Action on Alzheimer’s Prevention – case for support

Half of the risk for developing dementia and Alzheimer’s is preventable. Most of this risk relates to nutrition and lifestyle factors. Given that Alzheimer’s is not a reversible condition, the best hope for prevention lies in targeting those at risk, from age 50, and encouraging positive diet and lifestyle changes. We seek to test the effects of an e-based educational strategy for changing diet and behaviour on cognitive function after 1 and 2 years to help develop a model for effective action on Alzheimer’s prevention which could be applied nationally and globally.
Each day in the UK about 500 older people develop dementia. As a conservative estimate about twice as many develop Mild Cognitive Impairment (MCI), the precursor to dementia. The commonest 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.

So far drugs have only temporarily relieved symptoms of AD, but have not been effective in slowing disease progression. There are no potentially disease-modifying drugs in the pipeline – all recent clinical trials have failed. Contrary to popular opinion, only 1% of AD is directly caused by genes. Current aims to have a drug treatment by 2025 are theoretical, and not based on any convincing evidence, as pointed out by The Lancet. According to the WHO secretary general director-general Margaret Chan, in terms of a [drug] cure, or even a treatment that can modify the disease, we are empty-handed.

Currently, 766,000 people in Britain have dementia. In the next decade, if nothing changes, this is expected to exceed 1 million, according to the International Longevity Centre UK (ILC-UK). Current annual costs of dementia are estimated at £23 billion per year. Conservative estimates are that, by 2040, dementia will have cost the UK close to £400 billion – almost four times the current annual NHS bill.

Half of dementia is preventable

Yet, 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. 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 Health predict that up to one in three cases of Alzheimer’s disease can be averted if the strongest risk factors (high homocysteine, low physical exercise and educational attainment, mid-life smoking) were eliminated.

Eliminating these risk factors would equate to between 100 and 166 less people developing dementia every day in the UK, or 60,000 less people developing dementia in a year. However, if other known risk factors shown below were also targeted it is reasonable to predict that more than 200 people a day, or 80,000 a year, could be saved from dementia, or at least have it deferred for several years.

The ILC-UK have estimated that this would save the state £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 immense.

Known risk factors for dementia

The most well established risk factors for dementia are shown in the Table below. The Table shows two estimates: first, the estimated prevalence of the risk factor in the population (UK figures have been used where available): that is, what proportion of the population are currently thought to be exposed to the risk factor. The second estimate is called Population Attributable Risk (PAR) and is the percentage of cases of AD that might be caused by the risk factor. The higher the percentage, the greater would be the impact on AD of reducing this risk factor in the general population.

However, not all risk factors are easy to change and there is currently a varying degree of evidence that changing them will produce the estimated risk reduction. For example, it is not easy to change low educational attainment in the short-term, although encouraging more intellectual and social activity is possible, and there is some suggestive evidence that doing so reduces risk.

However, lowering a high homocysteine level with a B vitamin supplement is easy to change, and already there is evidence that this reduces both brain shrinkage (by up to nine times) and rate of memory decline in those ‘at risk’ with MCI.
Which risk factors have the biggest potential impact and are easiest to change?

We have therefore graded those that are easy to change (yes, moderate, no) and to the degree of evidence in existence that changing these would have an effect (strong, moderate, weak), based on intervention studies. Risk factors are ordered according to those that affect the most people, are most easy to change, and for which there is the best evidence that changing them will prevent or delay the onset of dementia.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Prevalence (%)</th>
<th>% of AD attributed to risk factor (PAR%)</th>
<th>Ease of changing</th>
<th>Evidence for effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>High homocysteine level, lowered by B vitamins</td>
<td>30</td>
<td>22</td>
<td>Yes</td>
<td>Strong</td>
</tr>
<tr>
<td>Low fish &amp; omega-3 intake</td>
<td>49</td>
<td>22</td>
<td>Yes</td>
<td>Moderate</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>34</td>
<td>22</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Low intake of polyphenol rich foods</td>
<td>75</td>
<td>up to 20</td>
<td>Yes</td>
<td>Weak</td>
</tr>
<tr>
<td>Mid-life smoking</td>
<td>20</td>
<td>11</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Mid-life high blood pressure</td>
<td>12</td>
<td>7</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Mid-life obesity</td>
<td>12</td>
<td>7</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Depression</td>
<td>14</td>
<td>8</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Diabetes and pre-diabetes</td>
<td>5</td>
<td>2</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Low educational attainment</td>
<td>24</td>
<td>12</td>
<td>Difficult, long-term</td>
<td>Weak</td>
</tr>
</tbody>
</table>

Please note that the evidence, based on intervention studies, is graded as weak for most risk factors because of the absence of studies, rather than the absence of evidence of effect from studies. This is largely because very little available funds for dementia research is spent on prevention research.

In the UK, since 2006, only 0.1% of research funds has been spent on prevention research (£156K out of £140.2 million up to October 2013). Given that half of dementia is preventable we continue to campaign for half of research funds to be spent on prevention research.
NUTRITION-RELATED RISK FACTOR REDUCTION

• HIGH HOMOCYSTEINE AND B VITAMINS
A high blood homocysteine level, above the level known to increase the rate of brain shrinkage (>10mcmol/l)\textsuperscript{13} occurs in approximately a third of the population over age 61.\textsuperscript{14} This risk factor is estimated to account for 22% of Alzheimer’s disease. Giving B6, B12, folic acid to people with high homocysteine (half the population over 65) has already shown a nine-fold reduction in brain shrinkage and a substantial reduction in rate of memory loss (cessation in some cases).\textsuperscript{15} This is the only proven disease-modifying treatment to date and is thus the strongest prevention factor. Testing those with MCI at risk for homocysteine, and treating them with inexpensive B vitamins is likely to slow cognitive decline in approximately 80 older people each day or 30,000 per year in the UK as a conservative estimate.\textsuperscript{16}

• FISH AND OMEGA-3 INTAKE
The average person in the UK consumes 1 to 2 fish servings per week (217g).\textsuperscript{17} A low fish/omega-3 intake versus high fish consumption accounts for 22% of Alzheimer’s cases and is associated with reduced brain volume.\textsuperscript{18} Eating one serving of oily fish a week is associated with halving the risk of AD.\textsuperscript{19} Supplements of one kind of omega-3 fish oil, called DHA, have been shown to enhance memory in adults\textsuperscript{20} who don’t eat fish, and to prevent memory loss in those in the early stages of memory decline.\textsuperscript{21} Studies giving supplemental omega-3 fish oils have shown improved cognition in older people and positive structural changes in the brain.\textsuperscript{22} But it’s not just oily fish. The more fish you eat, the better your memory test performance. Fish is also an excellent source of vitamins B12\textsuperscript{23,24}, D and choline, all essential for the brain.

• ANTIOXIDANT AND POLYPHENOL RICH FOODS
The more fruit and vegetables a person eats the lower is your risk of cognitive decline\textsuperscript{25} with vegetables being particularly protective.\textsuperscript{26} The best kinds of vegetables are carrots, cauliflower, broccoli, Brussels sprouts, cabbage, spinach and mushrooms. The best fruits are berries, especially blueberries and strawberries.\textsuperscript{27} Flavonoids and polyphenols, found not only in fruit and vegetables, but also in tea, red wine and dark chocolate, are associated with preserving memory\textsuperscript{28} and a number of mechanisms exist to explain their positive actions on cognitive performance.\textsuperscript{29} The most protective effect is found eating six servings (500g) a day of fruit and vegetables.\textsuperscript{30} In a population study it was found that those taking supplements of both vitamin C (1g) and vitamin E had more than half the risk of developing Alzheimer’s disease compared with those not taking these two supplements; either supplement on its own was not protective.\textsuperscript{31}

• BLOOD SUGAR CONTROL AND LOW GL FOODS
Keeping blood sugar level in the low-normal range, also reflected by a low glycosylated haemoglobin (HbA1C), which also means less insulin release, has been associated with lesser risk for dementia in several studies.\textsuperscript{32} Type 2 diabetes, the net result of losing blood sugar control, almost doubles risk for dementia.\textsuperscript{33} Diabetes is also associated with more rapid brain atrophy.\textsuperscript{34} Even people in the upper normal range of blood glucose have increased brain atrophy, impaired cognition and increased risk of dementia.\textsuperscript{35} In practical terms this means avoiding sugar as much as possible and eating slow-releasing ‘whole’ carbohydrate foods such as wholegrain bread or pasta and oat cakes. Eating white bread is associated with a poorer cognitive test performance, whereas high fibre bread is associated with better performance.\textsuperscript{36} Eating carbohydrate foods with protein, for example brown rice with fish, or porridge oats with seeds, further reduces the glycemic load (GL) of a meal. Best fruits in this respect are berries, cherries and plums while grapes, raisins and bananas are high GL. These kinds of foods are consistent with a Mediterranean diet which has also been shown to reduce risk.\textsuperscript{37}

• HEALTHY DIET
A study in Finland and Sweden compared those with the 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.\textsuperscript{38}
Identifying those at risk and encouraging prevention steps

Given that Alzheimer’s dementia is characterised by irreversible brain shrinkage, which is thought to begin thirty years before a diagnosis, any prevention strategy should be started early, and targeted at those ‘at risk’. A good indicator of those at risk is cognitive function assessing episodic memory, executive function and processing speed, the three domains proven to be predictive of Alzheimer’s, as well as homocysteine status. To assess these Food for the Brain has developed and offered early screening using a free online Cognitive Function Test (CFT) since 2012, targeted primarily at 50 to 70 year olds, who, by virtue of self-selection, have concerns about their memory. The CFT has been validated, in a pilot study, against the best available paper and pencil tests used in memory clinics.

Over 170,000 Cognitive Function Tests have been completed, including annual repeat testing, as part of a follow up. Those scoring poorly (the test is graded red, orange, green with orange representing 1 standard deviation from the mean, and red 1.5, which is consistent with those with MCI) are encouraged to visit their GP for diagnostic evaluation and request a homocysteine blood test, then act accordingly if their homocysteine value is above 10mcmol/l, as well as taking positive prevention steps. Each participant is then followed up on an annual basis and encouraged to repeat the test.

In January 2015 an upgraded CFT will be launched, including assessment of an individual’s dietary and lifestyle risk factors (medical risk factors are excluded), then giving the individual a personalised report, encouraging them to take action to reduce their risk through prevention measures. An example of a typical report is given below.

Does online prevention assessment and encouragement work?

It is hoped that, providing this personalised information to individuals will work to:

a. change dietary and lifestyle behaviour and consequently,
b. arrest, slow down or improve cognitive function.

The charity is seeking funding to test this proposition, and act on the results to find the most effective means of creating changes in behaviours that lead to reduced risk.

The outcome measures are the CFT score after 1 and 2 years indicating cognitive function; and assessment of dietary and lifestyle behaviours by online questionnaire.

We wish to test the impact after 1 and 2 years, using these outcome measures, of those individuals who:

a. receive only their CFT results and information of prevention steps.
b. receive their CFT results and information of prevention steps and have homocysteine testing and B vitamin supplementation if indicated.
c. receive their CFT results and information of prevention steps and either attend a prevention seminar or watch a series of prevention webinars.

The funds will also allow us to examine and analyse existing data to assess differences between those with high and low CFT scores, and issues relating to compliance and return testing; and to examine which aspects of the CFT are most predictive to thereby improve the accuracy and efficacy of the test.
FOOD FOR THE BRAIN
COGNITIVE FUNCTION TEST

Your Results
Date: 06/10/2014
Name: Stoyan

Your Cognitive Function Test result showed that you appeared to perform below the norm for your age. This may reflect early changes in your brain function or it may be due to other factors, including interruptions or technical problems during the test. To find out more about what your score means see the "Interpreting Your Cognitive Function Test Results" section of this program.

As it is known that early cognitive function problems can be a symptom of future cognitive impairment and Alzheimer’s Disease, we recommend that if you are concerned about your score, you visit your GP for a fuller assessment. Factors in your medical history that may affect your cognitive performance include heart disease, a history of stroke, Parkinson’s Disease, epilepsy, head trauma, B12 deficiency, medication, depression, acute infection and chronic stress. Some types of dyslexia may also affect your performance in this test.

Your Prevention Steps

UP ANTIOXIDANTS

EAT FISH AND SEEDS

MINIMISE SUGAR & REFINED FOODS – EAT A LOW GL DIET

KEEP PHYSICALLY, MENTALLY AND SOCIALLY ACTIVE

SUPPLEMENT B VITAMINS

LIMIT COFFEE – GREEN TEA IS BETTER

Your weakest area in relation to prevention steps is your intake of B vitamins (see below).

Your results and personalised Prevention Steps are also being emailed to you.

B vitamins

Your B vitamin status is not good. We recommend you check your homocysteine level. Having a higher intake and blood level of vitamin B12 and folate is associated with a quarter of the risk of developing Alzheimer’s. Vitamin B6, B12 and folate acid, especially in combination, lower blood levels of homocysteine, which is a key predictor of risk. Lowering your homocysteine, if above 10mcmol by supplementing high dose B6(20mg), folate acid (1000mcg) and B12 (500mcg) has been shown to greatly reduce the rate of brain shrinkage and memory loss in those at risk of Alzheimer’s. That is why it is VITAL to check your homocysteine level and, if above 10, speak with your doctor about supplementing high doses of B vitamins. Otherwise, supplementing a daily multivitamin or B Complex providing around 20mg of B6, 200mcg of folate acid and 50mcg of B12 is a sensible precaution. B12 absorption can greatly worsen with age, and is inhibited by the diabetes drug metformin, and antacids proton-pump inhibitor (PPI) medication. If you are taking these be sure your GP checks your homocysteine level.
The goal of this research is to find the most effective e-based strategy for encouraging and achieving positive diet and lifestyle prevention actions that are associated with a smaller decline in cognitive function as we age, and to encourage as many people as possible, both in the UK and abroad, to participate.

*In order to achieve these aims, we are seeking a total of £59,700 over a three year period.*

<table>
<thead>
<tr>
<th>Estimate of cost breakdown</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Part-time principal investigator and MSc student bursary</td>
<td>£36,100</td>
</tr>
<tr>
<td>Web-based technical CFT support and maintenance</td>
<td>£8,000</td>
</tr>
<tr>
<td>Seminar/webinar development &amp; delivery</td>
<td>£5,600</td>
</tr>
<tr>
<td>Outreach activities to encourage participation</td>
<td>£4,400</td>
</tr>
<tr>
<td>Publication write up and costs</td>
<td>£2,600</td>
</tr>
<tr>
<td>Management &amp; contingency</td>
<td>£3,000</td>
</tr>
</tbody>
</table>
References

5. Prevention dementia: a provocation”, International Longevity Centre July 2014 report
7. See ref 5 above.
11. See refs under 15 below.
12. Population Attributable Risk (PAR) Values from ref 5, 9 & 10
13. Smith AD et al, ‘Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial’, Public Library of Science ONE, 5(9) (2010);
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19. Morris M et al, Archives of Neurology 2003;volume 60; pages 940-946
27. Nurk E et al, 'Intake of flavonoid rich wine, tea, and chocolate by elderly men and women is associated with better cognitive test performance', J Nutr 139, 120–127
32. Arvaintakis Z et al, Arch Neurol, 2004; Yaffe K et al, Neurology, 2004
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