild cognitive impairment scored better on the Mini-Mental Status Exam and the Sleep Disorders Index when taking melatonin.[251]

But this is not just about the potential benefit of melatonin for sleep, but about understanding why sleep is so important for 'brain recovery' every single night. Consider how you feel when you have an hour or two less sleep just in one night. What the science shows clearly is that persistent short sleep duration at age 50, 60, and 70,

compared to persistent normal sleep duration, increases dementia risk by 30%.[252] This is another preventable risk factor ignored in the Lancet Commission's report. Sleeping problems not only predict a significant increase in dementia risk later in life, with the optimal being 7 hours, but insomnia is a major symptom of those with dementia.

Lack of sleep, however, is not so impactful on cognitive function in those who also exercise.[253] This is another reason why a 'systems-based' approach is so important.

# Sleeping pills triple risk for Alzheimer's

Insomnia is good for business. Last year sales were over $80 billion. The main type, called non-benzodiazepines or "zeds" are remarkably ineffective. A 2007 study by the American National Institutes of Health found that the newer drugs, like Ambien (zolpidem), made you fall asleep only 12.8 minutes faster than with a fake pill, and sleep for just 11 minutes longer. [254]

But at what cost? A review in the British Medical Journal[255] concluded they are associated with "major harm", including "four times the mortality", and that there was "little evidence of clinically meaningful benefit". Other studies show 'a generalized negative effect on cognitive function', and 'an increased [triple] risk of Alzheimer's', and 'risk for balance dysfunctions'.[256]

What's the alternative? Melatonin, which any doctor can prescribe, and it's precursor 5-HTP which is an amino acid - a type of tryptophan. Another amino acid, GABA, which you'll learn in a minute switches off adrenalin, in combination with 5-HTP, in a placebo-controlled trial, cut the time taken to fall asleep from 32 minutes to 19 minutes and

extended sleep from five to almost seven hours.[257] So that's much better, and safer, than zeds but neither are patentable, hence not profitable, hence rarely prescribed. For those in search of a good night's sleep my books *Upgrade Your Brain* and *The Stress Cure* (co-authored with Susannah Lawson) give several natural solutions to set yourself up for a good night's sleep.

# Alcohol is a big Alzheimer's driver

Most people use alcohol both to reduce stress and promote sleep. This is largely because alcohol causes an immediate increase in the calming neurotransmitter GABA by opening up GABA receptors, and the increased GABA then switches off adrenalin, at least for an hour or so. That's a main reason we use alcohol to relax. But there are two problems with this. First, the effect wears off, and drinking too much in the evening actually shuts down the GABA receptors the next day, so we get into a cycle of feeling more anxious and stressed. Secondly, alcohol is a neurotoxin and literally shrinks your brain.

A study of 36,678 MRI scans from UK Biobank shows that anything over 1 unit a day is associated with ever-decreasing white and grey matter in the brain.[258] A unit is a small glass of wine, half a pint of beer or a single shot of a spirit. A thorough study in the British Medical Journal in 2018, which followed over 9,000 people over 23 years, showed that both abstinence and drinking more than 14 units of alcohol a week, which is equivalent to a medium glass of wine (2.3 units) every day, also increases risk by 40%.[259] On the plus side a 125ml glass of red wine a day reduces dementia risk more than abstinence.[260] Red wine in

particular may be beneficial due to its higher levels of polyphenols (see page 9).

# Stress shrinks the brain

What is clear is that major stresses, and perceived and prolonged stress, age the brain and increase the risk of cognitive decline and dementia. This has been shown by tracking people who have had two or more major stressful events - such as the death of a spouse, child, or grandchild; divorce; financial or health problems - and also perceived psychological stress in adulthood and levels of neuroticism.[261]

There are two main stress hormones – adrenalin and cortisol. Adrenalin is short-acting, kicking in in under a second and lasting for up to an hour, but usually less.

Cortisol is long-acting, and its level cycles throughout the day. In the evening, and as we approach sleep, it should be reducing. In the morning, cortisol levels need to increase to kick-start our day. In the first hour of waking, there's a cortisol peak to get us going.[262] That is why it is probably better not to have coffee, which further promotes adrenal hormones, for at least an hour on waking. You may stop producing enough of your own cortisol and become dependent on the caffeine hit. If your cortisol level is high at night, you'll have difficulty getting to sleep, and if it's low in the morning, you'll have difficulty waking up.

If we get stuck in reacting stressfully, though, we have continuous elevated cortisol as a result, and many studies have linked this excess cortisol with worsening overall cognitive functioning, memory, the ability to get things together, slower thinking and worse social skills. Ultimately, this leads to a greater risk of dementia and Alzheimer's in later years.[263] My book, *The Stress Cure*, co-authored with

Susannah Lawson, shows you how to get out of reacting stressfully. It's not hard when you know how. Heartmath's Quick Coherence technique is one of our favourite skills to destress your brain *(see Resources)*.

What's actually going on in the brain is that cortisol is triggering these stress responses in the limbic brain, which includes the hippocampus. This part of the brain then feeds back to put the brakes on further cortisol release. But with prolonged stress, the brakes don't get fully applied, so we get into a negative loop of continued cortisol, leading to increased hippocampal brain shrinkage.[264]

# Women, hormones and Alzheimer's

More women than men develop Alzheimer's. Why? Could it be to do with the drop off in hormone levels during menopause?

Most people don't think of the sex hormones - oestradiol, progesterone and testosterone as important for the brain. But they are all 'neurosteroids' – that is, they are both made in the brain and throughout the nervous system by both neurons and those glial cells which fuel neurons. They protect the brain in many ways[265] and seem to reduce tau and amyloid-β (Aβ) accumulation[267]. Having low hormone levels can adversely affect brain function and affect different cognitive processes - such as decision-making, emotion recognition, attention, memory, and also emotions[268] - which are all important aspects of cognitive function.

This is particularly important since the decline in hormone levels with menopause parallels an increased risk of cognitive impairment and dementia, as well as mood

disorders, including depression and anxiety.[269] Post-menopausal women account for 60% of Alzheimer's diagnoses. Also, women who have an early menopause have a greater risk,[270] and those who have a surgical menopause (ovary removal) have around twice the risk of developing Alzheimer's.[271] In our own research of over 400,000 people taking the online Cognitive Function Test there is a marked acceleration in cognitive decline in women's scores, but not in those for men, starting around the age of 49.

The balance of oestradiol and progesterone is really important for optimal brain function.[272] Progesterone can "put the breaks on" the adrenal system, accounting for the often reported experience of feeling more stressed and anxious post menopause. Both oestradiol and testosterone are synthesised from progesterone, as is the stress hormone cortisol. If there is a lack of progesterone, and a demand for cortisol due to a perceived state of stress, this further creates a potential hormone deficiency, as progesterone is used up to make cortisol. Testosterone also has a beneficial effect, especially with respect to mood and cognition.[273]

For these reasons, there is a growing medical movement to prescribe bio-identical (body identical) hormones, often the oestradiol given transdermally. These are biochemically and metabolically different to synthetic hormones, which are prescribed in contraceptives and older types of hormone treatments.

Practitioners usually assess women's hormonal needs on the basis of symptoms and tests, and then prescribe combinations of 'natural' progesterone, oestradiol and testosterone, given in amounts equivalent to those produced before menopause. There is plenty of evidence of their benefit in relieving menopause-related symptoms, and reports of improved memory and cognition, but there is a lack of long-term studies tracking future risk for Alzheimer's.

Doing a placebo-controlled trial is not really possible or ethical, so the best evidence is likely to come from following women who do or don't have this hormone therapy. The first study of this kind, following 379,000 women over the age of 45, comparing those who didn't or did use transdermal hormone therapy, found that those using it have a 27% reduced risk of dementia.[274] The reduced risk for Alzheimer's was especially significant in those over age 65.

If you are a menopausal woman and you are concerned about your memory, or perhaps having other physical and psychological symptoms such as depression and anxiety, this is an avenue well worth exploring (*see Recommended Reading for books and Resources for websites and ways to find a practitioner prescribing natural hormone therapy*).

# Rebuilding the brain and its connections

Prevention is one thing, and the place to start, but can you 'reverse' Alzheimer's? This is a hot potato, not least because the disease is characterised by significant loss of brain cells, thus shrinkage of the hippocampal area. But, as we saw in the case of Simon Nicholls on page 36, even this might be reversible to some extent. Let's hope so.

There are two aspects to rebuilding:

- Making new dendritic connections between brain cells, which is happening all the time. This rewiring is especially important after a brain injury, as the neural network develops 'workarounds'. This is called 'neuroplasticity'.
- Making new brain cells, or 'neuro-regeneration', is a more challenging task and considered by some to be impossible - or at least a very slow process.

Some of the memory enhancers previously discussed may help. Having a lower homocysteine level, for example, helps those who've had a stroke recover faster.[275] So, too, does having a higher vitamin D level or supplementing vitamin D at levels above 2,000iu a day.[276] I recommend 3,000iu a day or 21,000iu a week, but most importantly, monitoring your vitamin D level to keep it above 75nmol/l (30 ng/ ml). A level of 100nmol/l may be optimal.

Remembering that neuronal membranes are made from phospholipids, eating phospholipid-rich foods such as fish and eggs, and supplementing with the phospholipids found in lecithin, could help recovery. Lecithin is available in 1,200mg capsules or in granules. Some lecithin granules are 'high-PC'. Combining B vitamins with choline is particularly helpful in stroke recovery, encouraging neuroplasticity.[277]

# The Bredesen protocol

In California, dementia expert Dr Dale Bredesen, author of *The End of Alzheimer's Program*, has been helping people recover from cognitive decline with a comprehensive approach tailor-made to each individual, covering all the factors in this book – and more. His 'proof-of-concept' trial in the Journal of Alzheimer's Disease,[278] involving 25 people diagnosed with various stages of cognitive decline, shows improvement in 84% of those with MCI or early dementia, which is an unprecedented result. When compared to the anti-amyloid antibody injections, these results are very impressive, as shown overleaf.

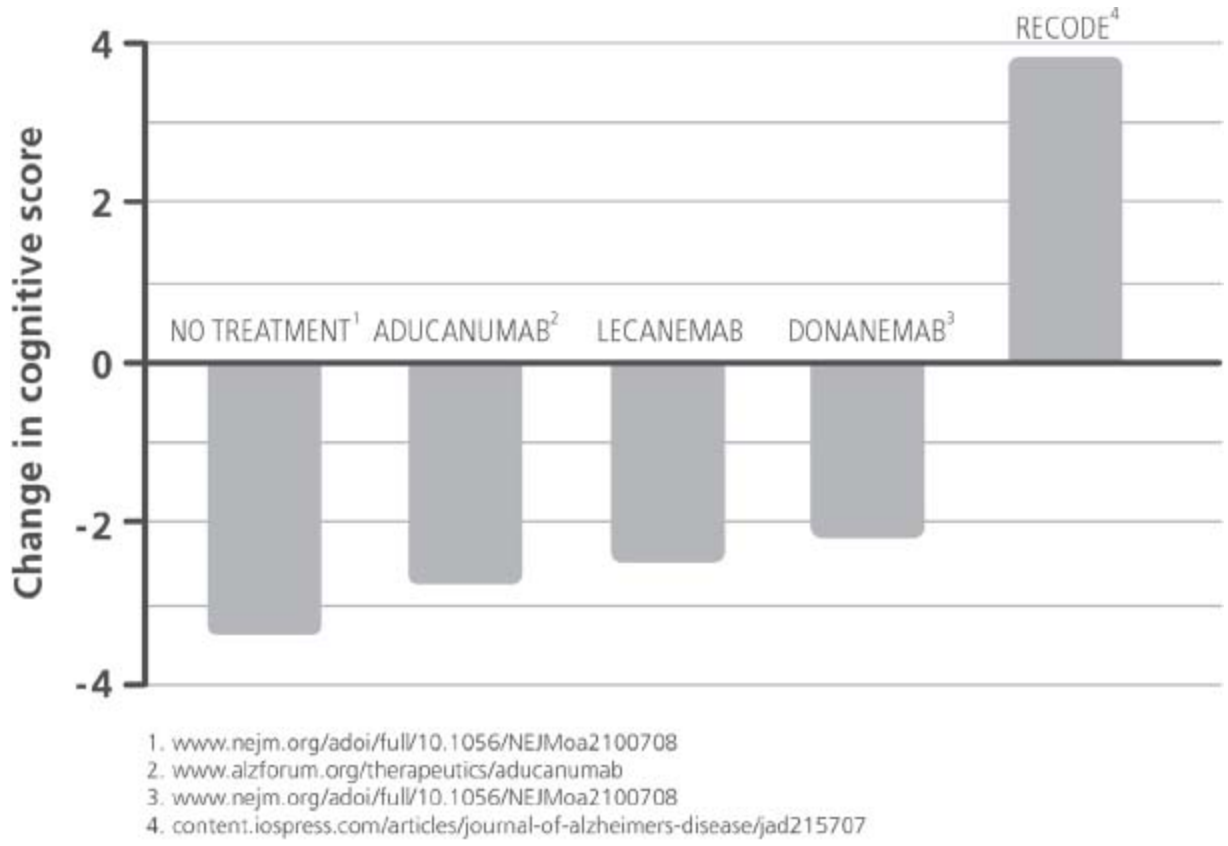


**Figure 23 – Change in cognitive performance with Dr Bredesen's RECODE precision nutrition approach compared to anti-amyloid treatments** *From Dr Dale Bredesen, used with permission.*

Dr Bredesen's protocol, while focusing on the importance of diet, brain support supplements and lifestyle, also considers other factors, such as mycotoxins, inorganic toxins (such as air pollution or mercury), chronic undiagnosed infections, sleep apnoea and other risk factors.

'Repeatedly we read that "nothing can be done",' he says, 'and you've pointed out that prevention can in fact be achieved, but our trial shows that it is not hopeless for those with MCI or even early-stage dementia.'

# Brain-friendly mushrooms and plants – Lion’s Mane, Reishi and Brahmi

Of the plants and fungi, my three favourites are Lion's Mane, Reishi and Brahmi. Lion’s Mane is particularly interesting, as it seems to stimulate neuroplasticity thanks to its two active ingredients, hericenones and erinacines, which enhance the brain’s own nerve growth factor (NGF), a hormone which encourages neuronal growth.[279] Lion’s Mane fungus has been shown to improve aspects of memory and cognitive function in three trials, on healthy volunteers,[280] those with mild cognitive impairment[281] and dementia.[282]

The best-researched mushroom, used for thousands of years in Japan for its anti-ageing properties, is Reishi. It is a potent antioxidant, thus protects the brain from damage.[283] Many people in Japan take it on a daily basis. The usual dose is 500 to 1,000mg a day (*see Resources*).

Brahmi(*Bacopa monnieri)* is an Indian adaptogenic herb that has been used traditionally to boost longevity and enhance cognitive function. Numerous trials conducted on Brahmi extracts, usually giving 300mg a day, have shown beneficial effects on memory retention and cognitive performance versus a placebo. A meta-analysis of nine trials involving 437 older people with memory problems reported improved cognition, better function and better attention.[284]

One of the hottest areas of brain research is the effects of various hallucinogenic compounds - notably psilocybin, LSD and the Amazonian plant potion ayahuasca, a rich source of DMT - on mental health and brain function. These compounds share the quality of activating a key brain receptor site, 5-HT2 receptors, for serotonin. As a group, they are all shown to be potential promoters of

neuroregeneration and neuroplasticity, helping make neuron connections and perhaps new neurons.[285] They also stimulate brain-derived neurotrophic factor (BDNF), a key brain signaller that stimulates growth. It's too early to know if they may have a role to play in neuro-regeneration in those with dementia.

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# In summary,

- **Get off sleeping pills** and take melatonin (5-10mg) if you struggle with sleep. (Read *Upgrade Your Brain* for more natural ways to sleep well).
- **Cut back on alcohol** to a maximum of 7 small glasses of preferably red wine or 7 spirit shots or 3.5pints of beer a week.
- **Build your stress resilience.** My book, *The Stress Cure*, co-authored with Susannah Lawson, shows you how. Consider learning HeartMath's Quick Coherence technique (*see Resources*).
- **Consider natural hormone therapy** if you are menopausal or post menopausal and suspect it's had an effect on your mind, mood and memory, consider being assessed for hormone deficiency. The same applies to older men. It's called the andropause. *See Resources for more details*.
- **Consider experimenting with Lion's Mane, Reishi or/and Brahmi** if you are struggling and have covered all the bases (*see Resources*)
- **To rebuild brain cells follow all the advice in this book.** No-one truly knows the effect of putting everything together. That's what we are researching at foodforthebrain.org.

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# Microbes and the Mind

In our model at foodforthebrain.org we include ‘healthy gut’. The gut, which includes the first part of the digestive tract - the mouth - is a rich field of hundreds of thousands of microbes: bacteria, viruses, fungi (yeasts), and protozoa that we can consider ‘not us’. But is this really true? Where do ‘we’ begin? There are about as many of them as there are cells in your body.[286]

Inside our 10-metre-long gut, which has folds called villi - making the surface area the size of a tennis court - lurk billions of bacteria, weighing about 0.5kg (1lb), with a combination of about 300 different species collectively known as our microbiome. But there are also over 140,000 viral species as well, and not all viruses are bad. Together we call them gut microbes.

Gut microbes can produce neurotransmitters, stimulate immune cells to make cytokines, which trigger inflammation and also produce metabolites such as butyric acid, which further feed bacteria but have knock-on effects in the brain, potentially helping stimulate neuroregeneration.[287]

Our gut expert at the charity is Dr David Vauzour, Associate Professor at the University of East Anglia. He says, “In addition, recent evidence has highlighted that microbes, whether commensal [normal residents of a healthy gut] or pathogenic, also have the ability to interact with their host and to regulate its immune system, therefore participating in the exchanges that lead to peripheral inflammation and neuropathology”.[288] Because of this intimate relationship, implicated in the development of Alzheimer’s disease.’

# Gum disease - a risk factor for Alzheimer’s

Also in our team is dentist Victoria Sampson. She enlightened me with evidence that those who have had gum disease for 10 or more years have a 70% increased risk of Alzheimer’s.[289]

Periodontitis is another word for gum disease, caused by a group of bacteria called red complex pathogens. *Porphyromonas gingivalis,* one of the main bacteria associated with gum disease, can lead to infection of the tissue holding the teeth in place, and as a consequence, symptoms such as bleeding gums and loose teeth.

The association between chronic gum disease and cognitive impairment has long been established, with several studies showing a strong correlation between periodontitis and Alzheimer’s disease. A study of over 2,000 people tested over 60 years for IgG antibodies to *P. gingivalis* found that those who had the highest levels of IgG antibodies were more likely to have poor delayed verbal recall and other cognitive problems compared to those with the lowest.[290] This is important since the presence of IgG antibodies demonstrates that the body has created an

inflammatory response to the bacterium, which is strongly associated with the Alzheimer's disease process.

Most patients with Alzheimer's disease exhibit neuroinflammation that is not dissimilar to a reaction to an infectious agent, like bacteria, leading to the activation of the brain's immune cells called the microglia, as well as a cascade of cytokine production – another hallmark of inflammation. Remember, it was that 'cytokine storm' that COVID-19 infection triggered. For this reason, infectious agents have been robustly studied as a key contributing factor to the development of Alzheimer's. However, a direct causal role is yet to be established.

Despite the lack of evidence for a causative role, associations between cognitive decline and bacterial infection have continued to be established. In another study, where more than 25,000 people aged 50 or older participated, researchers found that people who have suffered from gum disease for 10 years or longer are 70% more likely to develop Alzheimer's disease.[291] This study also highlighted that in those with chronic gum disease, there was a higher prevalence of depression, traumatic brain injury and hyperlipidaemia (raised cholesterol and triglycerides), which may all be contributors in the development of dementia. This research suggests that there may be various factors at play, rather than just gum disease on its own. That's why it is so important to have a multi-factorial systems-based approach.

# Gingipains destroy brain cells

*Porphyrmonas gingivalis*, one of the bacteria responsible for the infection, is not only found in those with gum disease, but has also been found at low levels in 25% of healthy individuals with no presence of oral disease[292]. However,

what more recent studies are showing is that there are multiple different strains of *Porphyromonas gingivalis*. Other strains of bacteria are also linked to cognitive impairment.[293] Some can be entirely benign in the mouth, and others can be extremely pathogenic by releasing virulence factors. A group of these virulence factors are proteins called gingipains, which are released by the bacteria that are responsible for damage to nerve cells in the brain, rather than just the bacteria on its own. Experiments carried out in mice that were infected orally by *P.gingivalis,* discovered that they later demonstrated signs of brain deterioration and infection, which are concurrent with humans showing symptoms of early-stage dementia.

In this same study, carried out by researchers from a variety of universities, brain tissue samples from approximately 100 people with and without Alzheimer's were analysed and tested for two different types of gingipain proteins. They also tested for the presence of gingipain DNA in both the cerebrospinal fluid and the saliva of people that had been diagnosed with Alzheimer's. What they found was that the level of gingipains in brain tissue of those with Alzheimer's was between 91% and 96% (for the two different proteins), in comparison to 39% and 52% in those without Alzheimer's. Furthermore, they found gingipain DNA in 7 out of 10 cerebrospinal fluid samples in those with Alzheimer's and 10 out of 10 for the saliva samples. *P.gingivalis* has, in addition, been shown to be extremely virulent – unlike other bacteria, broad-spectrum antibiotics rarely eradicate it and may lead to resistance to it.[294] It is also acid resistant meaning that it can survive in the stomach when ingested. In addition, *P.gingivalis* depends on the secretion of gingipains to maintain its survival. While drugs have been developed to block the neuroinflammatory action of gingipains, trials have yet to be completed on humans to assess the efficacy of them.[295]

So, how does this bacterium get into you, then the blood, and then into the brain? Researchers from the University of Central Lancashire in the UK, report that bacteria like *P.gingivalis* can enter from oral cavities into the bloodstream through a variety of daily activities, such as eating, brushing teeth and chewing. However, they mention in a study published in the Journal of Alzheimer's Disease, that the bacteria is more likely to enter the circulatory system after invasive dental treatment, which then goes on to trigger inflammation.[296] Dr. Sim Singhrao, Senior Research Fellow at the university, said: "We are working on the theory that when the brain is repeatedly exposed to bacteria and/or their debris from our gums, subsequent immune responses may lead to nerve cell death and possibly memory loss."

While we know that having dementia can lead to difficulties maintaining daily habits like brushing teeth properly, the findings of many studies suggest that gum infections precede the diagnosis of dementia.

# How to prevent periodontal disease

Besides the obvious dental hygiene habits like brushing teeth and the tongue after every meal to remove food and plaque, flossing and using an antibacterial mouthwash, there are also dietary measures that can be put in place to offer extra support.

For example, research shows that there is a strong association between type 2 diabetes and periodontal disease.[297] This may be due to the fact that increased levels of glucose in the blood, due to insulin resistance, can favour the growth of certain species of bacteria such as *P.gingivalis*. In addition, diabetes can lead to a

malfunctioning of the immune system, which leads to a decrease in antibody function and therefore more opportunity for bacterial infection. On that basis, it is wise to limit sugar, in all its forms, including the seemingly 'natural' alternatives to regular cane sugar such as fructose (*see Chapter 8*), as well as focusing on a low GL diet that helps to stabilise blood sugar levels. Also, limit fruit juice and ultra-processed foods, eating mainly foods in their natural, whole state, as Chapter 8 explains.

# Herpes – The Alzheimer's Connection

Another microbe that has been found in the brains of those with Alzheimer's is a type of herpes virus called cytomegalovirus, or HCMV.[298] It is not sexually transmitted and is one of nine herpes viruses, and normally lives harmlessly in the gut, but post-mortem studies of the brain of those who died of Alzheimer's find it present in over a third[299]. It appears to travel to the brain along a central 'vagal nerve' and researchers have found IgG antibodies against it, meaning that the immune system is activated in such a way that leads to brain inflammation.[300] "We think we found a biologically unique subtype of Alzheimer's that may affect 25 to 45% of people with this disease," said Dr Ben Readhead, an expert in neurodegenerative disease at Arizona State University, whose team made this discovery.

# Is mould toxicity an 'inhaled' driver of Alzheimer's?

Other researchers are monitoring the presence of mycotoxins, such as inhaled mould, in those with Alzheimer's.[301] In 2016, Alzheimer's expert Dr Dale Bredesen first described 'a type of Alzheimer's disease is the result of exposure to specific toxins, and is most commonly inhalational - a manifestation of chronic inflammatory response syndrome, due to biotoxins such as mycotoxins.' (Read his book *The End of Alzheimer's* for more details). He called it 'inhaled Alzheimer's'.

Moulds, called mycotoxins, are also capable of triggering the immune system to switch on neuro-inflammation, which has been associated with cognitive problems,[302] including Alzheimer's. This fits with the most common symptom reported by those exposed to mycotoxins in buildings, namely 'brain fog'. Whole books have been written on the subject such as *Breaking the Mold* by Dr Jill Crista. It is a difficult subject to research as mould produces a wide variety of symptoms and is also highly prevalent in old and cold houses - and remarkably difficult to get rid of.

One sufferer, Kirkland Smulders, describes her experience. "My mould toxicity caused chronic and terrifying neurological symptoms, such as repeated and widespread muscle twitches and tremor, as well as anxiety, insomnia and brain fog. It has taken me 2.5 years to detox the mould and I'm still not 100% better. My mother had Alzheimer's and our home in France, where she lived for 47 years, was mouldy."

Of course, association doesn't prove causation and while there is no direct evidence that mould exposure causes Alzheimer's disease, it could be, for those exposed, another straw that breaks the camel's back.

# Is ’toxic overload’ a preventable risk factor for Alzheimer’s?

What these three areas of concern – gum disease with P. gingivalis, herpes HCMV infection and mould exposure - have in common is that repeated exposure has the ability to trigger an immune response that leads to neuro-inflammation. There are likely to be many other microbes that can do this, and may become implicated in increasing risk for Alzheimer’s - and perhaps it is the total load that tips that inflammatory and immune response into hyperdrive. That then leads to accumulation of amyloid and p-tau as knock-on effects of increased inflammation in the brain.

# Brain-Friendly Bacteria

Of course, many of the more evidenced risk factors and prevention steps we’ve discussed - including increasing intake of omega-3 and antioxidants, and less sugar overload - all reduce inflammatory response. The primary antioxidant, vitamin C - while already being established as a key and preventable predictor of risk - also helps promote a healthy gut microbiome, which then keeps more harmful bacteria under control. Two studies have shown that supplementing vitamin C (1g a day; 3g+ a day) increases healthy gut bacteria such as bifidobacteria, while reducing unhealthy gut bacteria such as Enterocci.[303]

# Soluble Fibre

Also, eating a diet high in soluble fibre, such as in oats, chia and flax seeds, as well as raw vegetables, and reducing refined carbohydrates is also gut friendly. Soluble fibres have so many benefits. They help slow down sugar absorption, both to fuel gut bacteria to make butyric acid, a brain friendly gut fat,[304] and also lower the glycaemic load of your meal. They help prevent constipation and also help detoxify many gut toxins. The most soluble fibre of all is glucomannan fibre, from the Japanese Konjac plant, a type of tuber. Glucomannan, at modest daily doses of 4 grams a day of powder, usually taken as 1.5 grams (half a teaspoon) in a large glass of water before a meal, helps stabilise both blood sugar levels and cholesterol, as well as relieving constipation. It is also highly effective for weight control[305]. According to a recent review,[306] glucomannan can reduce the levels of glucose, cholesterol, triglycerides, and blood pressure and can enable weight loss, as well as preventing many chronic diseases through the regulation of metabolism - [making it] anti-diabetic, anti-obesity, laxative, prebiotic, and anti-inflammatory. It is widely used in Japan but hardly heard of in the UK. For these reasons, I developed a breakfast shake, *Get Up & Go* - rich in vitamins, minerals, and low in carbs with added glucomannan - which is one of my breakfast options (*see Resources*).

All these factors are taken into account in the COGNITION questionnaire that follows the Cognitive Function Test at foodforthebrain.org giving you a 'healthy gut' rating and personalised advice about what to do.

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# In summary,

- **Brush and floss your teeth on a daily basis.** Chew your food well, eating high fibre food, low in sugar and limit fruit juices.

- **Up your vitamin C intake** – it is a vital anti-viral agent and promotes healthy gut bacteria. Ideally take 500 or 1,000mg twice a day.
- **If your house has any signs of black or red mould or dampness** consider having it checked for mould. *See Resources for details of companies that can do this for you*.
- **Eat an anti-inflammatory diet rich in antioxidants and seafood.** Supplement omega-3 fish oil, a potent anti-inflammatory.

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# PART 3

# PREVENTION IN ACTION

Assess and personalise your own prevention plan so you have an action plan to follow, with doable diet changes backed up with brain-friendly recipes, sensible supplement choices and simple and effective lifestyle habits to put into action. Join the world’s largest ‘citizen science’ research revolution to help put an end to this largely preventable disease.


# Assessing and Reversing Your Risk with the Cognitive Function Test

The first step to personalising your Alzheimer's prevention plan is simple. Take two short online tests at foodforthebrain.org. First, you'll do the free, validated Cognitive Function Test. This takes about 15 minutes and requires no interruptions, so turn your phone off and put the cat out.

Then you'll complete the comprehensive COGNITION questionnaire all about your diet, lifestyle and medical history. It takes about 10 minutes to complete.

From this you'll be able to see your results on the Cognitive Function Test, your future Dementia Risk Index where 100% is the worst and 0% is what you're aiming for. Then, you'll see which domains are your weakest (red) and strongest (green). You'll see this in colour on the inside cover.

Ideally, also order the DRIfT test kit so you can measure what's actually going on in your body. You'll then be able to

see what your levels of the various risk factors are. i.e., do you do enough exercise, are you getting enough B vitamins - and which need attention to bring them into the green.

Depending on your results you'll be advised what to eat and supplement to bring your levels into the green. Once you achieve 'all green' you will have substantially reduced your future risk of cognitive decline and, ultimately, Alzheimer's.

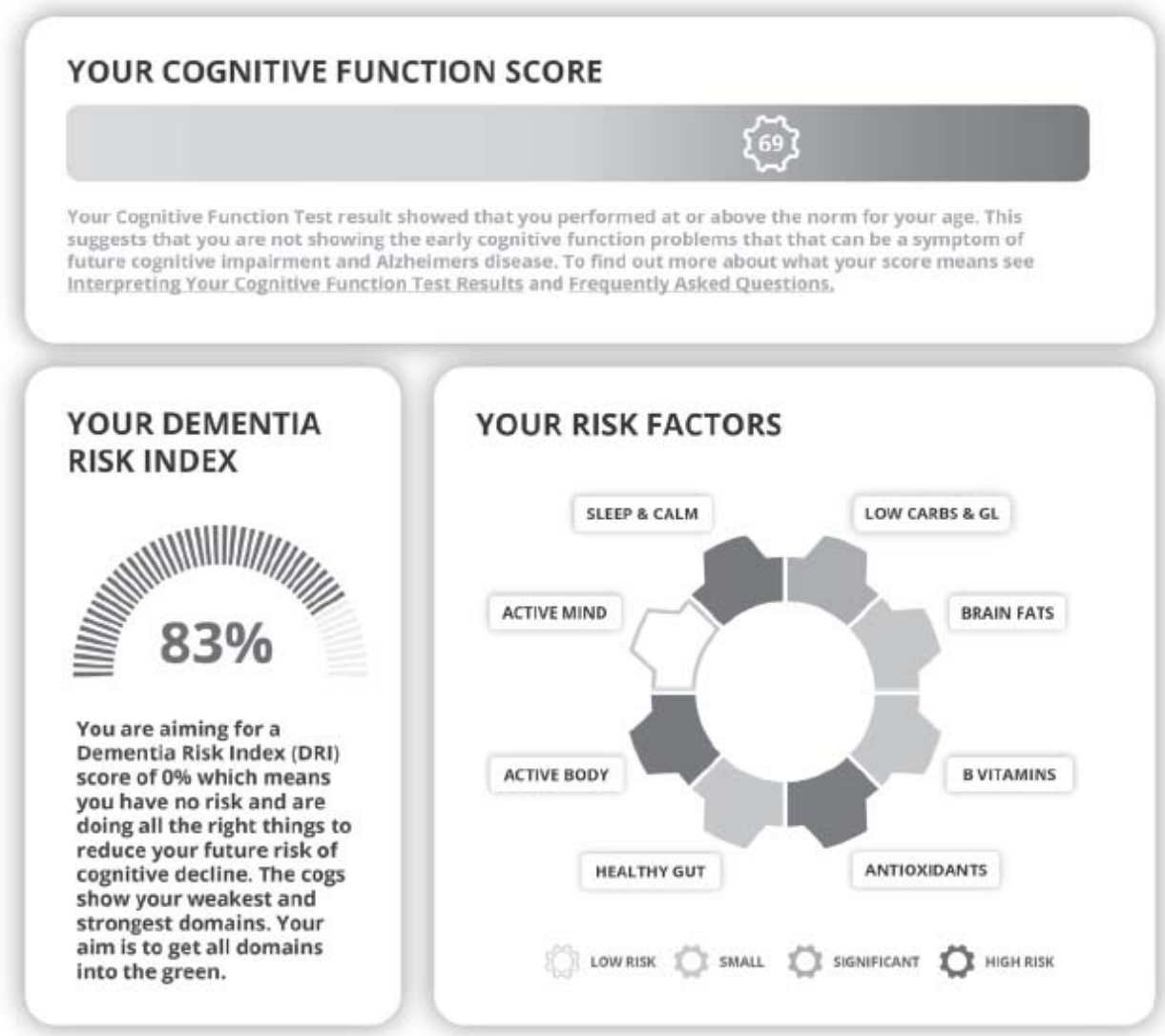



Figure 24 – Example of your DASHBOARD showing cognitive function and Dementia Risk

The Upgrade Your Brain cookapp at foodforthebrain.org/uybcookapp also lets you home in on the best recipes to target your red or amber zones.

If you want some one-to-one help with your Alzheimer's prevention strategy, the charity's virtual Brain Bio Centre at foodforthebrain.org/the-brain-bio-centre/ gives you details of practitioners you can consult.

Also, you will have become a 'citizen scientist' since all your anonymised results go into the COGNITION Biobank to help our researchers and others around the world find out what really works to prevent Alzheimer's. As a FRIEND of foodforthebrain.org (*see Resources*) they'll share this research with you to educate, encourage and empower you to make the right changes. See Chapter 15 to find out how you can be part of this global dementia prevention revolution.

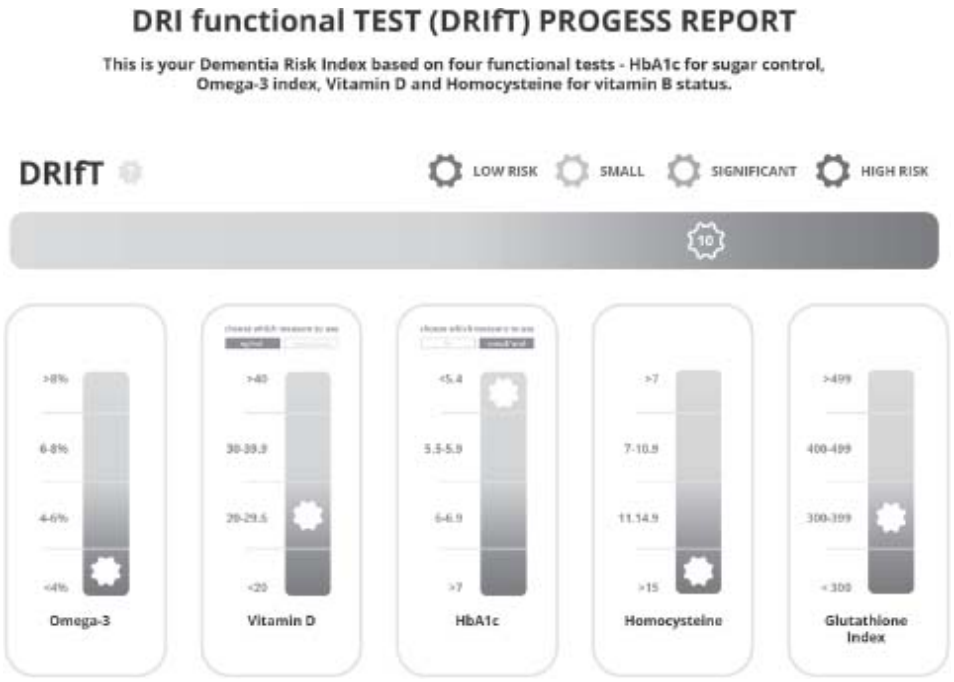



Figure 25 – Example of DRIfT dashboard tracking key biological biomarkers, combined into a DRIfT score

**TESTIMONIALS from people taking the Cognitive Function Test and joining COGNITION**

Here is a fraction of the positive feedback we've received from people taking the Cognitive Function Test, joining COGNITION and taking the DRIfT blood test:

*"I was alarmed to have a low Cognitive Function Test which advised me to see my GP. My mother has Alzheimer's so I knew to take this seriously. I took a homocysteine test which was high at 13mcmol/l despite a 'healthyish' diet.*

*I commenced the appropriate B vitamins and zinc, ate mostly an organic, vegetarian / pescatarian diet, lowered alcohol and did more exercise.*

*Six months later my homocysteine level was 6! Even better my Cognitive Function Test was back to normal. I noticed I was clear thinking, less stressed, sleeping better, feeling better all round. It's been a huge help, thank you."* Rebecca R

*"The Cognitive Function Test gives you real evidence on where your brain health is and what you can do about it. Since focusing on my diet, my blood sugar levels have stabilised so I get far fewer 'flat moods'. I've actively increased my consumption of the right kind of fats and B vitamins, feeling much more alert."* Anon

*"Since doing the Cognitive Function Tests I've taken on board your recommendations and I've increased my vitamin B complex intake and started doing puzzle books everyday to keep my brain active in different ways to normal. I also do more exercises and yoga daily. I love the fact that I can make these small changes myself and*

*hopefully reduce my chances of getting Alzheimer's or dementia."* Anon

*"After taking the Cognitive Function Test I've started taking Omega-3 vegan capsules. Having been vegetarian for nearly 50 years I have noticed an improvement in my concentration and ability to retain information."* Anon

*"I rely on the Cognitive Function Test every year to reveal how I'm progressing. There's always something in my diet and lifestyle that needs highlighting, so it pulls me back on track."* Rose L

*"I have taken the Cognitive Function Test for at least seven years now and find it very worthwhile. By monitoring sensibly what I eat as you advise and exercising within my limitations I have found that, despite being 84, my results have improved. One supplement I recommend is Solgar's Homocysteine Modulators which has reduced the level in my blood by several points which also lessens the risk of stroke & heart attack."* Jennifer W

*"In direct response to taking the Cognitive Function Test I have increased my weekly exercise routine by attending a Pilates class, worked weekly on my allotment, take a weekly swim and increased my evening walk routine (on the number of walks and distance.) I have cut down on my alcohol and meat intake as well. My sleep has also improved naturally from following a more healthy lifestyle.*

*What has also helped is reducing my working week to 3 days in preparation for my gradual retirement. On a cognitive aspect, I have*

*increased my reading consumption by listening to podcasts and audiobooks while I do chores. I now watch far less TV. I have focused a little more on building a positive network of friends and discarded the more unhealthy and occasionally toxic family relationships.*

*I have far less foggy days and now really enjoy feeling more energetic. My husband has also joined me in walking and eating more healthily. He barely drinks alcohol nowadays."*Julie J

*"I took the DRIfT blood test as my memory was very bad and it was your test that made me realise my brain fats were extremely low. Since then I have taken an excellent omega 3 supplement and my memory is improving massively. The results also gave me the confidence that my vitamin D and HbA1c were OK.*

*The cookapp is marvellous. For once I feel full after eating a meal. The meals are quick, easy to make and delicious. I love the way you can easily see whether you're getting all the omega and B vitamins and antioxidants. I now know what to supplement so I'm not wasting money on those I don't need.*

*I'm hoping my very, very short-term memory will also continue to improve with the use of the amazing app the meals, supplements, etc. What you've done with Food for the Brain is on another level."* Nora S

*"I've been doing the Cognitive Function Test for about 10 years. As a result, I've modified my diet to include more of the recommended foods & vitamins, play many more brain training games, taken steps to reduce stress and anxiety, increased my exercise schedule, been more aware of my gut/brain relationship and its impact on my health. I'm no longer worried that I'm losing my mental*

*abilities. Now, age 70, my cognitive function has improved. My memory is better, my vocabulary has improved and I'm no longer searching for that "right" word - it's springing to mind much more readily. People are even complimenting me on my great memory whereas in the past, I used to joke that I had the memory retention of a goldfish. Doing the test annually has given me confidence that ageing and Alzheimer's are not to be feared and has played a significant role in reinforcing the lifestyle changes I've made."* Diane

*"When I first used your Cognitive Function Test about 8 or 9 years ago, I noticed a steady decline in my cognitive function, which projected forward would have had me classified as suffering borderline dementia within five years. I started to reduce my homocysteine levels following your recommendations and over the course of 18 months, reduced my homocysteine from 15 to 6 mcmol/l, taking the test every six months. I then retook the Cognitive Function Test and was astounded to see my levels not only reversed, but back above the level of my first test. I have since retaken the Cognitive Function Test, and my levels remain steady at the elevated level. Consequently, I continue to follow the supplement regime recommended by Patrick."* Martin (age 75)

*"I've managed to finally force myself to get to bed at a reasonable hour and be up reasonably early so I can get more out of my day - and start to get over some of my addictions! It feels like I've developed the determination to stick at it.*

*I've been regularly having C8 and cod liver oil, and sometimes just a teaspoon of coconut oil. My ability to think clearly and make important connections between pieces of information and act on them is coming back.*

*And I’m talking about organising groups of people and inspiring them, not just working out where I put my keys. I am also feeling more present and in my body, and more positive generally.*

*I’m just very grateful that there are dedicated, well-educated common sense people like you in the world whose dedication makes my life easier. Thank you from the bottom of my heart!”* Chris E

*“Since joining COGNITION I control what I eat much more carefully, and I take more supplements, not just Vitamin C. I was already a subscriber to the Lumosity App and know my performance has improved since I became a Friend.*

*I definitely feel more mentally alert as well and my card play at bridge has improved a bit.*

*I have lost 2kg weight and am now the same weight as I was in 1980. Just can’t run as fast.”* Nigel B

*“I joined COGNITION because my memory was terrible! I’d forget something as soon as I’d said it or heard it and writing down what was said on the phone or conversations where I’d ask my friend, 'What did I just say?' - and she couldn’t remember either! My head and memory was as if there was concrete in my brain and it was really scary, as if nothing was going in and nothing coming out.*

*I’m very pleased with the results so far. My DRI has gone down from a start point of 52% to 37%! I have 4 green areas now - the rest are in yellow mode. I’ve really got a handle on keeping sugar intake very low.*

*I still get some brain fog but nowhere near as bad as it was. It's a nice feeling to start 'connecting' after at least 2 years of not being able to remember even the conversation I'd just had. To feel that 'word' come to mind that would have eluded you is just great! My memory returning to me!*

*My overall health improved slowly due to adding NAC and taking more DHA. I more recently added a B complex. It's the best thing I could have ever done.*

*But it's not just about vitamins either, as under the guidance of COGNITION, I do Wordle and Spelling Bee to stimulate my mind and I'm doing really well with it, dab hand you could say, getting genius sometimes and really doing well with Wordle too!*

*I've even managed to do a 3K run and I've got my anxiety under control. I get out more and am more aware of the need to socialise and get mental stimulation. I would NEVER have considered those two areas as part of getting cognition improvement! I've lost over a stone and kept it off. I'm more positive in life, embarking on projects and feel very excited to getting my life back. I could never have achieved it without the COGNITION programme. Thanks to COGNITION - life has improved SO MUCH!"*Janette M

"*As someone with a genetically raised risk of dementia (ApoE4), I am hugely grateful to foodforthebrain.org. Without it my only option would have been to wait for the worse to happen and hope it didn't. Regular medicine can offer no prevention or treatment.*

*Instead the charity has given me the possibility of reducing my risk with the bonus of getting healthier in the process. My raised risk means that the exercise I do*

*anyway doesn't just keep me feeling well every day, but has a clear goal. The same goes for the changes I'm making to my diet and the supplements I take. My threatening gene now seem more like a gift."* Jerome Burne, award-winning medical journalist.

*"Last December my husband, Nodge, was diagnosed with mixed dementia (vascular and Alzheimer's). He constantly lost his keys, wallet and glasses. He asked the same question and told the same stories repeatedly. He couldn't remember where he lived. He'd even got lost on the way to the toilet in the night. He couldn't join conversations because he couldn't follow them. He was unable to drive because he couldn't think about more than one thing at once. There were lots of signs of dementia.*

*At the Memory Clinic we had wanted to discuss a prevention programme but instead were given a virtual pat on the head and a pile of depressing leaflets about where to go for support. There was no hint of hope. By the time we left the clinic Nodge couldn't remember the diagnosis.*

*Nodge did their free on-line Cognitive Function Test, and questionnaire which works out your Dementia Risk Index and tells you what actions to take to reduce your risk. His score was 56% – it should be zero. The test not only measures your actual cognitive function but shows you what is driving your risk across eight domains.*

*We were both horrified at the yellow and amber results and decided to act immediately to rectify each area as recommended by the COGNITION 'brain upgrade' programme that sends you emails to read, things to watch and actions to take. Now there are zoom groups and text reminders.*

*Nodge started taking the recommended B vitamin supplements and omega-3 fish oils, radically changed his diet, cutting out all sugar and refined carbs and added two tablespoons of Ketofast (C8 oil) a day. We have both increased our exercise massively, joined social groups to stimulate the mind and started going to bed earlier to get more sleep.*

*In just three months the change has been remarkable. We both feel better. Our moods are better, our energy is better. Nodge is joining conversations, he's organising his own diary, he uses his computer without help, he's taken himself back to Morris Dancing practice and taken himself to a Dementia support group so he can show them his recovery.*

*Nodge has just repeated the online test at foodforthebrain.org.*

*In just three months his Cognitive Function has improved dramatically, more than doubling his score and his Dementia Risk Index has fallen from 56% to 43%. While before he had four out of eight domains showing red flags he's now only got to just below green – active mind and body – but he's working on them.*

*Honestly, I feel like I've got my husband back. I am so grateful to Food for the Brain."* Dorothy N

*"I had completely forgotten how to garden, apart from making compost which I'm an expert at. I had allotments for over 35 years so it was a shock. Since I've been following the COGNITION programme I've had the seeds out, got the pots ready for planting and planned when and where things should go.*

*We couldn’t discuss plans for the week or for holidays without getting muddled and cross because I couldn’t hold the idea of something in the future in my head. Now my brain is functioning better we can, once again, plan together. It’s been really exciting. We’re looking forward to getting increased improvements.”* Nodge N


# Your Alzheimer's Prevention Plan - Diet, Supplements & Lifestyle

Let's start with your diet. How do you work out the best diet to protect your brain and prevent cognitive decline? There are two ways to approach this question. One is to look at individual foods that reduce or increase the risk of cognitive decline and the other is to look at diets that reduce the risk, but these usually start with an assumption of what a healthy or not healthy diet is.

An example of this is a study in Finland and Sweden that compared those with a 'healthy' versus unhealthy diet in midlife for their future risk of developing Alzheimer's disease and dementia 14 years later. It found a 92% reduced risk of Alzheimer's in those following the healthiest diet.[307] This 'healthy' diet score assumed that vegetables and roots, berries and fruits, and bread, fish, coffee were good, and sugar, sausages, eggs were bad. (eggs are on my 'good' list – *see Chapter 5 and page 156 below*)

Another is the study in the British Medical Journal following over 30,000 people over a decade which found that those with a healthy diet were about seven times less likely to have age-related cognitive decline or dementia than those with an ‘average’ diet and about nine times less likely to develop dementia than those with an unfavourable diet. Their definition of a healthy diet was one high in fish, eggs, fruits, vegetables, legumes, nuts and tea.[308]

Studies on the Mediterranean-style diet, meaning eating more fruit, vegetables, legumes, nuts and seeds, as well as more fish, less meat and sometimes some wine, reported that high adherence versus low adherence reduced the risk of Alzheimer’s by a third.[309]

A variation of this, called the MIND diet invented by researchers at the Rush University Medical Center in Chicago, which had plenty of fruit and veg, reported that ‘People who scored highest for adhering to the Mediterranean diet had, on average, brain plaque and tangle amounts found in the brains of those 18 years younger.

A similar study in Holland reported that ‘better-diet quality related to larger brain volume, grey matter volume, white matter volume, and hippocampal volume. The better diet had a high intake of vegetables, fruit, whole grains, nuts, dairy, and fish and low intake of sugar-containing beverages.’[310] A recent study found that swapping one serving of processed meat with a serving of nuts and legumes, which could mean a vegetarian protein meal such as a nut roast or bean casserole or curry, was associated with a 19% lower risk of dementia.[311]

# Small changes make big differences

So, following a brain-friendly diet could reduce your risk of cognitive decline, dementia and Alzheimer's and lessen amyloid plaques and neurofibrillary p-tau tangles. Rush University's research found that ticking one good-food box — such as eating the recommended amounts of vegetables or fruits — reduced amyloid build-up to a level similar to those about four years younger.

In their study, the greatest result was found with those eating greens. Those in the top third of greens consumption had substantially less Alzheimer's-related pathology than those in the lowest third. Also, reducing bad foods makes a big difference. Replacing just 10% of ultra-processed food by weight in one's diet with an equivalent proportion of unprocessed or minimally processed foods was estimated to lower the risk of dementia by 19%.[312]

# *Brain-friendly foods*

So, what are the foods that are most protective for your brain and cognitive health?

- ***Fruit and veg.*** – The more you eat, the better, though the benefits start to plateau at 500g a day, which is about five to six servings. Of individual vegetables, carrots, cruciferous vegetables and citrus fruit were very positive, as were mushrooms. Berries are particularly protective, especially blueberries and strawberries.[313]
- ***Fish*** – is the most protective. Having 150g a day, which is one to two servings, reduces Alzheimer's risk by 20% and cognitive decline by up to 30% according to the latest review of all studies.[314] Another reported that eating fish once or more each week reduced the risk of Alzheimer's by a third compared with those who ate fish

less than once a week.[315] Oily fish, as a source of omega-3 fats, is the best.

- ***Eggs*** – eating more than 2 eggs a week almost halves Alzheimer's risk.[316] I recommend six eggs a week.
- ***Olive oil and nuts*** – Both olive oil and nuts reduce the rate of cognitive decline.[317] I favour olive oil high in polyphenols (*see Resources*) and pecans, walnuts, macadamia nuts high in omega-3. So are chia, flax and pumpkin seeds. Almonds are good for calcium and magnesium but not omega-3. Cashews are the highest in carbs, but still a good food. Peanuts are high in protein.
- ***Grains and potatoes*** – reach a plateau at 100 to 150g a day, which is one or two servings max. High-fibre bread was the most beneficial carb food. White bread increased risk. I opt for 'hard' scandanavian style rye breads such as sonnenbrot or pumpernickel or oat cakes. The more squishable the higher the GL.
- ***Tea & Coffee*** - some studies suggest coffee drinking might reduce risk, yet coffee increases homocysteine levels, which is a strong predictor of risk. One cup of coffee a day, in the morning, ideally not on waking but 30 to 60 minutes later, seems optimal.[318] However, the more tea you drink, the better.[319] The tea benefit has been confirmed more recently in a study in Singapore, with green tea being marginally better than black tea.[320] However, this benefit was not found in a UK Biobank study, which reported tea and coffee drinking to be associated with worsening cognition compared to abstainers.[321] My view is to drink tea, green over black, in preference to coffee, and limit your intake to one or two cups a day.
- ***Chocolate*** – peaks at 10g, or about 3 pieces – and let's say dark, 70%+, thus with less sugar, is more likely to be better, as sugar is a strong indicator of cognitive

decline. Cocoa, a rich source of flavanols, have shown improved cognition, possibly by improving circulation.[322] I make a hot chocolate with cocoa, cinnamon, nutmeg and sometimes a tiny bit of paprika or cayenne – with no sugar.

- ***Red wine*** may reduce risk in moderation, but there's a narrow window of benefit. Wine consumption reduces risk up to 125g a day, which is a small glass or 1.5 units. However, both abstinence increases risk, as does having more than 14 units of alcohol a week, which is equivalent to a medium glass of wine every day, according to a study in the British Medical Journal.[323] So, the sweet spot is that small glass of wine. Drinking half a bottle of wine a day, on average, gets you close to doubling your risk.

# The key components of the diet

Bearing all this in mind, the key components of a diet designed to protect brain health and reduce risk of cognitive decline are:

## *Eat essential fats and phospholipids*

- Eat an egg a day, or six eggs a week – preferably free range and organic. Boil, scramble or poach them, but avoid frying.
- Eat a tablespoon of seeds and nuts every day – the best seeds are chia, flax, hemp and pumpkin (all higher in omega-3). They're delicious sprinkled on cereal, soups and salads. The best nuts are walnuts, pecans, and

macadamia nuts, but all nuts, including almonds, hazelnuts and unsalted peanuts are good sources of protein and minerals.

- Eat cold-water, oily, carnivorous fish – have a serving of herring, mackerel, salmon or sardines two or three times a week (limit tuna, unless identified as low in mercury, to three times a month). Vegans need to supplement algal omega-3 DHA, as well as choline or lecithin capsules or granules, rich in phosphatidyl choline.
- Use cold-pressed olive oil for salad dressings and other cold uses, such as drizzling on vegetables instead of butter. Substitute frying with steam frying with olive oil, coconut oil or butter, e.g. for onions and garlic, then adding a watery sauce, such as lemon juice, tamari and water, to ‘steam’ for example, vegetables, perhaps with tofu, fish or chicken.

# *Eat slow-release carbohydrates*

- Eat wholefoods – wholegrains, lentils, beans, nuts, seeds, fresh fruit and vegetables – and avoid all white, refined and over-processed foods, as well as any food with added sugar.
- Snack on fresh fruit, preferably apples, pears and/or berries, especially blueberries.
- Eat less gluten. Try brown rice, rye (which contains a little gluten but less than wheat), oats, quinoa, lentils, beans or chickpeas.
- Avoid fruit juices. Eat fresh fruit instead. Occasionally have unsweetened Montmorency cherry juice or blueberry juice (made from unsweetened concentrate).

# *Eat antioxidant and vitamin-rich foods*

- Eat half your diet raw or lightly steamed.
- Eat two or more servings a day of fresh fruit, including one of berries.
- Eat four servings a day of dark green, leafy and root vegetables such as broccoli, tenderstem broccoli, kale, spinach, watercress, carrots, sweet potatoes, Brussels sprouts, green beans or peppers, as well as mushrooms. Choose organic where possible.
- Have a serving a day of beans, lentils, nuts or seeds – all high in folate.

# *Eat enough protein*

- Have three servings of protein-rich foods a day if you are a man, and two if you are a woman.
- Choose good vegetable protein sources, including beans, lentils, quinoa, tofu or tempeh (soya) and ‘seed’ vegetables such as peas, broad beans and corn.
- If eating animal protein, choose lean meat or preferably fish, organic whenever possible. Having one or more servings of unprocessed red meat more than daily versus less than half a serving a day on average, has been shown to increase dementia risk by 16%.[324] Processed meat (such as hamburgers, sausages and bacon) are also linked to increased risk and best minimised or avoided.

## *Eat gut-friendly fermented foods and fibres*

- Add sauerkraut, kimchi, live yoghurt, kefir, kombucha, fermented pickles and some unpasteurized soft cheese to your diet.
- Add chia seeds to oat-based cereals.
- Limit or avoid wheat. Have oatcakes instead of bread.
- Eat oats and oatcakes, beans, nuts, seeds, whole fruit and vegetables, having four servings of vegetables a day, raw or lightly steamed.
- Eat prebiotic-rich Jerusalem artichoke, garlic, leeks, onions, asparagus, barley and oats.

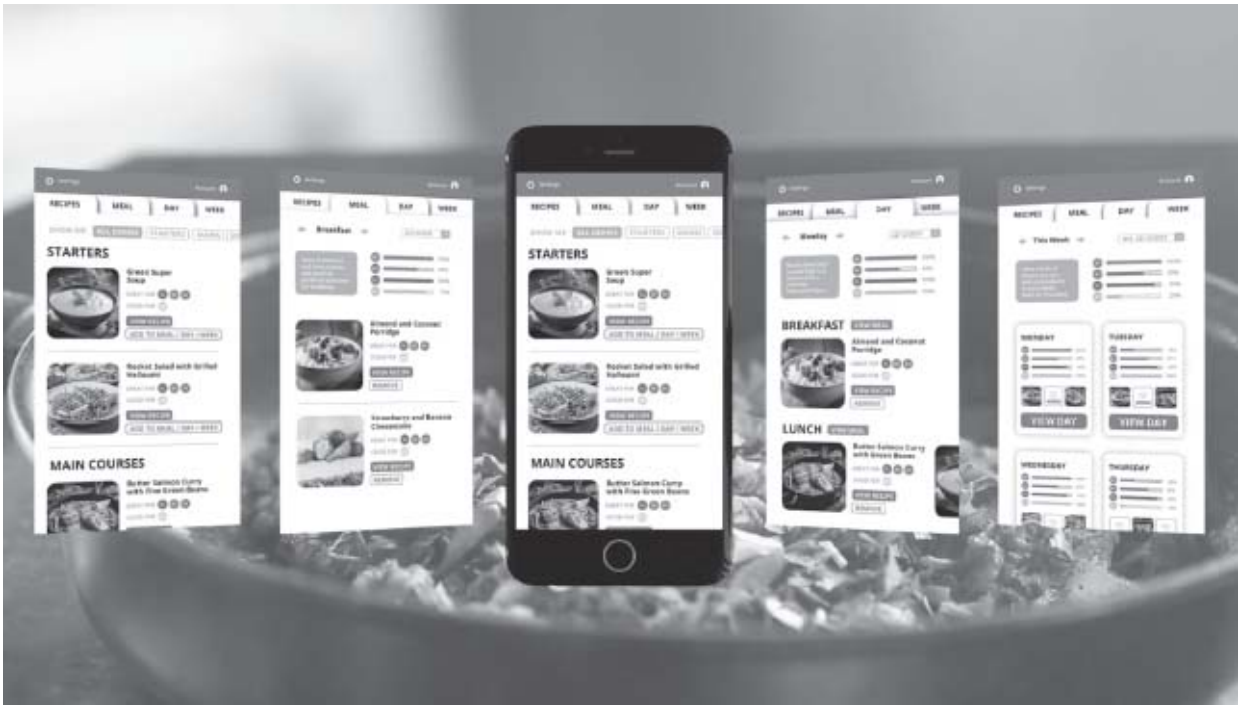
## *Avoid harmful fats*

- Minimize your intake of fried or processed food and burnt saturated fat on meat, and cheese.
- Minimize your consumption of deep-fried food. Poach, steam or steam-fry food instead.
- Minimize your intake of refined vegetables oils high in omega-6 (principally soybean oil, corn oil and sunflower oil).

## *Avoid sugar, reduce caffeine, and drink alcohol in moderation*

- Avoid adding sugar to dishes and avoid foods and drinks with added sugar. Keep your sugar intake to a minimum, sweetening cereal or desserts with fruit.

- Avoid or considerably reduce your consumption of caffeinated drinks. Don’t have more than one caffeinated drink a day. Tea is preferable to coffee.
- Drink alcoholic drinks infrequently, preferably red wine, to a maximum of one small glass (125g) a day.
- Have up to three pieces of dark chocolate per day, minimum 70% cacao, or drink unsweetened cacao with milk or plant milk.




# The Upgrade Your Brain cookapp makes this easy

It’s one thing knowing what to do, of course, and another thing doing it. The simplest way to push your diet in the right direction is the Upgrade Your Brain cookapp. There’s hundreds of delicious, relatively easy to make, recipes, each graded for:

- Antioxidant rich

- Brain fats rich
- B vitamins rich
- Low Glycaemic Load (GL)

If you pick a meal high in antioxidants but low in brain fats it shows you options of what to eat next to tick this box. If you want to lose weight it helps you hit the 45 GLs a day target, otherwise 60GLs is best. If you want to 'go keto' it helps you make daily menus giving
15 GLs, which is what you need to tip over into ketogenesis. *See details on page 188 in Resources to subscribe*. Here's a few examples of delicious meals that tick one or more of these boxes:

| Recipe | Anti-oxidants | Brain Fats | B Vitamins | Low GL |
|---|---|---|---|---|
| Almond & Coconut Porridge with Berries | ✓ | | | ✓ |
| Asian Scrambled Eggs | ✓ | ✓ | ✓ | ✓ |
| Celeriac and Watercress Soup | ✓ | | ✓ | ✓ |
| Super Greens Soup | ✓ | | ✓ | ✓ |
| Mackerel and Cucumber Salad with a Lemon-Yoghurt Dressing | ✓ | ✓ | ✓ | ✓ |
| Zingy Chickpea Chaat Salad | ✓ | | ✓ | |
| Miso Salmon with Courgetti 'Noodles' | | ✓ | ✓ | ✓ |
| Jerk Chicken with Cauliflower Rice | ✓ | | ✓ | ✓ |
| Steamed Salmon with Soy and Garlic Spring Greens | ✓ | ✓ | ✓ | ✓ |
| Lentil and Mushroom Shepherdless Pie with Cauliflower Mash | ✓ | | ✓ | ✓ |
| Grilled Halloumi and Rocket Salad | ✓ | | ✓ | ✓ |
| Quinoa Stuffed Red Bell Peppers with Feta | ✓ | | ✓ | ✓ |
| Smoked Salmon and Cucumber Bites | ✓ | ✓ | | ✓ |
| Rosemary and chilli roast nuts | ✓ | | ✓ | ✓ |
| Ginger, carrot and walnut loaf | ✓ | | ✓ | |
| Chocolate Espresso Mousse | ✓ | | ✓ | ✓ |

# Join COGNITION for step by step guidance and encouragement to change your diet

When you join the personalised interactive COGNITION programme you'll not only be given bite-size assignments to make the changes to your diet that will make the biggest difference (with reminders to keep you motivated and on track) but also lists top recipes from the Upgrade Your Brain cookapp. It takes approximately three weeks to break a habit and six weeks to make a new, good habit, so whatever you decide to do, you need to stick to it for at least a month.

Whether or not you sign up to COGNITION, which I suggest you do both for yourself and to help us research what really helps prevent Alzheimer's, by doing the free online Cognitive Function Test at foodforthebrain.org, you'll see which areas you need to focus on. For example, if you score red or amber on 'Brain Fats', focus on the 'Eat essential fats and phospholipids' section above. If 'Low Carb and GL' is your weak area, focus on the section 'Eat slow-release carbohydrates'. If it's 'Antioxidants' that comes up lacking, focus on the 'Eat antioxidant and vitamin-rich foods' section. If 'Healthy Gut' is your weakness, focus on 'Eat gut-friendly fermented foods and fibres'.

From the list of recommendations above, highlight three that you aren't currently following and want to focus on for the next month. Write them down in big letters and stick this on your fridge. Make a note, in a month's time, to do the same again, choosing three new areas to focus on.

# Supplements for Alzheimer's Protection

Anyone who says supplements are a waste of money is not a scientist or hasn't bothered to read the science. There is an extraordinary 'anti-supplement' mindset in mainstream medicine yet exactly the same kind of high-quality research done on supplements shows benefit way in excess of that shown by any anti-Alzheimer's drugs.

By now you will know that the evidence of benefit from supplementing B vitamins, omega-3, certain antioxidants especially vitamin C, possibly choline and phospholipids, is substantial. This all makes evolutionary sense since the estimated intake of nutrients that our ancestors, living, fishing and foraging along the water's edge, eating a high marine food diet as well as whole, organic plants – fruit and veg, nuts, eggs and occasional meat, cannot be achieved by what we eat today for a simple reason. We don't eat enough.

Not only is our food often downgraded and not organic, our ancestors ate at least twice as much because they exercised at least twice as much. So, we have half as much food to get our nutrients from. This simple fact explains why you have to supplement even a healthy diet both to achieve what our ancestors ate and for optimal Alzheimer's protection.[325] That was the conclusion of a study in the Journal of the Royal Society of Medicine looking at the nutrient intake of a mid-Victorian worker, not that this is necessarily 'optimal' by any means. Their intake of vitamins, minerals and essential fatty acids was so much higher than today. They concluded that "this constitutes either a persuasive argument for a more widespread use of food fortification and/or food supplements" to make up the difference.

## *Four nutrients are especially significant in this regard:*

- **Vitamin D** – It is now well established that anyone living far from the Equator has to supplement vitamin D for several months over the winter. In 2016, the UK government recommended that everyone supplement during the autumn and winter.
- **Vitamin B12** – Many people, especially over the age of 50, simply do not absorb vitamin B12 well enough from food alone to provide a sufficient supply. The ignorance regarding vitamin B12 is compounded in the UK by the inaccurate reference range for serum B12 of anything above 180pg/ml being sufficient (200pg/ml in the US). This is urgently in need of revision. In Japan, anything below 500pg/ml is considered deficient. Against this yardstick, two in five over 60 have B12 levels that are too low to stop accelerated brain shrinkage. Ignorance regarding B12, and the inability of doctors to prescribe it to those with cognitive concerns, is fuelling the epidemic of dementia. If your homocysteine is high you will need to supplement 500mcg a day to lower it. The RDA for B12 is 2mcg. My advice is to supplement at least 10mcg if your homocysteine level is normal.
- **Omega-3 DHA** – In the UK, doctors are not allowed to prescribe omega-3 supplements for any condition, be it depression or dementia, despite all the evidence of its benefits. I first wrote about omega-3 in 1981, and with each decade, recommendations have gradually increased. However, there is still no official Nutrient Reference Value for it. The current guideline is to have 250mg of combined EPA and DHA a day, but this is well below the level of DHA that confers the greatest protection from cognitive decline which is a daily intake of 500mg a day of DHA.
- **Choline** – despite clear evidence of the need for choline there is no recommended intake. Vegans can be assumed to be deficient unless supplementing. But most

of us are unless we eat lots of eggs and fish. The optimal daily intake of choline is around 400mg a day.

- **Vitamin C** – There are so many benefits in supplementing 1 or 2 grams of vitamin C a day. It is strongly associated with lessening risk for Alzheimer's but it also promotes healthy gut bacteria, is anti-viral, lessens cardiovascular and cancer risk, and supports immunity. While taking vitamin C every day won't stop you getting a cold upping your intake on first signs of an infection to 2 grams every two hours does reliably shorten cold duration by getting your blood level up to the level that is profoundly anti-viral[326] – this is what all animals that make vitamin C do when exposed to a virus. Other antioxidants discussed in Chapter 9 such as glutathione or NAC and vitamin E may also confer protection.

# Take the DRIfT test to determine what you need to supplement

The best way to find out whether or not you need more B vitamins, vitamin C or glutathione, vitamin D or omega-3 is to test your blood levels in the DRIfT test.

*If your homocysteine is high* (10 mcmol/l or more) you need more B vitamins – especially B6, B12 and folate.
*If your Glutathione Index is low,* below 500 you need more antioxidants – think vitamin C and glutathione or NAC. Magnesium also helps raise your Glutathione Index.
*If your vitamin D is low,* below 75nmol/l (30 ng/ml) you need to supplement more – probably 3,000iu in the winter.
*If your omega-3 index is below 8%* you need to eat more oily fish and/or supplement omega-3, providing 500mg of DHA.

Your test results will guide you on what to take. By doing so you'll be part of ongoing research to find out what intake of nutrients confers the best cognitive protection. You'll also be recommended to retest any components of the DRIfT test that were not optimal (in the green). In this way you'll learn how to optimise your nutrient levels. See foodforthebrain.org/drift and details in *Resources* on page 192.

# Building your own brain-upgrade supplement programme

In the absence of your DRIfT test results how do you put all this together into your own personal daily supplement programme? There are those supplements recommended for all (*see below*).

## *Recommended for all*

- 2 x high-strength multivitamin–mineral tablets, taken one with breakfast and one at lunchtime. (Note most high-strength multis are taken in two doses – follow the pack instructions. You want one that gives you at least 100mg of magnesium.)
- 2 x vitamin C 900mg, ideally with extra zinc, taken one with breakfast and one at lunchtime. Since your multi will provide some, the goal here, together with diet, is to achieve 2,000mg a day. If younger 1,000mg may be sufficient.
- 2 x essential omega-3 and omega-6: dosage 500mg of omega-3 (EPA+DPA+DHA; 50mg GLA), taken one with

breakfast and one at lunchtime. Judging by recent research, it may be wise to double or quadruple the omega-3 amount by adding in a high-strength DHA supplement, which is what I do. For brain function the optimal daily intake for DHA is around 500mg and for EPA, which is more associated with mood, 750mg. Omega-6 GLA is the precursor for Arachidonic Acid which is a vital component of neuronal membranes.

- 1 x ‘antioxidant formula’ (containing resveratrol, lipoic acid, glutathione, CoQ10 or Ubiquinol), taken with lunch or dinner.This is most important for those over age 50 and those undertaking lots of exercise, which increases the need for antioxidants. Ubiquinol is the fully reduced form of CoQ so several times more potent. It helps recycle glutathione.
- 1 x ‘brain-friendly formula’ with extra B vitamins and phospholipids, taken with breakfast. You can also increase your phosphatidyl choline intake by taking two 1,200mg lecithin capsules or a dessertspoon of lecithin granules. This is especially important for vegans and those not eating eggs.
- Homocysteine lowering B vitamins – this really does depend on your blood level of homocysteine. If it is above 10mcmol/l you’ll need to be supplementing 500mcg of B12, 400mcg of folate (preferably methylfolate), 20mg of vitamin B6 and homocysteine lowering formulas often provide some TMG, zinc and either glutathione or NAC and possibly some vitamin B2.

The above is what I take daily at the age of 67 with the exception of the homocysteine-lowering formula because my level is 7mcmol/l.

# Declaration of conflict of interest

I don't make supplements but I do get approached by companies that do. They want me to advise them about the right formulas and amounts to put in supplements. I do so, as I have in this book, based on studying all the science which I've been following over 45 years and make a point of keeping up to date. Some companies pay me royalties much like, but less than the royalties I receive from books. These royalties allow me to volunteer time at the charity to help push the Alzheimer's prevention project forward. For 'full disclosure' I always insist that my name is on the product if I'm being paid a royalty. Whether you take these or other brands of supplements doesn't matter as long as the amount of the nutrient is equivalent to the levels discussed in this book and above.

In the Resources section I list reputable companies that provide supplements with decent formulas. At the charity foodforthebrain.org/supplements they list all brands of supplements that meet the research criteria for the areas we've discussed in part 2 – homocysteine lowering B vitamin formulas; omega-3 supplements; antioxidants; vitamin D; phospholipids and sources of C8 oil.

# Developing your brain friendly lifestyle

In Chapters 10 and 11 we learnt the many key lifestyle factors that protect your brain and protect you from future risk of Alzheimer's. These include:

**Get active for 20 minutes**… and build and maintain muscle - Spend at least 20 minutes doing activities such as walking, gardening, housework or repairing things – anything that gets you moving. Don't limit yourself to 'exercise'– anything that gives you a faster heart rate and engages different sets of muscles is good.

**Build muscle** - Muscle mass best predicts both your brain volume and risk of cognitive decline in later years. Do some 'strength training' or activities that build muscle.

**Get balancing** - The brain works hard in exercise, especially if it involves complex movements and learning, such as learning to dance, or doing different movements in a yoga or t'ai chi class or running or walking on uneven surfaces. The brain is processing a lot of information, triggering patterns of muscle movement and keeping you in balance.

**Listen to music and dance along.** This ticks three boxes – brain stimulation, less stress, building coordination, engaging both body and mind.

**Read, watch or listen to stimulating content** – A simple yardstick is to ask, 'Am I learning anything? Am I using my mind?' Reading books or listening to podcasts can be great ways to stimulate your mind, depending entirely on what you engage with. I've had so many great guests on my podcast at podbean.patrickholford.

**Be social** - Aim to spend two hours a week or a couple of days spending time with other people in a social (not work) setting – groups, friends, family, etc.

**Test your brain in the morning** - Do Sudoko, the crossword, Wordle, Worldle, Brain HQ or Lumosity (*see Resources*).

**Learn something new and challenging -** Learning a new language, sport or musical instrument are all good - anything that you keep practising. The worse you are the better.

**Cut back on alcohol -** to a maximum of 7 small glasses of preferably red wine or 7 spirit shots or 3.5pints of beer a week.

**Build your stress resilience -** My book, *The Stress Cure*, coauthored with Susannah Lawson, shows you how. Consider learning HeartMath's Quick Coherence technique (*see Resources*).

**Brush and floss your teeth on a daily basis -** Chew your food well, eating high fibre food, low in sugar and stay away from fruit juices.

When you do the Cognitive Function Test you'll soon see your weakest areas that warrant attention. When you sign up for COGNITION you'll be given doable assignments to nudge you forward into building these kinds of brain-friendly habits into your life. As we've learnt it's all about interactions and adding in these lifestyle behaviours to a healthy diet and supplement programme is a winning formula for preventing Alzheimer's.


# The Global Citizen Science Alzheimer’s Prevention Revolution

Do you ever get the sense that, despite the real science steaming ahead, nothing really changes? I have the strong instinct that we are heading for another two-step dance that will involve creating a ‘disease’ called ‘high amyloid’, then having everyone over 50 tested, and then scaring people who may have no real problem that they have ‘high amyloid’ and need treatment with anti-amyloid drugs. It just feels like cholesterol/statins all over again, but with even worse evidence of benefit and much greater evidence of harm.

It is also clear to me that the common belief that ‘if the science were good enough, we’d be doing prevention’ is an illusion to excuse inaction.

# Real prevention is being hijacked

Real prevention is being hijacked as a dressing to pave the way for drugs that don't work. Almost every week – this one as an example – I watched a Channel 5 documentary, 'Will You Get Dementia?',[327] which covered a few soft targets for prevention, mainly hearing loss, with some gadget that could help some, then ends with the story that 'a cure is around the corner'.

Then I read an article in the Telegraph by Professor Tim Spector headed 'My mother got dementia at 85. Here's what I eat to reduce my risk'.[328] On the face of it, it all sounded reasonable. Eat nuts, fish, plants, less sugar, and limit alcohol to 14 glasses a week.

In the plant section, he says, "Studies have shown a link between low levels of these fatty acids and dementia, which suggests that our diet and gut microbes play a role in developing the disease." I'm all for eating plants and a healthy diet, but this one study (not studies) referred to was 'looking at fecal microbiomes and fecal short-chain fatty acid composition (SCFAs) between wild-type and AD model mice at different ages'.[329] I've not even mentioned it in this book because there is nowhere near evidence of an association, an established mechanism or a cause for Alzheimer's. The science just isn't there yet regarding the microbiome in mice, let alone humans.

But then there's this throwaway line at the end – 'Stick to real food and don't be fooled by adverts for supplements as they haven't been shown to be effective'. Of course, this statement is utterly wrong. The chapters in Part 2 on omega-3, homocysteine-lowering B vitamins, vitamin D, and vitamin C make this abundantly clear.

Why do people who should know better make these completely unscientific statements? It could just be

ignorance, but I think it is also a medical/cultural pressure because it is supplements, not exercise or eating fruit and veg, that challenge the pharmaceutical model. Perhaps they want to stay ‘in’ with the cultural and media powerbase.

The BBC, as an example, is remarkably anti-supplement. Yet the reality is that the simplest and probably most effective way to reduce your risk is to supplement omega-3 and take a homocysteinelowering B vitamin supplement. I’d prefer people to also eat fish and wholefoods, and quit sugar, but that’s a bit harder for some than taking two supplements. And, as you saw, it is these two supplements that have already outperformed the anti-amyloid treatments.

Based on all the evidence in Part 2 the charts below shows the kind of risk reductions that could be achieved by acting on all the evidence available. Much like the Lancet Commissions’ calculations, it is based on both how much a risk factor, if eliminated, lessens risk for dementia or Alzheimer’s and also how many people have the risk factor. For example, if 50% of people are low in omega-3 fats and increasing their intake or blood levels would reduce risk by 20%, then the contribution of this factor to the overall risk for all is 10% (half of 20%). These kind of risk reductions are ballpark as there are so many variables, including the age range you select, the overlapping factors and so on.

The most comprehensive such meta-analysis to date, published in 2020, based on 396 studies, authored by Professor Jin-Tai Yu, is also shown below. Everything above the dotted line means more risk, while everything below the dotted line means less risk – and the further from the line the bigger is the impact. Those shown as a star * have the highest level of evidence. So, homocysteine, for example, is both a big risk factor and has the highest level of scientific evidence.

Unlike the Lancet Commission in 2024, it includes diet, vitamin C, homocysteine (B vitamins), sleep but does not include high LDL cholesterol, nor visual and hearing loss. The

evidence for these last two are more recent. I believe ‘high LDL cholesterol’ is more an indicator of both bad diet and low vitamin C. If so, lowering cholesterol with statins is unlikely to be helpful. Neither factor in omega-3 or seafood intake, nor the combined effect of both, and vitamin D.

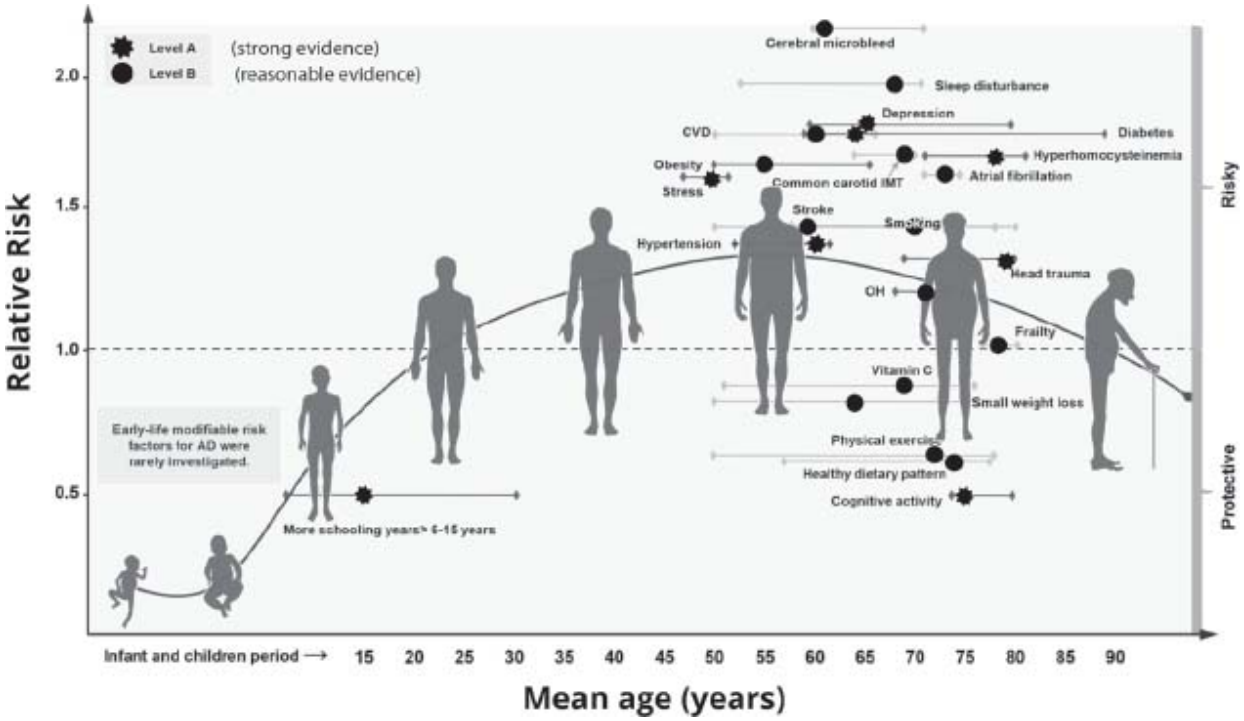



Figure 26 – Population Attributable Dementia Risk Reductions
*Used with permission of Professor Jin-Tai, Yu (J Neurol Neurosurg Psychiatry, 2020 vol. 91(11) pp. 1201-1209)*

The important point is that there is considerable agreement on the inclusion of most risk factors even if not always the % risk reduction that is achieved. The omissions largely relate to things that can be reduced by diet and supplements – B vitamins, vitamin C, D, omega-3, eating more marine food and much less sugar and refined foods. These omissions downplay the percentage risk reduction that can be achieved. The Lancet Commission has the lowest figure of 45% preventable. Professor Jin-Tai Yu’s team, analysing UK Biobank data, came up with up to 73% preventable[330] (but this excluded homocysteine as the UK Biobank never

measured it), while my ballpark figure suggests that most can reduce risk by over 90% if all risk factors are addressed. Obviously, 100% is achievable because most people never get Alzheimer's.

Now compare this to my ballpark estimates of the risk factors discussed in this book, most of which are largely under control. The chart shows you the kind of risk reduction you'd be likely to achieve if you had, and corrected, one of these risk factors. But not everyone has these risk factors. For example, not everyone smokes, drinks too much alcohol and is overweight. So, to work out the total contribution to a population's risk you have to take the prevalence into account (the first column). In this chart the approximate calculation, is that half of people don't achieve enough omega-3 from seafood or supplements, one in five have low vitamin D, a third have raised homocysteine in the brain shrinking zone (above 11mcmol/l) and a quarter drink too much and don't exercise enough.

To then work out the 'Population Attributable Risk' (the PAR in the chart) you multiply the two together. So, if correcting low omega-3 intake cuts your risk by 20%, and half of people have low omega-3, then the PAR is 10%. This means that, of the total risk of Alzheimer's (100%) 10% is driven by lack of omega-3 fats.

What about genes, you might wonder, or something like head injuries? If you take all these positive actions the current science suggests that it makes no difference if you have the ApoE4 or the MTHFR gene variant. Regarding head injuries - and strokes, for that matter - these events have already happened and can't be reversed (though there are steps you can take to support recovery). For that reason, I've chosen to focus only on the factors that are under your control.

| Prevalence | RISK as % out of 100 (PAR) | Positive Action | Impact on You (% risk reduction) |
|---|---|---|---|
| 50% | Low omega-3 index <5% 10% | Optimise omega-3 index to 8% | 20% |
| 25% | Low vitamin D <50nmol/l 5% | Vitamin D/sun exposure to 75nmol/l | 20% |
| 49% | Low eggs/choline 5% | Eating eggs/seafood for choline >400mg | 10% |
| 33% | High homocysteine >11µmol/l 13% | Homocysteine/B vitamins - below 10mcmol/l | 40% |
| 40% | High carb/sugar/HbA1c >6% 8% | Eat low carbs/ GL/prevent diabetes | 20% |
| 13% | Overweight/low muscle mass 3% | Healthy weight (high muscle/fat ratio) | 20% |
| 50% | Low fruit & veg/C & E 10% | Optimise antioxidants/veg & fruit/vitamin C | 20% |
| 25% | Excess alcohol >14 units 5% | Minimise alcohol | 20% |
| 10% | Smoking 2% | Don't smoke | 15% |
| 50% | Air pollution 3% | Minimise air pollution | 6% |
| 28% | Physical inactivity 6% | Active body | 22% |
| 15% | Inactive mind/social 3% | Active mind (not retiring early) | 22% |
| 30% | Hearing loss (untreated) 4% | Good hearing | 14% |
| 10% | Visual loss (untreated) 2% | Good vision | 20% |
| 15% | Bad sleep <7 hours 5% | Good sleep | 30% |
| 20% | High stress/depression 4% | Low stress | 22% |
| 20% | Menopausal (no natural HRT) 2% | Menopause | 10% |
| 15% | Poor gut health 3% | Healthy gut | 22% |
| 11% | Gum disease 3% | Healthy gums | 25% |
| 30% | Antacids 5% | Not on antacid (PPI) or metformin | 15% |

Figure 27 – Possible Population Attributable Dementia Risk Reductions (my estimates)

These numbers are obviously going to vary in different countries, and at different ages, so I've based it on the UK and people over 50. These calculations are estimates only, made by considering the existing evidence but not some perfect statistical calculation, as if that were even possible. However, the figures are unlikely to be far off of the truth and give a reasonable estimate of the kind of actions you can take to substantially reduce, if not eliminate your risk of developing Alzheimer's.

You might also wonder why, if you add up all the personal risk reductions you could achieve that it comes to well over 100%. This shows you that, even if you don't do everything it is theoretically possible to get to the point where you have no risk.

# We need a people-led Alzheimer's Prevention Revolution

Knowing that these actions can substantially, if not totally reduce your risk, our thinking is that instead of trying to influence the policymakers, who are heavily influenced by big pharma and big food, why not go straight to the people? We call this Citizen Science.

In the 40 years I've been in healthcare, I've seen very, very few of these critical prevention discoveries put into action despite the obvious benefits. Stopping smoking is perhaps the only one. Exercise is perhaps more popular. We are still eating sugar and processed foods, not eating fish, not supplementing vitamin D in the winter, and not taking

high doses of vitamin C upon viral infection. I've met so many brilliant, committed humanitarian scientists who are bitterly disappointed at how their research findings, which could have saved so many lives, have had close to no effect because health authorities haven't done the right thing.


It is time for Citizen Science - science and research done by people - funded by the people completing their Cognitive Function Test, further funded by those becoming FRIENDS of Foodforthebrain.org, who then share the results back to the public to educate and empower them to take the preventive steps necessary to virtually eliminate their risk of Alzheimer's. Also, all these preventive steps largely eliminate the risk for most other 21st century diseases, from obesity, diabetes, heart disease, arthritis and most cancers, putting nutrition right at the centre, as it should be.

The great news is that, in this digital age, we can do this. There need be no language or border that can stop us reaching people all over the world. This year alone, the Cognitive Function Test is now translated into Chinese, Japanese, Arabic, Portuguese, Spanish, German, French, and Polish with ambassadors in Australia, New Zealand, Canada, Brazil, India, Algeria, Kenya, Japan and China. The word is starting to spread very fast.

Let’s imagine you do the test and then contact all your friends over 40 to take the test. If two of them do and one of them then contacts all their friends over 40 and two of them do it. Now the number who take the test grows exponentially.

# The COGNITION Biobank will become the biggest research database for dementia prevention

To do ‘big research’ and understand what diet and lifestyle behaviours are really driving dementia, you need lots of data. Consider the analogy of driverless cars. Millions of dollars were spent employing hundreds of programmers struggling to create complex ‘rules’ about how a car should drive in every circumstance, factoring in other drivers, the weather, a pedestrian, a light changing to red. This is much like these statistical labyrinths of ‘systematic reviews’ like the Lancet Commission. But there are just too many variables and unusual circumstances and it all gets way too complex to end up making sense, because things get left out and interactions get ignored.

Then, along comes artificial intelligence. With advances in AI, it was discovered that you don’t need any ‘rules’ at all - you just need data of over 1 million drivers and what they do. Tesla happened to have this data and uses it to drive driverless cabs in California.

It can even prioritise data from 5-star Uber drivers, so driverless cars do, in effect, what a 5-star Uber driver would do in any circumstance. The more data, the better they drive.

What is the equivalent of a 5-star Uber brain? In other words, what is it that people whose cognitive function is excellent - and doesn't decline with age - do differently to you? I expect that foodforthebrain.org will have that amount of data within 2 years. The more people who do the Cognitive Function Test, complete the COGNITION questionnaire, and take the DRIfT blood test, the more we learn.

You don't even need a 'control' group because there will always be people who don't do something – they don't change their diet, don't eat fish, don't supplement, don't stop smoking, don't exercise for example – they are the 'controls'.

I believe this approach will make us less dependent on all these incredibly complicated 'systematic reviews and meta-analyses', with dozens of experts and incomprehensible statistics, – like the Lancet Commission – that not only ignored, but wouldn't even entertain, a scientific discourse relating to literally every one of the hard hitting diet-related risk factors, and even downgraded diabetes to contributing a mere 2% to dementia risk, when other equally prestigious groups calculated it to contribute ten times as much.

Does anyone truly believe what you put in your mouth has no effect at all on dementia risk, when your brain is literally made from food? If I search in the National Library of Medicine for 'nutrition' + 'dementia' there are just under 7,000 peer reviewed studies. The excuse that 'there isn't enough evidence,' just doesn't wash.

Even the best and biggest multi-factorial and global trial, like the FINGER study[331] which has 30,000 participants, struggles with all those confounding variables and interactions between risk factors. But this is an impressive number – a mammoth undertaking - and we look forward to learning from this research.

I am saddened, however, that homocysteine was dropped from the FINGER study panel of biomarkers, seemingly

around the time the Drug Discovery Foundation took over its funding, which is itself substantially funded by big pharma, who invest to then get a return on their investment when a drug gets to market. It is not unreasonable to think that the best way to eliminate the best competitor, homocysteine-lowering B vitamins, is to just stop testing it.
Encouraging people to do more exercise, not smoke, and be more socially active doesn't threaten drug sales, but an inexpensive B vitamin and omega-3 supplement that has three times the clinical effect and virtually stops accelerated brain shrinkage, with no adverse effects, most certainly does.

The key point is we have the ability right now to get the anonymised research data of several million people. Not from buy-in by a government or needing a great big grant with 'conditions attached', but simply by people telling people to do the free on-line Cognitive Function Test. From all these people, we want to find out what makes for a 5-star super brain with great cognitive abilities that doesn't decrease with age. Then, we can encourage you to do what they are doing. This is Citizen Science under all our collective control, not controlled by vested corporate interests.

Currently, the biggest databases for research are the UK Biobank, with 500,000 people, and the US NHANES, which tests about 5,000 people a year and has tested about 70,000 people over the past 16 years.

The COGNITION Biobank will soon be bigger and, unlike the UK Biobank, will keep testing people's cognitive function over time. You will be reminded to redo the Cognitive Function Test in six months so we can track your progress as you make changes – or don't. And we will encourage you to make those changes and also track your blood levels of biomarkers. The beauty of this approach is not just the vast amount of anonymised data which researchers all over the world can access to dive deep into so many areas of prevention, but also that it is effectively owned by the

people. Foodforthebrain.org is and always will be 100% charitable. There is no 'investment' option whereby rich people buy shares to make a fortune when the company gets sold. This creates a motive towards greed. It is inevitable.

What's stopping us from collectively changing the whole paradigm? Effectively, nothing. The ability to do this at speed is dependent on funds. If you want this revolution to happen faster become a FRIEND of the charity, or even better, a BEST FRIEND (*see Resources*), which means you get the DRIfT test and the Upgrade Your Brain cookapp and join COGNITION, which personalises your prevention plan with full support forever if you rejoin every year.

We hope and pray for a decent donation from a generous person who would like their money to help change the paradigm so we can accelerate this global movement and end this epidemic of Alzheimer's sooner. Some have even lent us money with no interest so we can shift up a gear. All have been repaid. If you'd like to find out more about making a donation of time, expertise, or money, email donations@foodforthebrain.org.

The cost savings for all of us and our economies are enormous. Our experts estimate that the actions in this book, even if only one in three participate, and those who do just change a couple of key behaviours, can reasonably result in a 30% reduction in the number of people developing dementia in any given year.

Associate Professor and health economist Apostolos Tsiachristas at the University of Oxford costed possible savings that would happen if doctors simply tested homocysteine in those over 60 and prescribed inexpensive B vitamins. '[This] is predicted to be a highly cost-effective policy that could save costs to the UK economy of approximately £60 million per year,' he said. It was also estimated it would additionally promote healthy longevity as well, adding 14 years to life expectancy.[332] That is just one prevention step. There are so many more.

The total cost saving of preventing 30% of dementia in the UK is estimated at over £13 billion and £600 billion a year globally.

Every person we can help, who doesn't get dementia, saves the state and their family £50,000 a year (rising to £80,000 when the condition becomes severe[333]), in addition to the terrible angst and difficulties faced by both the family and the individual. Isn't this worth shooting for?

# China leads the way in prevention

China is facing a 1 trillion dollar annual cost of dementia if nothing changes. This is a problem they have to solve. President of the China National Health Association, Wu YingPing, believes it is the combination of both diet, nutritional supplementation, and lifestyle that can impact dementia prevention in the 'silver-haired' community. "It is education, rather than medication, that we need and foodforthebrain's global campaign is something we fully support to help achieve this."

She is part of a group we have formed, together with the former Vice Minister of Health, Zhang Fenglou, and Minister of Health, Gao Qiang. "We must popularise prevention," he says. "With 300 million people over 60, this has to be our focus. Foodforthebrain's initiative is the way forward. It is something everyone can do right now for themselves."

**Patrick Holford with former Minister of Health, Zhang Fenglou** (to the left), **President of the China National Health Association, Wu YingPing and former Vice Minister of Health, Gao Qiang** (to the right)

We are planning to test up to 18 million people over 60 this year. If China can do it, why can't we? The reality is that every country in the world can get involved. All it takes is one enthusiast, as country representative, and about £5,000 for everything we are doing to be available in a different country and language.

But it all starts with you taking the Cognitive Function Test and then sharing it with others.

Alzheimer's may be the end stage of brain degeneration, but for many, that journey started in a sub-optimal maternal environment during pregnancy. Lack of the very same nutrients – omega-3, B vitamins, antioxidants, and too much

sugar – increases the risk of a child developing autism and ADHD. I discuss this in my book *Upgrade Your Brain*, *Optimum Nutrition for Your Child* and the cookbook *Smart Food for Smart Kids* (*see Recommended Reading*).

Children and teens, via their parents, are encouraged to complete the same Cognitive Function Test, plus the kids and teens version of the COGNITION questionnaire and another online test called the Strengths and Difficulties Questionnaire (SDQ).

In just the same way that you are shown your future risk and what is driving it, children and teens can also find out what steps they can take to reduce future risk of cognitive decline, which, on average, is declining with each year of life, and 'upgrade' their brains. The chart on page 46 (Figure 10) shows the average cognitive function score with age, with most hitting the danger zone in their 80's. But reduction in cognitive function starts from, at least, the age of 18. My belief is that it doesn't have to.

These children are our future, and with IQ levels falling and brain size reducing, our loss of mental health is becoming a major issue for the survival of our species, which depends on intelligence, cooperation, and healthy socialisation.

We hope to push that line up a few degrees as occurs in those who score in the 'green' for their Dementia Risk Index, just by making a few simple diet, supplement, and lifestyle steps in the right direction. These people in the green zone can reasonably be expected not to hit that cognitive danger zone before the age of 120, in other words, before they die.

We will all die; that is a fact. But none of us needs to die without our memories intact. Already, we are seeing that even those with the very rare early onset Alzheimer's genes, APP or Presenilin, decline much more slowly by taking these same Alzheimer's prevention steps.

It is time we took prevention seriously and woke up to the fact that not only is there no drug treatment, it is very

unlikely there ever will be one because there is no one cause – no one enzyme to block, no magic pill or injection or cure. Prevention is the cure for Alzheimer's – and you can get started right now.

Wishing you the best of health and happiness,

Patrick Holford
Founder of the Food for the Brain Foundation
Chair of the Scientific Advisory Board

# Recommended Reading


Dale Bredesen *The End of Alzheimer's,* also *End of Alzheimer's Program*, and *The Ageless Brain*, Penguin

Michael Crawford and David Marsh, *The Shrinking Brain*, Filament Publishing

Jill Crista, *Breaking the Mold*, Wellness Ink Publishing

Dr Marion Gluck, *It's Not Your Head It's Your Hormones*, Orion

Karl Herrup *How NOT to study a disease – The Story of Alzheimer's*, MIT Press

Patrick Holford, *Upgrade Your Brain*, Thorsons

Patrick Holford and Susannah Lawson, *The Stress Cure*, Piatkus

Patrick Holford, *Say No to Heart Disease*, Piatkus

Patrick Holford, *Say No to Diabetes*, Piatkus

Patrick Holford, *Optimum Nutrition for Your Child*, Piatkus

Patrick Holford, *Smart Food for Smart Kids*, Piatkus

Dr Malcolm Kendrick, *The Clot Thickens*, Columbus Publishing

Dr Louise Newson, *The Definitive Guide to the Perimenopause and Menopause*, Yellow Kite

Charles Piller Doctored: *Fraud, Arrogance, and Tragedy in the Quest to Cure Alzheimer's*, Simon and Schuster

# Resources

## Educational and health resources

### *Alliance for Natural Health International (ANH)*

The Alliance for Natural Health (ANH) International is a nonprofit organization founded in 2002 with a mission to safeguard and promote natural and sustainable approaches to regenerating and managing human health worldwide. They support approaches to health and self-care that work with, rather than against, nature, using the tools of ‘good science’ and ‘good law’. Through campaigns, actions, research and education, they have inspired and helped thousands of people, doctors, other practitioners and companies in the natural health sector to practise, access or adopt natural, diverse and sustainable approaches to managing human health, with due respect to our planet and its natural resources, on which we depend.

Their website, anhinternational.org, has an extensive repository of helpful information.

### *Alzheimer’s Prevention Expert Group (APEG)*

Alzheimer’s Prevention Expert Group (APEG) is a voluntary group of scientists, all experts in an aspect relating to the

prevention of cognitive decline.
See foodforthebrain.org/apeg

## *Alzheimer's Prevention Day*

World Alzheimer's Prevention Day, launched in 2024 by the APEG, exists to raise awareness of the importance of diet and lifestyle for the prevention of cognitive decline around the world. It includes a 30 question Alzheimer's Prevention Check, and 3 minute films from experts around the world of simple steps to take to reduce risk.
For more information see alzheimersprevention.info

## *Holford's Health Check (free)*

You can have your own personal health and nutrition assessment online using Patrick Holford's free Health Check. This provides you with a personalized assessment of your current health, and what you most need to change, including a metabolic check to gauge your risk of metabolic syndrome, and a BioAge Check.
Visit patrickholford.com and get your FREE Health Check.

## *Holford Health Club*

When you join the Holford Health Club, you'll receive a comprehensive health report after completing the 'Health Check' and unlimited access to address and support your needs as your health improves. You can also choose a free Patrick Holford-authored book from a choice of six when joining, Patrick Holford's regular health reports, plus instant access to all past reports online on important health issues; also get your personal health questions answered by Patrick Holford in the Holford Health Club members Facebook group; plus 20% off most seminars, webinars and events; up

to 30% off all books and supplements from Holfordnutrition.com

## *Brain Bio Centre*

The Brain Bio Centre is a resource to connect you with practitioners using the approach in this book. The Centre represents a collective of nutrition and mental health specialists working with individuals of all ages with a wide range of behavioural and mental health issues. Our registered nutritional therapy practitioners and psychiatrists are experienced in this area of nutrition and provide personalized nutrition and lifestyle recommendations tailored to your specific mental health needs.

Visit foodforthebrain.org/the-brain-bio-centre/

## *British Association for Nutrition and Lifestyle Medicine (BANT)*

The British Association for Nutrition and Lifestyle Medicine is the professional body of qualified nutritional therapists. You can search for a therapist by area and see their specialisms, should you need support with your health issues.

See bant.org.uk

In Ireland, see the Nutritional Therapists of Ireland at ntoi.ie

## *COGNITION®*

COGNITION is Food for the Brain's personalized, interactive brain-upgrade programme to help everyone dementia-proof their diet and lifestyle, based on the recommendations of our expert Scientific Advisory Board (foodforthebrain.org/sab). It guides you, step by step, with

interactive support, giving you the means to lower your Dementia Risk Index closer to zero, our goal being to get you under 10 % (in the green) within six months. How? You'll start receiving doable instructions, simple exercises and encouragements and reminders to make gradual changes to your diet and lifestyle, with supportive 'engagements', including access to free apps and an online forum where you can interact and learn from others and share what works for you. You'll have your own library of health-enhancing resources and can choose to receive text or email reminders, as well as being able to join our Facebook group and attend Zoom coaching sessions to help you achieve your goals. You'll have your own COGNITION Dashboard tracking exactly how you're doing as you move towards your goal of dementia-proofing your diet and lifestyle.

Visit foodforthebrain.org and take the Cognitive Function Test first to access COGNITION.

## *COGNITION for Smart Kids and Smart Teens*

This is Food for the Brain's personalized, interactive brain-upgrade programme for parents to assess and guide their children's habits for optimal mental health, happiness and emotional balance. From the age of 12, the 'teen' completes their own assessment and receives their own guidance.

See foodforthebrain.org/smartkids

## *Cognitive Function Test*

The Cognitive Function Test is the first-ever free, validated, digital version of what gets measured in memory clinics, tried and tested by over 450,000 people, available in several languages and smartphone friendly. It takes about 15 minutes to complete but must be done without interruptions. It is followed by the COGNITION questionnaire about your nutrition, lifestyle and medical history, which then assesses your Dementia Risk Index and lets you know exactly what's driving your future risk.

Visit foodforthebrain.org and, for China, foodforthebrain.cn and, for Japan, foodforthebrain.jp

The Cognitive Function Test is also available for researchers to use in a smartphone friendly version and in several languages.

Visit cognitivefunctiontest.info or email research@foodforthebrain.org.

# *Food for the Brain Foundation*

The Food for the Brain Foundation is a non-profit educational charity, founded by Patrick Holford, which aims to promote awareness of the link between learning, behaviour, mental health and nutrition; and to educate and provide educational material to children, parents, teachers, schools, the public, the catering industry, health professionals and the government. The website has a free Cognitive Function Test. It takes 15 minutes to complete. Depending on your score, it tells you what to do to improve your memory. The charity, and its work helping people prevent dementia, is funded by people becoming FRIENDS of the charity (donating monthly or annually). As a FRIEND, you have access to all educational information and receive regular updates.

For more information visit foodforthebrain.org

# *GrassrootsHealth*

GrassrootsHealth is a non-profit public health research organization founded in 2007, dedicated to promoting optimal health worldwide through research, education and advocacy, with a primary focus on the role of vitamin D. Through evidence-based nutrient education, resources and their citizen-science approach to research, they empower individuals to make informed decisions about their health, including mental health, and healthcare providers to move research into practice.

With a panel of 48 senior vitamin D researchers from around the world contributing to its operations, GrassrootsHealth has been running the world's largest public health intervention study – the D*action field trial – to solve the vitamin D deficiency epidemic worldwide. Participation involves measuring vitamin D (and other nutrient) levels from home, completing health surveys that include supplementation data, calculating how much supplementation might be needed to reach a target nutrient level, and retesting to determine if the target level has been achieved.

Learn more at grassrootshealth.net or daction.org

# *Institute for Optimum Nutrition (ION)*

The Institute for Optimum Nutrition, founded by Patrick Holford, offers both full and part-time degrees in nutritional therapy for those starting their nutrition journey. For medics, allied healthcare and CAM practitioners, ION offers a Graduate Diploma Integrative Functional Nutrition. Courses

are university validated. Additionally, ION offers a range of CPD and validated short courses.

Visit ion.ac.uk or visit them at Ambassador House, Paradise Rd, Richmond, TW9 1SQ 2JY, UK. Tel: +44 (0)20 8614 7800.

## *Institute of Functional Medicine (IFM)*

As the leading voice for functional medicine for more than 30 years, IFM is advancing the transformation of healthcare for patients and practitioners worldwide. It supports the confident and competent practice of functional medicine through high-quality education and certification programmes; partnerships across medical disciplines; and advocating on behalf of functional medicine clinicians and patients around the globe. IFM is a 501(c)(3) non-profit organization, and the only organization providing functional medicine certification along with educational programmes directly accredited by the Accreditation Council for Continuing Medical Education (ACCME), in line with the principles in this book.

For more information, or to find a functional medicine practitioner, please visit IFM.org

## *International Society for Orthomolecular Medicine (ISOM)*

The purpose of the International Society for Orthomolecular Medicine (ISOM) is to raise awareness and further the

advancement of orthomolecular medicine throughout the world by creating educational programmes and events for professionals and the general public; curating and providing information and resources related to orthomolecular medicine; and uniting existing and future orthomolecular groups and organizations. It is a registered charitable organization based in Canada.

For more information, visit isom.ca

# *MindHealth360*

MindHealth360's mission is to revolutionise mental healthcare for better patient outcomes. It aims to do this by providing a free, comprehensive, online source of information on mental health from an integrative/functional medicine perspective.

They advocate a 360° approach to mental health which takes into account the biochemical, psycho-spiritual, and lifestyle-behavioural factors which impact mental health. Check out their website and subscribe to their free newsletter.

Visit mindhealth360.com

# *Patrickholford.podbean*

Patrick Holford's highly informative podcasts with world-class experts in numerous aspects of health, including mental health.

To listen visit patrickholford.podbean

# *Pernicious Anaemia Society (PAS) and B12 Society*

PAS is an International Charity with the aim to provide an easy to understand explanation of Pernicious Anaemia to newly diagnosed patients. It quickly became obvious that there were serious issues with the way in which B12 deficiency in general, and Pernicious Anaemia in particular, is diagnosed and treated. For those concerned with B12 there's lots of really useful information on their website – pernicious-anaemia-society.org.

Also, visit the B12 Society to dig deep into the unfolding science relating to this essential brain-friendly vitamin.

Visit theb12society.com

# *Psychiatry Redefined*

Led by renowned integrative psychiatrist Dr James Greenblatt, Psychiatry Redefined provides the most comprehensive, scientific, practical, convenient and cost-effective training available in integrative and functional psychiatry. Their clinician-led online courses, fellowship programme, intensive programmes, and seminars and conferences will help you target and treat the root causes of mental illness, providing your patients with a greater chance of lasting recovery and wellness.

Learn more at PsychiatryRedefined.org

# *Upgrade Your Brain Cookapp*

Hundreds of recipes, completely in line with the principles of this book, are available in the Upgrade Your Brain Cookapp

that supports this book. The GL, antioxidant, brain-fat and B-vitamin status is given for each recipe, so you can build menus that support your brain health.

Available from foodforthebrain.org/UYBcookapp

# Measuring ketones and glucose

## *Keto-Mojo*

Keto-Mojo is an essential tool for measuring your level of ketosis and is widely recommended by researchers, hospitals, clinics, doctors and other healthcare professionals. The device measures your blood glucose and ketones with a single prick of your finger, and it comes with a free app that allows you to download all your readings onto your mobile phone so you can track unlimited results, view graphs and charts, and even share your data with your healthcare provider. The starter kit costs only £48 and you'll receive a 10 % discount (on meter kits only) when you use code FFB10 at checkout. Keto-Mojo will also make a donation to Food for the Brain Foundation to help with their research.

Visit keto-mojo.com

## *Ketoscan SMART*

This device measures breath ketones. You can use it as often as you like, and others can too. This pocket-sized ketone meter measures the concentration of ketonesin your exhaled breath, indicating when your body is burning fat and in ketosis. The KETOSCAN Smart has a removable pull

off, push on cartridge sensor meaning it does not need to be sent away for servicing. It’s the easiest to use and gives you readings on both the device and in an app, so you don’t need to link it to an app on your phone or computer, although that’s possible for keeping a record of your scores. It’s £179, but use this code to get £20 off – PH30.

Visit ketoscanmini.co.uk/product/ketoscan-smart/

# Natural hormone therapy

## *Bioidentical progesterone*

This is available as an over-the-counter cream in some countries, but in the UK it is only available on prescription as a licensed capsule, Utrogestan, in one fixed strength. There are, however, some advantages to transdermal application, such as a possible reduction in some of the unwanted side-effects, and transdermal creams can be prescribed by a practitioner and made by a compounding pharmacy.

## *The Marion Gluck Clinic*

One of the UK’s leading hormone clinics, whose doctors prescribe bioidentical hormones, and their academy also trains doctors in how to prescribe them.

Visit mariongluckclinic.com

## *Newson health*

Based on the work of Dr Louise Newson, Newson Health clinics specialise in helping women with menopausal and perimenopausal concerns.

Visit newsonhealth.co.uk Also see drlouisenewson.co.uk

## *Specialist Pharmacy*

Specialist Pharmacy compounds bioidentical progesterone and other hormones in various dosage forms, including transdermal creams, via a private prescription from a practitioner.

See specialist-pharmacy.com

## *Centre for Men's Health*

The Centre for Men's Health provides expert advice, diagnosis and treatment for men with Testosterone Deficiency Syndrome (Low T), erectile dysfunction (ED)/impotence, or prostate health concerns and health problems. Their team of doctors specializes in andrology, urology and men's sexual and general health. With 30 years' experience, the Centre for Men's Health clinics in London have helped thousands of men regain their well-being and vitality and return to a fulfilling sex life.

Visit centreformenshealth.co.uk

# Foods and food concentrates

## *CherryActive*

CherryActive is a deliciously healthy, low-GL cherry juice. It is sold in a highly concentrated format, so mix a 30ml (1fl oz) serving with 250ml (9fl oz) water. Each 946ml bottle contains the juice from over 3,000 cherries – that's half a tree's worth – and contains a month's supply. CherryActive is also available as a dried cherry snack and in capsules.

It's available in health-food shops and from active-edge.co.uk

## *Drop of Life olive oil*

This is a healthy extra virgin olive oil from a naturally evolved olive variety with an exceptionally high polyphenol level and with a low acidity. Thus, it can claim to help protect blood lipids (fat) from being oxidised.

Available from holfordnutrition.com

## *Get Up & Go with Carboslow*

This is a delicious breakfast shake combining wholefoods with vitamins, minerals, protein and super-soluble glucomannan fibre. (See page 141 for more about this.)

There is no need to take a multivitamin and mineral if you have Get Up & Go, since it provides optimal levels of all vitamins and minerals. Carboslow (glucomannan fibre) is also available on its own as a powder.

Available from holfordnutrition.com

# Stress management

# *HeartMath and the Inner Balance™ Coherence Plus*

This sensor and app are an innovative approach to improving wellness and performance through monitoring your heart rhythms and self-regulating your thoughts, feelings and physiology. The sensor clips onto your ear to monitor your heart rate variability (HRV) and enables you to practise HeartMath coherence techniques and bring yourself into a state of high stress resilience.

Use the code FFB10 to receive a 10% discount when buying from either the HeartMath UK store heartmath.co.uk or US store heartmath. org. HeartMath kindly make a donation to Food for the Brain to help their research.

Visit the above websites for resources, details of events, training, HeartMath Coaches and products.

# *Susannah Lawson*

Susannah Lawson, co-author of The Stress Cure, is a certified HeartMath trainer and practitioner, offering group training and one-to-one coaching. She is also a qualified nutritional therapist, kinesiologist and teacher/practitioner of subtle energy healing.

See susannah-lawson.co.uk for more details.

# *John Levine's Alpha Music – Silence of Peace*

Based on the centuries-old therapeutic use of specific musical scales and arrangements, the music of John Levine

helps you enter a more relaxed and peaceful state of mind. Silence of Peace is excellent for promoting a good night's sleep.

To download, visit silenceofmusic.com and use the code FFB. They will match your discount with a donation to the Food for the Brain Foundation.

# Tests

## *Adrenal stress test*

This test measures levels of the stress hormones cortisol and DHEA in saliva at periods throughout the day. This is available from Genova Diagnostics. Genova is a referral laboratory, so testing can be arranged only via a doctor, nutritional therapist or other registered healthcare professional.

Visit gdx.net

## *Dementia Risk Index functional (DRIfT) test*

This is a home-test pin-prick blood test for five tests: homocysteine for B-vitamin status; omega-3 and vitamin D for brain-fat status; HbA1c as a measure of blood sugar control; and glutathione index for antioxidant status.

It is available from foodforthebrain.org/tests/

# *Genetic testing*

Genetic polymorphisms can be tested through a buccal (mouth) swab. The Lifecode Gx APOE test examines genes involved in methylation, inflammation, toxicity and neuroprotection, including the APOE and MTHFR genes, which are risk factors for late onset Alzheimer's disease. Specialist, comprehensive panels including their comprehensive Methylation, Detoxification, Hormones and Metals and Minerals reports can be added on within 6 months of your initial test. Testing can be ordered directly from Lifecode Gx as a part of a package which includes support from a registered nutritional therapist, or arranged via a doctor, nutritional therapist or other registered healthcare professional. Available in the UK and internationally. Lifecode Gx offer a discount for packages purchased directly using code FFB and match your discount with a donation to Foodforthebrain.org to help progress research.

See lifecodegx.com

# *Glutathione Index (antioxidant status)*

Glutathione is the body's master antioxidant. When it is fully loaded, it's called 'reduced' (GSH), and once it is spent disarming oxidants, it is called 'oxidized' (GSSG). The glutathione index calculates the ratio between reduced and oxidized glutathione (GSH/GSSG) to give you an accurate measure of your antioxidant potential. It is the best way to check if you're eating enough antioxidants and polyphenols or need to increase your intake or supplement. It is part of the DRIfT 5-in-1 test and can be measured on its own.

Order from foodforthebrain.org/tests

# *HbA1c (long-term glucose measure)*

Haemoglobin A1c is a measure of how healthy average blood sugar levels have been in the past 3 months, and is a better representation of blood sugar health than a single glucose measurement, since glucose levels vary throughout the day. HbA1c is the compound formed in the blood when a haemoglobin molecule in a red blood cell binds with a glucose molecule in the blood; the resulting molecule is also known as glycated haemoglobin (sugar-coated or damaged red blood cells).

It can be a good indicator of glucose intolerance even in the absence of abnormal fasting glucose levels indicating the need to reduce your intake of sugar, carbohydrates and alcohol.

HbA1c is routinely tested by GPs and doctors to determine diabetes risk. A level above 6.5% (46 mmol/mol) is indicative of diabetes, while 6% (42 mmol/mol) is considered pre-diabetic. Optimal is below 5.4% (36 mmol/mol). It is part of foodforthebrain.org's DRIfT 5-in-1 test and can be measured on its own.

Order from foodforthebrain.org/tests

# *Homocysteine test*

Homocysteine can and should be measured through your GP but few GPs do this. Above 11 mcmol/l is associated with accelerated brain shrinkage; 7 mcmol/l or less is probably optimal.

Foodforthebrain.org have an accurate pin prick method to test this via a home test kit, available almost globally, except for China. It is part of their DRIfT 5-in-1 test.
Order from foodforthebrain.org/tests

# *Mineral analysis*

Your mineral levels can be measured by a hair tissue mineral analysis. This test is available from Mineral Check, or via a nutritional therapist, if you also want comprehensive interpretation.

Visit mineralcheck.com or call 01622 850 850.

# *Mould testing and home remediation services*

There are four steps: first test yourself, then detox yourself. Also, test your home then remediate to remove sources of mould. The lab Realtimelab.com test for people for mould toxicity in both the UK and US.

Pure Maintenance.com and ActionDry.co.uk both test homes and offer remediation. Buildingforensicsiaq.com tests and will offer solutions, but do not do remediation themselves.

In terms of detoxifying your body the key, ultimately, is to get your Glutathione Index in the healthy zone (above 700). Vitamin C, glutathione and/or NAC should help achieve this. Testing laboratories may advise you on detoxifying strategies. Ensuring your homocysteine level is low, ideally 7 or less, is also important as methylation is a critical detoxification pathway. Homocysteine and Glutathione Index are part of the 5-in-1 DRIfT test (*see above*).

# *Omega-3 test*

An omega-3 test measures EPA and DHA, the two very important omega-3 fatty acids that are found in fatty fish and other marine sources and are essential to our health.

The Omega-3 Index is a measure of the amount of EPA and DHA in red blood cell (RBC) membranes. The result is expressed as a percentage of total RBC fatty acids, and is a long-term and stable marker of omega-3 status. Experts recommend an Omega-3 Index of at least 8 % to minimise Alzheimer's risk.

This is available from foodforthebrain.org and is part of the DRIfT 5-in-1 test. Once you have your Omega-3 Index result, we will advise you what you need to eat and/or supplement to bring your score above 8%.

Order from foodforthebrain.org/tests

# *Vitamin D test*

A vitamin D test measures 25(OH)D3, the major circulating form of vitamin D in the blood and the commonly accepted measure of vitamin D status. Circulating 25(OH)D3 levels reflect endogenous production as well as vitamin supplementation. Optimal levels of 25(OH)D3 are certainly above 32ng/ml (80 nmol/l) and ideally over 40ng/ml (100nmol/l). It is part of the DRIfT 5-in-1 test and can be measured on its own.

Order from foodforthebrain.org/tests

# Brain Support Supplements

For each type of supplement (i.e., omega-3, homocysteine lowering formulas, etc) foodforthebrain.org have listed those products that fulfil the science-based criteria and where they are available. This is regularly updated.

Visit foodforthebrain.org/supplements

# *Holford supplements*

Patrick Holford has formulated a range of supplements to support optimal health, with a focus on brain health. The backbone of a supplement programme is an optimum multivitamin and mineral, with extra vitamin C and essential fats, both omega-3 and 6. These are provided in the Optimum Nutrition Pack.

If over 50, the enhanced version, the 100% Health Pack, provides extra antioxidants such as 'AGE Antioxidant' (*see below*) and 'Brain Food', a source of phospholipids.
Available from holfordnutrition.com and health food shops.

# *Antioxidant formulas*

A good all-round antioxidant complex should provide vitamin A (beta-carotene and/or retinol), vitamins C and E, zinc, selenium, glutathione or cysteine, anthocyanidins of berry extracts, lipoic acid and co-enzyme Q10 (CoQ10), ideally as ubiquinol, the active form of CoQ10.

Examples are Holford's 'AGE Antioxidant', Viridian's 'Antioxidant Formula' and Solgar's 'Advanced Antioxidant Nutrients'.

# *Brahmi*

Containing 300mg of Brahmi leaf, this is available from viridiannutrition.com and other suppliers.

## *Brain Food® Upgrade Pack*

This provides a daily strip of the three key building materials for braincell membranes. Includes ‘Connect’ – high-potency B12 plus other homocysteine-lowering B vitamins; ‘High Strength Omega-3’, which contains essential fats at potent levels (770mg EPA and 510mg DHA); and ‘Lecithin’, which contains one of the best natural sources of the phospholipid phosphatidyl choline, which is needed for brain health.

Available from holfordnutrition.com and health food shops.

## *CogniSave*

Regenerlife’s CogniSave is a comprehensive daily nutritional support system designed to support brain function. Each convenient five-inone supplement kit contains both phoshatidyl choline and serine, homocysteine support B vitamins, omega-3, and other supportive nutrients crucial for memory retention and overall brain health based on Patrick Holford’s research.

Available in the US and Canada. Visit regenerlife.ca/products/ cognisave-healthy-brain.

## *Chill Food*

‘Chill Food’ is a blend to calm and help sleep. It contains magnesium with amino acids, theanine, 5-HTP and GABA

precursors (glutamine and taurine), and hops. Take before bedtime. For a ‘reset’, it works well to have two in the evening.

Available from holfordnutrition.com and health food shops.

# Digestive Support

Includes probiotics, glutamine and digestive enzymes. Any decent digestive enzyme needs to contain enzymes to digest protein (protease), carbohydrate (amylase) and fat (lipase). Some also contain amyloglucosidase, which digests glucosides, found in certain beans and vegetables noted for their flatulent effects.

Try Solgar’s ‘Vegan Digestive Enzymes’ or Holford’s ‘DigestPro’, which contains both these enzymes, probiotics and glutamine.

Some people have low levels of betaine hydrochloride (stomach acid), a critical factor for B12 absorption. You can supplement this on its own, and if it helps digestion, this might be your problem. Try Biocare’s ‘Betaine plus HCl’.

# *Get Up & Go with Carboslow®*

A delicious breakfast shake combining wholefoods with vitamins, minerals, protein and super-soluble glucomannan fibre.

There is no need to take a multivitamin and mineral if you have Get Up & Go, since it provides optimal levels of all vitamins and minerals. It does not provide sufficient essential fats such as omega-3.

Available from holfordnutrition.com and health food shops.

# *Homocysteine support supplements*

These should include TMG, vitamin B6, riboflavin (vitamin B2), zinc, folic acid (ideally as MTHF) and vitamin B12, ideally as methylcobalamine. Options include Holford's 'Connect', Solgar's 'Gold Specifics Homocysteine Modulators' and Higher Nature's 'H Factors', Cytoplan's 'Methyl Factors' and Viridian's 'Homocysteine Support Complex'.

# *Ketofast®*

Ketofast is a pure form of C8 oil, the most effective MCT oil, together with carnitine, the critical co-factor in turning C8 into ketones. Each tablespoon provides 15ml of pure C8 derived from coconut oil, without any additives. Take up to 3 tablespoons max. (45ml). Each tablespoon also provides 166mg of carnitine. Each 450ml bottle provides 30 x 15ml servings, a month's supply.

Available from holfordnutrition.com and health food shops.

# *Lion's Mane and Reishi*

Pure organic concentrates are sold as Mico-Leo and MicoRei.

Available from hifasdaterra.com

# *Mood Food*

Supports the ‘feel-good factor’. Contains B vitamins, L-tyrosine and 5-HTP, TMG, zinc and chromium.

Available from holfordnutrition.com and health food shops.

## *Omega-3*

The most important omega-3 fats are DHA and EPA, the richest source being cod liver oil. The most important omega- 6 fat is GLA, the richest source being borage (also known as starflower) oil.

Try Holford’s ‘Essential Omegas’, which provides a highly concentrated mix of EPA, DHA and GLA, Holford’s ‘Omega-3 High Strength’ providing 500mg of DHA and 750mg of EPA. Viridian’s Rainbow Trout Oil and, for vegans, their Vegan DHA & EPA, are available in independent health food stores. Holford’s ‘Brain Food Upgrade’ provides 510mg of DHA and 750mg of EPA in two capsules.

Available from holfordnutrition.com and health food shops.

## *Phospholipids and phosphatidyl choline*

Holford’s ‘Brain Food’ provides eight nutrients, including key B vitamins such as B12, B3 and B5 (pantothenic acid), as well as folic acid and phospholipids, both phosphatidyl choline and phosphatidyl serine, to support the healthy functioning of the brain, with specific nutrients contributing to psychological function and normal mental performance (see holfordnutrition.com). Holford’s Brain Food Upgrade pack’ provides two capsules of high-phosphatidyl choline

lecithin, also available on its own as ‘High PC lecithin’. Lecithin and lecithin capsules, available in health food stores, also provide phosphatidyl choline.

Available from holfordnutrition.com and health food shops.

## *Vitamin D*

Vitamin D comes in two forms: D2 from plants and D3, mainly extracted from lanolin in the wool of sheep. D3 is more effective.

Many companies sell vitamin D products. Holford’s ‘Vegan D3’, derived from lichen, provides 3,000iu. Cytoplan have a vegan D3 product (2,500iu) derived from lichen. Viridian has a 2,000iu capsule and drops, available in independent health food shops. Other good brands include Nutrigold, Lamberts, Higher Nature and Natural Health Products.

# Index

**A**
AA. See arachidonic acid abstinence, 104, 127–28, 157
acetylcholine, 55
acid, 138
    arachidonic, 41, 49, 54, 165
    butyric, 135, 141
    linoleic, 49
    lipoic, 165
    methylmalonic, 73–74
Ackley, Sarah, 6, 30
Active, Cherry, 109
ADAS (Alzheimer's Disease
    Assessment Scale), 4
ADHD, 35, 40–41, 46, 179
adrenalin, 62, 128
air pollution, 26, 57, 98, 106–7, 132
Aisen, Paul, 82
alcohol, 15, 20, 23, 37, 97, 104, 127–28, 133, 148, 168, 172
almonds, 56, 114, 156–57
Alois Alzheimer, 16
Alzheimer, 8, 13, 102
    developing, 18, 20, 52, 87, 118, 129, 174
    preventing, 168
Alzheimer's disease, 2, 51, 56, 66, 68, 72–74, 77–78, 89, 97, 136, 138–40
Alzheimer's Disease Assessment
    Scale (ADAS), 4
Alzheimer's prevention, 14, 29, 34, 37, 45–47, 63–64, 69, 120, 146, 162, 180
Alzheimer's Prevention Day, 183
Alzheimer's Prevention Expert
    Group (APEG), 36, 92, 182–83
Alzheimer's Research UK (ARUK), 7, 67
Alzheimer's Society, 4, 7, 67, 70, 88
amino acids, 12, 16–17, 71, 127, 196
    toxic, 11, 62
amyloid plaques, 2–7, 9, 11, 13, 15–16, 19, 36, 80, 95, 97, 155
Amyloid Precursor Protein, 3, 17
Amyloid Probability Score (APS), 36–37
anaemia, 73
anti-amyloid drugs, 3, 5–6, 8, 19, 29–30, 35, 63, 67, 86, 131–32, 169–70

anti-depressant, 71, 114
antioxidants, 96, 106–16, 119–20, 126, 133, 140, 142, 149, 158, 160–61, 164–65, 179
anxiety, 26, 35, 41, 94, 113–14, 129–30, 140, 149, 151
APEG. *See* Alzheimer's Prevention Expert Group
ApoE4, 16–21, 23, 29, 36–37, 54, 58, 95, 172
Apostolos Tsiachristas, 88, 178
APS (Amyloid Probability Score), 36–37
arachidonic acid (AA), 41, 49, 54, 165
arthritis, 35, 96, 175
rheumatoid, 13
ARUK. *See* Alzheimer's Research UK
aspirin, 80–81
ATP, 93, 97, 99
Atrophic glossitis, 65
autism, 40–41, 46, 65, 113, 179
autophagy, 93, 104

**B**

B2, 23
B12
absorbing oral, 73
high dose, 77
insufficient, 70, 73–74
methyl, 23
B12 and folate, 20–21, 62, 71, 81, 83
B12 and folic acid, 85
bacteria, 135–38, 140
BDNF (brain-derived neurotrophic factor), 23, 133
beans, 56, 81, 90, 114, 158–59, 197
berries, 109, 115, 154, 156, 158, 161
Beydoun, May, 89, 118
biomarkers, 14, 32, 34, 44–45, 58, 73, 111–12, 176–77
Bipolar disorder, 65
Blackcurrants, 108
blood-brain-barrier, 64
blood glucose, 60, 94–95, 99, 188
blood pressure, 60, 93, 141
bloodstream, 18, 109–10, 138
blood sugar, 45, 92, 94–95, 113, 123, 139, 141, 148
blood tests, 10, 32, 34–35, 37, 99
amyloid, 8
Brahmi, 132–33
brain, 2–4, 13–14, 21–22, 35–37, 41–43, 48–50, 53–60, 91–101, 103–7, 109, 111–13, 117–19, 121–30, 132–33, 135–41, 153–56, 167, 179–81
brain atrophy, 66, 78, 80, 95
Brain Bio Centre, 183

brain cells, 2, 36, 98, 102, 111, 119, 130–31
brain damage, 53, 75–76
brain degeneration, 58, 137
brain-derived neurotrophic factor (BDNF), 23, 133
brain energy, 97, 100, 102
brain fats, 13, 41, 48–49, 51, 53, 55, 57, 59, 61
brain fog, 42, 92–94
brain function, 41, 102, 129, 133, 165
brain health, 43, 148, 157, 188
brain injury, 25, 131
brain pathology, 14, 25
brain recovery, 105, 126–27, 129, 131, 133
brain's blood supply, 58
brain scan, 2, 37, 76
  advanced, 63
brain shrinkage, 7, 63, 68, 72, 75–77, 79, 82, 84–85, 95, 99
  accelerated, 11, 70, 74, 81, 163, 177
brain shrinkage and cognitive decline, 68, 99
brain size, 41, 48, 76, 180
brain swelling, 4, 88
brain volume, 36–37, 53, 55, 122–23, 155, 167
Bredesen, Dale, 36, 131–32, 139, 181
Burne, Jerome, 69
B-vitamin intake, 21
B-vitamins
  complex, 37
  family, 78
  intake, 163
  and omega-3
  approach, 88
  status, 58, 85–87, 89, 106–7, 188, 192
  treatment, 84–85
B-Vitamins, Treatment Trialists
  Collaboration, 79

**C**

cacao, 103, 109, 159
caffeine, 128, 159
calcium, 156
cancer and dementia, 98
carbohydrates, 59, 95, 99, 104–5, 121, 141, 156
Cardiovascular diseases, 26, 64, 80, 86
cataracts, 119–20
causative genes, 17, 19, 22
CDR. See Clinical Dementia Rating
cells, 41, 110–11, 135
  fuelling, 100
  immune, 135–36

nerve, 137
repairs, xxii
Charles Piller, 3
cholesterol, 8, 11, 18–19, 24, 26, 48, 56, 58–59, 96, 137, 141, 169, 171
high cholesterol, 58–60
choline, 21–23, 26, 54–56, 61–62, 75, 91, 131, 157, 162, 164
circulation, 43, 109, 116, 157
Citizen Science, 32, 44, 174–75, 177
Clinical Dementia Rating (CDR), 4, 6, 30, 35, 63, 76, 86
coconut oil, 100–101, 104, 150, 158
coffee, 103
COGNITION diet and lifestyle questionnaire, 47
COGNITION Biobank, 146, 175, 177
COGNITION programme, 33, 151–53, 162, 168, 177
cognitive benefits of omega-3s and homocysteine, 51
cognitive decline, 27, 46–47, 66, 68, 74, 126, 128
Cognitive Function Test, 8, 15, 31, 33, 46–47, 141, 145, 147–50, 152, 168, 175–77, 179–80
cognitive impairment, 10, 22, 46, 65–66, 68, 71, 82, 129, 136–37
diagnose Mild, xxv
improved, 87
vascular, 65
cortisol, 128–30
COVID-19 infection, 136
Crawford, Michael, 41, 48, 125, 181
Crista, Jill, 140, 181
Cunnane, Stephen, 101

**D**

DALYs (Disability Adjusted Life Years), 40
dark chocolate, 108, 159
DASHBOARD showing cognitive function, 146
David Marsh's book, 48
DCD (diabetic cardiovascular disease), 86
Dementia Risk Index (DRI), 31, 33, 44, 47, 145, 151–53, 180
deposits, amyloid, 7, 36
depression, 26, 35, 41, 65, 113, 126, 129–30, 137, 164
DHA. *See* docosahexaenoic acid
diabetes, 13–14, 29, 35, 86, 92–99, 112, 119–20, 138, 175, 181
diabetes and dementia, 13, 86, 94, 100, 102, 119–20
diet
anti-inflammatory, 23, 142
dietary guidelines, 59
dietary intake, 44, 52–53, 55, 109
healthy, 97, 154, 163, 168, 170
high marine food, 48, 163
and lifestyle, 15, 20, 29, 39, 148
and supplements, 90, 172

Disability Adjusted Life Years (DALYs), 40
diseases, neurodegenerative, 51, 139
disorders, 99, 113, 129
DNA, 16, 75, 108
docosahexaenoic acid (DHA), 50, 52–54, 84, 86, 90, 125–26, 151, 164–65
Down's Syndrome, 17
DRI. *See* Dementia Risk Index DRIfT (Dementia Risk Index functional), 44
DRIfT blood test, 32–33, 45, 53, 57, 60–61, 81, 112, 145, 147, 149, 164–65, 176–77
drug trials, anti-amyloid, 5–6, 8, 35, 84
Durga, Jane, 78
Dyall, Simon, 50
dysfunction, 21
    cerebrovascular, 14, 71
    erectile, 64, 190
    metabolic, 94
    mitochondrial, 98

**E**
early-onset Alzheimer, 3, 17
Ede, Georgia, 105
eggs, 21, 33, 50, 55–56, 61, 74, 90–91, 131, 154, 156–57, 163–64
Einstein, Albert, 99
enzymes, 4, 10–11, 16, 21–22, 103, 111, 114, 180
EPA, 53, 90, 165
    combined, 164–65
exercise, 20–21, 26–27, 29, 37, 61, 122–23, 147–49, 152, 167, 172, 176–77
experts, leading Alzheimer's prevention, 66–69
eye, 119–20, 125

**F**
fats, 18, 37, 48, 53, 93–96, 100, 110, 122–23, 148, 161
    essential fats, 157, 162
    long-chain, 100
fatty acids, 37, 41–42, 49–52, 119, 170
    essential, 125, 163
fatty liver disease, 93, 99
fibre, 99, 104, 159, 162
FINGER study, 176
fish, 20–21, 33, 50, 55, 59, 90, 131, 154–56, 158, 170
flavanols, 108–9, 116, 157
flax, 61, 115, 156–57
floss, 142, 168
folate, 15, 20–21, 23, 33, 41–42, 62–63, 68, 71–74, 78, 80–81, 83, 90, 107, 113–15, 166
folic acid, 23, 70, 75, 77–78, 83, 85–86, 90
food
    processed, 155, 159, 174

protein-rich, 158
ultra-processed, 37, 93–94, 96, 104, 139, 155
Fortier, Melanie, 101
Fredrik Jernerén, 84
fructose, 42, 73, 92–94, 96–99, 102, 104, 139
fungus, Lion’s Mane, 28

**G**
G8, 8
GABA, 94, 127
Gao Qiang, 179
Garrard, Peter, 44, 67, 87–88
Geller Dementia Commission, 88
genes, 1, 3, 16–26, 54, 62, 71, 75, 172
gingipains, 137–38
gingivalis, 136, 140
GL. *See* glycemic load
glial cells, 41, 129
Gluck, Marion Dr, 181
glucomannan, 141
glucose, 13, 32–33, 41–42, 44, 92–94, 96, 99–102, 104, 123, 138, 141
glutathione, 12, 23, 32, 44, 72, 75, 106–15, 164–66
glycaemic load (GL), 20, 95, 109, 141, 156, 160, 162
Greenblatt, James, 188
grey matter volume, 155
GSH/GSSG, 112, 114
gum disease, 26, 136–38, 140
gut, 26, 99, 135, 139, 141, 170

**H**
Harris, William, 50
HbA1c, 44, 92, 94–95, 99–100, 113, 149
HDL (High-Density-Lipoprotein), 18, 60
head injuries, 14, 26, 172
healthy gut, 45, 135, 141–42, 162, 164
heart, 16, 150
heart attacks, 11, 15, 36, 80, 148
heart disease, 11, 35–36, 40, 59, 96, 98, 175, 181
Herrup, Karl, 9, 181
High-Density-Lipoprotein (HDL), 18, 60
high fructose corn syrup, 92, 94, 104
hippocampus, xix, 35–37, 109, 129–30
home test kit, 32, 44, 60, 81, 112
homocysteine, 11–14, 20–24, 32–33, 36–37, 44, 62–84, 86–87, 90, 96, 113–16, 163–64, 166, 171
Hybrid Diet, 104
hybrid latte, 103
hyperhomocysteinemia, 68

hypertension, 64, 96

**I**
IgG antibodies, 136, 139
immune system, 135, 138–40
improvement, cognitive, 36, 86
increased risk of ApoE4, 20
increased risk of cognitive
    impairment and dementia, 95, 129
index, body mass, 95, 122
infection, 13, 136–37, 164
    bacterial, 136, 138
    herpes HCMV, 140
    viral, 174
inflammation, 13, 19, 26, 42, 73, 78, 94, 120, 135–36, 138, 192
    increased, 140
    reducing, 56
insomnia, 35, 41, 126, 140
Institute for Optimum Nutrition (ION), 186
Institute of Functional Medicine (IFM), 186
insulin, 13, 62, 75, 94
insulin resistance, 13–14, 26, 42, 92, 94, 96–97, 101–2, 123, 138
intervention, 20, 29, 36–37, 57, 66–67, 69, 72, 80, 83, 119–20
    nutritional, 44
ION. *See* Institute for Optimum Nutrition
IQ, 40–41, 180
Isaacson, Richard, 36
Ismail, Zahinoor, 56

**J**
Jin-Tai Yu, 67, 69, 110, 171–72
Johnson, Richard, 92, 97
joining COGNITION, 147, 150

**K**
Kahn, Ronald, 94
Kendrick, Malcolm, 59, 181
ketogenic diet, 20, 42, 102, 104, 160
ketones, 42, 92–93, 100–102, 104
Kowalski, Konrad, 112

**L**
Lancet Commission, 25, 50–52, 57–59, 67–70, 88, 96, 98, 119–20, 122, 126, 171–72, 175–76
Lawson, Susannah, 127–28, 133, 168, 181
LDL (Low-Density-Lipoprotein), 18–19, 58–59, 171
lecanemab, 4–5, 19, 29
lecithin, 55, 61, 90, 131, 157, 166

Lee, Kate, 88
legumes, 154–55
Levine, John, 191
Levitin, Daniel, 121
life expectancy, 89, 178
lifestyle, 1, 15, 19–22, 31–34, 37, 39, 43–45, 148–49, 178
    factors, 31, 45, 117, 119, 121, 123
light, 22, 84, 119, 175
Lion's Mane, 28, 132–34
lipids, 18
liver, 71, 93–94, 99–100, 104
liver cirrhosis, 112
Livingston, Gill, 69
Low-Density-Lipoprotein (LDL), 18–19, 58–59, 171
lowering homocysteine, 11–12, 63–64, 69, 75, 77
low GL diet, 20, 104, 108, 139
LSD, 133
Lustig, Robert, 97, 102

**M**
magnesium, 114–16, 156, 164–65, 196
marine food, 42, 48, 50, 90, 172
Marsh, David, 181
matter
    grey, 55, 117, 127
    particulate, 106–7
    white, 53, 60, 65
McCaddon, Andrew, 67, 80
MCI. *See* mild cognitive impairment MCT oil, 100–101, 103
meat, 33, 49, 55, 74, 90, 97, 155, 158–59, 163
medial temporal lobe, 35, 50
Mediterranean diet, 20, 37, 155
medium chain triglycerides (MCTs), 100
melatonin, 126–27, 133
membranes, 41–42, 53–54
    neuronal, 41, 49, 53, 58, 62–63, 75, 131, 165
memory, 4, 21–22, 63, 72–73, 100–102, 109, 121, 128–30, 133–34, 149, 151, 185
    improved, 54, 87, 130
    loss, 3, 11, 76, 78, 84–85, 92, 94–95, 133, 138
menopause, 26, 28, 129–30, 134, 181, 189
mental health, 34, 40–41, 56, 113, 115, 133, 180
mercury, 107, 132, 157
metabolic syndrome, 60, 65, 96, 183
metabolism, 92, 98, 141
methionine, 68, 71, 113
methylation, 12–13, 15, 21–22, 41, 44, 62–63, 71–75, 85, 87, 107
methyl-folate, 72, 78, 90, 166

microbes, 135, 137, 139–41
mild cognitive impairment (MCI), 22, 35, 60, 76, 79–80, 82, 86–88, 126, 131–33
Miller, Joshua, 67, 80
mind, 105, 123–25, 134–35, 137, 139, 141, 152, 167
MIND diet, 155
minerals, 61, 141, 157, 163
mini-strokes, 75
mitochondria, 13, 93, 97, 102
    damaged, 93, 104
modifiable risk for Alzheimer's disease and dementia, 45
mould, 26, 139–40, 142
MTHFR, 17, 21–23, 113, 172
muscle, 16, 26, 37, 117, 122–23, 167
    twitches and tremor, 140
mushrooms, 28, 132, 156, 158
music, 43, 121–22, 167, 191
mycotoxins, 132, 139–40

**N**

NAC. See N-Acetyl-Cysteine
N-Acetyl-Cysteine (NAC), 72, 106–7, 109, 111–13, 115–16, 164, 166, 194, 210
natural hormone therapy, 130, 134, 189
natural selection, 18
nerves, 2, 117, 132
neural tube defects, 63, 65
neurodevelopmental impairment, 41
neuro-inflammation, 136, 139–40
neurons, 41–42, 58, 74, 93–94, 100, 102, 117, 126, 129
neuro-regeneration, 36, 131, 133
neurotransmitters, 16, 41, 55, 135
Newson, Louise, 181
nutrients, 23, 27, 42–43, 51, 107, 110, 162–63, 165–66, 179
    essential brain, 48, 56, 90
    supplemental, 20
nutrition, 11, 15, 31–32, 34, 37, 98, 175–76
nuts, 56, 61, 81, 90, 114–15, 154–59, 163, 170

**O**

oestradiol, 129–30
oily fish, 50, 52–53, 58, 60, 90, 156, 164
olive oil, 20, 100, 156, 158
omega-3, 25–26, 32–33, 48–55, 57–59, 61–63, 82–89, 96, 114–15, 120, 156–57, 164–65, 170–72
    DHA, 20, 41, 48–50, 60, 85–87, 90, 119, 125, 164, 210
DHA vegan, 60, 90, 157
    EPA, 53
    fats, 27, 42, 54, 120, 156, 170, 172
    low, 96, 172

marine, 51
non-DHA, 52
optimising, 96
in protecting memory, 87
omega-6, 42, 159, 165
AA, 119
optimum nutrition, 20, 22, 125, 179, 181
orthomolecular medicine, 20
osteoporosis, 65
oxidants, 13, 42, 106, 119
dangerous, 114
oxidation, 13, 41–42, 44, 75, 107, 125

**P**

PAHs (polycyclic aromatic hydrocarbons), 107
pain, 71, 79, 82, 113
Parkinson's disease, 35, 41, 63, 65
PC. *See* phosphatidyl choline periodontal disease, 65, 138
Perlmutter, David, 97
Pernicious Anaemia Society, 73, 187
P.gingivalis, 137–38
pharma, 7, 12–13, 30, 79, 83
phosphatidyl choline (PC), 48–50, 54–56, 61, 87, 90–91, 157, 166
phosphatidyl ethanolamine (PE), 54
phosphatidyl inositol (PI), 54
phosphatidyl serine (PS), 54, 91
phospholipids, 21–22, 41–42, 48–51, 53–55, 57, 61–62, 87, 90–91, 131, 157, 162, 166
and B12, 42
and omegas, 49
Phospholipids, and Vitamin D, 48
placebo-controlled trial, 22, 53, 72, 76, 127, 130
randomised, 29, 63, 98
plants, 42, 56, 108, 132, 170
plaques, 3–4, 36, 138
podcasts, 59, 124, 149, 167
pollution, 15, 27, 31, 43, 106–7, 110
and smoking, 107
polycyclic aromatic hydrocarbons (PAHs), 107
polyphenols, 42, 108–9, 128, 156
Population Attributable Risk (PAR), 66, 171–72
Porphyromonas gingivalis, 136–37
precursor, 62, 112–13, 165 5-HTP, 127
adrenalin, 62
glutathione, 112–13
N-Acetyl-Cysteine, 72, 112
prediabetes, 120
predictive genes, 17–18, 22

pregnancy, 63, 65, 179
presenilin, xix, 3, 17, 180
progesterone, 28, 129–30
proteins, 3, 16–18, 61, 113, 137, 156–58, 191, 197
    amyloid, 3, 17, 74, 93
    precursor, 17
    toxic, 10
Proust, Marcel, 121
p-tau, 2, 7–8, 10–13, 15, 25, 36, 74, 98, 140
    formation, 12
    treatment, 13
p-taum, inhibitor drugs, 11

**R**

radicals, free, 107, 112–13
raised homocysteine, 33, 63–64, 66, 68–70, 73, 75, 78–80, 82, 85, 89, 96, 172
    lack of B12, 80
red blood cell (RBC), 53, 94
red blood cells, sugar-damaged, 104, 108, 128, 133, 157, 159, 168
refined carbohydrates, 14, 97, 141
Refsum, Helga, 66, 75
Reishi, 132–33
relationship, gut/brain, 149
resistance training, 122
response, inflammatory, 65, 136, 140
retinol, 119, 195
riboflavin, 113, 197
Rutjes, Anne, 83

**S**

SAD diet, 19
S-adenosyl-methionine, 71
schizophrenia, 41, 65, 113
Schrag, Matthew, 3
Scientific Advisory Board, 2, 69, 101, 180
scientist, citizen, 34, 146
SDQ (Strengths and Difficulties Questionnaire), 180
seafood, 26, 31, 53, 69, 89–90, 142, 171–72
seeds, 56, 61, 81, 90, 114–15, 153, 155, 157–59
    flax, 141
    pumpkin, 114–15, 156
serotonin, 16, 133
Serum B12, 74, 163
shrinkage
    brain, 17, 35, 37, 48, 76–77, 82, 99, 130, 181
    declining cognition, 77
    reducing, 22
Singhrao, Sim, 138

skin, 16, 57, 106
SLE (Systemic lupus erythematosus), 65
sleep, 27–28, 31, 42–43, 45, 114, 125–28, 133, 148, 152, 171
  apnoea, 132
  extended, 127
  optimizing, 37
  and physical activity, 45
  and reducing stress, 28
Smart Kids & Teens, 179, 181, 184
SMASH, 60, 90
Smith, David, 2, 6, 12, 63–64, 66–67, 69, 75, 84
smoking, 15, 26, 29, 31, 43, 57, 73, 106–8, 118, 174
  and air pollution, 43, 57, 107
social interactions, 121
soluble fibres, 141
soya, 56, 158
Spector, Tim, 170
Spelling Bee, 151
Spencer, Jeremy, 109
spina bifida, 63
statins, 5, 8, 11, 59, 80–81, 171
  cholesterol-lowering, 58–59
stimulation
  brain and body, 121
  cognitive, 20
  mental, 151
  muscle, 122
  neuronal, 43
strawberries, 108, 115, 156
Strengths and Difficulties Questionnaire (SDQ), 180
strength training, 122, 167
stress
  anxiety, 149
  prolonged, 128–29
  reducing, 28, 37
  resilience, 133, 168
Sudoko, 124, 167
sugar, 14, 20, 42, 59, 73, 94–98, 104, 120–21, 142, 152, 154, 157–59, 168, 170, 172, 179
  avoiding, 37
  and carbs, 59, 121, 152
  consumption, 92
  corn, 98
  cravings, 92
  excess, 139–40
  and fructose, 92–94, 96
  glycaemic load, 92
  intake, 151, 159

and limiting fruit juices, 142
quit, 170
and refined foods, 172
regular cane, 139
sugars, refined carbohydrates, 14, 97–98
Super Greens Soup, 161
supplements, 33–35, 53, 56–58, 60–61, 72–73, 78, 81, 90, 107–8, 114–16, 148–50, 162–66, 170, 172
5-HTP, 127
for Alzheimer's Protection, 162
antioxidant, 110, 112
B12, 78
cacao extract, 109
fish oil, 52, 54
glutathione, 112, 116
high-strength DHA, 165
homocysteine lowering B vitamin, 74
magnesium, 114, 116
mineral, 83, 116
omega-3, 60, 90, 142, 164, 170
personalised, 34
vitamin B6, 81
vitamin D, 56
system
adrenal, 129
circulatory, 100, 138
drug regulation, 71
nervous, 129
systems-based science, 15, 28–29, 43
systems breakdown, xix, 25, 27, 29, 31, 33, 35, 37

**T**

TAI (tau accumulation-inhibitor), 12
tangles, 2
neurofibrillary, 2, 36, 74, 155
tau, 1, 10, 12–13, 36–37, 129
tau accumulation-inhibitor (TAI), 12
Tauist's delusion, 2–3, 5, 7, 9, 11–13, 15
tea, 154, 156, 159
black, 156
green, 156
teenagers, 40, 99, 180, 184
teeth, 136, 142, 168
brushing, 138
gum infections, 138
tooth decay, 11
Tessier-Lavigne, Marc, xxvii
test

amyloid, 8
cognitive, 53, 60
test kit, 5-in-1
DRIfT blood, 34, 44, 78
testosterone, 129–30
thalidomide, 64
TIA. *See* transient ischemic attack Tibetans' yak-butter tea, 103
time outdoors, 57
TMG, 71–72, 166
tofu, 158
toxins, 15, 107, 139–40
transient ischemic attack (TIA), 26, 71, 75
treatment
amyloid, 7
disease-modifying, 11
eye, 119
hormone, 130
invasive dental, 138
non-drug, xxi, xxvi
triglycerides, 60, 96, 137, 141
medium chain, 100, 104
tri-methyl glycine, 71
Turknett, Josh, 28

**U**

UK Biobank, 52, 127, 172, 177
ultraprocessed foods (UPFs), 97
Upgrade Your Brain cookapp, 61, 81, 91, 104–5, 115, 146, 160, 162, 177, 188
US Food and Drug Administration, 31
US National Institutes of Health, 14, 69, 89, 118
UV exposure, 56–58

**V**

Vauzour, David, 135
vegans, 53, 60, 157, 164, 166
vegetables, 15, 59, 96, 108–9, 114, 154–56, 158–59, 197
antioxidants, xxiii
high intake of, 20, 42, 155–56, 158
raw, 141
root, 158
vegetarian, 147–48
viruses, 135, 164
herpes, 139
vision, 43, 84, 98, 119–21
loss, 26, 119, 121
vitamin, deficiency, 69
vitamin B. See folate
vitamin B2, 71, 115, 166

vitamin B6, 15, 62, 72, 81, 113, 166
vitamin B12, 41, 56, 68, 71, 73, 77–78, 83, 87, 163, 197
vitamin C, 109–10, 142
vitamin D, 20, 48
vitamins
  and antioxidants, 96, 149
  low, 33, 56, 171–72
  oxidised, 110
  phospholipids, 166
  supplementing, 61, 83, 107, 116, 131, 141, 163–64, 174
volume
  grey-matter, 54
  hippocampal, 155

**W**
walnut loaf, 161
walnuts, 61, 115, 156–57
water, 14, 110–11, 121, 125, 141, 158, 190
watercress soup, 161
waterside ape, 48
weight, 104, 122–23, 150, 155, 160
  weight loss, 141
    Ozempic, 103
wheat, 158–59
white matter
  lesions, 53, 65
  volume, 155
wholefoods, 158, 170
wine, 104, 127–28, 155, 157
Witte, Veronica, 54
women, 20, 28, 70, 106–7, 129–30
  post-menopausal, 129
Wood, Tommy, 15, 28, 50, 118
Wordle, 124, 151, 167
World Alzheimer's Prevention Day, 183
World Dementia Council, 70
Worldle, 167
Wu YingPing, 178–79

**Y**
yoga, 122–23, 148, 167

**Z**
Zhang Fenglou, 179
zinc, 23, 71–73, 147, 165–66

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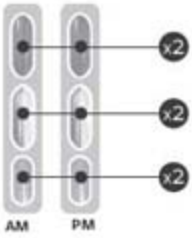


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