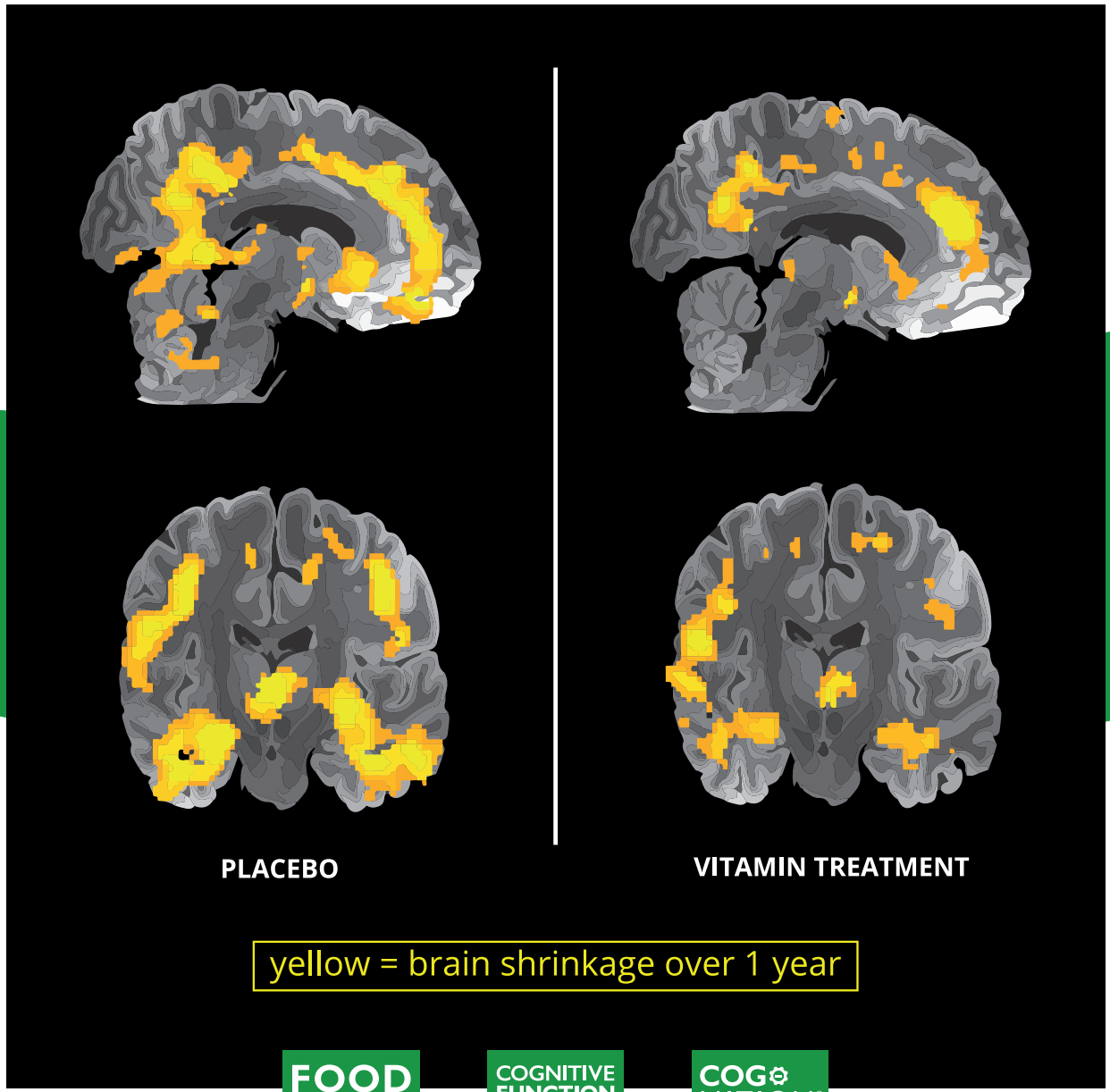
Alzheimer's is PREVENTABLE

A MANIFESTO FOR **CHANGE**



FOOD FOR THE BRAIN FOUNDATION

COGNITIVE FUNCTION TEST
FOOD FOR THE BRAIN

COGNITION®
UPGRADE YOUR BRAIN

1% OF ALZHEIMER'S IS 'IN THE GENES'

IDENTIFY YOUR RISK

PROTECT YOUR BRAIN

FOOD FOR THE BRAIN FOUNDATION

Food for the Brain Foundation

We are a not-for-profit charity wishing to create a future where the importance of nutrition in optimising mental wellbeing and brain health, as a means of both prevention and treatment, is understood by all and implemented by many.

SCIENTIFIC ADVISORY BOARD

Our advisors are a world class team of leading scientists who are committed to reducing mental illness, including Alzheimer's disease risk.

Professor Emeritus David Smith
University of Oxford and former Deputy Head of the Faculty of Medical Science.

Professor Jin-Tai Yu
Vice Director of the Institute of Neurology, Fudan University, Shanghai, China.

Professor Peter Garrard
Director of the dementia research group in the St George's, University of London Neuroscience Research Section (Molecular and Clinical Sciences Research Institute), specialising in dementia and cognitive disorders.

Professor Julia Rucklidge
Director of the Mental Health and Nutrition Research Lab, University of Canterbury, New Zealand, specialising in children's mental health and nutrition.

Professor Emeritus Robert Lustig
Division of Endocrinology, University of California and Member of the Institute for Health Policy Studies at the University of California, San Francisco.

Professor Jeremy Spencer
Professor of Nutritional Biochemistry and Medicine at the University of Reading.

Dr Celeste De Jager Loots
Expert in neuropsychological assessment and development & validation of cognitive tests.

Dr Kristina Curtis
Expert in Digital Behaviour Change Interventions that promote effective engagement.

Dr Tommy Wood
Assistant Professor of Pediatrics and Neuroscience at the University of Washington, Seattle.

Dr Simon Dyall
Clinical Neuroscience programme lead at the University of Roehampton and a Director of the International Society for the Study of Fatty Acids and Lipids.

Dr David Vauzour
Senior Research Fellow and Principal Investigator at Norwich Medical School, University of East Anglia, UK specialising in diet, gut health and the brain.

Dr Phuong Leung
Founder of individual Cognitive Stimulation Therapy (iCST) Dementia Education Training and is a research fellow at UCL.

Dr William Grant
Expert in the the role of solar UVB exposure and vitamin D in reducing the risk of disease, including dementia.

Patrick Holford
Founder of the charity, a psychologist, turned nutritionist and retired visiting professor, specialising in nutrition and mental health, author of 46 books and is in the Orthomolecular Medicine Hall of Fame. In 1984 he founded the Institute for Optimum Nutrition. He is the Chair of the Scientific Advisory Board.

"Alzheimer's is not an inevitable consequence of ageing, nor is it all 'in the genes'. It is largely a preventable disease and we know quite a lot about what people need to do to help prevent it. Simple diet and lifestyle changes, made achievable in Food for the Brain's COGNITION programme, could cut the risk of developing this terrible and avoidable disease by at least a third."

Professor David Smith, Emeritus Professor of Pharmacology

Founding Director, Oxford Project to Investigate Memory and Ageing (OPTIMA), University of Oxford

Prevention is the only way forward, and we can make it happen

Half of the risk for developing dementia and Alzheimer's is preventable. Only 1 in 100 cases are caused by genes. Most of this risk relates to nutrition and lifestyle factors which we can change. Given that Alzheimer's is not a reversible condition, the best hope is prevention and targeting those at risk, from age 50 or younger, and encouraging positive diet and lifestyle changes in the areas shown to impact cognitive function. We offer, and are testing the effects of, an e-based educational strategy for supporting those positive diet and lifestyle changes to help deliver a **viable model for effective action on Alzheimer's dementia prevention which could be applied nationally and globally.**

We estimate that a targeted prevention approach will prevent a third of dementia, saving lives, suffering and £billions of healthcare costs. This manifesto explains what you can do to dementia proof yourself and how you can help reach others.

The Situation

Each day in the UK alone around 800 older people are diagnosed with dementia.[1] As a conservative estimate about twice as many develop Mild Cognitive Impairment (MCI), the precursor to dementia.[2] The most common form of dementia is Alzheimer's disease (AD), accounting for two in three dementia cases. It is irreversible and develops slowly over many years. About 80% of dementia cases are attributed to Alzheimer's and vascular dementia, which share common risk factors. Many of these people will be referred to NHS memory clinics, but after a diagnosis of MCI has been made there is nothing presently that can be done to help them often leaving those affected feeling hopeless.

There are 790 Dementia Diagnoses per day in the UK

the equivalent of 7 double decker buses

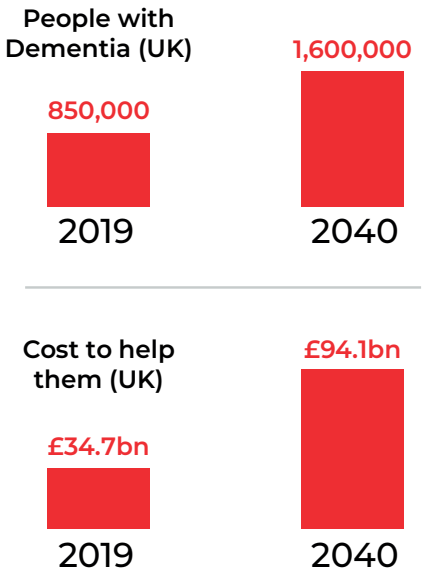
Someone in the world develops dementia every 3 seconds.[3]

Dementia is huge and growing

Currently, around 900,000 people in UK have dementia.[4] By 2050 this will be over 1.53 million.[5] Globally over 50 million have dementia. By 2050 this is expected to increase to 152 million.[6]

Current UK costs of dementia are estimated at £34.7 billion per year.[7] (£40K per person). Conservative estimates predict that, by 2040, dementia will have cost the UK close to £400 billion[8] – four times the current annual NHS bill.

The global annual cost of dementia is estimated as $818 billion and expected to be $2 trillion by 2030. This represents 1% of GDP.

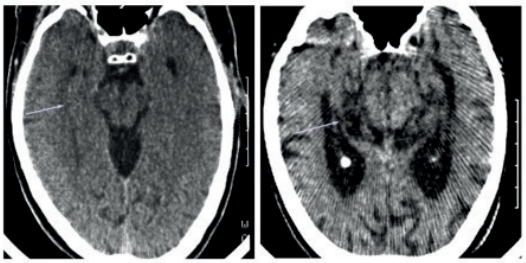


References for all statements and studies in this manifesto are at https://foodforthebrain.org/aiprefs/

The Problem

Changes in the brain start happening up to 30 years before a diagnosis of mild cognitive impairment (MCI), dementia or Alzheimer's. **There is no way to reverse the brain mass loss found in those with Alzheimer's.** Therefore, early diagnosis of subtle cognitive decline to identify those at risk is vital, followed by preventive action to reduce that risk.

Temporal-lobe-oriented CT in confirmed Alzheimer's disease



Control aged 66: no pathology

16 mm

Demented aged 66: Alzheimer pathology

2 mm

Measuring Cognitive Function

In 2011 we digitised and validated the **standard Cognitive Function Test** used to assess cognitive health and screen for MCI and dementia and made it available, for free, online. **To date over 370,000 have taken the test,** demonstrating huge appetite for this sort of tool.

COGNITION®

UPGRADE YOUR BRAIN

The Cognitive Funtion Test measures the critical aspects that indicate risk:

EPISODIC MEMORY
EXECUTIVE FUNCTION AND ATTENTION

Decline in these aspects of cognition, plus an accelerated rate of brain shrinkage, are the hallmarks of cognitive impairment.

The Cognitive Function Test is available for use by research groups needing an accurate assessment of cognitive function, such as Weill Cornell Medicine in New York.

VALIDATION RESEARCH

International Journal of Geriatric Psychiatry

"The online CFT was shown to be suitable for self-administration in an online format..."

USER SURVEY

THE EUROPEAN JOURNAL OF PSYCHIATRY

OTHER RESEARCH

alzheimer's association | Alzheimer's & Dementia® THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION | Weill Cornell Medicine

Featured Article | Open Access

Individualized clinical management of patients at risk for Alzheimer's dementia

In 2018 we introduced a risk factor questionnaire and commenced a research project to inform the building of an interactive, effective means of changing key diet and lifestyle behaviours to reduce risk and asked **University College London and NHS researchers** to test it, and explore barriers and weaknesses to increase compliance and behaviour change.

Out of 4,826 participants, **88% found it useful and 37% made diet or lifestyle changes as a result.** Our goal is to substantially improve these percentages.[9]

Preventing Alzheimer's is the solution

To prevent something you have to know, and tackle, the cause(s). The causes of Alzheimer's are mostly known and approximately half of the risk is attributed to modifiable risk factors – most importantly, things you can change.

The cause is not a build-up of amyloid protein and plaques. This is a consequence of the disease process. Over a hundred failed trials of amyloid lowering drugs, **thirty of which effectively lowered amyloid but made no difference to cognition**, have established this beyond reasonable doubt.[10] There are no potentially disease-modifying drugs in the pipeline. Current aims to have a drug treatment by 2025 are theoretical, and not based on any convincing evidence, as pointed out by The Lancet.[11]

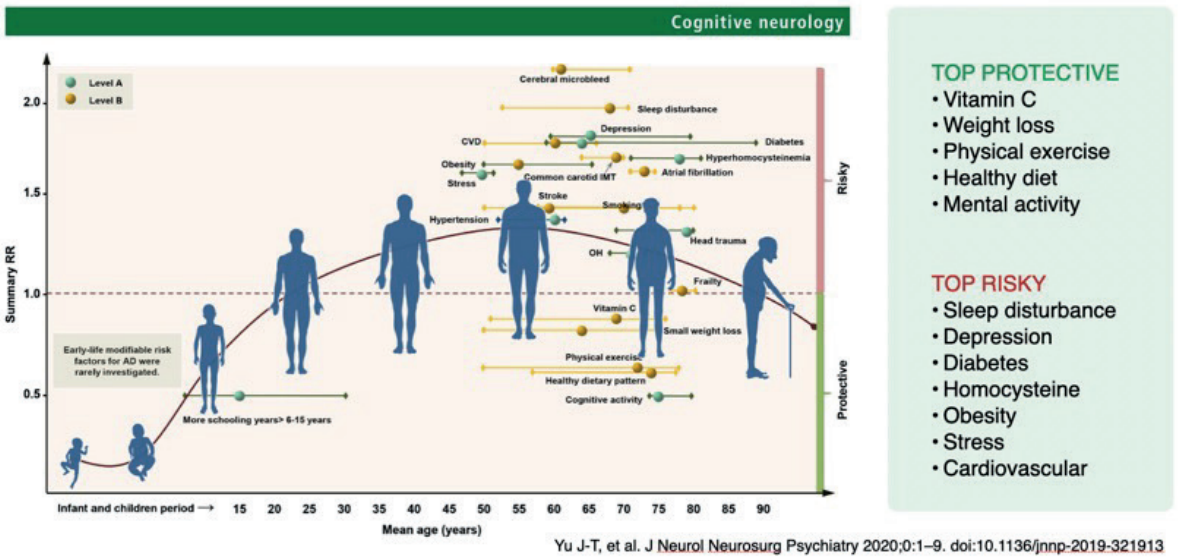
Just one in 100 cases of Alzheimer's is caused by mutations in genes (presenilin, APP) which account for most of the familial, early onset cases.[12]

There are genes, notably the ApoE 4 gene variant, which can increase risk but the odds can be mitigated by changes in diet and lifestyle.[13]

> *"In terms of a [drug] cure, or even a treatment that can modify the disease, we are empty-handed."*
>
> Former WHO Director-General Margaret Chan

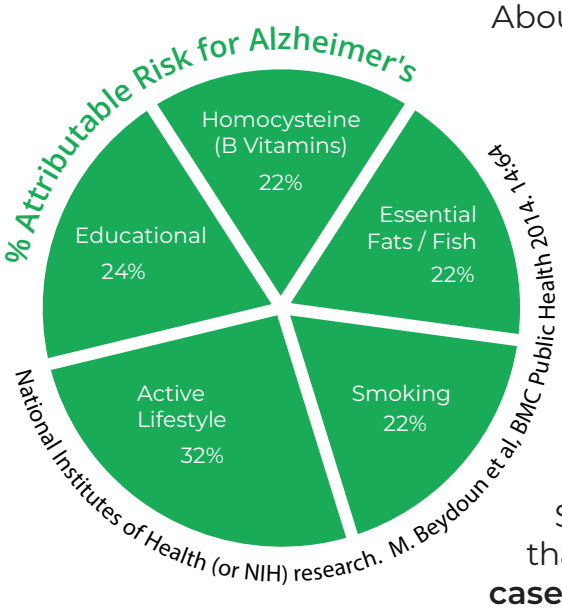
Prevention is the solution - not genes or drugs

There are diseases, such as diabetes, hypertension and stroke, which increase risk but our experts hold the view that these diseases are not primarily the cause but the consequence of diet and lifestyle factors. This means that reducing these risk factors will also reduce the risk of developing these diseases. A win win.
A meta-analysis of 396 trials confirm the potential impact of risk reduction.[14]



Yu J-T, et al. J Neurol Neurosurg Psychiatry 2020;0:1–9. doi:10.1136/jnnp-2019-321913

Half of dementia risk is preventable



About half of all the risk for dementia is due to modifiable risk factors, according to a statement from world leading dementia experts, and thus is, theoretically, preventable. Although it would be ideal, it is unlikely that we will achieve the goal of modifying all the known risk factors in all individuals, hence the number of cases of dementia that could be prevented will be less than this.[15]

According to the international group of 111 scientific and medical dementia experts from 36 countries it is possible right now to cut the number of people who will develop Alzheimer's by a fifth. Scientists at the US National Institutes of Aging found that **risk factors for Alzheimer's that account for most cases are high homocysteine, low physical exercise, low educational attainment, and mid-life smoking.**[16]

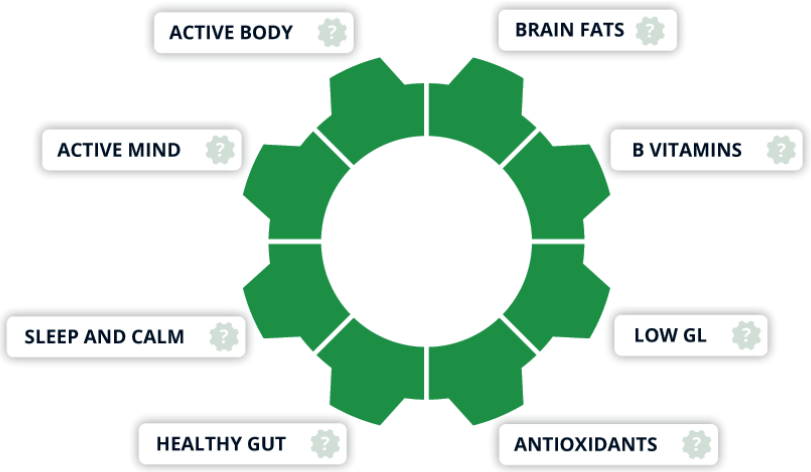
But if all known modifiable risk factors are targeted this could reduce the incidence of dementia by a third. That means 260 less people diagnosed a day in the UK, or 95,000 less in a year.

The ILC-UK have estimated that this would save the country £1.12bn a year, and £42.9billion by 2040. However, the saving for private individuals who pay to support themselves, would be many times higher and of course, the relief of personal and family suffering would be unquantifiable.

The 8 Prevention Steps

There are 8 key aspects of one's diet and lifestyle and the good news is that it is possible for us all to make positive changes in every one of these domains – thereby reducing your risk of cognitive decline.

That's why we've built COGNITION – a personalized, interactive brain upgrade programme to support people in making positive and lasting changes in these key areas, thereby dementia-proofing their diet & lifestyle.



Upgrade Your Brain with COGNITION

COGNITION® puts prevention into action – one person and one small step at a time. COGNITION is a personalized, interactive brain upgrade programme to help everyone dementia-proof their diet and lifestyle.

Our Cognitive Function Test calculates your Dementia Risk Index (DRI) based on proven risk factors that you can change which, collectively, account for at least half your risk.

COGNITION® 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 6 months.

How? When you sign up to COGNITION, you'll start receiving doable instructions, simple exercises and encouragements to make gradual and sustainable changes to your diet and lifestyle, with supportive 'engagements' ranging from an App that measures your number of daily steps to an online forum where you can interact and learn from others and share what works for you. Step by step, we support you in reducing your risk and measuring your progress along the way.

Why six months?
It takes three weeks to break a habit, six weeks to make a new habit and 26 weeks (6 months) to hard-wire a habit.

COGNITION is highly personalised, guiding you to make the specific changes that will have the most impact on your particular risk. At the end of each month you'll be able to check that domain and see the progress you make next with the goal being to bring each domain into the green.

At the end of eight months you'll re-measure your Cognitive Function (CFT) and your Dementia Risk Index and see how, when the DRI goes down, CFT improves or stabilises in the optimum green zone.

Reaching Millions of People

There is no limit to the number of people who can get involved and dementia-proof their diet and lifestyle – except funding for outreach. **We need this to go viral.**

our goal is to reach **10 million people** in 10 years

Some of our outreach ideas include:

Ongoing **mass PR and social media** campaign

High profile ambassadors to help spread the word

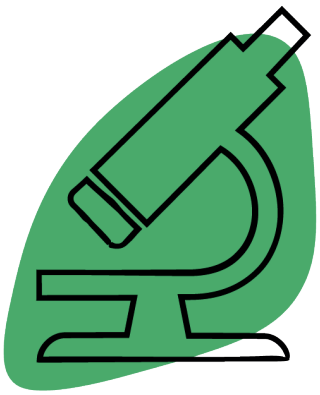
A compelling, scientific, informative feature-length **documentary for streaming with 3 half hour episodes** for TV (think Netflix), and worldwide distribution. See trailer here

COGNITION costs £5 a month, or £50 per annum donations. We use these funds to continually research and improve the app's ability to drive positive behaviour change to **be more effective and to reach more people**

Research and Development

We plan to do or support the following research:

- Micro research into each domain to improve effectiveness in positively changing behaviour – **Dr Krystyna Curtis** (behaviour change) working with **Dr David Vauzour** (gut health), **Dr Simon Dyall** (omega-3), **Professor Julia Rucklidge** (healthy diet), **Professor David Smith** (B vitamins) and others.
- Correlations between Cognitive Function Test (CFT) scores and Dementia Risk Index (DRI) scores on sign up and over time to answer the question – how does reducing risk factors impact cognitive function?
- A definitive large randomised controlled trial of B vitamins with Omega-3 versus placebo in a MCI population – 3-5 year trial – **Professors David Smith & Peter Garrard**
- Impact of vitamin D on CFT scores - a study by **Dr William Grant**



Thinking Big - Costs & Consequences

These are the funds we'd need to reach 10 million people and dementia-proof their diet and lifestyle and do the research to establish the impact of these prevention actions beyond doubt.

COGNITION — £1 million
Product improvement and research to measure and improve to maximise effectiveness and reach

RESEARCH — £5 million
To test if the combination of B vitamins with omega-3, given to those with MCI and raised homocysteine does prevent or delay conversion to Alzheimer's

TESTING HOMOCYSTEINE — £100,000
Establishing a direct and inexpensive way to offer homocysteine testing, partnering with laboratories – self-funding after set up

MARKETING TO REACH MILLIONS — £550,000
£100,000 – PR and ambassador programme
£250,000 –TV series 'Reclaim Your Brain'
£100,000 – Advertising
£100,000 – Fund to provide COGNITION for free to disadvantaged at risk groups

Total cost £6.65 million

Expected Impact

1 million fewer people develop dementia

£180 billion pounds of health spending saved

A twenty-fold return on investment

How? 10 million people engaged, 30% fewer develop dementia, saving 1 million from dementia. (3 in 10 develop dementia, costing £40K each a year.) This would reduce the number to 1 in 10. Thus, 1 million fewer people will not be expected to develop dementia, saving £40 billion a year. The average duration of dementia is 4.5 years before death. So that's a total of £180 billion saved.

The effect per million pounds donated is 130,000 people saved from dementia, saving £5.2 million per year and £23.4 million in 4.5 years. That's a twenty fold return on investment.

Resetting the Paradigm to Prevention

How You Can Help

There is only one way forward with dementia, and that is prevention. To change the paradigm requires indisputable proof and an established way to action. Help us reach and positively change people's diet and lifestyle habits for the better and research the effects on cognitive health.

TAKE PART

Do the Cognitive Function Test and sign up to COGNITION.
We appreciate your support, feedback and suggestions.

TELL OTHERS

Tell everyone you know, especially those over age 40.
We can give you a standard email to personalise.

MAKE A DONATION

Everything you see has been achieved from individuals giving whatever they can. Every little bit helps. To date everything we've built has cost over £50,000 funded by individual donations. We now need to raise £40,000 to complete and launch COGNITION. Donate here.

BECOME A 'FRIEND OF FOOD FOR THE BRAIN'

Gain wider access to our webinar series as well as exclusive content by making regular donations or a significant one-off donation. Join here.

BECOME A SUPPORTING PARTNER

Your organisation can actively support your own employees' wellbeing program by giving them access to our menu of webinars as well as gaining our brain healthy catering accreditation.

HOST A 'HOW TO PREVENT ALZHEIMER'S' EVENT

If you can get a group of people together we'll provide a speaker with ticket sales and donations to the Alzheimer's Prevention Project.

SHARE THIS MANIFESTO WITH YOUR HEALTHCARE WORKER

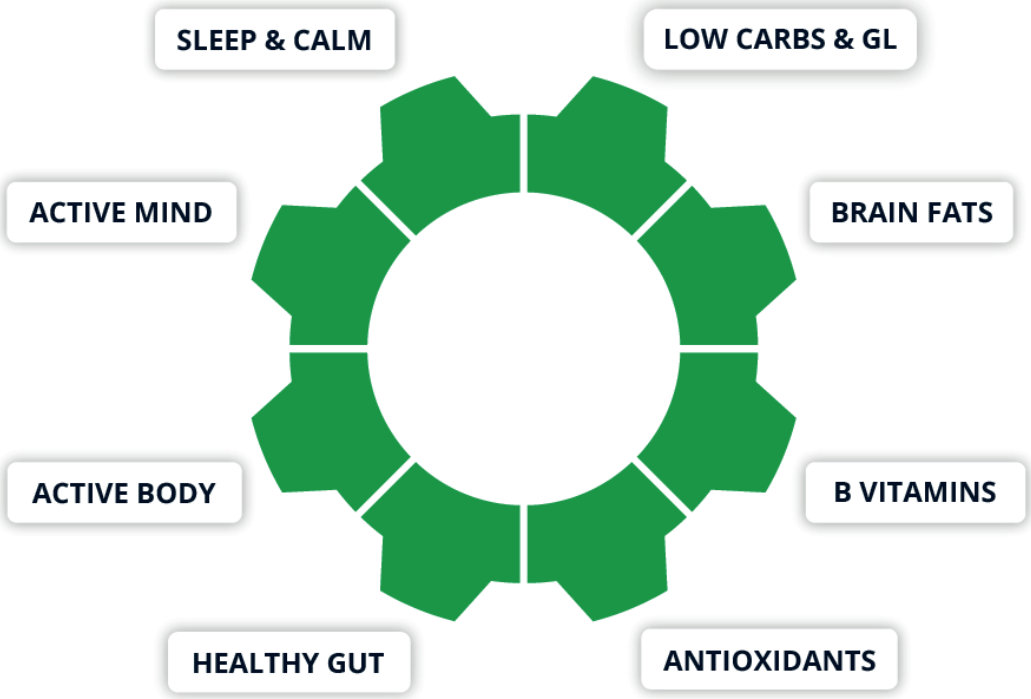
GPs don't learn much about nutrition in medical school. Every statement here is referenced with live links to studies. Your doctor will appreciate receiving this vital information.

STAY IN TOUCH

Sign up at www.foodforthebrain.org to receive our regular updates.
Contact us to get involved at info@foodforthebrain.org

Summary of Evidence for Prevention

1. **Low GL**
   Eat a low Glycemic Load (GL) diet
2. **Brain Fats**
   Up Brain fats – Omega-3, Phospholipids & vitamin D
3. **B vitamins**
   Keep Your Homocysteine Low with B vitamins
4. **Antioxidants**
   Eat and Drink Anti-Ageing Antioxidants & Polyphenols
5. **Healthy Gut**
   A Healthy Gut is a Healthy Brain
6. **Active Body**
   Exercise and Keep Physically Active
7. **Active Mind**
   Keep Yourself Socially and Intellectually Active
8. **Sleep & Calm**
   Sleep Well, Stay Calm and Live Purposefully



Domain 1 – Eat a Low Glycemic Load (GL) Diet

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.[17] Type 2 diabetes almost doubles risk for dementia.[18] Diabetes is also associated with more rapid brain shrinkage.[19] Even people in the upper normal range of blood glucose have increased brain atrophy, impaired cognition and increased risk of dementia.[20]

For instance, one trial measured HbA1c and glucose levels in several thousand elderly people over the course of almost seven years.[21] 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.

But even more important than loss of glucose control is the loss of insulin control. 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.[22] The same year, an Italian study also established a link between heightened insulin levels and declining mental function.[23] Similarly, a Puerto Rican study found that people who consumed large amounts of sugar doubled their risk of suffering poor cognitive function,[24] while another US study discovered a strong correlation between blood sugar level and memory loss.[25] Two studies – one in Ireland[26] and the other in the United States[27] –established a link between high dietary glycemic 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[28] and cognitive decline, especially in those with the ApoE4 gene.[29] 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.[30] This cognitive decline starts young. Cognitive decline in overweight children is associated with a high GL diet[31] and adolescents with metabolic dysfunction driven by a high GL diet have been shown to have shrinkage of the hippocampal area of the brain and cognitive deficits[32] [33].

> *"Those who ate the healthiest diet had an 88% decreased risk of developing dementia and a 92% decreased risk of developing Alzheimer's disease."*

In practical terms this means avoiding sugar as much as possible and eating fewer carbohydrates and, when you do, eating 'whole' carbohydrate foods such as wholegrain bread or pasta and oat cakes since the fibre in these foods helps 'slow release' the sugars. Eating white bread is associated with a poorer cognitive test performance, whereas high fibre bread is associated with better performance.[34] Eating carbohydrate foods with protein, for example brown rice with fish, or porridge oats with seeds, or fruit with nuts, further reduces the glycemic load (GL) of a meal. Best fruits in this respect are berries, cherries and plums. These kinds of foods are consistent with a Mediterranean diet which has also been shown to reduce risk.[35] A Scandinavian study compared those with a healthy versus unhealthy diet, including the above criteria, in mid-life for future risk of developing Alzheimer's disease and dementia 14 years later. Those who ate the healthiest diet had an 88% decreased risk of developing dementia and a 92% decreased risk of developing Alzheimer's disease.[36]

Domain 2 – Up Brain Fats

Omega-3, Phospholipids & vitamin D

The omega-3 fat docosahexaenoic acid (DHA) is the most abundant polyunsaturated fat in the brain, concentrated in the grey matter and synapses.[37] DHA is incorporated into membrane phospholipids, where it affects the properties of the membrane, for example, maintaining membrane fluidity. DHA, along with the other omega-3 fats (EPA and DPA) and their mediators are involved in a wide variety of processes in the brain, such as making neurons, synaptic connections, and the regulation of inflammation .[38]
Fish, especially cold-water oily fish, contain high levels of EPA and DHA and epidemiological studies consistently show that an elevated fish intake is associated with decreased risk of neurodegenerative diseases such as Alzheimer's disease[39] [40]Recent estimates suggest that worldwide many populations are currently consuming DHA and EPA at levels well below the recommendations issued by many international authorities (GOED), with blood levels estimated to be low to very low for most of the world, which may increase global risk for chronic disease[41] .

DHA supplementation appears to show the greatest promise, particularly in the early stage before the onset of memory loss symptoms[42] ,and at levels at or above 1000 mg per day43. Interestingly, positive association have also been found between walnut consumption and cognitive performance[44]. Walnuts are a source of the omega-3 fat alpha-linolenic acid (ALA) and also a range of antioxidants.

Phospholipids

Phospholipids, rich in eggs and seafood, are abundant in the brain. They become attached to omega-3 DHA in neuronal cell membranes, a process that requires methylation, dependent on B vitamins which play a key role in generating DHA enriched phosphatidyl choline (PC)[45], which is one type of phospholipid.
Another phospholipid, phosphatidylserine (PS), has been found to be low in post-mortem samples from Alzheimer's disease patients[46] Interestingly, phosphatidylserine supplementation may benefit cognition in the elderly [47] but as PS is highly enriched with DHA (Kim et al. 2014), it is currently unclear whether the potential beneficial effects of PS on cognition are due to the intact PS or DHA.
Phosphatidylethanolamine (PE) is also enriched in DHA, whereas much lower levels are found in phosphatidylcholine (PC) and phosphatidylinositol (PI)[48] Although PC is not highly enriched in DHA, higher plasma concentrations of PC-DHA are associated with reduced risk of dementia and AD[49], and post mortem samples from AD show depletion of PC-DHA in grey matter[50].

A number of trials have investigated the effects of providing multinutrient supplements containing a range of nutritional factors with the aim of supporting phospholipid biosynthesis. For example, a combination supplement containing DHA, EPA, and uridine monophosphate, choline, vitamins B, C and E and selenium, has shown promise in those with MCI[51]

Vitamin D

The primary source of vitamin D is exposure to sunlight. Seafood provides the most dietary vitamin D. Supplements of vitamin D can be derived from animal or fungal source (mushrooms and yeast). Vitamin D helps neurotransmission and exerts anti-inflammatory and neuroprotective activities within the brain by reducing inflammation and the oxidative stress.[52]

Vitamin D deficiency increases risk of AD.[53] In a study in France involving 912 elderly patients followed for twelve years, a total of 177 dementia cases (124 AD) occurred: 25(OH)D deficiency was associated with a nearly three-fold increased risk of AD.[54] Supplementing 800iu (20mg) a day for 12 months has been shown to improve cognitive function.[55]

Domain 3 – Keep Your HCY Low with B Vitamins

B vitamins are essential for many aspects of brain function. They are essential for healthy methylation, which is needed to build brain cell membranes and neurotransmitters that pass messages between brain cells. Hence B vitamins, especially B6, B12 and folate, are essential for the brain's structure, 'talking' and 'listening'. When in short supply, blood levels of homocysteine go up, indicating faulty methylation.

Both high homocysteine (Hcy) and low folate and B12 levels increase risk for Alzheimer's disease (AD).[56, 57] The higher the Hcy and the lower the folate and B12 the greater is the rate of cognitive decline.[58]

An International Consensus Statement in 2018 concluded that moderately raised plasma total Hcy (> 11µmol/L), found in half of those over age 70[59], is a main cause of age-related cognitive decline and dementia.[60] Two major meta-analyses of hundreds of studies conclude that raised Hcy is one of the best evidenced risk factors for AD and accounts for around a fifth of all risk[61, 62].

Homocysteine-lowering B vitamin treatment

Raised Hcy can readily be lowered by supplementation with B vitamins[63]. Randomised Controlled Trials show:

- In those over 50 with raised Hcy (>13µmol/L), but not diagnosed with cognitive impairment, supplementing folic acid (0.8mg/d) for three years resulted in a significant improvement in cognition compared to placebo (the FACIT trial).[64]
- The VITACOG trial on people with Mild Cognitive Impairment by Professor David Smith and his group of the OPTIMA Study at the University of Oxford, showed that Hcy above 11 µmol/L, correlated with accelerated brain shrinkage and cognitive decline. Those given daily folic acid (0.8mg/d), vitamin B12 (500 µg/d) and B6 (20mg/d) had a significant 30% reduction in the rate of brain shrinkage versus placebo[4] and almost a nine-fold reduction in shrinkage of the medial temporal lobe, which is a key area of the brain that shrinks in AD.[65] In addition, the B vitamins slowed cognitive and clinical decline. [66] *(see cover image, used with permission from Douaud[42] Yellow denotes area of significant atrophy)*

Treatment with B vitamins later in the disease process, in those diagnosed with AD, has shown modest benefit in those in the mild stage but not in those with moderately severe AD.[67]

B vitamins and Omega-3 are synergistic

Dr Jerneren at Oxford University analysed the data from the previous VITACOG study but divided the participants into those with a high, medium and low blood level of omega-3 at the start of the trial. Those with low omega-3 status showed no beneficial effect from the B vitamins while those with high omega-3 showed a 73% decrease in rate of brain shrinkage down to that seen in healthy elderly who do not develop dementia.[68] Those with a high omega-3 status showed the largest cognitive benefits to B vitamin treatment.[69]

Two trials in China on people with mild cognitive impairment have shown slowing of cognitive decline in those given folic acid and B12[70] or with a combination of folic acid and the omega-3 fatty acid DHA.[71]

These studies suggest that Hcy-lowering B vitamins can, at least, slow cognitive decline in people with a raised Hcy level over age 50 and those over 70 with Mild Cognitive Impairment and may also slow cognitive decline in those with mild AD, but not in moderate to severe AD.

Homocysteine is both a marker and a cause of brain damage

Three reviews confirm the growing evidence supporting raised Hcy levels as a likely primary predictor and cause of the brain damage that identifies AD.[72] [35] [40] Hcy and its derivatives are neurotoxins and indicate disrupted methylation, which leads to raised levels of amyloid and tau proteins and associated plaques and neurofibrilliary tangles found in the Alzheimer's brain. Raised Hcy leads to increased oxidative stress, brain damage and impaired circulation.

Domain 4 – Eat and Drink Anti-Ageing Antioxidants & Polyphenols

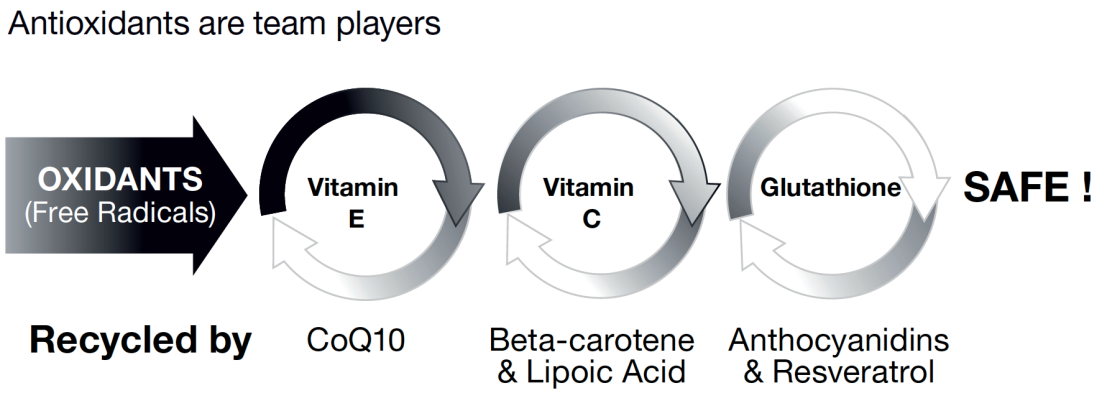
Antioxidants and polyphenols are plant-based nutrients that protect the brain. The older you are the more your brain needs to disarm harmful oxidants, the toxic by-products of the brain's energy creation, and to reduce inflammation. Smoking[73] and long-term exposure to polluted air[74] are significant risk factors for Alzheimer's dementia.

The more fruit and vegetables a person eats the lower is their risk of cognitive decline[75] with vegetables being particularly protective.[76] The best kinds of vegetables are carrots, cauliflower, broccoli, Brussels sprouts, cabbage, spinach and mushrooms. The best fruits are berries, especially blueberries and strawberries.[77] [78] Polyphenols, found not only in fruit and vegetables, but also in tea, especially green tea, red wine and the cacao in dark chocolate, are associated with preserving memory[7980] and a number of mechanisms exist to explain their positive actions on cognitive performance.[81] Olive oil is also promising in this regard.[82] The most protective effect is found eating six servings (500g) a day of fruit and vegetables.[83] Those in the top fifth of consumption of these kind of foods and drinks have half the risk of dementia.[84] A randomised controlled trial found cognitive improvement with a Mediterranean style diet with extra virgin olive oil or nuts.[85]

A number of key vitamins, as measured in food and in the blood, correlate with decreased risk. These include vitamin C[86], both in food and supplements[87] and vitamin E in supplements.[88]

In a population study it was found that those taking supplements of both vitamin C (1g) and vitamin E substantially reduced risk of developing Alzheimer's disease compared with those not taking these two supplements; either supplement on its own was not protective.[89] Vitamin E was found to be beneficial in mild to moderate AD by slowing decline of cognition.[90] A study supplementing vitamin E and selenium was not found to be protective. N-acetyl cysteine[91], a precursor of glutathione, Co-enzymeQ10[92] and resveratrol[93], found in red grapes, is also neuroprotective.

These nutrients, together with anthocyanidins in blue/red foods and beta-carotene in orange foods are team players in disarming harmful oxidants that age the brain, however they also have roles when acted on by the gut microbiome producing secondary metabolites involved in liver function, detoxification and cell signalling with anti-inflammatory effects supporting brain function, as well as reducing cardiovascular risk and hence supply of nutrients and oxygen to the brain.[94]



Domain 5 – A Healthy Gut is a Healthy Brain

A healthy gut is essential for a healthy brain. In recent years it has become establish that there are many ways in which the gut communicates with the brain, and vice versa. This includes the production in the gut of neurotransmitters including serotonin, dopamine, noradrenaline and GABA which directly influence the brain; the gut's ability to absorb critical brain-friendly nutrients such as vitamin B12; its role in controlling inflammation and eliminating potential brain-damaging toxins; and role of the gut microbiome - the balance of trillions of bacteria that populate our gut.

Two gut-related predictors or Alzheimer's – periodontal disease and lack of stomach secretions required for vitamin B12 absorption – illustrate this microbiome -gut-brain connection.
Having periodontal (gum) disease, a consequence of infection and dysbiosis, is associated with a significant increase of cognitive decline[92] with increasing dental visits correlating with Alzheimer's[93].

Decreasing production of stomach acid, required for vitamin B12 absorption, is a common occurrence in those over age 50. Two in five over 61 have low blood levels of B12.[94] Gastritis[95], irritable bowel syndrome (IBS)[96],gut infections such as H.pylori[97], long term use of PPI antacids[98,99] and antibiotics[100] have all been implicated or associated or with increased risk of cognitive decline and dementia.

The intestinal gut barrier functions much like the blood brain barrier, ideally allowing nutrients to pass while rejecting toxins and ant-nutrients. The integrity of the gut barrier is affected by alcohol, gliadin[101] in wheat, a lack of antioxidants and anti-inflammatory omega-3 fats which influence the microbiota[102]. Gut inflammation may play a role in cognitive decline.[103]

The role of the microbiome in the gut affecting cognition is a new frontier for research.[104,105] A study giving aged rats a fecal transplant from young rats showing significant changes in cognition[106] illustrates the potential role for probiotics, prebiotics and diets that promote a healthy microbiome.

While there is little clinical trial evidence yet there is a growing body of evidence that restoring gut health and eating a digestion friendly diet is correlated with and likely to be beneficial for protecting cognition.[107]

Domain 6 – Exercise and Keep Physically Active

Movement is one of the most powerful ways to reduce of risk cognitive decline. In fact, brisk walking was the first activity that was shown to increase the size of the hippocampus – the area of the brain critical for memory – in older adult humans! [111] In that study, participants who were randomised to walk briskly for 40 min three times per week saw an increase in the size of the hippocampus compared to a control group after a year. Participants started with the 10 minutes of walking, increased it by 5 minutes every week. In addition to walking, almost any exercise can improve brain health, and one of the ways it does that is through the production of brain-derived neurotrophic factor (BDNF).[112] Exercise particularly helps improve the amount and quality of sleep we get,[113] and decreases inflammation,[114] both of are critical factors in long-term brain health.

Resistance training or weight training also improves brain health and cognitive function in several ways. Improving strength and muscle mass is associated with better function of brain white matter - the areas of the brain responsible for making fast connections between brain areas or between the brain and the body.[115] Other studies have shown that loss of muscle mass is associated with lower brain volume and dementia,[116] and muscle mass was also positively correlated with cognitive function in individuals from the UK biobank study.[117] Only four sets per week of resistance training, which can be done in a few minutes, is enough to see benefit.[118]

The final important area of movement and dementia risk is movements that involve coordination or balance. A recent meta-analysis suggested that exercise involving coordination are the best at improving cognitive function.[119] For instance, one study showed that participants who did dance-based exercise saw greater improvements in the size of the hippocampus.[120] You could even combine resistance and coordination movements by doing something like yoga or pilates.

Domain 7 – Keep Yourself Socially and Intellectually Active

The term “use it or lose it” is very pertinent for preventing cognitive decline in older adults. Keeping the brain active plays an important role in building cognitive resilience throughout life, and helping to preserve memory in later life.

Engaging in Mentally and Socially Stimulating Activities

Research indicates that individuals who keep their minds active exhibit better cognition than those who do not engage in these activities. Mental stimulation is often perceived as an activity that provides opportunities to keep minds active, concentrate and stay alert. Mentally stimulating activities include reading, brain-stimulating games, art and crafts, communication, physical activities, reminiscence, problem-solving and social contacts.[121] A study of those training to be London taxi drivers over four years, showed an increase in brain volume[122].

Social participation predicts psychological outcomes in later life. Social participation with others, particularly within friendship groups, has been indicated to become incrementally more important for mental well-being as people age. Research has demonstrated that older adults are at particular risk of becoming lonely, and that loneliness is associated with impaired cognition and poor psychological and physical health in older adults[123].

Loneliness is strongly correlated with negative health outcomes and premature death, to a similar extent to what is seen with other risk factors, such as obesity and smoking [124, 125, 126, 127, 128, 129, 130].

Creativity and Languages

Research suggests that bilingualism and multilingualism may help to prevent memory loss in older adults. Individuals who are bilingual have been observed to exhibit better cognitive function and reserve than individuals who are monolingual. Additionally, bilingualism has been associated with lower incidence of Alzheimer’s disease and enhanced ability to increase learning and memory. Neuroprotective benefits of bilingualism have been demonstrated even in individuals who have taken up language learning in later life, as just 4 months of language learning has been associated with improved cognitive function in older adults [131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141 .

Engaging in creative activities, such as music and art, may also prevent memory loss. Music in itself has been suggested to improve memory, orientation, irritability, agitation and language in individuals with Alzheimer’s disease. A further study found that the benefits of music therapy demonstrated positive effects on cognition and memory in older people. Furthermore, art therapy has also been suggested to be beneficial for improving cognition, as well as generally promoting psychological well being in old age [142, 143, 144].

Domain 8 – Sleep Well, Stay Calm and Live Purposefully

A person’s emotional health, reflected in levels of anxiety, depression, lack of purposeful activities, positive attitude and social interaction, as well as sleep, are associated with increased future risk of cognitive impairment and dementia.

Those reporting anxiety have a 35% higher risk of developing Alzheimer’s disease in a meta-analysis of six studies.[145] Social isolation and depression are risk factors for dementia in later life.[146] Depression is also more prevalent in those with dementia.[147] People with positive age beliefs, which also reduces stress, are less likely to develop dementia.[148] Conversely, negative thinking is associated with accelerated cognitive decline.[149]

A meta-analysis of studies on sleep found that disturbed sleep increases future risk of dementia. Combining 23 studies insomnia was significantly associated with 27% higher risk of cognitive disorders.[150] Those getting too little (six hours or less) or too much (over 8 hours) had greater risk. A recent study of people in their 50s and 60s getting six hours of sleep or less were 30% more likely to be diagnosed with dementia later compared to those getting seven hours.[151]

Potentially beneficial interventions include meditation and mindfulness, which has been shown to lessen depression in those with dementia[152]; heart rate variability (HRV) biofeedback which has been shown to lessen depression, anxiety, and improve attentional skills as well as sleep quality and stress management in older adults[153]; yoga having beneficial effects on cognitive functioning, particularly on attention and verbal memory possibly through improved sleep, mood, and neural connectivity.[154]; and improved social interactions with facilitated meeting and discussion groups being associated with improved cognition and increased brain volume.[155]

References for all statements and studies in this manifesto are at https://foodforthebrain.org/aiprefs/

Supporting Organisations
as of May 2023

Sponsors

"Alzheimer's is not an inevitable consequence of ageing, nor is it all 'in the genes'. It is largely a preventable disease and we know quite a lot about what people need to do to help prevent it. Simple diet and lifestyle changes, made achievable in Food for the Brain's COGNITION programme, could cut the risk of developing this terrible and avoidable disease by at least a third."

Professor David Smith, Emeritus Professor of Pharmacology

Founding Director, Oxford Project to Investigate Memory and Ageing (OPTIMA), University of Oxford

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