

Review

Approaches to reduce the incidence of cognitive decline and dementia

David Jolley

Abstract

The health of older people is of importance in all countries of the world. Life expectation is increasing most markedly in low and middle income countries so that the number and distribution of older people is expanding. Dementia is an age related condition, rare before the age of 60, but affecting 30% of people in their late eighties and beyond. It is a syndrome with a range of aetiologies, which leads to dependency, cost of care and early death. Despite investments in recent years there is, for most cases, no magic medicinal treatment which will arrest or improve the life-course of dementia once it is established. It is now understood that certain risk factors make it more likely that individuals will develop dementia. The Lancet Commission has recently reviewed these, identifying twelve factors which are potentially remediable with the possibility of reducing worldwide incidence of dementia by up to 40%. In addition enlightened approaches to care - 'tertiary prevention' - can reduce the burden of adverse symptoms and have been associated with increased life expectation for people with dementia. These factors are reviewed here.

Key words

Age, Dementia, Incidence, Prevention, Risk Factors

Introduction

The motivation for clinicians working in the field of mental health of older people from the 1970s onwards has been to improve services and treatment for older people with psychiatric disorders, including dementia. The task has been focussed on people who have developed, often quite severe or advanced mental illnesses. This has been extended in association with the scientific community to gain a better understanding of the nature of these conditions, including factors which lead them to occur, as well as to search for approaches which might reduce their incidence or resolve their symptoms.^{1,2}

The number of people living into old age (60 years +) is increasing as survival into late life is achieved by more: there were 962 million aged 60+ by 2017, two thirds living in Low and Middle Income countries (LMIC).³

A proportion of older people begin to show impairment of cognition, an estimated 46.8 million people world-wide, have dementia. By 2050 it is predicted it will be over 150 million. Great age is the strongest predictor of having dementia. The prevalence varies between communities but everywhere it is age related. In the UK a rough estimate is that 2% in their early 60s have dementia of some sort and degree, rising to 5% in the early 70s, 10% in the early 80s and 30% amongst 90 year olds.⁴

Most research has been conducted in High Income Countries where the expectation of survival into late life has been long established. Yet the majority of older people, at risk of dementia live now in LMIC. This will become more so in the years ahead. Professor Martin Prince and his colleagues established a research programme to address this mismatch: 10/66 – ten percent of publication about older people, coming from the 66 percent of the world population in LMIC. They have produced assessment tools which are not biased by education, literacy or numeracy and established that dementia is found in all communities – prevalence varies from 4.8% in rural China to 12.6% in Cuba.⁵

Dementia is characterised by impaired memory, loss of communication skills and loss of the ability to do things. It is a major cause of disability, dependency on others and shortens life expectation. It is costly for individuals, for families and for society. It is said that amongst middle aged and older people dementia or Alzheimer's disease is more feared than cancer.⁶

Risk factors for dementia and prospects for primary prevention

Genetic factors account for some cases of dementia, particularly amongst relatively young people, but inheritance is importance in only 1% of cases of Alzheimer's disease and vascular dementia. Their contribution is greater for frontotemporal dementia and Huntington's chorea and other rare conditions. This means that for 99% of dementia we look to other factors which contribute to its development.

An important and influential review by The Lancet Commission published in 2017 and updated in a publication 2020 has identified twelve modifiable risk

factors.^{7,8} These papers have reviewed articles which achieve a high standard and include systematic reviews and meta-analyses. It is accepted that there will be other modifiable factors identified by research in the future; the current twelve are given in the Box 1.

Box 1: Modifiable risk factors for dementia
<ol style="list-style-type: none"> 1. Less education 2. Hypertension 3. Hearing impairment 4. Smoking 5. Obesity 6. Depression 7. Physical inactivity 8. Diabetes 9. Low social contact 10. Excess alcohol 11. Traumatic brain injury 12. Air pollution
<p>Based on Lancet Commission.^{7,8} Sl 1-9 were listed in 2017; sl 10-12 were added in 2020.</p>

It is estimated that these risk factors contribute 40% to the incidence of dementia. This raises the prospect that attention to them could reduce the incidence by that amount. The potential for corrective action is greatest in LMIC and amongst the poorest and most deprived.

People with dementia have more health problems than age, gender, ethnicity and social circumstance matched controls. They have more admissions to hospital than age, gender, ethnicity and social circumstance matched controls and are more likely to develop delirium when ill. They have a reduced life-expectation and have died more often of COVID-19 than age, gender, ethnicity and social circumstance matched controls. Modelling in the UK predicts the years ahead will include more old people who are well and independent, but also more with complex care needs.

Life course model of dementia genesis

The Lancet Commission presents a life course model of dementia genesis.⁷ A summary of the identified factors associated with dementia are discussed below.

Education: Education in childhood and beyond builds on the cognitive reserve of an individual. Lack of education leaves neurobiological development of the brain incomplete and vulnerable to the development of pathologies later in life. Involvement with a full education is powerfully associated with well-developed cognition and with resilience in the face of stress, including neuropathology – so reducing the likelihood of dementia.

Physical health: Maintenance of good physical health through life has a positive and protective effect on cognition. If neuropathology begins to develop, people who remain physically fit and active show less deterioration.

Exercise: Exercise has positive effects via weight loss and reduced likelihood of diabetes, and the production of

‘feel good’ emotions. Taking into account differences in age, generation, morbidity, gender, social class and culture, observational studies confirm that exercise improves normal cognition and reduces the incidence of dementia.

Maintenance of cognitive activity: People who read, play games or are involved with betting in middle age and later life, have a lower incidence of dementia.

Poverty and inequality stunt the growth of cognitive abilities and make the development of dementia more likely and more rapidly progressive.

Smoking and air pollution have toxic effects within the body and brain, mainly via the vascular system.

Retirement is associated with a drop in cognitive function. More demanding jobs sustain cognition and staying in work for more years is associated with retained cognitive ability. It is not clear that marketed computer programmed cognitive training programmes are effective.

Loss of hearing: People with hearing impairment in middle age and beyond are more likely to develop dementia; if they use a hearing aide, this reduces the effect.

Traumatic Brain Injury (TBI) has now been demonstrated to predict development of dementia. Mild TBI equates to concussion, severe TBI will include fractured skull, cerebral oedema, brain injury or bleeds. Severe TBI is associated with widespread hyper-phosphorylated tau.⁹ Common causes include road traffic accidents and sports injuries. There is currently great awareness of the damage associated with recurrent head trauma in professional soccer and other contact games.

Hypertension: the Framingham Studies demonstrated that a systolic blood pressure above 140 mm Hg in middle age predicted higher incidence of dementia. Control to below 120mm Hg reduces the incidence. But a Cochrane Review found no evidence that statins or aspirin in late life reduced the incidence of dementia.

Diabetes: Type 2 diabetes increases the incidence of dementia. It is not clear whether good control of diabetes is protective of deterioration in cognition.

Combined effects of cardiovascular risk factors: Using a scoring scheme which takes into account smoking, diet, physical activity, BMI, fasting blood glucose, cholesterol and blood pressure; low scores are associated with low incidence of dementia. High scores relate to reduced whole brain volume and to hippocampal atrophy.

Excessive alcohol: Heavy drinking (four drinks per day for men, three drinks per day for women) is associated with brain shrinkage, cognitive decline and a threefold increase in the incidence of dementia. Moderate drinkers have a slightly lower incidence of dementia than abstainers.

Obesity and weight control: Being obese – BMI equal or greater than 30 – is associated with a higher incidence of

dementia, but simply being overweight is not. Losing weight in middle age by diet improves attention and memory.

Smoking: Smokers have a higher incidence of dementia, which falls when they stop smoking, even in later life. It is not known if passive smoking leads to more dementia.

Depression: There is a complex relationship between dementia and depression. Depression may be mistakenly diagnosed as dementia. An episode of depression may be followed by a developing dementia. Depression may occur during the course of dementia. Treating depression in the presence of dementia is difficult. It is not known whether effective treatment of depression is protective against dementia.

Social contact: Low social contact is associated with more dementia. Cohabitants have a lower incidence of dementia than people who are long-term single or widowed.

Air pollutants: Exposure to nitrogen dioxide, carbon monoxide and/or particulate matter, as in traffic - is associated with more dementia.

Sleep: Less than five hours sleep per night, or more than eight hours sleep are associated with higher incidence of dementia

Diet: Studies of individual components of diet: vitamins, high plant content (Mediterranean or Nordic) do not show convincing evidence that they reduce the incidence of dementia.

Estimates of the contribution of factors to the genesis of dementia

Various estimates of the contribution of factors to the genesis of dementia have been proposed along with the potential for reducing incidence of dementia if they are addressed. **Population Attributable Fraction (PAF)** is a concept which gives a value to the effect there would be on incidence of a disease, if the actual status of a factor at present were returned to an average population level. This can be used to estimate benefits which might be attained by improved conditions within the dimension of one factor.¹⁰ **Communality** is a measure of how much of the impact of one factor overlaps with others.¹¹

Some recent considerations

Biomarkers: There is interest in looking for changes amongst people who may develop dementia but are clinically normal.

Scans: Dementia is signified by loss of brain volume, reduced size of the hippocampus, entorhinal cortex and medial temporal cortex. Scans are costly and are not justified outside a research context.

Molecular markers: In blood or cerebrospinal fluid, amyloid beta and tau biomarkers can be identified amongst people with no clinical evidence of dementia.

Research does not find their presence predicts development of the clinical syndrome.

Plaques can be seen in 3% of normal people aged 50-59, but in 40% of people aged 80-89. Amyloid imaging is therefore not a diagnostic test for dementia. If it is negative it certainly rules out Alzheimer's disease. If it is positive the subject may be normal or have Alzheimer's disease.

Whole population screening for dementia produces no advantage but may do no harm.

LATE – Limbic predominant, Age related TPD-43 Encephalopathy: A newly recognised fairly common dementia in very late life: LATE – Limbic predominant, Age related TPD-43 Encephalopathy is a condition quite recently identified. It affects mainly people in their 80s and older, is a milder, more slowly progressive condition with sclerosis of the hippocampus seen at post-mortem.¹²

Multi-domain interventions: These interventions including diet, physical exercise and cognitive training do seem to be useful especially in the 65-76 age group and with people who have been most educationally deprived.

'Tertiary' prevention: The concern thus far has been with primary or secondary prevention of dementia, by recognising and addressing factors which relate to the incidence of dementia. There remains value in reducing the impact of established dementia on the lived experiences of individuals and families, and the demand and cost of services

Medication: Cholinesterase inhibitors have a useful but modest impact on progress of cognitive decline and useful activities. They are no longer funded in France as they are deemed to be not cost-effective.

Neuropsychiatric symptoms

These can be helped by low dose antipsychotics (but beware of unwanted effects) and tailored activities. Non-drug therapy is not effective for **psychotic symptoms**. These can be helped by low dose antipsychotics (but beware of unwanted effects). Other medications such as tranquillisers or antidepressants are being widely prescribed because of directives not to use antipsychotics. They do not work but they do have high levels of death, falls and hospital admission. **Depression** is not easily treated in dementia. **Agitation** has mostly been investigated in care homes, tailored activities can be effective. There is no medication which is useful for **apathy**. Tailored activities are effective. Hypnotics are not effective for **sleeplessness** and are associated with falls, hospital admissions and death. Diet and tailored activities are the best option. There is evidence that cognitive rehabilitation delivered to individuals (not groups) can produce useful improvements in functioning.

Carers

Identifying carers and their needs, including education and support of distressed carers can reduce their symptoms and reduce the cost to services.

Comorbidities and related points

Comorbidities: Comorbidity is common in dementia. Almost 70-80 percent of people with dementia seen in primary care have two or more other pathologies, identification and treatment of these is always worthwhile. Recently COVID-19 is sweeping the world. It has preferentially attacked older people, particularly those with dementia, who are suffering the highest death rates.

Delirium: It is often seen as a complication of dementia. Delirium arising de novo may be followed by a subacute syndrome of progress to dementia. Approaches to reduce the incidence of delirium in hospital are recognised.

Hospital admissions: Older people with dementia, especially if living alone, are more liable to admission to hospital than are others with similar physical illnesses. In hospital they do not do well. They are more prone to delirium and falls, stay longer in hospital, are more likely to die or to be discharged to a care home. All these phenomena are unhappy for the individual and family and a source of unease and expense to the services. Approaches to better care at home are valued. Specialised liaison services have been found to improve outcomes and reduce costs.

Frailty: The mental frailty of dementia is often associated with physical frailty and the associated dependency and vulnerability to additional illnesses.

End of Life: Dementia is now confirmed to be the most common cause of death in High Income countries under normal circumstances. The last weeks of life with dementia may be difficult – complicated by pain, agitation, physical dependency, and loss of weight, difficulty with feeding and hydration, and vulnerability to infections. There is increasing awareness of the advantage of a palliative approach to modify symptoms. Hospices can play a very helpful role within the spectrum of services.¹³

The best of news

Good news is that follow up studies in the UK and elsewhere have begun to find that the incidence of dementia using exactly matched methodology in successive cohorts is falling. Cognitive Function and Ageing studies one and two 1989 – 1994 and 2008-2011 found a 20% drop in incidence in the three centres – Nottingham, Cambridgeshire and Newcastle. The drop was most marked in men where it was almost 50% in some age bands. The lowering of incidence found in Nottingham and Cambridgeshire was not matched in Newcastle where the measure rose a little. This difference is probably related to the socio-economic conditions; Newcastle experienced more difficulties and loss of employment.¹⁴ Overall the incidence of dementia fell in the least and moderately deprived areas and rose in the most deprived areas. This is not a controlled experiment but a careful report of a naturalistic change. It seems probable that improvement in many of the 12 factors (Box 1) will have played a part in achieving a pooled effect. It

is tempting to believe that general improvement in socio-economic circumstance and a move toward equality will have benefits

In summary, compared with the state of knowledge in 1970s we have come a long way. There is now a better understanding of the nature and complexity of dementia and its distribution throughout the world. Factors have been identified by rigorous research, which increase the likelihood that individuals will develop dementia. Many of these are potentially remediable - a sober estimate is that if these are fully addressed, incidence of dementia will fall by 40%. We are already seeing that incidence is falling in some countries where socio-economic circumstances and health care are best developed.

The Lancet Commission summarises these findings and suggests an effective strategy to reduce the incidence of dementia worldwide. Life-long education has the potential to reduce incidence by 7%. Identifying and correcting hearing loss could reduce incidence by 8%, smoking by 5%, depression and social isolation by 4% each, traumatic brain disease by 3%, hypertension, physical inactivity, and air pollution by 2% each, alcohol excess, obesity and diabetes can reduce dementia incidence by 1% each.⁷

Conclusion

Compared with the situation in the 1970s this is a position of hope: a better understanding of the nature and aetiology of conditions which produce dementia means that primary preventive measures can be taken which could reduce the incidence of dementia, with all the personal and societal costs associated with it, by something like 40%. Although there is limited benefit to derive from anti-dementia medication, there is much which can be done to improve the experience of life with dementia, for individuals with the condition and those who care for them – a tertiary prevention strategy.

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