Parliamentary Office of Science and Technology

postnote

February 2007 Number 278

ALZHEIMER'S & DEMENTIA

In the UK, an estimated 750,000 people suffer from Alzheimer's and other dementia disorders. Dementia makes independent living either difficult or impossible in the later stages. As the UK population ages, the number of cases are predicted to rise over the next two decades placing a significant demand on health and social services. This POSTnote reviews current understanding of the causes of dementia, the hopes for interventions, and the UK's current position in terms of handling future demand for services.

Background

What are dementia-related disorders?

Dementia is a syndrome that in most cases is caused by an underlying disease of the brain and loss of brain tissue. There are several diseases which give rise to dementia, such as Alzheimer's and Parkinson's with dementia (Box 1), known as subtypes. Functions affected include memory, orientation, thinking, comprehension, calculation, judgement, learning and language. Dementia is a progressive disorder and is accompanied by deterioration in emotional control, social behaviour and loss of independent function and decision-making. The cause, course and symptoms of dementia depend on numerous factors. It is difficult to distinguish between some of the different subtypes, to predict the timescales over which a person's cognitive abilities decline, and what behavioural symptoms a sufferer may experience. At present, no biological interventions are available which alter or reverse the underlying degeneration of brain cells.

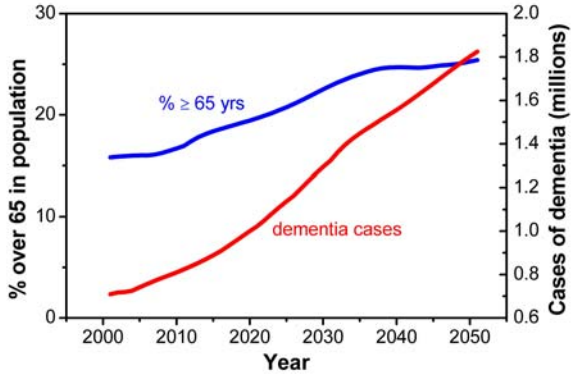
Dementia in an ageing population

The risk of developing dementia is strongly associated with ageing, although inheritable early-onset dementia does occur very rarely in people under 65 years. Population studies show that the prevalence (number of cases) roughly doubles every 5 years over the age of 60 (Table 1). The UK population is projected to increase to 69.3 million in 2051 from 60.5 million in 2006[1]. Should prevalence rates remain unchanged over the next few decades, and as the population ages, the total number of dementia cases could more than double, from 750,000 in 2006, to 1.8 million in 2051 (Figure1).

Table 1: Prevalence rates of dementia by age[2]

Age-group (years)	Prevalence of dementia (%)
60-64	0.9
65-69	1.5
70-74	3.6
75-79	6.0
80-84	12.2
≥85	24.8

Figure 1: Projected percentage of UK population over 65 years old, and estimated total cases of dementia[1,2]



Diagnosis and care of people with dementia

Currently, dementia is diagnosed through a series of tests to assess cognitive decline. In the 'very mild' stage, suspicion is raised when someone has trouble with memory, learning and, perhaps, mild personality changes. A formal diagnosis maybe made when there is impairment of social or occupational function. Gradually one or more 'activities of daily living' such as dressing or bathing are also affected. The moderate stage sees growing impairment of language and memory and increased reliance on a carer. Behavioural disturbance and psychological symptoms can happen at any stage of the illness. The greatest impact on sufferers, carers and society is concentrated in those in the severe stages (~17-28% of people with dementia over 65). Dementia is a key factor in the need for nursing-home placement; 62-74% of residents in care institutions have dementia[3].

Box 1. Causes and risk factors for dementia

Brain changes in dementia
At birth, the brain is composed of over 100 billion nerve cells (neurons). In dementia, neurons in certain parts of the brain die due to an underlying disease. At death, an Alzheimer's brain may have lost up to 50% of its weight.

Subtypes of dementia disorders
Four major causes of dementia are Alzheimer's (~55%), vascular dementia (~20%), dementia with Lewy bodies (~15%), and frontotemporal dementia (~5%). Less common causes are Parkinson's with dementia, and rarer forms such as Creutzfeldt-Jakob and Huntington's disease.

Pathological hallmarks
Microscopic changes in the brain underlying dementia are different for different subtypes, as are the regions in the brain where these arise. In Alzheimer's, two hallmarks are protein 'tangles' inside neurons and 'plaques' on the outside, found mainly in the region responsible for memory. In many cases, there is an overlap of these distinct hallmarks[4].

Early-onset genetic risk factors
Much has been discovered from studies of the genetics of rare, hereditary forms of dementia. In early-onset hereditary Alzheimer's, mutations in three genes that alter a protein (Aβ) have been identified. Aβ forms amyloid plaques, one hallmark of Alzheimer's. For other subtypes, numerous other genes have been identified, and this search is ongoing.

Late-onset genetic factors
Much less is known about the genetic and non-genetic risk factors for late-onset dementia. One genetic risk factor has been identified in Alzheimer's where carrying a copy of a gene for a protein called *'apoE ε4'* (present in 25% of the population) triples the chance of developing the disease. Carrying two copies of the gene (~2% of the population) increases this risk to ~6-15 fold.

Other risk factors
Although environment plays a part, twin studies suggest that genes probably contribute ~80% of the risk of developing Alzheimer's. Population studies have suggested some tentative environmental risk factors, including diabetes, diet, risk factors associated with vascular disease such as hypertension and obesity, and low educational attainment and mental ability.

Issues

Dementia is immensely important to UK health and social care policy. For instance the direct and indirect economic costs alone have been estimated at ~£7-15 billion (1998/99 prices)[5,6], more than coronary heart disease, cancer, and stroke combined. Key issues include provision of early diagnosis, treatment, interventions and long-term care, as well as research funding/infrastructure.

Early diagnosis and monitoring disease progression

Currently, few cases of dementia are diagnosed early. Early detection would have two advantages. First, sufferers and families could plan legal, care and financial matters for the future. This is a key issue voiced by current sufferers and carers. Second, if interventions slow disease progression, the earlier the diagnosis, the greater the potential to prevent irreversible cognitive damage. This would need to be combined with better methods for monitoring disease progression. Several new diagnostic approaches are in development (Box 2). Their use up to now has been largely confined to research. An ideal system would be cheap, simple, able to differentiate between dementia and other conditions such as depression, and able to distinguish the different types of dementia (Box 1).

Box 2. Early diagnosis & monitoring

Psychometric tests
The 'Mini-Mental State Examination' is widely used as a screening tool to assess cognitive impairment. It is easy to use but is culturally and socially sensitive, and results can vary from day to day. More sensitive tests have been developed, but are not in wide clinical use.

Brain-imaging
New imaging techniques allow researchers to visualise changes in the brain. *Structural imaging* (**CT** and **MRI scans**) highlight changes to certain affected areas in the brain, and *functional imaging* (**PET and SPET scans**) can be used to monitor physiological changes. Monitoring single patients over time can indicate disease progression. PET-imaging with the use of a dye can visualise amyloid plaques in Alzheimer's; a possible indicator of disease progression.

Biological markers in bodily fluids
Biological indicators in cerebrospinal fluid or blood have been investigated widely as markers for the onset of dementia. For instance, circulating levels of abnormal proteins are being examined as biomarkers for Alzheimer's.

Another issue is how early can dementia be diagnosed? It has been estimated that biological changes may occur 10-20 years before a diagnosis is made. Early signs of memory problems may result in people earning the diagnostic tag of 'mild cognitive impairment' (MCI). The usefulness of MCI depends on two factors: the proportion of MCI patients going on to develop dementia; and the time scale over which this might occur. Considerable confusion remains over these. For example, some definitions of MCI include almost all people over 65, and others almost none. Some studies suggest that 12-15% of MCI patients will develop mild dementia each year, but this may not be applicable in the general population. New diagnostics (Box 2) may help to target interventions to this group, as some techniques may predict ~80% of this subset. Uncertainty over MCI poses ethical issues for doctors, who have to decide what to tell MCI patients about their increased risk of dementia.

Interventions

There are a variety of potential interventions for dementia. These include drugs (Box 3), non-pharmacological interventions (e.g. cognitive retraining; information and advice), and supporting those affected to live more independently using assistive technology (Box 4). Drugs that treat cognitive symptoms of Alzheimer's disease have been in the limelight due to recent guidance on their use by the National Institute of Health and Clinical Excellence (NICE).

NICE appraisal of current Alzheimer's drugs
Four drugs can be used to treat the cognitive symptoms of Alzheimer's disease. Each costs the NHS ~£1,000 per patient per year, or £50 million per year in total. An

Box 3. Dementia drugs.

Current drugs

Four drugs are currently used to treat cognitive symptoms in Alzheimer's Disease. They interact with mechanisms that allow brain cells (neurons) to communicate with each other. Three, called acetylcholinesterase (AChE) inhibitors, help to maintain levels of the signalling molecule acetylcholine by delaying its breakdown. The drugs are based on work suggesting that depletion of this molecule and associated loss of 'cholinergic neurons' are an underlying factor in Alzheimer's. A fourth drug, memantine, blocks the action of another signalling molecule, high levels of which are implicated in neuronal dysfunction. Many clinical trials suggest the drugs provide modest cognitive benefits for~40% of Alzheimer's sufferers for ~6-18 months, but do not slow down the underlying disease. Some trials suggest wider benefits, such as reduced carer time, but some show that the drugs do not reduce the risk of institutional care.

Emerging drugs

New drugs are based on firmer knowledge about the disease mechanism, targeting the root cause of brain degeneration rather than symptoms, but take 15-20 years to develop. There are around 640 drugs under various stages of development for neurodegenerative disorders. A handful of these target Alzheimer's disease. Possible targets include 'amyloid plaques' and 'protein-tangles' (Box 1). Drugs targeting such features are in late stages of clinical development, with some results expected in 2007 or 2008. A 'vaccine' is also under development, and other drugs highlighted in population studies may also prove beneficial.

appraisal by NICE in 2001 recommended the use of acetylcholinesterase (AChE) inhibitors (Box 3) in the treatment of mild and moderate Alzheimer's. In a new appraisal in 2006 NICE recommended that:

- AChE-inhibitors for mild stages of Alzheimer's are not cost-effective. An economic measure commonly used to assess this, the 'quality adjusted life year' (QALY) was calculated to be ~£56,000-72,000.
- AChE inhibitors for moderate stages Alzheimer's are cost-effective (£23,000-35,000 per QALY).
- Memantine (Box 3) was not recommended as a treatment option except as part of clinical trials.

Response to NICE recommendations

A number of bodies appealed against the 2006 appraisal, feeling that it was not transparent enough, and did not place sufficient value on wider benefits of using the drugs. There was criticism for not factoring in:

- reduced carer time;
- reduced prescription of other drugs (neuroleptics);
- wider health service costs;
- cumulative benefits of early diagnosis/treatment;
- reduced overall treatment costs due to only ~40% of patients responding to treatment.

The appeal was not upheld. Underlying much of the appeal process was whether a measure like the QALY could adequately capture the complex benefits of the subtle cognitive improvements seen with these drugs. Broader measures that might address this in future, are being developed. The Royal College of Psychiatrists has criticised the guidance suggesting it will discourage early-diagnosis, and noting that the test used to categorise patients is culturally and educationally biased and, thus, an inadequate sole guide for treatment.

Box 4. Assistive technology or telecare

Telecare devices support memory, communication and safety, enabling people with dementia to live more independently. Devices range from calendar-clocks that aid orientation, to sensors that detect gas, floods, and falls and that alert carers or community alarm centres. Their use has been restricted to pilot studies with growing evidence for positive outcomes. However, there is no national strategy on how telecare should be implemented and what technologies would provide the most effective outcomes. The Department of Health announced a two-year £80 million 'Preventative Technologies' grant which started in 2006, but future security of funding is uncertain.

Funding provision of long-term care

Reviews of the current system for care funding highlight its ambiguity and unfairness for dementia sufferers. A Commons Health Select Committee report[7], drew attention to the partition between health (free at the point of delivery) and social care (means-tested). This has led to two parallel streams for funding care (Box 5), and raises a number of issues concerning the fairness of eligibility criteria for dementia sufferers. First, there is confusion over exactly who is eligible for which stream as there is significant overlap between the criteria. Similar language is used, for example, in the criteria for the top-tier of Registered Nursing Care Contribution (*RNCC*) in England, and for Continuing Care (*NHS CC*) (Box 5). In practice, the system discriminates against dementia sufferers as it tends to place them in the *RNCC* stream compared with, say, terminal cancer patients, who are more likely to have costs met by the *NHS CC* stream. Second, there is considerable variation in the way that the criteria are applied by different Strategic Health Authorities, and the Health Ombudsman has highlighted that many have been unlawfully denied funding[8]. Often, funding can fluctuate as the disease progresses, which can be distressing and disruptive for carers and sufferers.

In contrast, Scotland provides free personal and nursing care at a cost of ~£140 million (0.2% Scottish GDP). Reviews of this system by the Scottish Executive Health Committee and others, highlight free personal care as having made provision for those with dementia more equitable[9]. A similar move in England & Wales would cost ~£1.75 billion, but would have to be considered in the context of the wider debate on reform of long-term care provision. The Department of Health (DH) is currently devising a 'national framework' to clarify some of the confusion over criteria, and is expected to report in 2007. It has no plans to introduce free personal care.

Service provision reform

Service provision for the elderly, particularly dementia sufferers, has been criticised for being non-integrated, and non-informative[10]. The challenge in coming years is delivering the DH's vision of choice, patient-centred care, carer support, seamless service provision and prevention,

Box 5. Long-term care funding now & in the future.

When does the NHS fully pay for long-term care?
The 'NHS Continuing Care' (NHS CC) stream meets all personal and nursing cots, as well as housing costs in a nursing home. Eligibility is assessed by Strategic Health Authorities to comply with the 'Coughlin Judgement' and other case law, where the primary care need is health.

When is care means-tested?
The Registered Nursing Care Contribution (RNCC) is an assessed tiered (England) or fixed payment (elsewhere in the UK) by the NHS towards registered nursing-care. Personal care costs are means-tested, except in Scotland where these are fully met. An asset threshold in the region of £21,000 is used, above which a person must pay towards their care. Housing costs associated with care homes are means-tested.

How should long-term care be funded in the future?
Opinions differ but key factors are affordability, sustainability and fairness. **The Royal Commission** suggested free personal care, implemented in Scotland. **The Wanless Social Care Review** suggested a non means-tested 'Partnership model', with the state contributing 66%, and the rest met equally by the individual and the state. The **Joseph Rowntree Foundation** suggested a number of improvements, including reform of the current benefits system[11].

How much is it going to cost in the future?
Projections[12] suggest that demographic pressures mean spending on care would need to increase from 0.96% GDP (2002) to 1.95% GDP in 2051. Free nursing care would change this from 1.18% (2002) to 2.40% GDP in 2051.

on the ground[13]. An important issue is how best to integrate health and social services. Options here include greater support for multidisciplinary health and social care teams, providing locally pooled budgets, and a 'Single Assessment Process', to ensure person-centred care across agencies.

One important role, recognised by the DH, NICE and the Scottish Intercollegiate Guidelines Network, is that of 'memory assessment centres'. The hope is that these will aid early diagnosis, prescribe interventions and advice, signpost services, and be the focus of integrated teams. However, the centres are not usually community-based, and may be less viable in the wake of the NICE drugs appraisal. Another issue is the lack of 'descriptive' population data (how do sufferers currently access services, and what outcomes work best?) which are needed to address effective service provision. Given that dementia is a major factor in service demand (~30% of occupants of hospital beds over 65 years of age[14], and ~62-74% of residents in care institutions suffer from dementia), greater emphasis on training of health and social care professionals is another important issue.

Research financing & infrastructure

Public and charitable expenditure on Alzheimer's disease research in 1999 was £5.5 million and the figure spent by the pharmaceutical industry is likely to be many times more than this. The DH has set up a UK Clinical Research Network specifically for dementia and other neurodegenerative disorders, to aid the conduct of clinical trials. The EU allocated €40 million to support funding into Alzheimer's in the FP6 programme, which supports collaborative research in the Union. In contrast, the US National Institute of Health spent $656 million on Alzheimer's disease research in 2005. A recent House of Lords report[15], highlighted the need for a better strategy for UK research into ageing, including dementia. Recommendations included a dedicated strategic body, and specialised fellowships/career development awards. Also highlighted was the need for infrastructure support for more population studies. These would be needed in future to address the question of whether the UK's population will be at increased risk on account of increasing rates of obesity, high blood pressure, and heart disease rates (Box 1).

Overview

- Numbers of people affected by dementia are set to increase from 750,000 to 1.3 million in 2031.
- The economic costs of dementia are thought to be in the region of ~£7 to £15 billion.
- Clearer biological targets for treatment have been identified, and new drugs are likely in 5-10 years.
- The current system for funding long-term care is seen as inequitable for dementia patients.
- There is scope for a more integrated approach to service provision for dementia patients.

Endnotes

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POST is grateful to Dr Walraj Gosal for researching this briefing. to NESTA for funding his parliamentary fellowship, and to all contributors and reviewers. For further information on this subject, please contact Dr Peter Border, at POST.

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