Promoting brain health

Developing a prevention agenda linking dementia and other non-communicable diseases

A science and policy discussion document prepared by the UK Health Forum for a meeting on 30 January 2014
Acknowledgements

This discussion document was written by Dr Oliver Mytton (Specialty Registrar in Public Health), while on secondment to the UK Health Forum from Oxford University Hospitals NHS Trust. The document was edited by Rosie Leyden at Wordworks and Jane Landon.

Expert Group
The author is grateful to the Expert Group, which provided valuable oversight of this work, highlighted references and sources of information, and helped in the interpretation of the findings. Members of the group also commented on earlier drafts of the report. The group consisted of:

Charles Alessi, National Association of Primary Care and Public Health England
Carol Brayne, University of Cambridge
Shah Ebrahim, London School of Hygiene and Tropical Medicine
Joe Korner, Stroke Association
Jane Landon, UK Health Forum
Eugene Milne, Public Health England
Modi Mwatsama, UK Health Forum
Jess Smith, Alzheimer’s Society
Paul Springer, Age Related Diseases and Health Trust
Marc Wortmann, Alzheimer’s Disease International.

Angelique Mavrodaris (University of Cambridge) provided the case study concerning the Coventry and Warwickshire Living Well with Dementia Strategy.

Peer review
An earlier version of this discussion document was reviewed by Lawrence Whalley (Professor Emeritus of Mental Health, University of Aberdeen) and Ruth Peters (Research Fellow, Faculty of Medicine, Imperial College).
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>5</td>
</tr>
<tr>
<td><strong>Background: dementia and a public health perspective</strong></td>
<td>6</td>
</tr>
<tr>
<td><strong>Science review</strong></td>
<td>12</td>
</tr>
<tr>
<td>Alcohol</td>
<td>14</td>
</tr>
<tr>
<td>Diet</td>
<td>19</td>
</tr>
<tr>
<td>Physical activity</td>
<td>22</td>
</tr>
<tr>
<td>Smoking</td>
<td>25</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>28</td>
</tr>
<tr>
<td>Diabetes</td>
<td>32</td>
</tr>
<tr>
<td>Obesity</td>
<td>35</td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td>38</td>
</tr>
<tr>
<td>Summary of science review</td>
<td>42</td>
</tr>
<tr>
<td><strong>Policy review</strong></td>
<td>43</td>
</tr>
<tr>
<td>Considerations in developing a prevention agenda linking dementia and</td>
<td>57</td>
</tr>
<tr>
<td>other non-communicable diseases</td>
<td></td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td>60</td>
</tr>
<tr>
<td>**Appendix 1: NICE framework for the prevention and management of</td>
<td>63</td>
</tr>
<tr>
<td>cardiovascular disease</td>
<td></td>
</tr>
<tr>
<td><strong>Appendix 2: Search terms used for the science review</strong></td>
<td>64</td>
</tr>
<tr>
<td><strong>References</strong></td>
<td>66</td>
</tr>
</tbody>
</table>
List of Tables

**Table 1:** Dementia diagnosis at post-mortem of 50 patients from the Rush Memory and Aging Project 6

**Table 2:** Summary of systematic reviews on the effects of alcohol on dementia 18

**Table 3:** Summary of systematic reviews on the effects of diet on dementia 21

**Table 4:** Summary of systematic reviews on the effects of physical activity on dementia 24

**Table 5:** Summary of systematic reviews on the effects of smoking on dementia 27

**Table 6:** Summary of meta-analysis undertaken on the effects of blood pressure or blood pressure lowering on dementia 31

**Table 7:** Summary of systematic reviews on the effects of diabetes on dementia 34

**Table 8:** Summary of systematic reviews on the effects of obesity on dementia 37

**Table 9:** Summary of meta-analysis undertaken on the effects of serum cholesterol or serum cholesterol lowering on dementia 41

**Table 10:** UK Government dementia strategies and plans 49

**Table 11:** National dementia strategies and plans for countries other than the UK 50

**Table 12:** Other dementia strategies and plans (including those of non-governmental organisations) 51

**Table 13:** UK and international dementia charities’ information on prevention of dementia 52

**Table 14:** Dementia guidelines in the UK 52

**Table 15:** Government strategies for selected non-communicable diseases (England) 53

**Table 16:** UK health charities: To what extent does their advice on healthy living emphasise benefits for dementia and other diseases? 54

**Table 17:** UK Government strategies on alcohol, smoking, physical activity and nutrition 55

**Table 18:** UK advocacy organisations’ information provided on the behavioural risk factors and health 55

**Table 19:** UK guidelines on alcohol, smoking, physical activity and nutrition 56

**Table 20:** Existing intervention studies related to dementia 60

List of Figures

**Figure 1:** Prevalence of dementia by age in England, 2008-11 7

**Figure 2:** The relationship between behaviours, novel and established risk factors, and cardiovascular disease 8

**Figure 3:** The determinants of health 10

**Figure 4:** Prevention and reduction of dementia risk 61
Introduction

The past few years have seen a growing focus on dementia, both worldwide and in the UK. In the UK it is estimated that around 700,000 people live with dementia, and that it costs the economy £17 billion per year. Over the next 30 years this is forecast to grow to 1.4 million people, with costs of £50 billion per year. This is a significant challenge for both health and social care, and both systems will need to adapt. (Department of Health, 2009) In recognition of dementia’s importance, the Prime Minister established a ‘dementia challenge’. It has three main domains: driving improvements in health and care, creating dementia-friendly communities, and improving dementia research. (Department of Health, 2012)

The World Health Organization has described dementia as a “public health priority”. (Alzheimer’s Disease International and WHO, 2012) As with other major non-communicable diseases, the WHO report stresses a role for primary prevention, alongside other important components of a response, such as health and social care readiness. However, the 2010 report from the Agency for Healthcare Research and Quality was pessimistic about opportunities for prevention of Alzheimer’s dementia. (Williams et al, 2010)

Recent results from a large UK study – the Cognitive Function and Aging Study – suggest that the incidence of dementia (and age-specific prevalence) have declined in the past 20 years. The number of adults with dementia is now thought to be 670,000 (or 6.5% of the population over the age of 65 years). This is less than the estimates based on earlier research (880,000 people, or 8.3% of older adults over 65 years of age). (Matthews et al, 2013) Studies in other countries have produced similar conclusions. This may suggest that dementia is more preventable than previously thought. It raises the prospect of not merely responding to dementia by increasing and adapting current services, but actively seeking to prevent or delay the onset of future cases. This may mitigate the rise in the burden of dementia expected in the coming 30 years.

Various risk factors for dementia have been proposed. Some of these – alcohol consumption, diet, physical activity and smoking – are shared with other non-communicable diseases. Public health action and advocacy in these areas are relatively well established. If the science supports action in these areas concerning dementia, it may be possible to integrate dementia prevention with the prevention of the other non-communicable diseases.

This report seeks to review the scientific evidence base linking the four behavioural risk factors of alcohol consumption, diet, physical activity and smoking (as well as related ‘biological’ risk factors: obesity, diabetes, blood pressure and blood cholesterol) with dementia. It also sets out where current dementia policy and practice are with regard to these four behavioural risk factors and dementia, contrasting this to other non-communicable diseases. This document sets out two reviews: a science review and a policy review.
Background: dementia and a public health perspective

Dementia and its sub-types

Dementia is a serious loss of general cognitive ability. This may include memory loss, difficulties with thinking or problem-solving, and difficulties with language. The symptoms are normally progressive. It is a syndrome rather than a diagnosis, meaning that it is a cluster of different signs and symptoms. It can be caused by a variety of underlying disease processes.

The most commonly recognised form of dementia is Alzheimer’s dementia, which accounts for around 50-75% of all dementias. It is characterised by the development of amyloid plaques and neurofibrillary tangles in the brain. Vascular dementia is also very common, and may account for up to 40% of dementias. Vascular dementia is characterised by many small infarcts (or mini-strokes) within the brain that cumulatively cause damage to the brain. It may present differently to Alzheimer’s dementia, progressing in a step-wise fashion, being associated with other signs of neurological disease, and with cardiovascular disease.

While there are diagnostic criteria that may be used to distinguish between the two major forms of dementia, it is often hard for doctors to reliably distinguish between these two types of dementia. Examination of the brains of people with dementia often also shows elements of both types of disease process happening in the same person. (See Table 1; Schneider et al, 2007) Moreover it now appears that both Alzheimer’s dementia and vascular dementia share the same cardiovascular risk factors. For these reasons, many people often do not distinguish between these two types, or may refer to ‘mixed dementia’.

Table 1: Dementia diagnosis at post-mortem of 50 patients from the Rush Memory and Aging Project

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed</td>
<td>28 (56%)</td>
</tr>
<tr>
<td>Alzheimer’s</td>
<td>15 (30%)</td>
</tr>
<tr>
<td>Vascular</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Lewy body</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

Note: The Rush Memory and Aging Project was a longitudinal community-based study of people with dementia.


Other important types of dementia include Lewy body dementia (in which patients have Parkinson’s-like features), fronto-temporal dementia (which often involves a change in personality), and Huntington’s dementia (which is often inherited and has a young age of onset). While these dementias may be less common, they place different demands on carers and the health system.

Epidemiology of dementia

The prevalence of dementia rises sharply with age (see Figure 1). In England the prevalence in those aged 90 years and older is over 30% (1 in 3 people). (Matthews et al, 2013) The prevalence of dementia is particularly high among residents in care homes (over 60%) and older people admitted to hospital (over 40%). (Matthews et al, 2013; Sampson et al, 2009)
However, the majority of people with dementia (over 95%) live in the community. (Matthews et al, 2013)

The pattern of dementia seen in the UK largely seems to be replicated in other countries, although there has been limited work that has compared different geographical areas. These studies can be helpful for pointing to clues to the causes of disease. Recent studies (from the US, UK, Sweden and the Netherlands) have compared the prevalence of dementia over time. (Rocca et al, 2011; Matthews et al, 2013; Qiu et al, 2013; Schrijvers et al, 2012) Comparisons between different times are difficult and should be interpreted with caution. However, the studies do use standardised instruments and select people at random from the population, so they should not simply reflect differences in how doctors are diagnosing dementia over time.

These recent studies suggest that, over the past 20 to 30 years, the age-specific prevalence of dementia or cognitive impairment has fallen in some countries. For example, the Cognitive Function and Ageing Study (CFAS), based in the UK, suggests a reduction in dementia risk of around 20% over a 20-year period (from 1989-1994 to 2008-11). The fall in incidence over time suggests that risk of dementia may be modifiable, and supports the idea that dementia may be (at least in part) prevented.

The preferred explanation for the reduction in dementia is favourable changes in vascular risk factors. These changes have come about partly due to better and wider use of medications and partly due to changes in behaviours (notably much lower smoking rates). Other explanations are also proposed: changes in education, changes in employment and fewer head injuries.

**Figure 1: Prevalence of dementia by age in England, 2008-11**

Different perspectives on the causes of dementia

Much has been written about what causes dementia. To a certain extent the answer depends on one’s perspective.

A laboratory researcher may talk about plaques or neurofibrillary tangles. A psychiatrist or neurologist may talk in terms of lack of brain volume (as seen on scans of the brain), or may talk in terms of loss of brain transmitters (acetyl-choline) for which he or she can offer treatment in the form of acetyl-choline esterase inhibitors (e.g. Aricept). An epidemiologist may talk about risk factors (e.g. hypertension, obesity, physical activity and smoking). While these answers are all different, they may all be compatible.

A similar picture could be described for heart disease, with different professionals having different perspectives on cause and approach to treatment (and prevention). The cardiologist may talk in terms of fatty plaques that develop in the arteries and then rupture, preventing the flow of oxygenated blood to the heart’s muscle. The GP might point to cardiovascular, or medical risk factors (e.g. blood pressure and cholesterol) that he or she routinely treats. The public health practitioner might point to behaviours (e.g. smoking, lack of physical activity or poor diet), or may go further and point to the underlying drivers of behaviour (e.g. the built environment, education, income and cultural norms).

To a large extent we avoid these divisions with heart disease, and have an integrated approach to prevention and management. For cardiovascular disease there is recognition about how these levels of explanation are related (see Figure 2), and there are multiple points at which it is possible to intervene to prevent disability and death. This model shows how behaviours (labelled ‘lifestyle risk factors’ in Figure 2) contribute to the development of biological or medical risk factors (e.g. hypertension or diabetes), which in turn contribute to the development of disease within the body, resulting eventually in symptoms. Similarly for dementia, while there has been a significant focus on biological and molecular pathways concerning Alzheimer’s dementia, many scientists believe that dementia is best explained by an interaction between genetic and environmental factors. (Whalley et al, 2006)

Figure 2: The relationship between behaviours, novel and established risk factors, and cardiovascular disease


Multi-factorial causation

The model shown in Figure 2 is multi-factorial. Smoking, physical activity and poor dietary patterns all contribute to, or cause, the development of heart disease. The relationship between any one risk factor and heart disease is ‘probabilistic’, in that it increases (or reduces) risk. There are tools to quantify how different factors (e.g. smoking, family history of heart disease, presence of diabetes, and age) affect one’s risk of heart disease (e.g. Q-Risk and the Framingham Risk Score).

Most dementias are also multi-factorial (or ‘probabilistic’) with different factors (e.g. genes, behaviours or environment exposures, and age) affecting risk of development of dementia. For dementia two very important factors are age (as outlined in Figure 1), and mutations in the APOE gene. Huntington’s dementia is unusual and might be considered more ‘deterministic’ (i.e having a single-cause). For Huntington’s dementia, possession of a single gene defect invariably results in development of the disease.

Life-course approach

A life-course approach suggests that different factors may exert different effects on the development of disease at different stages in life. Such a model has been advocated for dementia and outlines which factors might be important at which periods of life. (Whalley et al, 2006) This model also introduced the idea of ‘cognitive reserve’, that is, that early and mid-life events may enhance cognitive development and offer protection against age-related decline in cognition and dementia. This model suggests that a fall in cognition with age is inevitable and progressive, such that anybody, if they lived sufficiently long, would develop dementia. Prevention efforts might not stop a person developing dementia, but they would delay the point at which dementia developed. Again this is very similar to cardiovascular disease, where preventive efforts in reducing risk (e.g. stopping smoking or reducing blood pressure) may only delay the age at which cardiovascular disease occurs.

A population-based approach to prevention

A population-based approach to prevention recognises the wider influences or determinants on people’s health and well-being (see Figure 3). These approaches would seek to change or modify these determinants, recognising that an individual’s capacity to change and live a healthy life may be limited by these determinants.

Reduction in smoking prevalence over the past 50 years in the UK has been impressive, and provides a good example of a population-based approach to prevention. It is often argued that the greatest changes came from wider changes in society driven by legislation (e.g. taxes on tobacco, smoke-free legislation, restrictions on marketing, banning sales to children, and visual labels on cigarette packs). These actions worked on the wider determinants of health to create the right social and cultural conditions to support people to live smoke-free. Other more individually focused approaches (e.g. smoking cessation clinics, or brief advice from healthcare practitioners) are also important, and are likely to have had greater success because of work to address the underlying determinants. Such changes could not have been brought about by education alone.

1 Throughout this report the term ‘prevention’ is used. This should be interpreted as either delaying the onset of dementia or reducing the risk of the future occurrence of dementia.
Population-based approaches, and the use of new evidence-based treatments, explain much of the substantial fall in heart disease seen in many developed countries since the 1960s. (O’Flaherty et al, 2013; Smolina et al, 2012) Similar population-based approaches are advocated for the prevention of other non-communicable diseases (diabetes and cancer) and may offer much greater potential for altering the dementia burden than individual approaches (e.g. education) alone.

Figure 3: The determinants of health

![The Determinants of Health](source)

Source: Adapted from Dahlgren and Whitehead, 1991.

**Integrating dementia and other non-communicable diseases**

Given the substantial overlap between the risk factors for the major non-communicable disease (e.g. stroke, cancer, diabetes and heart disease) and dementia, there may be the potential to integrate preventive strategies. It may represent a means to rapidly develop a prevention agenda for dementia. It may also represent a means both to strengthen messages around healthy living and to better advocate for policies to support health. Given that the evidence base about what may prevent dementia is weaker than for other non-communicable diseases, it may also represent a safer place from which to develop a dementia prevention strategy.

For these reasons, and reflecting the expertise of the UK Health Forum, this report focuses on the shared risk factors between dementia and non-communicable diseases. These are: physical activity, smoking, alcohol and diet. We will refer to these as behavioural risk factors.

The report is divided into two main parts:

First a science review, which outlines the epidemiological evidence linking these four behaviours and dementia. The science review is presented first, so that science may inform the policy. The science review also considers the evidence linking dementia and four other

---

2 Integration with other non-communicable diseases should not be seen as a complete dementia prevention strategy. As the Background section outlines, there may be other important risk factors (e.g. head injuries and depression) that it might be appropriate to include within a broad dementia prevention strategy. These other risk factors are less commonly shared with the other non-communicable diseases and may require a different policy response.
risk factors: diabetes, obesity, blood pressure and serum cholesterol. These are principally included to strengthen the case linking the four behavioural risk factors and dementia.

Second a policy review, which outlines what dementia prevention strategies have been developed and the extent to which these overlap with other non-communicable disease strategies. It also contrasts the development of prevention strategies for dementia with those for other non-communicable diseases.
Science review

This science review describes the epidemiological evidence linking the four behavioural risk factors – alcohol, diet, physical activity and smoking – and dementia. It also considers four medical risk factors: blood pressure, diabetes, obesity and serum cholesterol.

We include these medical risk factors in the science review to strengthen the case linking the behavioural risk factors to dementia. Different behavioural risk factors (notably diet and physical activity) are important in preventing the development of medical risk factors. For example, regular physical activity, a healthy diet (e.g. low in salt, and high in vegetables and fruit) and moderate alcohol consumption, may reduce blood pressure and prevent the development of hypertension. Consequently, if raised blood pressure was to be linked to dementia, this would suggest that diet, physical activity and alcohol consumption would have a role in causing dementia through their effect on blood pressure.

The review addresses the following questions:

1. Is there an association between behavioural risk factors and dementia (Alzheimer’s dementia, vascular dementia, or any dementia)?
2. Is there an association between medical risk factors and dementia (Alzheimer’s dementia, vascular dementia, or any dementia)?
3. What is the nature and magnitude of these associations, and how do they vary with age?
4. Is there any evidence suggesting that treatment of medical risk factors may prevent dementia?

Method

Study overview
The protocol for the science review was reviewed by an expert committee comprising academic and policy experts (see page 2 for membership).

Search strategy and study selection
This review used a set of search terms to identify systematic reviews (including meta-analyses) of observational (and trial) studies for four behavioural risk factors (alcohol consumption, diet, physical activity and smoking), and four medical risk factors (blood pressure, diabetes, obesity, and serum cholesterol).

The search took the general form of: Systematic Review (review[Title/Abstract] or meta-analys*[Title/Abstract]) AND Dementia (dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]) AND “Risk Factor”. The full search terms used for each risk factors and number of papers identified are shown in Appendix 2. Searches took place between 29 August and 27 October 2013.

While these medical risk factors may also represent fruitful areas for dementia prevention, this report does not consider interventions that would require drug treatment. This partly reflects the expertise of the UK Health Forum. It also partly reflects our feeling that a higher level of evidence (e.g. randomised controlled trials) is likely to be necessary before drug treatment can be recommended for the prevention of dementia. In contrast, observational evidence may be sufficient to justify interventions to change behavioural risk factors.
All titles and abstracts were then screened manually by the author of this report, to identify relevant systematic reviews.

**Inclusion criteria and study selection**
Studies were included in the review if they fulfilled the following criteria:
1. A systematic review (including meta-analysis) of either observational studies (cohort studies, case-control studies) or trials
2. Explicitly considered the association between one of the eight risk factors and dementia (either any dementia, vascular dementia or Alzheimer’s dementia)
3. Published in a peer-reviewed journal
4. Human studies.

Non-systematic reviews, and reviews where there was no clear description of how papers had been identified for inclusion, have been excluded. Studies based on genetics or animal models or that explored biological mechanisms were not included.

**Data extraction**
For all systematic reviews the following data were extracted: author, year of publication, study type (e.g. trials, cohort study, case-control study), population (region of the world and age), number of individual studies included in the review, outcome (any dementia, vascular dementia, Alzheimer’s dementia); summary of key findings with relative risk where appropriate; and key limitations (identified either by the paper’s authors or by the author of this report).

The summary of the key findings for each review is based on the author’s (OM’s) interpretation of the paper. The overall interpretation, synthesis of the evidence base and discussion of limitations represent the author’s (OM’s) interpretation and understanding. They should not be considered definitive, but as the basis for discussion at the meeting.

**Peer review**
The science review has been reviewed by two experts in the field (Lawrence Whalley and Ruth Peters – see page 2).
Alcohol

Brain damage or profound cognitive impairment (e.g. foetal alcohol syndrome and Wernicke-Korsakoff syndrome⁴) can occur due to heavy alcohol intake. Alcohol-related dementia has also been described as a discrete condition, but there is very limited work to estimate its prevalence. (Ridley et al, 2013; Oslin and Cary, 2003)

Conversely alcohol (in small or moderate amounts) is cardio-protective. A U- or J-shaped relationship has been described between alcohol consumption and cardiovascular disease. (Nichols et al, 2012) It might therefore be expected that dementia (or at least the dementias that are associated with vascular risk factors) might exhibit a similar relationship.

Levels of alcohol consumption in the UK are at a high level, compared to other countries and historical trends. If alcohol consumption is an important risk factor for dementia, this might suggest that a larger burden of dementia due to alcohol will occur in due course. (Gupta and Warner, 2008)

Findings

Three systematic reviews of the relationship between alcohol consumption and dementia were identified. Two of these systematic reviews undertook a meta-analysis. The majority of the evidence is from studies conducted in older people (aged 65 years and over). The two meta-analyses largely drew their findings from different studies.

The two meta-analyses both suggest that small or moderate alcohol consumption (compared to no alcohol) protects against dementia (Alzheimer’s dementia and any dementia). (Anstey et al, 2009; Peters, Peters et al, 2008)

The relationship for vascular dementia may also be protective. The Anstey meta-analysis found a protective relationship (RR=0.75; 95% CI 0.57-0.98; comparing moderate with non-drinkers), while the Peters meta-analysis found a non-significant relationship (RR=0.82; 95%CI 0.50-1.35; comparing moderate with non-drinkers). The effect sizes in the two studies are similar.

Both studies also considered the risk in heavy drinkers. In the Anstey meta-analysis those classified as ‘heavy drinkers’ appeared to have no increased risk compared to non-drinkers (pooled RR=0.92, 0.59-1.45 for Alzheimer’s; 1.36, 0.68-2.71 for vascular dementia; 1.04, 0.69-1.56 for any dementia). The number of studies examining ‘heavy drinkers’ was small, those studies had limited power, and the definition of ‘heavy drinker’ varied (e.g. 14 units a week for a women, to more than 4 drinks a day). (Anstey et al, 2009) Peters et al did not specifically examine the risk in heavy drinkers compared to low, moderate or non-drinkers, but they did consider the relationship between level of consumption and dementia risk. They report that the majority of studies showed a J-shaped curve. (Peters, Peters et al, 2008)

Both studies commented on the wide heterogeneity in the measurement of alcohol consumption in the primary studies (e.g. units, drinks, standard drinks, ml per day, drinks of

---

⁴ Wernicke-Korsakoff syndrome is characterised by a profound amnesia and confabulation. It is caused by thiamine deficiency most commonly in chronic alcoholics but may also be caused by malnutrition. It is not a form of dementia because it only affects one cognitive domain, memory, while dementia is a loss of global cognitive ability.
wine), which made it difficult to combine studies. Neither study attempted to formally characterise the optimum amount of alcohol consumption to prevent dementia.

Moreover the studies covered in both of the meta-analyses give widely varying estimates of how much alcohol should be consumed to reduce dementia risk. For example, “for dementia, benefit [in terms of reduction of dementia risk] was shown for more than one drink per day, weekly or monthly wine consumption, 250-500ml [per day] (usually wine), more than three drinks per day and for 1-28 units per week.” (Peters, Peters et al, 2008) Neither study attempted to compare low to moderate alcohol consumption with high alcohol consumption, as the primary studies had not tended to address this question.

The third systematic review was a narrative review. (Piazza-Gardner et al, 2013) It argued that the current evidence base does not provide adequate information for a concrete cause-effect association between alcohol and Alzheimer’s dementia. It emphasised a number of limitations with the present epidemiological literature concerning alcohol consumption and dementia. It suggested further research should be undertaken before clinical recommendations are made.

**Study limitations**

It can be particularly difficult to make comparisons across the different observational studies on alcohol consumption and dementia for several reasons. The different studies have used different methods to quantify total alcohol consumption (e.g. units, standard drinks, and frequency of drinking). They are often from different countries and so the observed differences may reflect different patterns of alcohol consumption (e.g. binge drinking vs consumption with meals) or different types of alcohol being consumed, rather than being attributed to the quantity of alcohol consumed.

Most studies asked participants what their current drinking status was at study enrolment, and did not consider past drinking behaviour. Using this classification may classify previously heavy drinkers as non-drinkers, which may over-estimate the risk of dementia in non-drinkers. (Roizen et al, 2013; Peters, 2013) Many of the studies include only older adults. One should be cautious about extrapolating to younger adults based on evidence in older adults.

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or have failed to adjust adequately. These other factors may include other behavioural risk factors (smoking, diet, physical activity), age, socio-economic status, employment, social engagement, genetic factors and head injuries (associated with alcohol use and recognised as a risk factor for dementia). While many of the primary studies have adjusted for age and socio-economic status, adjustment for other risk factors is variable.

While there are unique studies to each review, the reviews include many of the same primary studies. One should not assume that having more review studies suggests more evidence.

---

5 Binge drinking in mid-life, for example, has been linked to increased dementia risk. (Järvenpää et al, 2005) However, this study did not adjust for total alcohol consumption, so it is not clear whether the excess risk is due to the total volume of alcohol drunk or the pattern of drinking.
Discussion

The observational studies suggest that alcohol consumption (at least in small or moderate amounts compared to abstinence) is beneficial in terms of reducing dementia risk, among older people. They do not provide consistent evidence that heavy alcohol consumption is associated with increased risk of dementia compared to abstinence. Very limited work has quantified the increased risk for heavy drinkers compared to moderate drinkers.

The absence of better evidence about whether heavy alcohol is associated with increased risk is surprising. This may reflect a variety of issues with the design of present studies: heavy drinkers who experience poor health may have been excluded due to the study design or the late age of enrolment, when heavy drinkers may have developed cognitive problems before the age of 65 (Kim et al, 2012); there may be incomplete follow-up of heavy drinkers either due to death due to other diseases, or as a result of other habits associated with high consumption of alcohol; non-consumers of alcohol appear to have lower cognitive performance than drinkers and so the observed effects (on dementia) may simply be reflecting baseline differences in cognition (Anstey et al, 2009).

Despite the absence of good observational data to support a U-shaped or J-shaped relationship between alcohol consumption and dementia, this relationship is suggested by many authors (Peters, 2012; Kim et al, 2012; Letenneur et al, 2004). Studies published after the publication of the two reported meta-analyses have failed to clarify the picture, with some supporting the idea of a U-shaped relationship (Weyerer et al, 2011) and others refuting it (Lobo et al, 2010). A U-shaped or J-shaped relationship would be similar to the relationship observed for cardiovascular disease, so may support the idea of dementia being a vascular disease.

Policy implications

The evidence does not consistently show that heavy alcohol consumption (compared to no alcohol consumption) is associated with excess risk of dementia. However, some evidence points to a U- or J-shaped relationship between consumption and risk of dementia. The clinical evidence also suggests that heavy alcohol consumption is likely to be linked to dementia. As with cardiovascular disease, it might therefore seem most appropriate to assume a U-shaped relationship with dementia.

As with cardiovascular disease, it could be sensible to put the emphasis on discouraging heavy consumption of alcohol, with less emphasis being given to the possible benefits of small or moderate consumption. It could also be helpful to use the term ‘alcohol-related brain damage’ for which there is a stronger body of evidence showing the dangers of excessive alcohol consumption, throughout the life course.

Policies that discourage harmful excessive alcohol consumption could be supported as measures to reduce the incidence of alcohol-related brain damage, including alcohol-related dementia.

Research suggestions

Future research should consider the importance of the age at which alcohol is consumed (particularly the mid-life period) on risk of subsequent dementia; consider the effect of type of alcohol (e.g. beer, wine or spirits) on risk of dementia; seek to identify what level of
alcohol consumption may be associated with reduced and increased risk of dementia; and seek to describe the epidemiology, including time course, of alcohol-related brain damage in the UK. As randomised trials will be difficult to achieve, other means to examine the nature of the relationship between alcohol consumption and dementia should be considered (e.g. Mendelian randomisation).

**Alcohol-related dementia and alcohol-related brain damage**
There are several diagnoses of cognitive impairment in adults that are related to alcohol use. The most commonly recognised in the UK is Korsakoff syndrome, characterised by profound memory impairment (in particular, difficulty forming new memories). Cognitive impairment associated chronic alcohol excess which is reversible on cessation is also described.

Alongside these syndromes it has been proposed that a true alcohol-related dementia may exist. A set of consensus-based criteria was proposed by Oslin and Cary (2003) and the diagnosis (albeit based on a different set of criteria) was included in the *Diagnosis and Statistical Manual of Mental Disorders version IV*. The Oslin and Cary criteria emphasise the ways in which alcohol-related dementia is different to other dementias (e.g. younger age of onset and clear history of excess alcohol consumption – 35 standard drinks a week for men, and 28 standard drinks for women – over a period of five years). The term alcohol-related brain damage has also been used, and this would include a broader set of syndromes of cognitive impairment attributable to alcohol. (Ridley et al, 2013) This broader term recognises the diagnostic difficulty of distinguishing between alcohol-related dementia and Korsakoff syndrome.

Prevalence rates for alcohol-related dementia vary markedly from 3% of dementia cases in neurology clinics to 24% of dementia cases in nursing homes. (Ridley et al, 2013) The proportion of dementias attributable to alcohol also varies markedly by age, being 22% of all dementias among those under the age of 65 years, and 1.4% of all dementias in those aged above 65 years. (Ridley et al, 2013)

Estimating the true prevalence may be hard not only because of differences in diagnostic criteria and the difficulty in reliably quantifying past alcohol consumption, but also because population-based surveys may miss many people who abuse alcohol, as they may be homeless or in temporary accommodation. Concern has also been expressed that the burden of alcohol-related dementia or alcohol-related brain damage may be liable to rise in the UK due to shifting patterns of alcohol consumption. (Gupta and Warner, 2008) At present there are no direct data to support (or refute) this hypothesis.
<table>
<thead>
<tr>
<th>Study Source</th>
<th>Population</th>
<th>Study types</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piazza-Gardner et al, 2013</td>
<td>Europe, Asia and North America. Mid-life and older persons</td>
<td>Prospective Case-control (n=19)</td>
<td>7/19 papers report that alcohol is protective. 3/19 report that alcohol was a risk factor. 9/19 report no association.</td>
<td>No quantitative summation. Primarily sought to consider whether alcohol was protective or harmful, rather than considering U- or J-shaped relationships.</td>
</tr>
</tbody>
</table>
| Anstey et al, 2009                  | Europe, Asia and North America. Predominantly older persons | Prospective (n=15)               | Risk for low-moderate consumers vs non-consumers:  
• for unspecified dementia 0.74 (0.61-0.91)  
• for Alzheimer’s dementia 0.72 (0.61-0.86)  
• for vascular dementia 0.75 (0.57-0.98). | Small to moderate alcohol consumption not quantified. Includes only people aged 55 years and older. Limited adjustment for confounders. |
| Peters, Peters et al, 2008          | Europe, Asia and North America. Older people (over 65 years) | Prospective (n=20) Case-control (n=3) | Risk for low-moderate vs non-consumers:  
• for unspecified dementia 0.63 (0.53-0.75)  
• for Alzheimer’s dementia 0.57 (0.44-0.74)  
• for vascular dementia 0.82 (0.50-1.35). | Small to moderate alcohol consumption not quantified. Includes only older people. Limited adjustment for confounders. |
Diet

Diet is an important risk factor for many non-communicable diseases. Diet might be expected to be important for dementia risk because of its effect on cardiovascular risk factors (obesity, hypertension, serum cholesterol and diabetes). Other mechanisms have also been proposed. For example, some of the micronutrients found in fruit and vegetables can act as antioxidants or neuro-protective agents, so may have a role in preventing dementia.

While there have been significant shifts in dietary patterns in the past 30 years – for example, in fat consumption and fruit consumption – it is widely thought that there remains significant scope to improve health in the UK by changing diet. (Murray et al., 2013)

Findings

Four systematic reviews were identified. One was a systematic review and meta-analysis of the effects of a Mediterranean diet on all chronic diseases, which included a meta-analysis of the effects on Alzheimer’s dementia (one study) and Parkinson’s disease (two studies) combined. (Sofi et al., 2008) Two of the four studies explicitly considered the effects of a Mediterranean diet (or adherence to a Mediterranean diet) on dementia. One considered the effects of vegetables and fruit, and one took a comprehensive look at evidence around diet and dementia.

Three of the systematic reviews reported that a Mediterranean diet was associated with a reduced risk of Alzheimer’s dementia or any dementia. Estimates of the effect size varied from an 11% to a 48% risk reduction. (Lourida et al., 2013)

One systematic review that considered specifically the effects of vegetables and fruit on dementia concluded that regular vegetable consumption was associated with reduced risk of Alzheimer’s dementia. No association was observed for fruit. This finding was corroborated by another systematic review. (Lee et al., 2010) Fish consumption was also highlighted as being protective. (Lee et al., 2010)

Study limitations

The follow-up of many of the diet studies was short (two to four years). If the disease process takes five or ten years to develop, the association with diet might be explained by a poor diet being an early sign of dementia (e.g. reduced appetite or interest in food) rather than the poor diet contributing to the development of dementia.

Only a limited number of dietary factors have been explored, and the absence of systematic reviews for other dietary factors should not be interpreted as evidence that other dietary factors are not important. Most of these studies enrolled participants in (and measured) diet in late life. One should be cautious about extrapolating findings from older adults to younger adults.

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include other behavioural risk factors (smoking, alcohol, physical activity), age, socio-economic status, employment, social engagement and genetic factors. In particular diet can be very strongly patterned by socio-economic status. While many of the primary
studies have adjusted for age and socio-economic status, adjustment for other risk factors is variable.

While there are unique studies to each review, the reviews include many of the same primary studies. One should not assume that having more review studies suggests more evidence. Of particular note, the evidence linking a Mediterranean diet with dementia, which appears in three of the reviews, largely comes from four American studies that are all part of one project (the Columbia Project). One should not assume that there is a lot of evidence pointing to the benefit of the Mediterranean diet in preventing dementia because it appears in three of the systematic reviews.

Discussion

Regular vegetable consumption and consuming a Mediterranean diet may protect against dementia, particularly Alzheimer’s dementia. The evidence concerning vegetables may be more convincing. It has been observed in several large cohorts in both Europe and America, including those followed from mid-life. The association was also observed in those studies that had adjusted for other healthy behaviours (physical activity and smoking) linked to dementia. The null association for fruit has been consistently observed, including in some of the same studies that find a positive association for vegetables.

A Mediterranean diet is one characterised by: high vegetables; high fruit; high complex carbohydrates; high fish; low meat and poultry; low dairy and milk; and use of olive oil in preference to other oils and spreads. Its efficacy in preventing heart disease among patients at high risk of cardiovascular disease has been shown in a randomised controlled trial. (Estruch et al, 2013) While there is additional evidence that some of these components are associated with reduced risk (vegetables and fish), it remains unclear which parts of the Mediterranean diet are relatively more important in terms of reducing dementia risk.

As mentioned elsewhere in this report, several of the cardiovascular risk factors (hypertension, obesity, hyperlipidaemia and diabetes) are implicated in dementia. Diet is an important risk factor for these conditions. For example, specific dietary patterns, such as DASH (Dietary Approaches to Stop Hypertension) or the Mediterranean diet, as well as specific components (salt, potassium, and pulses) can lower blood pressure. (Jayalath et al, 2014; He et al, 2013; Appel et al, 2006) It would therefore seem likely that diet will have an important role in the development of the dementia, even though the observational evidence (to date) is noticeably limited.

Policy implications

There is some evidence that diet, particularly regular consumption of vegetables, can reduce the risk of dementia. In addition, diet is important in the development of other risk factors (e.g. diabetes and hypertension) for which the evidence is more established. Measures to promote healthy eating could be supported as part of a strategy to reduce the incidence of dementia.

However, one should be careful about over-interpreting these early studies (e.g. putting too much emphasis on a Mediterranean diet or on vegetables) as only a limited number of dietary factors and patterns have been studied. The broad message (and direction for policy) could be that a healthy diet may offer protection against dementia.
Research suggestions

Only limited work has considered the effects of diet on dementia. In addition several important dietary components (e.g. fat composition, red meat, sugar and refined carbohydrates, and fibre) as well as other dietary patterns (e.g. DASH) have not yet been explored. Future studies should consider mid-life diet, as other work suggests that mid-life may be a particularly important period.

Table 3: Summary of systematic reviews on the effects of diet on dementia

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Study types</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lourida et al, 2013</td>
<td>Europe, North America and Australia. Mid-life and older persons</td>
<td>Prospective (n=6) Cross-sectional (n=1)</td>
<td>5/7 studies reported statistically significant beneficial effect of adherence to Mediterranean diet on risk of Alzheimer’s dementia (11-48% reduction) 1/7 reported a beneficial effect (not-significant). 1/7 reported a null effect.</td>
<td>Only considered Mediterranean diet. Limited adjustment of other confounders. Short follow-up.</td>
</tr>
<tr>
<td>Loej and Walach, 2012</td>
<td>Europe and North America. Mid-life and older persons</td>
<td>Prospective (n=9)</td>
<td>8/9 studies found that higher vegetable (or fruit and vegetable) consumption was associated with a lower risk of dementia or cognitive decline. All five studies that examined the association between fruit consumption and dementia or cognitive decline reported null associations.</td>
<td>No meta-analysis. Only considers vegetables and fruit. Limited adjustment of other confounders. Short follow-up.</td>
</tr>
<tr>
<td>Sofi et al, 2008*</td>
<td>USA. Mean age 77 years</td>
<td>Prospective (n=1)</td>
<td>Mediterranean diet associated with reduced risk of Parkinson’s disease and Alzheimer’s dementia on meta-analysis. Only one study (Scarmeas et al, 2006) considered Alzheimer’s dementia: relative risk 0.83 (95% CI: 0.70-0.98) for a two-point increase in diet score.</td>
<td>Single study in a small cohort (2,258 participants). Only considered Mediterranean diet. Short follow-up.</td>
</tr>
</tbody>
</table>

* Meta-analysis combined two studies with outcome of Parkinson’s disease and one study with outcome of Alzheimer’s dementia. The study population refers only to the study that considered Alzheimer’s dementia.
Physical activity

Insufficient physical activity is an important risk factor for cardiovascular disease, some cancers, type 2 diabetes, obesity and poor skeletal health. (Haskell et al, 2007) Regular physical activity is also increasingly recognised as being important for mental well-being, including cognition and risk of dementia. (Haskell et al, 2007; Bull et al, 2010)

The benefits of physical activity in terms of dementia prevention or delay are specifically stressed in the recently updated UK guidelines on physical activity. (Bull et al, 2010) Physical activity may protect against dementia by modifying cardiovascular risk factors (blood pressure, lipids, diabetes and obesity), which are risk factors for dementia. It has also been hypothesised that physical activity may more directly influence brain function and plasticity – for example, by stimulation of brain-derived nerve growth factors.

Physical activity levels are very low in the UK, so increasing physical activity may represent an important strategy to prevent or delay the onset of dementia.

Findings

A total of four systematic reviews concerning the effects of physical activity on dementia were identified, two of which included a meta-analysis. No systematic reviews (or trials) of physical activity on delaying or preventing dementia were identified. However, one systematic review of trials of physical activity on cognition was identified and is included in Table 4.

The longitudinal studies suggest that regular physical activity protects against dementia, Alzheimer’s dementia and vascular dementia (see Table 4). One review repeated the meta-analysis restricting the analysis to studies with stronger methods (including adequate adjustment for confounders such as age, socio-demographics and vascular risk factors), and found that the relationship between physical activity and Alzheimer’s dementia remained strong (RR=0.55; 95% CI 0.36-0.84). (Hamer and Chida, 2009) The doses of physical activity studied vary tremendously from study to study (e.g. 4 hours per week, any exercise, any sports, highest quintile, twice per week, or 2 miles per week of walking). The systematic review of randomised trials of physical activity in healthy older people without cognitive impairment found that aerobic exercise interventions were associated with an improvement in some aspects of cognitive function. The extent to which these improvements are maintained and are related to dementia is unclear.

Study limitations

While most of these studies enrolled participants in late life, many studies have also included participants in mid-life. This gives us greater confidence about making statements about mid- and later life. Different studies have used different doses of physical activity, ranging from physical activity twice per week to at least 60 minutes per day, which may make it difficult to interpret the meta-analyses in terms of how much physical activity is necessary.

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include other behavioural risk factors (smoking, alcohol and nutrition), age, socio-economic status, employment, social engagement and genetic factors. It is reassuring
that studies that consistently adjusted for these risk factors and had other elements of a
stronger study design still found a strong protective effect due to physical activity.

While there are unique studies to each review, the reviews include many of the same
primary studies. One should not assume that having more review studies suggests more
evidence.

Discussion

While the reported associations appear to be strong and consistent (observed in several
cohort studies in both mid- and later life, in three different continents), several issues
remain. Some studies have made adjustment for other healthy behaviours (e.g. nutrition or
not smoking) that might be causally related to a reduced risk of dementia. The required
amount of physical activity to reduce the risk of dementia is unclear. A dose-response
relationship has not been described, with most studies comparing only two groups (high vs
low physical activity).

The type of physical activity required for dementia prevention is unclear. Most studies use
overall physical activity (considering both duration and intensity), although some have
studied (and found benefits associated with) walking. Others have postulated that resistance
training, which is recommended for older people, may have an additive role on cognition.
(Liu-Ambrose and Donaldson, 2009)

There is also some evidence from randomised trials of physical activity in older people
showing benefit in terms of cognition (Barnes et al, 2013; Lautenschlager, 2010; Angevaren
et al, 2008), although this work is in its infancy. Many of the trials are of short duration, and
it is unclear how the observed changes in test scores apply to everyday living. Often the
physical activity is undertaken as a group, and it is unclear if the benefits relate to physical
activity, the resultant social engagement, or a combination of both.

The mechanisms of action remain unclear. Are the effects of physical activity largely
mediated through cardiovascular risk factors? The timing of physical activity with respect to
neuro-degeneration has not been accurately described. Findings from other risk factors
might point to mid-life as being a critical period, but the relative contribution of physical
activity at different points in the life course has not been clearly described.

Policy implications

There is consistent evidence to suggest that regular physical activity can prevent or delay the
onset of dementia, including both Alzheimer’s dementia and vascular dementia. While the
amount of physical activity that will yield benefits is uncertain, it would seem most prudent
to continue to recommend the standard doses of physical activity for good health (i.e. in the
UK, 150 minutes per week of moderate, or 75 minutes of vigorous physical activity, or
combinations of both).

Given the very low levels of habitual physical activity in the UK (Townsend et al, 2012),
increasing physical activity among adults appears to offer significant potential as a strategy
to delay or prevent the onset of dementia. Policies that promote physical activity should be
supported as measures to reduce the incidence of dementia.
Research suggestions

Future research should seek to clarify: the effect of exercise at different points in the life course; the type of exercise that offers benefits; and the dose-response relationship. A randomised trial of physical activity to reduce dementia may be attractive, but given the other substantial benefits of physical activity such a trial may not be practically or ethically feasible.

Table 4: Summary of systematic reviews on the effects of physical activity on dementia

<table>
<thead>
<tr>
<th>Population</th>
<th>Study types</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aarsland et al, 2010</td>
<td>Europe, North America and Japan. Mid-and later-life</td>
<td>Prospective (n=24; of which 5 were suitable for meta-analysis)</td>
<td>Relative risk of vascular dementia: 0.62 (0.42-0.922). Only considers vascular dementia.</td>
</tr>
<tr>
<td>Paterson and Warburton, 2010</td>
<td>Europe and North America. Older adults (60 years and over)</td>
<td>Prospective trials (outcome = cognition) Cross-sectional (n=34)</td>
<td>Majority of articles (71%) reported a positive association between physical activity and a measure of cognition. Evidence from trial data was more equivocal (with 58% showing a positive association). No formal quantification or pooling of effect. Unclear what effect adjustment for other risk factors has on observed relationship.</td>
</tr>
<tr>
<td>Lee et al, 2010</td>
<td>Europe and North America. Mid- and later life</td>
<td>Prospective (n=9)</td>
<td>8/9 studies exhibited a significant positive association between physical activity and dementia. The extent to which other behaviours (smoking, alcohol, diet) have been adjusted for is unclear.</td>
</tr>
<tr>
<td>Hamer and Chida, 2009</td>
<td>Europe, North America and Asia. Mid- and later-life</td>
<td>Prospective (n=16)</td>
<td>Relative risk (comparing highest to lowest physical activity) was 0.72 (0.60-0.86) for dementia and 0.55 (0.36-0.84) for Alzheimer’s dementia. Many studies have not adjusted for other behaviours, and it is unclear what effect this has on overall outcome.</td>
</tr>
<tr>
<td>Angevaren et al, 2008</td>
<td>Older people (over 55 years) without cognitive impairment</td>
<td>RCTs (n=9)</td>
<td>8/11 studies reported that aerobic exercise resulted in improvement in at least one aspect of cognitive function. (The largest effects were on cognitive speed, and auditory and visual attention.) Cognition rather than dementia. Tend to be short-term trials; unclear if benefits are sustained. No estimate of overall effect.</td>
</tr>
</tbody>
</table>
Smoking

Smoking is linked to a wide range of non-communicable diseases. It also has an important role in the development of vascular disease, which suggests it would be associated with dementia, particularly vascular dementia. Smoking appears to have a role in cerebral atrophy, decline in blood perfusion to the brain and white matter lesions, all of which may be important in the development of dementia. (Peters, Poulter et al, 2008)

Conversely, it has been suggested that one ingredient within cigarettes – nicotine – might have a protective role on cognition through its action on nicotinic acetylcholine receptors in the brain or even inhibition of amyloid formation. (Peters, Poulter et al, 2008; Anstey et al, 2007)

Smoking prevalence has declined markedly over the past 40 years. If smoking is causally related to dementia, this may have had a role in mitigating the rise in the burden of dementia over the past 10 to 20 years. (Matthews et al, 2013) Smoking prevalence in the UK remains at 20%, and further reductions towards a smoke-free society may have the potential to contribute further to reductions in incidence of dementia.

Findings

Four systematic reviews were identified. Three of these formally pooled estimates for relative risk in a meta-analysis.

The earliest study found mixed results. Analysis of case-control studies suggested that smoking was protective of Alzheimer’s dementia. Cohort studies suggested a null association for ever-smokers and a raised risk for current-smokers (those smoking at baseline). (Almeida et al, 2002) The three subsequent systematic reviews all report that current smoking was associated with increased risk of dementia, vascular dementia or Alzheimer’s dementia (Lee et al, 2010; Peters, Poulter et al, 2008; Anstey et al, 2007), although a non-significant association for vascular dementia was found in one meta-analysis. (Peters, Poulter et al, 2008) The raised risk is typically in the region of 50-100%. There is a suggestion of a dose-response relationship for smoking and dementia. (Lee et al, 2010) Results for former smokers (classified as former smokers at baseline) compared to never smokers tend to show a null effect. (Anstey et al, 2007; Peters, Poulter et al, 2008)

The two large meta-analyses have not directly addressed the question of life-course effects and whether smoking in mid-life compared to older age contributes differently to the increased risk. However, it should be noted that positive and strong associations have been observed for mid-life studies. For example, the HHP-HAAS studies, which enrolled participants between the ages of 46 and 67 years and then followed the participants for 25 years, found an odds ratio of 2.55 for medium smokers (95% CI: 1.22-5.58) (for Alzheimer’s), and 2.93 for heavy smokers (95% CI: 1.37-6.53). (Tyas et al, 2003)

Study limitations

While most of these studies enrolled participants in late life, many studies have also included participants in mid-life. This gives us greater confidence about making statements about mid- and later life.
Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include other behavioural risk factors (physical activity, alcohol and diet), age, socio-economic status, employment, social engagement and genetic factors. Many studies adjusted for demographic and health factors that may influence the association. However, the extent of this and the variables adjusted for vary from study to study. (Peters, Poulter et al, 2008) It is also unclear what the effect of adjusting for these variables, if any, has on the observed associations. Adjustment for vascular risk factors (e.g. serum cholesterol) or other markers of health (e.g. heart disease), which has been done by several studies, may be inappropriate as such risk factors and diseases may be in the causal pathway between smoking and dementia.

Some of the evidence cited comes from case-control studies. Evidence from these studies is generally considered weaker (in comparison with evidence from prospective or longitudinal studies). Such studies can be very unreliable at measuring the true effect due to the difficulty of adjusting for confounding. With respect to dementia and smoking, close matching by age would be very important as non-smokers tend to be older (as smokers die young) and older age is a strong predictor of dementia. Studies that do not properly account for the higher attrition rate of smokers will under-estimate the effect of smoking on cognitive decline and dementia. (Weuve et al, 2012)

While there are unique studies to each review, the reviews include many of the same primary studies. One should not assume that having more review studies suggests more evidence.

Discussion

The prospective studies and comparisons of current smokers against non-smokers are most likely to give the truest estimate of the effect of smoking on dementia. These studies consistently show that smoking is associated with an increased risk of dementia, Alzheimer’s dementia, and possibly vascular dementia. In addition, studies published after the large meta-analyses also provide evidence linking smoking to dementia and cognitive decline. (Collins et al, 2009; Rusanen et al, 2011)

The apparent null association for former smokers, in most studies, might appear inconsistent with the hypothesis that smoking causes dementia, as one might expect a residual effect of past smoking on dementia to persist after quitting given the long latency seen between other exposures and development of dementia. However, former smokers are a broad group of people that may include people who have smoked very little or given up a long time ago, as well as recent heavy smokers, so one might not expect to observe much if any effect. It is also worth remembering that some studies have detected an increased risk of dementia among former smokers. (Anstey et al, 2007)

Policy implications

There is reasonable evidence that smoking is associated with dementia. Measures that discourage smoking could be supported as part of a strategy to reduce the incidence of dementia.
Research suggestions

Future studies should be explicit about which studies have adjusted for which potential confounders, and undertake a sensitivity analysis around adjusted estimates. Any such analysis needs to be undertaken with care, as some factors that have been adjusted for (e.g. serum cholesterol) may be on the causal pathway, so adjustment may lead to an under-estimate of the true relationship. This may be particularly important for vascular dementia.

Table 5: Summary of systematic reviews on the effects of smoking on dementia

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Study types</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al, 2010</td>
<td>Asia and European populations. Mid-life and older people</td>
<td>Prospective (n=4)</td>
<td>4/4 studies report that smoking is associated with dementia or Alzheimer’s dementia. Current smoking, but not past smoking, was associated with increased risk. Association was stronger the higher the number of pack years of smoking.</td>
<td>The extent to which other behaviours (physical activity, alcohol and diet) have been adjusted for is unclear.</td>
</tr>
<tr>
<td>Peters, Poulter et al, 2008</td>
<td>North America, Asia, Europe and Australia. Mid- and later life.</td>
<td>Prospective Case control (n=50)</td>
<td>Risks for current smokers against never smokers for Alzheimer’s dementia (1.59: 95% CI 1.15-2.20), vascular dementia (1.35: 95% CI 0.90-2.02), dementia unspecified (1.16: 95% CI 0.90-1.50), and cognitive decline (1.20: 95% CI 0.90-1.59). Risks for ex-smokers compared to non-smokers for Alzheimer’s dementia (0.99: 95% CI 0.81-1.23), vascular dementia (1.05: 95% CI 0.72-1.54), dementia unspecified (0.90: 95% CI 0.75-1.07) and cognitive decline (0.90: 95% CI 0.74-1.10).</td>
<td>The extent to which other behaviours (physical activity, alcohol and diet) have been adjusted for, and their effect on estimates, are unclear.</td>
</tr>
<tr>
<td>Anstey et al, 2007</td>
<td>North America, Asia, Europe and Australia. Mid- and later life.</td>
<td>Prospective (n=19)</td>
<td>Current smokers (compared to non-smokers at baseline) had an increased risk of Alzheimer’s dementia (RR=1.79; 95% CI 1.43-2.23), vascular dementia (RR=1.78; 95% CI 1.28-2.47) and for any dementia (RR=1.27; 95% CI 1.02-1.60).</td>
<td>The extent to which other behaviours (physical activity, alcohol and diet) have been adjusted for, and their effect on estimates, are unclear.</td>
</tr>
<tr>
<td>Almeida et al, 2002</td>
<td>North America, Asia and Europe. Mid- and later life.</td>
<td>Prospective (n=8) Case-control (n=21)</td>
<td>Pooled odds ratio for case control studies (based on adjusted odds ratio) was 0.82 (95% CI: 0.70-0.97) for Alzheimer’s dementia comparing smokers with non-smokers. For cohort studies: for ever smokers the risk was 1.10 (94-1.29) and for those smoking at baseline the risk was 1.99 (95% CI 1.33-2.98) for Alzheimer’s dementia, compared to non-smokers.</td>
<td>Only considered Alzheimer’s dementia. Largely weighted to case-control studies.</td>
</tr>
</tbody>
</table>
Blood pressure

Elevated blood pressure is thought to be an important risk factor for the development of dementia. It may contribute to small vascular events (small infarcts) that lead to direct damage to brain tissue. Raised blood pressure may also promote fluid and protein leakage from blood vessels, which are thought to have a role in the development of plaques and tangles that are characteristic of Alzheimer’s dementia. (Hoffman et al, 2009) Elevated blood pressure is also a strong risk factor for stroke, and stroke is associated with a doubling of the incidence of dementia. (Savva et al, 2010)

While hypertension is commonly managed medically, it can also be prevented or treated by modifying diet, moderating alcohol consumption, increasing physical activity and losing body weight. While detection and treatment of hypertension have much improved, the UK analysis for the Global Burden of Disease Study suggests that there is still considerable scope to improve health through the better management of raised blood pressure. (Murray et al, 2013)

Findings

A total of eight systematic reviews were identified. Each had different criteria for including studies within the review and meta-analyses. Some reviews include data from both observational studies and trials; some only from observational studies; and some only from trials. The reviews have also made different decisions about which types of trials or observational studies to include.

The summary results from the meta-analyses are shown in Table 6. They show mixed results for the effect of hypertension on dementia. Several studies report a small significant effect of hypertension on any dementia or Alzheimer’s dementia. (Peters, Beckett et al, 2008; Power et al, 2011; Chang-Quan et al, 2011) Other studies report null associations or small non-significant associations. (McGuinness et al, 2009; Guan et al, 2011; Chang-Quan et al, 2011) Studies that have looked at vascular dementia (in older persons) report much larger effects (Sharp et al, 2011; Chang-Quan et al, 2011), as have studies that have looked at mid-life hypertension. (Barnes and Yaffe, 2011) The one study that explicitly sought to compare mid- and late life found a null or inverse association in later life, and suggested that mid-life diastolic hypertension might be important. This study only considered Alzheimer’s dementia. (Power et al, 2011)

Study limitations

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include behavioural risk factors (physical activity, alcohol, diet and smoking), other biological risk factors (obesity, diabetes, and serum cholesterol), age, socio-economic status, employment, social engagement and genetic factors. Many studies adjusted for demographic and health factors that may influence the association.

Many of the observational studies (of the effect of hypertension on dementia) took place during a period when anti-hypertensives were increasingly being used to prevent cardiovascular disease. It therefore seems plausible that many study participants with raised blood pressure are likely to have received treatment. It is unclear the extent to which this
happened and has been adjusted for in different studies. This might lead to an under-
estimate of the effect of raised blood pressure on dementia.

The observational studies (considering the effect of treatment of hypertension on dementia) may be biased. Patients may be more liable to be treated if they are in good health, and it may be their good health rather than the treatment of hypertension that is causing (or predicts) their lower risk of dementia. This might lead to an over-estimate of the effect of treatment on the reduced risk of dementia.

The trial data should be treated with caution. Most of the trials were primarily designed to test the effect on cardiovascular disease (heart disease and stroke), with dementia as a secondary end-point. Consequently these trials were poorly designed to detect a difference in dementia, often being too small or having too short a follow-up. Consequently, a negative trial result may suggest that anti-hypertensives have no effect in preventing dementia, or may reflect the trial being too poorly designed to detect an effect.

Discussion

While the summary findings may appear to give a mixed picture, some of these differences may be explained by the different types of trial included in the reviews. The greatest risk from hypertension may occur in mid-life. (Ballard et al, 2013; Wilson et al, 2011) In contrast, the risk in later life appears lower, although it has also been observed that a fall in blood pressure may precede the diagnosis of dementia. (Skoog et al, 1996) Studies mixing both periods (mid- and late life) consequently may estimate much lower effects of raised blood pressure. However, the authors of one review that specifically sought to tease apart mid- and late life effects (albeit only for Alzheimer’s) concluded that they were uncertain of a causal role for raised blood pressure in Alzheimer’s dementia.

Despite the epidemiological evidence pointing to benefits of blood pressure lowering in mid-life, most trials of blood pressure lowering (for pragmatic reasons) have been in an older population. While one study reports no (significant) effect for anti-hypertensives, the other reports a protective effect, although the point estimates for both studies are similar (0.87 vs 0.89). (Peters, Beckett et al, 2008; McGuinness et al, 2009) Even the more conservative estimate (an 11% reduction) is consistent with a useful protective effect (and in line with the effects of anti-hypertensive agents on other vascular diseases). Presently it is not generally accepted that treatment of raised blood pressure can reduce the risk of dementia or vascular dementia. (Alzheimer’s Disease International and WHO, 2012)

While the epidemiology may suggest that the effects of blood pressure are more pronounced for vascular dementia compared to Alzheimer’s dementia, prospective cohorts of patients treated with anti-hypertensive agents suggest similar effects on both vascular and Alzheimer’s dementia. (Guan et al, 2011; Chang-Quan et al, 2011) The similar estimates may also reflect the practical difficulties of distinguishing between vascular and Alzheimer’s dementia.

---

6 There are also other important differences between these reviews. Peters, Beckett et al (2008) include the PROGRESS trial which enrolled patients with a previous stroke or TIA (transient ischaemic attack). In contrast, McGuinness et al (2009) included the SCOPE trial in which many participants in the placebo group were allowed to be treated and consequently the observed blood pressure difference between the placebo and control group was minimal.
The meta-analyses to date have not clearly delineated the independent effects of blood pressure, separate from other vascular risk factors on dementia. While blood pressure studies to prevent dementia are relatively advanced compared to other trials of treatment to prevent dementia, compared to cardiovascular disease the work is still at an early stage. A recent meta-analysis of the effect of blood pressure on cardiovascular disease (stroke and ischaemic heart disease) included 124 studies and 1.2 million people. (Peters, Huxley et al, 2013)

Policy implications

The evidence is tending to suggest that reducing raised blood pressure, particularly during mid-life, may help prevent dementia. However, it should be noted that the evidence from trials is not yet sufficient to recommend the use of anti-hypertensives to prevent dementia.

Policies and strategies (both behavioural and pharmacological) that reduce hypertension may reduce the incidence of dementia. Mid-life may be a more important period to target, but benefits may also occur from treatment in older age.

Research suggestions

Given the limited research into anti-hypertensives to prevent cognitive decline in older adults, and the limitations of past studies, it seems sensible to continue to pursue trials of anti-hypertensives in older adults. Studies of the effect of treatment of mid-life hypertension on dementia are also needed. Pragmatically, quicker answers may be gleaned by following up existing cohorts of people enrolled in past trials of anti-hypertensive medications. Further research should also seek to clarify and establish the effect of age on the relationship between blood pressure and dementia, for both vascular and Alzheimer sub-types. The importance of class (or type) of anti-hypertensive should also be considered.
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Study types</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barnes and Yaffe, 2011</td>
<td>Europe, North America and Asia. Mid-life.</td>
<td>Prospective (n=5)</td>
<td>Odds ratio for dementia among those with mid-life hypertension compared to those without 1.61 (1.16-2.24).</td>
<td>Based on a systematic review of past meta-analyses; then re-analysed data for mid-life studies only. Unclear if estimates used are adjusted for other vascular risk factors. Alzheimer’s dementia only.</td>
</tr>
<tr>
<td>Chang-Quan et al, 2011</td>
<td>Europe, North America and Asia. Mid-life and later life.</td>
<td>Prospective RCTs (n=14)</td>
<td>Significantly lower risk of any dementia (0.87; 95% CI 0.77-0.96) or vascular dementia (0.67; 95% CI 0.52-0.87). Risk for Alzheimer’s 0.90 (0.79-1.03) and for cognitive impairment 0.97 (0.92-1.03); includes sub-analysis for controlled trials for Alzheimer’s 0.79 (0.63-1.09), vascular dementia 0.76 (0.57-1.00) and any dementia 0.87 (0.76-1.01).</td>
<td>A large proportion of studies had older cohorts (aged over 65 years) and did not undertake a sub-analysis by age. Unclear if estimates used are adjusted for other vascular risk factors.</td>
</tr>
<tr>
<td>Guan et al, 2011</td>
<td>Europe, North America and Asia. Mid-life and later-life.</td>
<td>Prospective RCTs (n=2)</td>
<td>Risk of Alzheimer’s dementia in those with hypertension compared to those without: 1.02 (95% CI 0.91-1.14). Risk of Alzheimer’s dementia in those treated with anti-hypertensives compared to those not treated: 0.90 (95% CI 0.79-1.03).</td>
<td>A large proportion of studies had older cohorts (aged over 65 years); sub-analysis by age. Unclear if estimates used are adjusted for other vascular risk factors.</td>
</tr>
<tr>
<td>Power et al, 2011</td>
<td>Europe, North America and Asia. Mid-life and later-life</td>
<td>Prospective (n=18)</td>
<td>Relative risks for: hypertension (RR(Σ) = 0.97 [95% confidence interval = 0.80-1.16]); a 10-mm Hg increase in systolic BP (RR(Σ) = 0.95 [0.91-1.00]); and a 10-mm Hg increase in diastolic BP (RR(Ω) = 0.94 [0.85-1.04]). Suggestion of an inverse association between late-life hypertension and Alzheimer’s dementia.</td>
<td>Alzheimer’s dementia only. Unclear if estimates used are adjusted for other vascular risk factors. Estimates shown are for random effects; stronger effects were observed using fixed effects.</td>
</tr>
<tr>
<td>Sharp et al, 2011</td>
<td>Europe, North America, Middle East and Asia. Mid-life and later life</td>
<td>Prospective (n=6) Cross-sectional (n=5)</td>
<td>Odds ratio of incident vascular dementia associated with hypertension 1.59 (95%: 1.29-1.95, p &lt; 0.001) for prospective studies, and 4.84 (95%: 3.52-6.67, p &lt; 0.001) for cross-sectional studies.</td>
<td>Limited follow-up in prospective studies (median 4.9 years, range 3.2-10 years). All estimates are based on unadjusted odds ratios.</td>
</tr>
<tr>
<td>McGuinness et al, 2009</td>
<td>Europe, North America and China. Later life (60-89 years)</td>
<td>RCTs (n=4)</td>
<td>Odds ratio 0.89 (95% CI: 0.74-1.07), with considerable heterogeneity between trials.</td>
<td>Used random rather than fixed effects. Trials were in older people.</td>
</tr>
<tr>
<td>Peters, Beckett et al, 2008</td>
<td>Europe, North America and China. Later life</td>
<td>RCTs (n=4)</td>
<td>Hazard ratio 0.87 (95% CI: 0.76-1.00, p=0.045).</td>
<td>Used fixed rather than random effects. Trials were in older people.</td>
</tr>
</tbody>
</table>
Diabetes

Diabetes mellitus is associated with changes in cognition, such as slowing of mental speed and impaired learning. Cognitive decline may also be accelerated in those with type 2 diabetes. (Allen et al, 2004) Diabetes is closely linked with the metabolic syndrome and raised cardiovascular risk, so might conceivably be linked to dementia, and particularly vascular forms of dementia. Besides vascular explanations for an association between diabetes and dementia, it has also been suggested that glucose may have a direct toxic effect and that insulin may have a role in the breakdown of amyloid proteins. (Biessels et al, 2006)

The prevalence of diabetes (type 1 and type 2) in the UK is currently at 5% and rising. It also increases with age, with a prevalence of around 8% in mid-life, and over 13% in later life. (Diabetes UK, 2012) If diabetes is important in the aetiology of dementia, these trends will have important implications for the future incidence of dementia. Diabetes is also often preventable by adoption of healthy behaviours, which may suggest scope to reduce the future incidence of diabetes.

Findings

A total of five studies were identified. Four were systematic reviews of prospective studies, examining the association between diabetes and dementia. One was a Cochrane review considering the effect of diabetes treatment on risk of dementia and cognitive decline.

The four systematic reviews of prospective studies present a consistent picture of an increased risk of dementia among people with diabetes compared to people without diabetes (see Table 7). The excess risk associated with diabetes appears to be of the order of 50% to 100%. (Biessels et al, 2006; Profenno et al, 2010) Both mid-life and late-life diabetes appear to confer excess risk. Estimates of the risk of Alzheimer’s dementia when adjusted for other vascular risk factors appear similar to the unadjusted risk. (Profenno et al, 2010; Lu et al, 2009) The excess risk for vascular dementia may be greater than that for Alzheimer’s dementia. (Lu et al, 2009)

The Cochrane review found no evidence that treatment of diabetes prevented cognitive impairment or dementia (Areosa and Grimley Evans, 2002) although there was some evidence that more aggressive treatment of diabetes was associated with improvement in various indices of cognitive function. However, most studies were of short duration, with only one study having a follow-up greater than 12 months.

Study limitations

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include behavioural risk factors (physical activity, alcohol, diet and smoking), other biological risk factors (obesity, serum cholesterol blood pressure), age, socio-economic status, employment, social engagement and genetic factors. Many studies adjusted for demographic and health factors that may influence the association.

The methods (self-report, medical records and blood glucose testing) and timing (at baseline or additionally during follow-up) vary between studies. This may lead to misclassification of study participants who have diabetes as non-diabetic. Such misclassification would tend to
lead to a higher estimation of the risk among the non-diabetic population, and consequent under-estimation of the true risk of diabetes. Such effects are likely to be modest given the relatively low prevalence of diabetes in most populations observed. (Biessels et al, 2006)

The trial data should be interpreted cautiously. The null findings may be due to limitations of the study design (e.g. follow-up that is too short). Studies have tended to compare routine diabetes care with more intensive diabetes care. Routine care may be optimal care, and the failure to find benefit does not imply that routine care does not offer benefits in terms of cognition over sub-optimal care.

Discussion

The four systematic reviews of prospective studies all suggest that diabetes confers an increased risk of dementia. The persistence of the positive association after adjustment for other cardiovascular risk factors (Body Mass Index and hypertension) (Kloppenborg, 2008; Profenno et al, 2010) suggests that the association cannot simply be explained by other cardiovascular risk factors. Recent research has shown a dose-response relationship between hyperglycaemia and dementia risk. (Crane et al, 2013)

While the Cochrane review does not appear to match the other evidence, the review is now several years old and had only identified trials of short in duration (less than one year), which may have been too short to detect an effect on dementia. Subsequent trials have also failed to find improvements in cognition from either more intensive glucose-lowering treatment (Launer et al, 2011) or specific blood pressure treatment. (Patel et al, 2007)

The raised risk applies to both Alzheimer’s and vascular dementia, although there is a suggestion of a stronger association for vascular dementia. (Lu et al, 2009; Kloppenborg et al, 2008) In contrast to other vascular risk factors, diabetes appears to confer a similar risk in both mid- and late life. (Kloppenborg, 2008) However, this may be because those with diabetes in later life developed the disease in mid-life, and it was the presence of the disease in mid-life, rather than later life, that led to the development of dementia.

Policy implications

Diabetes is associated with raised risk of dementia (both vascular and Alzheimer’s). Aggressive treatment of diabetes (or its vascular complications) may seem like an attractive strategy to reduce risk in those with diabetes, but at present there is no evidence that such treatment reduces the risk of dementia. Strategies and interventions that aim to prevent diabetes (such as promoting physical activity and improved nutrition) could reduce the incidence of diabetes and so could contribute to reducing the future burden of dementia.

Dementia due to diabetes is likely to become a greater issue, both because of the rising prevalence of diabetes in the UK and because people with diabetes are increasingly living to an older age.

Research suggestions

There is a reasonable body of evidence linking diabetes to dementia. Understanding the risk factors (e.g. co-morbid vascular risk factors) and mechanisms that drive the association between diabetes and dementia may be important for understanding which elements of diabetes treatment are important in reducing the risk of dementia. Long-term follow-up of
existing cohorts of patients randomised to intensive vs non-intensive treatment of diabetes may be a pragmatic means to gain earlier insights into the efficacy of diabetes treatment in reducing dementia risk.

Table 7: Summary of systematic reviews on the effects of diabetes on dementia

<table>
<thead>
<tr>
<th>Population</th>
<th>Study types</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profenno et al, 2010</td>
<td>North America, Europe and Japan. Mid- and later life</td>
<td>Prospective (n=10)</td>
<td>Diabetes in mid- and late life associated with increased risk of Alzheimer’s dementia. Pooled relative risk 1.54 (95% CI: 1.33-1.79), 1.64 (1.29-2.09) when restricted to studies adjusting for BMI and vascular risk, and 2.06 (1.49-2.85) when additionally adjusting for APOE4 allele. The study also included obesity. It reports that obesity and diabetes are independent risk factors.</td>
</tr>
<tr>
<td>Lu et al, 2009</td>
<td>North America and Europe. Mid- and later life</td>
<td>Prospective (n=15)</td>
<td>Relative risk for Alzheimer’s dementia of 1.39 (95 CI: 1.16 to 1.66), and 2.38 for vascular dementia (95 CI: 1.79 to 3.18). Restricted analysis to studies that had adjusted for confounders, including cardiovascular co-morbidities.</td>
</tr>
<tr>
<td>Kloppenborg et al, 2008</td>
<td>North America and Europe. Mid- and later life</td>
<td>Prospective (n=14)</td>
<td>5/9 studies reported significant association with any dementia. 6/11 reported significant association with Alzheimer’s dementia; and 6/10 for vascular dementia. Odds ratio generally higher for vascular dementia than Alzheimer’s dementia; no clear difference for mid-life vs later-life diabetes observed. Adjustment for vascular risk factors did not appreciably change the risk.</td>
</tr>
<tr>
<td>Biessels et al, 2006</td>
<td>North America, Japan, Europe and Israel</td>
<td>Prospective (n=14)</td>
<td>Risk of both Alzheimer’s dementia and vascular dementia increased among people with diabetes. Both mid-life and late-life diabetes appear to be associated with dementia. Risk in late life around 50-100% increase. Limited and variable adjustment for confounders in included studies.</td>
</tr>
<tr>
<td>Areosa and Grimley Evans, 2002</td>
<td>Europe and North America. Later life</td>
<td>RCTs (Cochrane review) (n=5)</td>
<td>No evidence that diabetes treatment affects cognition or dementia risk. Most studies (4/5) were short-term (12 months or less) and all focused on cognitive function, rather than dementia. Study is old.</td>
</tr>
</tbody>
</table>
Obesity

Obesity might be linked to dementia. It is associated with the metabolic syndrome (insulin resistance, hypertension and hyperlipidaemia) and cardiovascular disease, both of which are likely to contribute to the development of dementia. The causes of obesity (insufficient physical activity and/or poor diet) are also associated with dementia. There may also be direct effects on dementia. Some of the hormones important for appetite (e.g. insulin and leptin) are affected in obesity and may have a role on brain development and repair. (Fadel et al, 2013; Elmquist and Flier, 2004) While this may suggest that associations between obesity and dementia are likely, it may be difficult to tease apart how and why obesity may contribute to dementia.

The prevalence of obesity among adults in the UK is 26% and has risen dramatically in the last two to three decades. Such trends may continue. (Wang et al, 2011) If obesity were linked to dementia, this would be likely to have significant implications for the future burden of dementia.

Findings

A total of six systematic reviews were identified, five of which undertook a meta-analysis. No treatment trials (effect of weight loss on risk of dementia) were identified.

The studies consistently suggest a U- or J-shaped relationship between Body Mass Index (BMI) and dementia, with a raised risk for those who are overweight, obese or underweight, compared to those of normal weight. A dose-response relationship has been demonstrated, with the risk for obesity being greater than the risk for overweight. The relationship is stronger for mid-life obesity than late-life obesity, where weak, null or even negative associations with dementia are described.

It is unclear whether the risks are different for Alzheimer’s and vascular dementia. One meta-analysis appears to suggest a weaker relationship with obesity for vascular dementia (Anstey et al, 2011), while an earlier meta-analysis appears to suggest a stronger relationship between obesity and vascular dementia in comparison with Alzheimer’s dementia. (Beydoun et al, 2008) However, in each paper the difference in risk between vascular and Alzheimer’s dementia is not significant.

Study limitations

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include behavioural risk factors (physical activity, alcohol, diet and smoking), other biological risk factors (serum cholesterol, diabetes and blood pressure), age, socio-economic status, employment, social engagement and genetic factors. Many studies adjusted for demographic and health factors that may influence the association. Some studies have also adjusted for hypertension and/or diabetes.

Given the strong suggestion of different effects between mid- and late life, one should interpret cautiously studies that have mixed the two periods.
Discussion

Mid-life overweight, obesity and underweight are associated with a raised risk of dementia (both vascular and Alzheimer’s dementia) in later life. The importance of body weight in later life remains unclear. Loss of body weight may be an early sign of dementia, which may mask the true relationship between body weight and dementia in later life. Alternatively, body weight in later life may be relatively unimportant in conferring later risk of dementia.

It appears that the relationship between mid-life obesity and dementia cannot simply be explained by hypertension or diabetes, as the strength of the relationship appears similar after adjustment for these risk factors. No studies appear to have adjusted for the behavioural risk factors (physical activity and diet) that contribute to obesity and may independently influence risk of dementia. It therefore seems possible that obesity serves as a marker for increased risk of dementia, and that the relationship between obesity and dementia could be explained by insufficient physical activity or poor diet.

Policy implications

Mid-life obesity is consistently associated with raised risk of dementia (both vascular and Alzheimer’s). Strategies and interventions that aim to prevent obesity in middle age (such as promoting physical activity and improved nutrition) could reduce the incidence of dementia. Weight loss in people who are obese may have a role in prevention of obesity. However, sustained weight loss is difficult to achieve, and the effects of reversing weight gain on dementia risk have not been explored. This emphasises the importance of preventive strategies.

The independent effect of obesity may suggest that the excess risk associated with obesity cannot readily be managed by medical treatment (anti-hypertensive agents and anti-diabetic agents), which emphasises the importance of specific measures to prevent weight gain or to reduce body weight.

Research suggestions

There is a reasonable body of evidence linking obesity to dementia. Areas of research that could inform public health practice include: clarification as to whether late-life obesity is important for risk of dementia after accounting for any effect of early dementia leading to loss of body weight (prevalence of obesity in later life is high and rising); understanding the effects of weight loss in mid-life on dementia risk in old age; and understanding the risks associated with early life (child, adolescent and early adult). There will also be benefit in further disentangling the relative components (behavioural and metabolic) to understand the mechanisms by which obesity may cause dementia.
Table 8: Summary of systematic reviews on the effects of obesity on dementia

<table>
<thead>
<tr>
<th>Study population</th>
<th>Study types</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loeff and Walach, 2013</td>
<td>Prospective</td>
<td>North America and Europe. Mid- and late life.</td>
<td>U-shaped relationship between mid-life BMI and dementia. Relative risk of all dementia for obesity = 1.91 (95% CI: 1.40-2.62), and for overweight = 1.34 (95% CI: 1.08-1.66) compared to normal BMI. Late-life BMI (over 60 years) negatively associated with dementia, but this may be related to low BMI being a marker of an underlying dementia process rather than causative.</td>
</tr>
<tr>
<td>Anstey et al, 2011</td>
<td>Prospective (n=11)</td>
<td>North America and Europe. Mid- and late-life populations.</td>
<td>U-shaped relationship between mid-life BMI and dementia. Relative risk for low BMI: 1.96 (95% CI: 1.32-2.92) for Alzheimer’s. Relative risk for overweight: 1.35 (1.19-1.54) for Alzheimer’s, 1.33 (1.02-1.75) for vascular dementia, and 1.26 (1.10-1.44) for any dementia. Relative risk for obesity: 2.04 (1.59-2.62) for Alzheimer’s, and 1.64 (1.34-2.00) for any dementia. (All relative to normal BMI.) Lack of consistent adjustment for health and demographic factors as well as for diet, alcohol, smoking and physical activity.</td>
</tr>
<tr>
<td>Lee et al, 2010</td>
<td>Prospective (n=6)</td>
<td>North America and Europe. Mid- and late-life populations</td>
<td>4/6 studies report an association between BMI and dementia. 2/6 describe no association. (One of these reported a null association after adjustment for multiple confounders.) Lack of consistent adjustment for health and demographic factors as well as for diet, alcohol, smoking and physical activity.</td>
</tr>
<tr>
<td>Profenno et al, 2010</td>
<td>Prospective (n=6)</td>
<td>North America and Europe. Mid- and late-life populations (Alzheimer’s only)</td>
<td>The relative risk for Alzheimer’s dementia was 1.54 (95% CI: 1.31–1.79) for obesity. Adjustment for abnormal glucose or insulin and diabetes did not alter the effect size: 1.61 (95% CI: 1.40-1.86). Marked heterogeneity within obesity studies, may relate to different risks at different ages.</td>
</tr>
<tr>
<td>Beydoun et al, 2008</td>
<td>Prospective (n=10)</td>
<td>North America and Europe. Mid- and late-life populations</td>
<td>Relative risk (age over 60 years): 3.10 (95% CI: 2.19-4.38) for Alzheimer’s, 5.01 (2.97-8.43) for vascular dementia; and 1.74 (1.34-2.26) for any dementia. Describes U-shaped relationship between BMI and dementia; low BMI associated with raised risk. When stratified by baseline age, see much greater effects for those aged under 60 years compared to those over 60 years.</td>
</tr>
<tr>
<td>Kloppenborg et al, 2008</td>
<td>Prospective (n=9)</td>
<td>North America and Europe. Mid- and late-life populations</td>
<td>5/9 studies reported an association between high BMI and an increased risk of dementia. The risk of any dementia was increased in 5/7 studies, of Alzheimer’s dementia in 1/5 studies, and of vascular dementia in 1/3 studies. Studies that measured BMI at mid-life generally showed a more consistent association and larger odds ratios for dementia.</td>
</tr>
</tbody>
</table>
Serum cholesterol

Serum cholesterol is important in the development of atherosclerosis and cardiovascular disease, including stroke, so it might be expected to be implicated in vascular dementia. Membrane cholesterol is thought to play an important role in the formation of amyloid plaques found in Alzheimer’s dementia, and cholesterol is also essential for synapse formation and maturation. Consequently, it has been suggested that serum cholesterol may be important for both dementia and cognition.

Around 60% of the UK adult population are classed as having high cholesterol. (Townsend et al, 2012)

Findings

Five systematic reviews were identified (see Table 9). Two reviews were of prospective studies of serum cholesterol and dementia. Three reviews considered the effect of statins (lipid-lowering agents) on dementia: one was a review of trials, and two reviews included a mixture of both trials and observational studies.

The prospective studies suggest that mid-life cholesterol is a risk factor for Alzheimer’s dementia or any dementia (see Table 9). There were no positive studies for mid-life cholesterol and vascular dementia. No meta-analysis of mid-life cholesterol and dementia has been undertaken.

For late-life cholesterol, the studies describe a more mixed picture. (Kivipelto and Solomon, 2006) A formal meta-analysis reported a null association between late-life total cholesterol and dementia (any dementia, vascular dementia or Alzheimer’s dementia). (Anstey et al, 2008) A limited number of studies have looked at the effect of specific types of cholesterol (low-density lipoprotein or high-density lipoprotein), and null results are reported.

Trial data suggest that statin treatment in old age has no effect on dementia, although this statement is based on a single trial that was under-powered and not designed to detect differences in dementia. (McGuinness et al, 2009) A second study considered only cognition as an outcome and not dementia, but also had a null finding. Observational studies (principally nested case control studies) suggest that statins may have a beneficial effect in reducing the incidence of dementia, but the effect is not seen in high-quality cohort studies. (Muangpaisan et al, 2010)

Study limitations

Confounding factors may explain some or all of the observed associations, either because the studies have failed to adjust for these factors or failed to adjust adequately. These other factors may include behavioural risk factors (physical activity, alcohol, diet and smoking), other biological risk factors (obesity, diabetes and blood pressure), age, socio-economic status, employment, social engagement and genetic factors. Many studies adjusted for demographic and health factors that may influence the association.

The prospective studies have not consistently adjusted for other risk factors (e.g. physical activity, obesity or hypertension), so residual confounding may explain the observed relationships. Studies have used different cut-offs for high and low cholesterol, which may account for some heterogeneity.
Given the strong suggestion of different effects between mid- and late life, one should interpret studies that have mixed the two periods (or averaged serum cholesterol over the life course) with caution. This may explain some of the null associations for the relationship between sub-components of cholesterol and dementia, where the mid- and late-life cohorts have not been separated.

The trial data should be interpreted with caution as it comes from studies primarily designed to test the effect of statin treatment on the prevention of heart disease and stroke. For example, the Heart Protection Study had a limited follow-up (five years) and the number of incident events was small (63 cases of dementia).

The positive findings in observational studies (considering the effect of statin treatment on dementia) may be due to confounding by indication (e.g. a propensity to offer statin treatment to those perceived to be in better health, with those in better health being at lower risk of dementia). The existing observational studies (of statin use) predominantly focus on older people, so may have missed the period when statin therapy may be most likely to prevent dementia.

Discussion

Prospective studies suggest that mid-life but not late-life total cholesterol is an important risk factor for dementia. The apparent null association for vascular dementia is surprising, but may reflect that studies on vascular dementia are less frequently carried out, and more likely to be under-powered.

It is noticeable that the findings in older age appear much more mixed, with no clear evidence of an association. It has been suggested that the dementia process might reduce serum cholesterol. (van Vliet, 2012) Consistent with this finding, one study (Stewart et al, 2007), which considered the change in cholesterol between mid- and late life, found that a decline in cholesterol preceded the development of Alzheimer’s dementia (although not of vascular dementia). It should also be noted that serum cholesterol appears to fall at older ages. (Chokshi et al, 2012) These effects may, in part, explain the inconsistent or null associations between late-life cholesterol and dementia.

The evidence around lipid-lowering with statins is mixed. These studies have tended to address the effect of statin therapy in late life, and were primarily designed to look for an effect on heart disease and stroke. In contrast, the observational epidemiology is pointing towards mid-life cholesterol (rather than late-life cholesterol) as being important. Observational studies of statin treatment may give a better indication of the potential benefits of statin therapy on dementia if they have a longer follow-up or have followed people since mid-life. However, these observational studies are particularly prone to bias. While some of these studies suggest a benefit from statin treatment, these tend to be the studies with a weaker design.

Policy implications

Mid-life cholesterol appears to be an important risk factor for later development of dementia. Late-life cholesterol does not appear to be important in the development of dementia. There is very limited evidence, to date, to suggest that lipid-lowering therapy, in the form of statins, may prevent or delay the onset of dementia. However, such research
has focused on older people, and the efficacy of statin therapy, particularly in mid-life, for the prevention of dementia has not been adequately tested.

Policies to lower lipid levels in mid-life, either behavioural or pharmacological, may reduce the incidence of dementia in later life.

Research suggestions

Observational epidemiology research on cholesterol and dementia is still young and requires further consolidation. Focusing on mid-life cholesterol (including the sub-types), considering different age periods within mid-life and different thresholds for cholesterol will be important. With new research on mid-life cholesterol and dementia (Solomon et al, 2009; Zambon et al, 2010; Mielke et al, 2010), the role of mid-life cholesterol (including LDL and HDL) on dementia (including vascular dementia) could be re-examined and a formal meta-analysis should be considered.

The effect of lipid-lowering, including trials of statins in mid-life, deserves further study. While trials of mid-life statin therapy on late-life dementia risk may be the ‘gold standard’, such trials would take many years to yield results, and may be impractical to undertake given the widespread use of statins.
Table 9: Summary of meta-analysis undertaken on the effects of serum cholesterol or serum cholesterol lowering on dementia

<table>
<thead>
<tr>
<th>Study population</th>
<th>Study types</th>
<th>Exposure</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muangpaisan et al, 2010</td>
<td>North America and Europe. Late life.</td>
<td>Prospective (including nested case control) and trials (n=7)</td>
<td>Statins</td>
<td>No association between statin use and risk of vascular dementia. Protective effect of statin use on dementia was demonstrated, but only in a nested case control study of lower quality and one recently published cohort study. In most other cohort and high-quality studies, statin use did not show a beneficial effect.</td>
</tr>
<tr>
<td>McGuinness et al, 2009</td>
<td>Europe.</td>
<td>Trials (n=2)</td>
<td>Statins</td>
<td>Heart Protection Study found no difference in dementia incidence between control (31) and statin arm (31). PROSPER reported no difference in cognition between the two arms.</td>
</tr>
<tr>
<td>Beri et al, 2009</td>
<td>North America and Europe. Late life.</td>
<td>Prospective and trials</td>
<td>Statins</td>
<td>Evidence for improving outcomes for dementia was conflicting and inconclusive.</td>
</tr>
<tr>
<td>Anstey et al, 2008</td>
<td>Europe, North America and Asia. Mid- and late life.</td>
<td>Prospective (n=26)</td>
<td>Mid-life total cholesterol (TC)</td>
<td>Two studies report mid-life TC associations with Alzheimer's dementia, and both reported a positive relationship (OR=2.8, 1.2-6.7; 3.1, 1.2-8.5); one of these also reported a positive relationship for any dementia. Only one study specifically examined the association between mid-life TC and vascular dementia and observed a null association (OR=1.0, 0.99-1.01).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Late-life total cholesterol (TC)</td>
<td>5 studies show no association between late-life TC and Alzheimer's dementia, 2 for vascular dementia, and 3 for any dementia on meta-analysis.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Low-density lipoprotein (LDL) and high-density lipoprotein (HDL)</td>
<td>0/5 studies report significant associations between HDL and any dementia, or Alzheimer's dementia, or vascular dementia.</td>
<td></td>
</tr>
<tr>
<td>Kivipelto and Solomon, 2006</td>
<td>Europe, North America and Asia. Mid- and late life.</td>
<td>Prospective (n=12)</td>
<td>Mid-life total cholesterol (TC)</td>
<td>4/5 studies describe a positive relationship between mid-life TC and subsequent dementia or Alzheimer's dementia.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Late-life cholesterol</td>
<td>Findings from the seven studies are mixed. No clear relationship observed.</td>
<td></td>
</tr>
</tbody>
</table>
Summary of science review

There is some observational evidence to link the four behavioural risk factors (alcohol, diet, physical activity and smoking) and dementia. There is also observational evidence linking other vascular risk factors (diabetes, blood pressure, obesity and serum cholesterol) to dementia. Given the importance of the behavioural risk factors in the development of these vascular (or medical) risk factors, this may strengthen the evidence linking these behaviours to dementia.

The observational evidence is of variable quality (e.g. consistency of observed associations, replication in different populations, and adjustment for confounders). The evidence for physical activity and smoking appears stronger than for alcohol and diet. While there are some short-term trials of physical activity in older people, definitive evidence from trials of the importance of these behaviours in preventing dementia (or delaying cognitive impairment) is lacking. Most of the evidence has emerged in the last 10 years.

The nature of the evidence at present largely permits us to comment on whether there is an association. Some work has looked at how the association may be modified by age or genetic factors (APOE gene), but less work has considered how the associations may vary for other sub-groups (e.g. different ethnic groups). This work tends to suggest that mid-life may be particularly important, but no work was identified that explored early life, and benefits from intervention in late life may exist. Very little work (in terms of systematic reviews) has considered how the risk factors may interact to cause dementia.

The nature of the observed associations between three of the behavioural risk factors (smoking, physical activity and diet) and dementia is similar to those observed for cardiovascular disease and other non-communicable diseases. The favoured pattern for the relationship between alcohol consumption and dementia risk (a J- or U-shaped relationship) is similar to that observed for cardiovascular disease. Broadly this supports the hypothesis linking vascular disease and dementia (both Alzheimer’s dementia and vascular dementia). A case can be made for aligning advice around the prevention of dementia with the prevention of cardiovascular disease. However, additional factors (not considered here) might also be important in the prevention of dementia.
Policy review

This policy review seeks to establish the extent to which reducing the risk of dementia is being considered as part of the current response to dementia in the UK and other countries. It considers the response from government bodies, professional groups and the third sector. It also seeks to identify areas of good practice that the UK may learn from.

The review addresses the following questions:

1. What is the nature and extent of present dementia prevention strategies at a country level?
2. What other preventive work is being undertaken or being recommended (e.g. by charities and other non-governmental organisations)?
3. To what extent is prevention included in present guidelines on dementia?
4. Do government strategies for other non-communicable diseases (NCDs) include prevention? Are the strategies integrated with other NCDs, including dementia?
5. Do UK-based disease charities, when they offer advice on disease prevention, integrate with other disease including dementia (i.e. emphasise the co-benefits of changing behaviour)?
6. Do government strategies on the four behavioural risk factors link to other NCDs and dementia?
7. Do UK-based bodies that advocate for action on the four behavioural risk factors justify action by making links to NCDs and dementia?
8. Do UK guidelines on healthy behaviours link to NCDs and dementia?

Method

Review overview
The protocol for the policy review was reviewed by an expert committee comprising academic and policy experts (see page 2 for membership). The expert committee also met on 9 September 2013 to review the findings and highlight gaps in the literature.

Search strategy
The internet was searched for key government and non-governmental organisation documents. The review considered documents published by government (UK and devolved nations), other government agencies (e.g. NICE), charities, health advocacy organisations and professional bodies. An expert panel provided guidance on appropriate documents to review.

The aim was not to produce an exhaustive and complete list, but to give an idea of the nature and extent of what is happening at present.

Data extraction
The policy and advocacy documents were grouped into the following categories: dementia, other NCDs, and behavioural risk factors. Documents concerning dementia were reviewed for the extent to which prevention was incorporated within that strategy or guidance. Documents concerning other non-communicable diseases were reviewed for the extent to which prevention was integrated with other non-communicable diseases, including dementia. Documents concerning behavioural risk factors were reviewed for the extent to which links are made with different non-communicable diseases, including dementia. Key words (e.g. “dementia” or “prevention”) were used to scan the contents of the documents.
**Case studies**

Examples of innovative practice were identified during the process of reviewing the documents, or highlighted by the policy experts. They have been followed up by direct correspondence with those involved and are set out as case studies. The case studies have been included as examples of concrete action. Inclusion of a case study does not imply endorsement of the work described.

**Findings: Dementia**

Table 10 sets out current government dementia strategies in the UK. The focus of these strategies is on diagnosis of dementia, and care of those who have been diagnosed. Both Wales and Northern Ireland have set out specific actions around prevention of dementia, primarily around awareness-raising and making links with other NCD prevention strategies (see the case studies).

Table 11 sets out government dementia strategies in countries other than the UK. Only a small number of countries have dementia strategies. The focus tends to be on awareness-raising, diagnosis and provision of care, and support to those who have been diagnosed. The Finnish strategy stands out as one that has explicitly included prevention. They have developed messages around ‘brain health’, emphasising the different behaviours at different stages of life that promote ‘brain health’. By focusing on ‘brain health’ the focus shifts from disease to health, and away from a single disease (or set of disorders) to overall cognitive and mental functioning. Emphasis in terms of benefits for a younger audience may be different – for example, focusing on coping with stress and well-being – while the type of behaviours encouraged will be the same regardless of age.

Table 12 sets out the dementia strategies of non-governmental bodies. Notably *Dementia – a public health priority*, which was jointly produced by Alzheimer’s Disease International and WHO in 2012, included a large section on prevention. It recommended that: “primary prevention should focus on targets suggested by current evidence, namely: improving access to education and countering risk factors for vascular disease, including diabetes, midlife hypertension, midlife obesity, smoking, and physical inactivity.” It also stressed the need for further research, the importance of dementia surveillance and the need to evaluate prevention programmes. Reports produced by national charities calling for a dementia strategy have also tended to include prevention (e.g. in India and Canada).

Table 13 outlines the information on prevention of dementia produced by dementia charities both in the UK and other countries. The UK-based dementia charities give advice on the prevention of dementia on their websites. They also discuss some of the co-benefits in terms of other non-communicable diseases (see Table 13). Charities in other countries take a similar approach. The Australian website and resources are particularly well developed, with a dedicated website (Your Brain Matters) that emphasises links between physical health and brain health and includes an App to record and help change behaviour.

Table 14 outlines the dementia guidelines in the UK. Clinical guidelines in the UK concerning dementia seldom discuss the opportunity for prevention.
Wales published its National Dementia Vision for Wales in 2010. Wales has a large elderly population, being a place that people move to from other parts of the UK on retirement. Consequently, preparing and planning for dementia is particularly important. The dementia plan is based on a social determinants model of health. It has a focus both on care and support for those with dementia, as well as prevention and early diagnosis. It emphasises: supporting individuals; strengthening communities; improving infrastructure and access to care; and changing the economic, cultural and environmental conditions.

The plan set an explicit action to integrate dementia prevention into existing healthy living campaigns. Literature that encourages healthy living now also stresses the benefits in terms of improved mental well-being (including preventing dementia) alongside the benefits that are more traditionally emphasised (e.g. cancer and heart disease prevention). A Dementia – how to reduce your risk leaflet has been produced. The focus has been on integration within existing campaigns and materials rather than running new ‘dementia-specific’ campaigns, to avoid confusion with existing messages. They are also exploring explicit training for GPs in giving advice on the behaviours that may reduce the risk of dementia.

Dementia is also integrated within the 2012 National Mental Health Strategy, which takes a life-course approach, seeking to intervene in childhood, early adult life, mid- and later adult life, to prevent, delay or mitigate the onset of mental illness. Preventing dementia also comes under other work with a broader focus of supporting healthy ageing.
Case study: Coventry and Warwickshire Living Well with Dementia Strategy

Coventry has a relatively young population and high levels of international migration compared to the rest of the UK. While the population is on average younger, it is anticipated that migrant communities will settle and age in the city, emphasising the need for responsive services for older people, which take into account different cultural perceptions regarding ageing and dementia.

Coventry’s Living Well with Dementia Strategy highlights the importance of prevention and of people understanding the risk factors for dementia. One of the 12 outcomes of the strategy is “knowledge about how to reduce the risk of developing dementia.” Specific objectives set to realise this outcome include:

- People having an awareness of risk factors for dementia and how to manage and reduce these risks. The Coventry and Warwickshire Dementia Portal (www.livingwellwithdementia.org) provides support and information on reducing the risk of dementia, and tips on adopting healthy behaviours
- All schools having access to ‘dementia awareness’ sessions that include information about preventing the onset of dementia
- Public health schemes, such as Active for Health, being ‘dementia-friendly’
- Making education for GPs accessible, to ensure that awareness of the benefits of healthy behaviours in relation to dementia is carried through to patients and the public
- GPs and other health and social care professionals understanding the value of early diagnosis and intervention in enabling people to live well with dementia.

Coventry City Council is a member of the Dementia Action Alliance and is committed to being a ‘Dementia-friendly Community.’ For Coventry, this also entails people knowing more about reducing their risk of developing dementia. Dementia Friends information sessions and the Dementia Portal are being used to disseminate this message.
Findings: Other non-communicable diseases

Table 15 includes government strategies for non-communicable diseases other than dementia. While all strategies include primary prevention, the benefits are usually only emphasised with respect to the disease of concern. Links to other non-communicable disease are limited. The Cardiovascular Disease Outcomes Framework (2013) is notable for acknowledging links with vascular dementia. However, even within this document the integration is relatively superficial; there are no specific areas for action or things that should be done differently because of the link with vascular dementia. The NHS Health Checks are an example of integrated practice (both in terms of integration across different diseases and integration of pharmacological and behavioural approaches) that includes dementia.

Table 16 sets out the information provided by UK-based charities that are concerned with the major non-communicable diseases. Understandably, the advice offered regarding prevention has a focus on the benefits in terms of reducing the risk of the disease that is the charity’s primary focus. However, some charities – for example, the British Heart Foundation and Breakthrough Breast Cancer – are emphasising the wider health benefits of adopting healthy behaviours. No charity has been identified (other than the dementia-specific charities) that makes the link between the adoption of certain health behaviours and the prevention of dementia.

Findings: Behavioural risk factors

UK Government strategies to address tobacco consumption and harmful alcohol consumption make connections with a wide range of non-communicable diseases (see Table 17). However, neither document makes links to the effect of these substances on dementia or cognition. The obesity strategy makes links between obesity and a range of non-communicable diseases (although not dementia). There are no corresponding strategies for physical activity or nutrition.

Table 18 outlines the advocacy organisations working for action on the behavioural risk factors of alcohol, smoking, physical activity and nutrition. These organisations emphasise a wide range of health outcomes associated with each behavioural risk factor. Links between physical activity and mental well-being are stressed, and in the case of Sustrans the specific connection with dementia is mentioned. It is also noteworthy that the recently published national guidance on recommended physical activity levels (2010) includes a section setting out the evidence base concerning physical activity and dementia. It specifically states that, “the UK physical activity guidelines for adults should be supported by commentary that outlines the health benefits derived from the recommended dose of physical activity with a special emphasis on the role of physical activity in aiding the prevention of mental illness (such as depression and dementia).” However, links are not made to dementia or cognition for alcohol, tobacco or nutrition.
Summary of policy review

Dementia policies and strategies developed elsewhere in the world tend not to address primary prevention. The main exceptions are those from Finland, Wales, Northern Ireland and Alzheimer’s Disease International/WHO. Even in these examples, the reach and extent of prevention appears modest compared to other major non-communicable diseases. Clinical guidelines on dementia give no or very limited acknowledgement to prevention. This may partly be explained by the quality of the evidence base, although the ADI/WHO report suggests that the quality of evidence is sufficient to warrant action in several areas. It is also notable that the major UK dementia charities do offer information on prevention.

The prevention picture for other major non-communicable diseases in the UK is different. Strategy documents have prevention as a core theme. However, these tend to focus on the benefits for that particular disease, and show limited integration between diseases – for example, by acknowledging the importance of shared risk factors and potential co-benefits. The NHS Health Checks are an example of integrated practice. The pattern for non-integration tends to be mirrored by UK charities representing different diseases, although some do discuss the wider health benefits of adopting healthy behaviours (e.g. the British Heart Foundation and Breakthrough Breast Cancer).

Considering strategies and guidelines focused on healthy behaviours, there seems to be a marked difference between physical activity and other behaviours. Strategies and guidelines focused around physical activity tend to make the connection with dementia. In contrast, links between dementia and alcohol, smoking and nutrition are not made in either strategy documents or guidelines. These differences may in part reflect the current evidence base. There was a very clearly worded statement in the recent UK physical activity guidelines concerning mental well-being (including dementia) and physical activity. Despite this, the links between physical activity and mental health are not always emphasised, being omitted from recent NICE guidance and Sport England publications.
Table 10: UK Government dementia strategies and plans

<table>
<thead>
<tr>
<th>Country</th>
<th>Title</th>
<th>Year</th>
<th>Key areas</th>
<th>Publisher/source</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>Prime Minister’s Dementia Challenge</td>
<td>2012</td>
<td>Improving health and care; creating dementia-friendly communities; improving dementia research. (The May 2013 update advocates a public health agenda with a prevention focus.)</td>
<td>Department of Health <a href="http://dementiachallenge.dh.gov.uk/about-the-challenge/">http://dementiachallenge.dh.gov.uk/about-the-challenge/</a></td>
</tr>
<tr>
<td>Scotland</td>
<td>National Dementia Strategy for Scotland</td>
<td>2010</td>
<td>Quality of care; staff training; increased diagnosis; care in appropriate settings; supporting research.</td>
<td>Scottish Government <a href="http://www.scotland.gov.uk/Topics/Health/Services/Mental-Health/Dementia">http://www.scotland.gov.uk/Topics/Health/Services/Mental-Health/Dementia</a></td>
</tr>
<tr>
<td>Wales</td>
<td>National Dementia Vision for Wales</td>
<td>2010</td>
<td>Strengthening individuals; strengthening communities; improving access to services; tackling underlying determinants of disease – including health promotion initiatives.</td>
<td>NHS Wales <a href="http://www.wales.nhs.uk/healthtopics/conditions/dementia">http://www.wales.nhs.uk/healthtopics/conditions/dementia</a></td>
</tr>
<tr>
<td>Country</td>
<td>Title</td>
<td>Year</td>
<td>Key areas</td>
<td>Publisher/source</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------</td>
<td>-------</td>
<td>----------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Australia</td>
<td>National Framework for Action on Dementia 2006-10</td>
<td>2010</td>
<td>Care and support; access and equity; information and education; research; workforce and training.</td>
<td>Department of Health and Aging</td>
</tr>
<tr>
<td>Cyprus</td>
<td>Cyprus Strategic Plan For Alzheimer’s Disease</td>
<td>2010</td>
<td>Increased awareness; early diagnosis and intervention; improved medical care; improved social care.</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>Denmark</td>
<td>Danish National Dementia Plan</td>
<td>2011</td>
<td>Timely diagnosis; better communication between care providers; improved health and social care.</td>
<td>Social Ministry</td>
</tr>
<tr>
<td>Finland</td>
<td>Finnish National Memory Programme 2012-2020</td>
<td>2012</td>
<td>Promoting brain health, including a focus on prevention; combating stigma; better care; supporting research and professional education.</td>
<td>Ministry of Health and Social Services. (See also the Alzheimer’s Europe website and Alzheimer’s Disease International website.)</td>
</tr>
<tr>
<td>France</td>
<td>National plan for ‘Alzheimer and related diseases’ 2008-2012</td>
<td>2008</td>
<td>Improving quality of life for patients and carers; research strategy; public awareness and tackling stigma.</td>
<td>Ministry of Health. (See also Alzheimer’s Disease International website.)</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>Korea’s War on Dementia</td>
<td>2010</td>
<td>Awareness raising; diagnosis; carer support.</td>
<td>Ministry of Health and Welfare. (Alzheimer’s Disease International: <a href="http://www.alz.co.uk/plans/republic-of-korea">http://www.alz.co.uk/plans/republic-of-korea</a>)</td>
</tr>
<tr>
<td>Norway</td>
<td>Dementia Plan 2015</td>
<td>2007</td>
<td>Care for people with dementia (day programmes, adapting living facilities, knowledge and training).</td>
<td>Norwegian Ministry of Health and Care Services</td>
</tr>
<tr>
<td>USA</td>
<td>National Plan to Address Alzheimer’s Disease</td>
<td>2012</td>
<td>Prevention and treatment of Alzheimer’s (research); enhancing care; support for patients and families; raising public awareness; improving data.</td>
<td>US Department of Health and Human Services (<a href="http://aspe.hhs.gov/daltcp/napa/NatlPlans.html">http://aspe.hhs.gov/daltcp/napa/NatlPlans.html</a>)</td>
</tr>
</tbody>
</table>

Note: This list of countries with plans has been taken from the Alzheimer’s Disease International website http://www.alz.co.uk/alzheimer-plans.
Table 12: Other dementia strategies and plans (including those of non-governmental organisations)

<table>
<thead>
<tr>
<th>Country/region</th>
<th>Title</th>
<th>Year</th>
<th>Key areas</th>
<th>Publisher/source</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>Dementia India Report 2010</td>
<td>2010</td>
<td>Priorities identified: increased funding; awareness-raising; diagnosis and identification; community support, carer support. Includes a section on prevention, particularly around the need for further research.</td>
<td>Alzheimer’s and Related Disorders Society of India <a href="http://www.alzheimer.org.in/dementia_2010.pdf">http://www.alzheimer.org.in/dementia_2010.pdf</a></td>
</tr>
</tbody>
</table>
### Table 13: UK and international dementia charities’ information on prevention of dementia

<table>
<thead>
<tr>
<th>Charity</th>
<th>Document</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>International Alzheimer’s</td>
<td>Dementia Action Alliance Benefits of timely diagnosis.</td>
<td>Emphasises overlap in terms of causes (and prevention) of heart disease, stroke and diabetes with dementia (both Alzheimer’s and vascular dementia).</td>
</tr>
</tbody>
</table>

### Table 14: Dementia guidelines in the UK

<table>
<thead>
<tr>
<th>Body</th>
<th>Document</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE</td>
<td>Clinical Guidelines 42: Dementia October 2012</td>
<td>Primarily focused on supporting people with dementia and their carers, but includes a section on prevention (smoking, alcohol, obesity).</td>
</tr>
<tr>
<td>SIGN</td>
<td>Management of Patients with Dementia (86) 2006</td>
<td>Remit excludes prevention.</td>
</tr>
<tr>
<td>Royal College of Physicians</td>
<td>No publications on dementia.</td>
<td></td>
</tr>
<tr>
<td>Royal College of General</td>
<td>Diagnosis and Early Intervention in Primary Care. Care of People with Dementia in Primary Care</td>
<td>Focuses on clinical aspects; no information on prevention.</td>
</tr>
<tr>
<td>Practitioners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td>Strategy document</td>
<td>Does the strategy include the following?</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td>Cancer: Improving Outcomes, 2011</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Cardiovascular disease</strong></td>
<td>Cardiovascular Disease Outcomes Strategy, 2013</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>National Service Framework for Diabetes, 2001</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>Healthy Lives, Healthy People, 2011</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Respiratory disease</strong></td>
<td>An Outcomes Strategy for Chronic Obstructive Pulmonary Disease (COPD) and Asthma in England. National strategy to transform respiratory disease care</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Mental health</strong></td>
<td>No Health Without Mental Health, 2011</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Liver disease</strong></td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Long-term conditions</strong></td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>NHS Health Checks (NHS Choices website)</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Table 16: UK health charities: To what extent does their advice on healthy living emphasise benefits for dementia and other diseases?

<table>
<thead>
<tr>
<th>Area of primary focus</th>
<th>Charity</th>
<th>Publication</th>
<th>Includes dementia?</th>
<th>Includes other diseases?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>Cancer Research UK</td>
<td>Healthy living web pages (<a href="http://www.cancerresearchuk.org/cancer-info/healthyliving/introducingcancerprevention/can-cancer-be-prevented">http://www.cancerresearchuk.org/cancer-info/healthyliving/introducingcancerprevention/can-cancer-be-prevented</a>)</td>
<td>No</td>
<td>Largely emphasises the benefits of healthy living in terms of cancer risk reduction; benefits of behaviour change in terms of other diseases not conveyed.</td>
</tr>
<tr>
<td>Prostate Cancer UK</td>
<td>Can I reduce my risk? (<a href="http://prostatecanceruk.org/information/who-is-at-risk/can-i-reduce-my-risk">http://prostatecanceruk.org/information/who-is-at-risk/can-i-reduce-my-risk</a>)</td>
<td>No</td>
<td>Specific to prostate cancer, does advise that physical activity may help “other health problems”.</td>
<td></td>
</tr>
<tr>
<td>Breakthrough Breast Cancer</td>
<td>Breast cancer risk – the facts</td>
<td>No</td>
<td>Encourages women to think of the wider benefits of changing behaviour, and provides a good overview of the broader health benefits of particular healthy behaviours.</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>British Heart Foundation</td>
<td>Preventing heart diseases (<a href="http://www.bhf.org.uk/heart-health/prevention">http://www.bhf.org.uk/heart-health/prevention</a>)</td>
<td>No</td>
<td>Emphasises the benefits in terms of heart disease; alcohol page stresses additional harms of excess alcohol (liver damage, cancer), and the diet page diabetes; gives advice on behaviour change strategies.</td>
</tr>
<tr>
<td>Kidney Research UK</td>
<td></td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>Association for the Study of Obesity (ASO)</td>
<td>About obesity ([Taken from International Association for the Study of Obesity webpage, as no equivalent document on ASO website: <a href="http://www.iaso.org/resources/aboutobesity">http://www.iaso.org/resources/aboutobesity</a>]</td>
<td>No</td>
<td>Sets out a wide range of health effects of obesity.</td>
</tr>
<tr>
<td>Mental health</td>
<td>MIND</td>
<td>Depression (<a href="http://www.mind.org.uk/mental_health_a-z/7980_depression">http://www.mind.org.uk/mental_health_a-z/7980_depression</a>)</td>
<td>No</td>
<td>Limited information on prevention; does discuss how lack of physical activity, poor diet and alcohol can contribute to depression. Includes importance of physical activity and healthy diet</td>
</tr>
</tbody>
</table>
Table 17: UK Government strategies on alcohol, smoking, physical activity and nutrition

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Strategy document</th>
<th>Links to NCDs?</th>
<th>Links to dementia?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>The Government’s Alcohol Strategy, 2012 (Predominantly England and Wales only)</td>
<td>Yes. (Also considers social impacts.)</td>
<td>No</td>
</tr>
<tr>
<td>Smoking</td>
<td>Healthy Lives, Healthy People: A Tobacco Control Plan for England, 2011</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Physical activity</td>
<td>* Obesity: A Call to Action (England only)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nutrition</td>
<td>* Obesity: A Call to Action (England only)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

*No specific strategies for physical activity or nutrition.

Table 18: UK advocacy organisations’ information provided on the behavioural risk factors and health

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Body</th>
<th>Document</th>
<th>Links to NCDs?</th>
<th>Links to dementia?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>Alcohol Health Alliance</td>
<td>Health First: An Evidence-based Alcohol Manifesto</td>
<td>Yes, and social consequences.</td>
<td>No, nor impact on cognition or Wernicke-Korsakoff Syndrome</td>
</tr>
<tr>
<td>Smoking</td>
<td>ASH</td>
<td>Smoking and Disease</td>
<td>Yes</td>
<td>No, nor impact on cognition.</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Sustain</td>
<td>Sustain Guide to Good Food - Getting the Balance Right</td>
<td>Yes</td>
<td>No, nor impact on cognition.</td>
</tr>
<tr>
<td></td>
<td>Which?</td>
<td>Which? Food policy website (<a href="http://www.which.co.uk/about-which/who-we-are/which-policy/food/">http://www.which.co.uk/about-which/who-we-are/which-policy/food/</a>)</td>
<td>Yes, and considers the broader environmental impact of food.</td>
<td>Avoids direct link with health; only discusses nutrients.</td>
</tr>
<tr>
<td>Risk factor</td>
<td>Body</td>
<td>Document</td>
<td>Links to NCDs?</td>
<td>Links to dementia?</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------------------------</td>
<td>-----------------------------------------------</td>
<td>----------------</td>
<td>---------------------------------------------</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity</td>
<td>Department of Health</td>
<td>UK Physical Activity Guidelines (May 2010)</td>
<td>Yes</td>
<td>Yes. (Specifically discusses benefits of regular exercise in preventing dementia.)</td>
</tr>
<tr>
<td></td>
<td>NICE</td>
<td>Public Health Guidelines 44: Brief advice on physical activity (May 2013)</td>
<td>Yes</td>
<td>No. (Includes benefits for mental health, but does not include benefits in terms of cognition or dementia.)</td>
</tr>
<tr>
<td>Nutrition</td>
<td>NHS Choices</td>
<td>Eatwell Plate</td>
<td>Yes (but limited information; evidence base not presented as it is for physical activity)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>British Dietetics Association</td>
<td>Food Facts</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Considerations in developing a prevention agenda linking dementia and other non-communicable diseases

The science should inform the development of policy – both whether the evidence justifies action, and what types of action might be justified. Action in some areas where the evidence may be considered stronger may be more appropriate than in other areas. This section outlines some considerations when considering possible policy responses.

Strength of evidence

The evidence linking the four behavioural risk factors – alcohol, diet, physical activity and smoking – to dementia is largely observational. There is also some early trial evidence, notably around physical activity (more often linked to cognitive function than dementia) and anti-hypertensives (that has yet to reach the threshold that proves the benefits of treatment).

Observational evidence often provides important evidence that causal relationships exist, but it cannot provide definitive evidence. Sometimes in the past it has provided misleading evidence (for example, antioxidants for prevention of cancer, or folic acid and hormone replacement therapy for the prevention of heart disease). However, often observational studies have provided evidence that has guided important action to protect health (e.g. tobacco, physical activity, various toxins and cancer, blood pressure and heart disease, and identification of important side effects from medications). Evidence in some of these other areas has grown and strengthened over time.

While most authors suggest the likely explanation for the observed associations between the four behavioural risk factors and dementia is a causal relationship (i.e. the risk factors have a role in the development of dementia), the evidence is not definitive. Some people argue that, because the best evidence suggests an association, we should act now to prevent future disease. They also emphasise that the suggested action (alignment with current messages for best practice) is likely to lead to improvements in other non-communicable diseases, even if there is no impact on dementia. Others are cautious, given the present evidence base, and point to potential harms that might ensue from acting.

Potential harms from acting

Potential harms from initiating public health actions to reduce the prevalence of dementia that have been raised during the compilation of this document include:

Creating anxiety and guilt: Putting out messages that dementia may be caused by doing (or not doing) activity X may create (unnecessary) anxiety and fear about the later development of dementia in people who are currently well. Related to this, some people have suggested that there is no demand or appetite for information about dementia prevention, and it would not be appropriate to force such information on people, particularly when information or services to support action may be absent. Messages about disease prevention may also create feelings of guilt in those who are newly diagnosed with dementia (i.e. that the disease is of their making).

It may be possible to mitigate these effects by the delivery and targeting of any messages. The issues are shared with other non-communicable diseases, and lessons may be learnt from these.
**Inappropriate use of resources:** If the evidence base is ‘weak’, it may be a poor use of limited resources to develop a prevention agenda for dementia, rather than spending resources on evidence-based activity where the gains on investment may be considered more certain. Some might suggest that, because so much is still unknown, acting might be just as likely to introduce harm as benefit – for example, a drive to encourage physical activity could lead to displacement of cognitive activities important for dementia prevention (e.g. education, occupational activities and social engagement), or increase the incidence of head injuries (due to more sport) which might increase the risk of dementia.

**Undermining public confidence in health advice:** If best current advice on preventing dementia was shown to be incorrect in the future, this might undermine public confidence in official health messages. It may be possible to mitigate this by communicating some of the uncertainty in the current evidence base when offering advice. For example: “The best evidence we have at present suggests that you can reduce your dementia risk by doing X or Y.”

**Size of potential benefits**

There are reasonable estimates of relative risk for the different risk factors. At the individual level these may be more readily translated into estimates of benefit from changing behaviour. Estimates of the potential benefit at the population level (i.e. reduction in the number of people living with dementia) may help inform decisions about whether to act. Other factors, beyond the strength of the relationship between the risk factor and dementia, will influence the potential population health gains. These will include the proportion of the population exposed to the risk factor, inter-relationships between risk factors, and how modifiable the risk factor is.

One estimate suggests that a 10% to 25% reduction in seven risk factors for Alzheimer’s dementia could potentially prevent as many as 184,000 to 492,000 cases in the USA, or around 6% to 17% of cases. (Barnes and Yaffe, 2011) However, these estimates have been criticised and such modelling is not easy to undertake. (Norton et al, 2013)

**Period of life to target**

The epidemiological evidence suggests that mid-life may be a particularly important period for prevention of dementia. Conversely, a life-course approach may suggest that we should think broadly about opportunities for prevention throughout the life course. The early years may be an important period for the development of healthy behaviours that can be sustained throughout life.

Even if mid-life is an important period with relatively large effect sizes, interventions in old age (with smaller effects at the individual level) may still be important. The benefits from interventions in old age will be realised more immediately. Older people are more likely to live to an age where they will be at risk of developing dementia, so a greater proportion of older people might be expected to benefit from interventions designed to reduce their risk.

**Better evidence**

It may be appropriate to wait for better evidence to accrue, which may inform more targeted and evidence-based action. However, the nature of the evidence may remain
largely observational for several more years. Intervention studies may take 20 or more years, if it is necessary to intervene 5, 10 or even 20 years before the development of dementia. Despite this, some studies are underway, although most of these are either of short duration or focused on success of risk factor modification. These existing intervention studies are set out in Table 20. Intervention studies may also be practically or ethically hard to undertake: would it be reasonable to randomise people in middle-age to physical activity or no physical activity, given the known benefits in terms of mortality and disease prevention? (Kim, 2011)
Table 20: Existing intervention studies related to dementia

<table>
<thead>
<tr>
<th>Trial title</th>
<th>Lead institute</th>
<th>Study aims and design</th>
<th>Study completion date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevention of dementia by intensive vascular care</td>
<td>University of Amsterdam, Netherlands</td>
<td>A randomised controlled trial to investigate if interventions aimed at vascular risk factors reduce the incidence of dementia or the burden of functional disability in people aged 70-78 years.</td>
<td>January 2013</td>
</tr>
<tr>
<td>Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)</td>
<td>National Institute for Health and Welfare, Finland</td>
<td>A multi-centre intervention study (six sites: Helsinki, Kuopio, Oulu, Seinäjoki, Turku and Vantaa) to test the effect of a two-year multi-domain lifestyle intervention (nutritional guidance, exercise, cognitive training, increased social activity, and intensive monitoring and management of metabolic and vascular risk factors) in 60-70 year old people at increased risk of dementia and cognitive impairment. Will include seven-year follow-up.</td>
<td>April 2014 (for two-year data)</td>
</tr>
<tr>
<td>Austrian Polyintervention Study to Prevent Cognitive Decline After Ischemic Stroke (ASPI)</td>
<td>Danube University, Austria</td>
<td>A two-year randomised controlled study to test if intensive polyintervention therapy including lifestyle modifications targeted at reduction of modifiable risk factors of stroke can reduce the risk of cognitive decline in those who have had a stroke.</td>
<td>November 2014</td>
</tr>
<tr>
<td>INovative Midlife INtervention for Dementia Deterrence (In-MINDD)</td>
<td>Dublin City University, Ireland (with European collaborators)</td>
<td>A multi-stage study. In the first phase a literature review and expert consensus will be used to identify modifiable mid-life risk factors. In the second stage this will be used to develop a model to estimate an individual’s risk of dementia, and prescribe recommendations (lifestyle change) to reduce risk (including strategies for behavioural change). In the third stage an initial evaluation of the model, its use and impact on behaviour, will be undertaken.</td>
<td>Not stated</td>
</tr>
</tbody>
</table>

For more information see:
- [http://controlled-trials.com/ISRCTN29711771](http://controlled-trials.com/ISRCTN29711771) (for Dutch trial)
- [http://www.inmindd.eu/](http://www.inmindd.eu/) (for In-MINDD)
**Areas of potential action**

The population perspective (outlined in the *Background* section) would suggest that preventive action should be broad-based. A potential model could be the NICE model for the prevention of cardiovascular disease (see Appendix 1; NICE, 2012). This includes individual-orientated and population-based approaches. This would suggest action could be taken at local, national and regional level. Action by the health sector and those outside health could contribute to the prevention of dementia.

Based on the NICE model, an example of how this might look is set out in Figure 4. The components included are indicative and for discussion. They are not intended to be exhaustive. The inclusion of components and their delivery should be informed by the evidence base. The model only includes elements that overlap with other non-communicable diseases. Other important risk factors (head injuries, illicit drug use, depression, education and occupation) are consequently excluded.

**Figure 4: Prevention and reduction of dementia risk**

<table>
<thead>
<tr>
<th>Modifiable individual risk factors</th>
<th>Individual fixed risk factors</th>
<th>Population-wide risk reduction</th>
<th>Reducing individual risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol intake</td>
<td>Genes (APOE4)</td>
<td>Plain packs (tobacco)</td>
<td>Drug and alcohol services</td>
</tr>
<tr>
<td>Diet</td>
<td>Family history</td>
<td>Marketing of food and tobacco</td>
<td>Smoking cessation services</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Pre-existing medical conditions</td>
<td>Safe spaces for physical activity</td>
<td>Brief interventions (tobacco, physical activity, alcohol)</td>
</tr>
<tr>
<td>Smoking</td>
<td>(diabetes, stroke)</td>
<td>Investment in active travel</td>
<td>Weight management services</td>
</tr>
<tr>
<td>Body weight</td>
<td></td>
<td>Minimum unit pricing for alcohol</td>
<td>Physical activity and nutrition interventions</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum cholesterol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Based on the NICE model for prevention and management of cardiovascular risk. Not comprehensive; illustrative only.
Summary

Some of the risk factors for dementia and other non-communicable diseases are shared. It has been suggested that prevention approaches for dementia could be ‘joined-up’ with prevention approaches for other non-communicable diseases. Linking dementia to existing preventive approaches may strengthen existing work. It might also contribute to mitigating the anticipated rise in dementia cases expected as the population ages. It could represent a ‘quick-win’ in terms of developing prevention approaches around dementia. Other policy responses focusing on risk factors that are less commonly shared with other non-communicable diseases might also be part of the response to prevent dementia, but have not been explicitly considered in this report.

The evidence linking behavioural risk factors (alcohol consumption, diet, physical activity and smoking) and other vascular risk factors (blood pressure, diabetes, obesity and serum cholesterol) with dementia largely comes from observational studies. The overall message is broadly that “What is good for the heart is good for the head.” While the existing evidence may suggest that modifying these risk factors could reduce the incidence of dementia, the evidence is not definitive. Scientific consensus may guide interpretation of the existing evidence base, and the extent to which is supports policy action.

The policy review shows that a few countries and regions are beginning to develop dementia prevention strategies. It is an area that governments, charities and professional bodies are beginning to consider. Presently most preventive strategies only provide information (on which behaviours may prevent or delay onset). This contrasts with prevention approaches for other diseases, which are more established, and more integrated with other non-communicable diseases. Other disease prevention strategies include a range of approaches (besides education and awareness-raising) to change behaviour, including both individual-level and population-level approaches.

In considering whether the evidence base is sufficient to support prevention policies, one should consider potential harms arising from action as well as potential benefits in reducing risk of dementia. As with other non-communicable diseases, shared preventive action should be broad-based, encompassing both individual-level and population-level approaches. This suggests that action at local, regional and national level could support strategies to prevent dementia by supporting people to live healthily (e.g. action focused around alcohol consumption, diet, physical activity and smoking). Action by the health sector (e.g. brief advice, signposting to services, and provision of information) will be important. However, many of the determinants of health lie outside the health sector and modifying these will be important to achieve the large-scale behaviour change that could result in much greater reductions in the incidence of dementia.

---

7 Be Head Strong. The Alzheimer’s Association: http://www.alz.org/we_can_help_be_heart_smart.asp
Appendix 1:
NICE framework for the prevention and management of cardiovascular disease

Appendix 2:
Search terms used for the science review

### Alcohol (search undertaken 27 October 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alcohol [Title/Abstract]</td>
<td>171,514</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>125,707</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analysis*[Title/Abstract]</td>
<td>904,042</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>141</td>
</tr>
</tbody>
</table>

**Included in review:** 3

### Diet (search undertaken 26 September 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>diet[Title/Abstract] or nutrition[Title/Abstract] or fat*[Title/Abstract] or fruit*[Title/Abstract] or vegetable*[Title/Abstract] or sugar*[Title/Abstract] or fish*[Title/Abstract] or meat*[Title/Abstract] or carbohydrate*[Title/Abstract] or fibre[Title/Abstract]</td>
<td>954,721</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>124,669</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analysis*[Title/Abstract]</td>
<td>896,093</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>510</td>
</tr>
</tbody>
</table>

**Included in review:** 4

### Physical activity (search undertaken 27 October 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>physical activity[Title/abstract] OR exercise[Title/Abstract]</td>
<td>210,842</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>125,707</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analysis*[Title/Abstract]</td>
<td>904,042</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>201</td>
</tr>
</tbody>
</table>

**Included in review:** 5

### Smoking (search undertaken 29 August 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>((cigarettes[Title/Abstract]) OR tobacco[Title/Abstract]) OR smoking[Title/Abstract]</td>
<td>187,059</td>
</tr>
<tr>
<td>2</td>
<td>(dementia[Title/Abstract]) OR Alzheimer*[Title/Abstract]</td>
<td>124,029</td>
</tr>
<tr>
<td>3</td>
<td>(review[Title/Abstract] or meta-analysis*[Title/Abstract])</td>
<td>890,355</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>112</td>
</tr>
</tbody>
</table>

**Included in review:** 4
### Blood pressure (search undertaken 27 October 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>hypertension[Title/Abstract] OR anti-hypertensive*[Title/Abstract] OR &quot;blood pressure&quot;*[Title/Abstract]</td>
<td>41465</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>125,707</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analys*[Title/Abstract]</td>
<td>904,042</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>373</td>
</tr>
<tr>
<td></td>
<td>Included in review</td>
<td>7</td>
</tr>
</tbody>
</table>

### Diabetes (search undertaken 5 September 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>diabetes[Title/Abstract] OR hyperglycaemia[Title/Abstract] OR &quot;blood sugar&quot;*[Title/Abstract]</td>
<td>317,454</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>124,183</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analys*[Title/Abstract]</td>
<td>891,890</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>596</td>
</tr>
<tr>
<td></td>
<td>Included in review</td>
<td>4</td>
</tr>
</tbody>
</table>

### Obesity (search undertaken 20 September 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Obesity [Title/Abstract]</td>
<td>126,388</td>
</tr>
<tr>
<td>2</td>
<td>dementia[Title/Abstract] OR Alzheimer*[Title/Abstract]</td>
<td>164,460</td>
</tr>
<tr>
<td>3</td>
<td>review[Title/Abstract] or meta-analys*[Title/Abstract]</td>
<td>894,904</td>
</tr>
<tr>
<td>4</td>
<td>1 AND 2 AND 3</td>
<td>169</td>
</tr>
<tr>
<td></td>
<td>Included in review</td>
<td>4</td>
</tr>
</tbody>
</table>

### Serum cholesterol (search undertaken 29 August 2013)

<table>
<thead>
<tr>
<th>Search</th>
<th>Query</th>
<th>Items found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(cholesterol[Title/Abstract]) OR (statin[Title/Abstract])</td>
<td>180,313</td>
</tr>
<tr>
<td>2</td>
<td>(dementia[Title/Abstract]) AND (review[Title/Abstract])</td>
<td>5,695</td>
</tr>
<tr>
<td>3</td>
<td>1 AND 2</td>
<td>106</td>
</tr>
<tr>
<td></td>
<td>Included in review</td>
<td>5</td>
</tr>
</tbody>
</table>
References


He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ. 2013 Apr 3; 346: f1325.


Lautenschlager NT. Twelve months of resistance training can improve the cognitive functioning of older women living in the community. J Physiother. 2010; 56 (3): 200.


Peters SA, Huxley RR, Woodward M. Comparison of the sex-specific associations between systolic blood pressure and the risk of cardiovascular disease: a systematic review and meta-
analysis of 124 cohort studies, including 1.2 million individuals. Stroke. 2013 Jul 2. [Epub ahead of print].


