

BBC Smart Thinking: Cheating Dementia.

Summary of BBC Dementia Panel Discussion

Wednesday 6 January 2010, The Royal Institution, London

Older age is clearly the strongest risk factor for the development of Alzheimer's disease and other forms of dementia, with dramatic implications for the number of individuals with dementia worldwide as people live longer. In this context interventions to prevent, delay the onset, or mitigate the impact of Alzheimer's disease and other forms of dementia will be vital but there is confusion and contradiction over the available evidence. The BBC commissioned a panel of independent experts, chaired by Alzheimer's Society, to review the key studies and give an opinion regarding the most promising lifestyle and medical factors that could provide opportunities to reduce the risk of Alzheimer's disease or other forms of dementia.

Dr Ann Hale, Head of Public Health Research at Alzheimer's Society undertook a literature review focussing on MEDLINE, EMBASE, PsycINFO and evidence based reviews. Identified papers were circulated to members of the panel, and any additional key research papers identified by the panel members were also circulated. In total more than 70 original research papers or review articles were considered by the panel.

The panel members were:

Professor Clive Ballard (Chair), Director of Research, Alzheimer's Society

Professor Dag Aarsland, University Hospital Stavanger

Dr Sarah Aldred, University of Birmingham

Professor Philip Bath, University of Nottingham

Dr Jacqueline Birks, NHS Oxford

Professor Carol Brayne, Institute of Public Health, University of Cambridge

Professor Mia Kivipelto, Karolinska Institute, Sweden

Dr Marcus Richards, Medical Research Council

Professor John Starr, Royal Victoria Hospital, NHS Lothian

Professor David Smith, Founding Director OPTIMA, University of Oxford

Professor Raj Kalaria, University of Newcastle

When interpreting the views of the panel it should be acknowledged that this was not a formal systematic review and that the evidence considered by the panel, whilst comprehensive, was not an exhaustive collection of the relevant literature. It should also be acknowledged that consensus was achieved by discussion, with several members who were unable to attend providing written summaries of their views. Therefore, consensus did not follow a rigorous structured consensus process.

In considering the topics that were discussed, it is important to bear in mind that there are many established risk factors for Alzheimer's disease and dementia as a whole, such as age and genetic factors, which were not considered as they are not amenable to "prevention". There is also strong evidence that factors such as education and type of occupation may impact upon the risk of developing dementia, but again were not included as they were not felt to be easily addressable as a prevention measure. The selection of medical conditions which may create opportunities for prevention is rather more arbitrary and conditions such as stroke, diabetes, depression and Down's syndrome were not considered by the panel. High plasma homocysteine was debated by the panel, and thought to probably be associated with an increased risk of developing Alzheimer's disease. However, the panel considered that further work was needed to determine whether the associated risk could be ameliorated with vitamin therapy. High blood pressure and high cholesterol were considered, as they were felt to be potentially amenable modifiable medical risk factors rather than "diseases" per se.

Potential Factors Considered and the level of evidence

| | Level of evidence | Comments |
|---------------------------|--------------------------|--|
| Lifestyle | | |
| Best Evidence | | |
| Obesity in mid-life | Probable | Potential risk increase for Alzheimer's disease –20%. Based on 10 studies with >20,000 people. All prospective studies >2 yrs follow-up, age >40. |
| Physical Activity/Regular | Probable | Potential risk reduction 18-45%. Based on 13 prospective studies |

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| Exercise | | focusing on AD and/or dementia with >150,000 participants. Higher aerobic fitness was highlighted. |
| Smoking (current) | Probable | Potential risk of AD and cognitive decline in current smokers (RR=1.70; 95% CI: 1.25, 2.31). Analysis sample size was 26,374. |
| Alcohol use | Probable | Risk reduction 26-28%. Based on 15 longitudinal studies of 2-8 years, with >14,000 participants. Comparisons made with “non-drinkers”. A couple of studies focused on red wine, but most examined general alcohol intake. Thresholds of modest drinking varied between the individual studies. |
| High Blood Pressure in Mid-Life | Probable | 24% or greater increased risk in all studies, and more than 2 fold increased risk in some. More than 15 years follow-up in most studies, with total >16,000 participants. Biggest differences in studies using 160/95 as threshold for high blood pressure |
| Elevated cholesterol in mid-life | Probable | 40% or greater increase in risk in all studies. All 5 midlife studies >15 years follow-up and total of >15,000 participants. |
| Other factors considered: | | |
| Mediterranean diet (which contains whole grains, fish and olive | Possible | |

| | |
|-----------------------|--|
| oil) | |
| Social networks | Possible |
| Cognitive stimulation | Good evidence for modest but significant impact on cognition, but Insufficient evidence regarding dementia risk |
| Vitamin supplements | Insufficient evidence |
| Oily Fish | Insufficient evidence |
| Dietary vitamins | Insufficient evidence |

Potential Targets for Prevention: Intervention studies

It is important to note several general points before considering specific individual interventions. Firstly, the potential value of any intervention must be balanced against the potential impact on quality of life. This may particularly apply to the management of potential medical risk factors in older individuals, where over-enthusiastic intervention may lead to side effects and a reduction in quality of life. Secondly, many of the intervention studies so far conducted are not representative of people in mid-life or later life in the general population, so some caution has to be used when interpreting the implications of these studies for benefit and harm in real life settings.

Epidemiological studies demonstrate a clear relationship between taking antihypertensive drugs and reduced incidence of dementia in people with hypertension, but the evidence from randomized controlled trials is more variable, with only one of 3 clinical trials showing a significant reduction in incident dementia. The overall health benefits of antihypertensive therapy are well established but the evidence pertaining to a possible additional benefit with respect to a reduction in incident dementia with antihypertensive drug treatment adds further impetus behind the importance of achieving antihypertensive treatment to best practice guidelines. A number of studies have also shown that various lifestyle interventions, including a low salt diet, can be effective in achieving modest reduction in blood pressure, although these studies have not specifically examined the impact on dementia. Further studies to determine whether specific antihypertensive drug therapy or lifestyle interventions to reduce blood pressure may confer additional benefits in the reduction of incident dementia will also be important.

Elevated mid-life cholesterol is clearly a risk factor for dementia. Epidemiological studies do suggest an association between statins and reduced dementia risk and

preliminary intervention studies also indicated potential benefit. Therefore, it is disappointing that statins have failed to impact upon cognitive function or incident dementia in more rigorous randomized controlled trials. In part this may be explained by the design of the studies, which are difficult to interpret as they have not focused on the age group where the risk was measured in the longitudinal studies. The reality is that it is unlikely that long-term trials could ever be undertaken where there is already evidence of the effectiveness of statins to reduce the risk for other medical conditions. Again lifestyle interventions can also be effective in reducing cholesterol, but the impact on dementia has not been studied.

There are far fewer studies examining interventions based upon lifestyle related risk factors. There are a number of clinical trials examining the potential value of vitamin supplements, summarised as part of the Cochrane review for evidence based medicine. The conclusion is that published studies provide no consistent evidence either way about whether B vitamin supplements (folic acid, vitamin B12, or B6) are effective in reducing dementia. Vitamin E supplements, on the other hand, do not appear to be effective. Several recent cohort studies have highlighted the potential for adherence to a Mediterranean diet, containing whole grains, fish and olive oil, to reduce the risk of incident AD, but further studies are needed. Following recommended dietary advice from the Food Standards Agency and following recommended dietary vitamin intakes is recommended for general health.

There is no convincing evidence at this stage that specific interventions focusing on particular types of cognitive stimulation can reduce incident dementia, although in older individuals there may be limited benefits in specific aspects of cognitive functioning.

Exercise appears to be an important target from the epidemiological studies, with additional encouraging evidence of benefit from preliminary intervention studies. The benefits are likely to be greatest as part of an active lifestyle across the whole lifespan.

Smoking is clearly a major health risk, and existing interventions to reduce smoking may also help in reducing the risk for Alzheimer's disease and other dementias. The protective effect of modest alcohol intake is clear from the epidemiological studies. As general advice, sensible modest drinking may also help reduce the risk of

Alzheimer's disease, although it should be noted that heavy drinking can directly cause brain damage and dementia.

Clinical obesity in mid-life is another clear risk factor for developing dementia. Developing interventions to treat obesity and to reduce obesity at a population level will be increasingly important for general health and for reducing the risk of dementia.

With respect to the likely benefits in reducing the risk of developing dementia, the panel, therefore, are of the opinion that the 4 most important factors are

Exercise (across age groups)
Reducing mid-life obesity
Bringing blood pressure to optimal levels in midlife
Reducing cholesterol in mid-life

As many of the key risk/preventative factors overlap, the most promising approach is likely to be a more general intervention to promote healthy living, with a strong emphasis on exercise as a key component as this is highlighted as a significant lifelong risk factor for dementia and AD from the epidemiological studies.

It is important to note that based upon this evidence the panel believe that it is possible to reduce the risk of developing dementia. It is also important to note that the size of this risk reduction is probably in the region of 15-20% for any particular individual combining the best healthy lifestyle factors. The potential impact of prevention at a population level has been estimated using mathematical modelling factoring in the likely number of people where specific risk factors can be modified, the impact of modifying these risk factors and the increasing number of people developing dementia as the age of the population increases. Using this approach it has been estimated that the number of people with dementia could be reduced by 2% a year from 2012 with the right intervention programmes. This doesn't sound a lot, but given that there will be more than a million people with dementia by 2026, we could potentially prevent or delay dementia in 80,000 of these individuals. In addition the same prevention interventions will give additional benefits for other important health outcomes such as heart disease, stroke and diabetes.