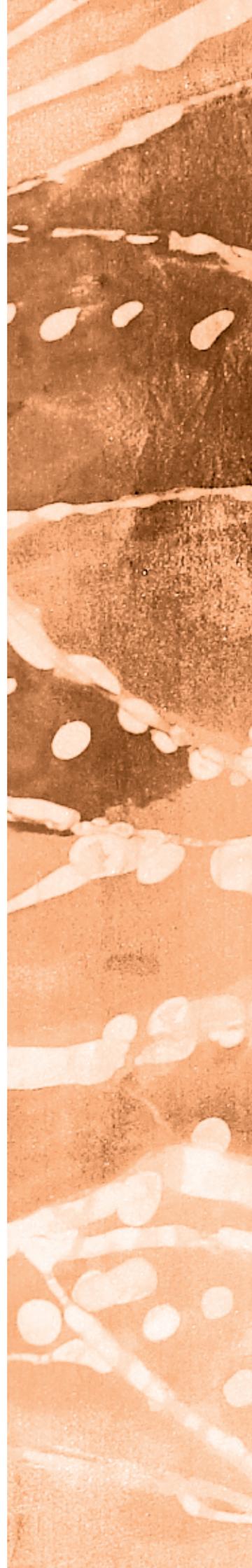


Chapter 8

Research



Chapter 8 – Research

Introduction

8.1 This Chapter will focus on two specific ethical issues posed by research into dementia. First, it will discuss how research should be prioritised, given both the ‘Cinderella status’ of dementia and the inherent tension between the longer-term and unpredictable aim of seeking cures and the shorter-term and perhaps more immediate goal of enhancing quality of life. Secondly, it will consider the particular difficulties which arise when involving people with cognitive impairment in research studies.

How should research be prioritised?

“Surveys of carers show that what is wanted is a better understanding of the causes, so they might become preventable. Surveys of dementia sufferers indicate that there is more concern regarding quality of life issues.” *Anonymous consultation respondent*

“... the emphasis of resource allocation, prioritisation, performance targets, research funding, education and training has all been skewed towards higher tech treatments and ‘sexier’ conditions such as cancer or ischaemic heart disease which affect younger people and away from the needs of older people with incurable long term conditions.” *British Geriatrics Society, consultation respondent*

8.2 While there have been major advances in recent years in dementia research, the 2007 report *Dementia UK*, produced by the London School of Economics and King’s College London for the Alzheimer’s Society, highlighted the relatively low priority given to dementia research compared with that devoted to other diseases. A survey of research papers on long-term conditions published since 2002 demonstrated that while 23.5 per cent were concerned with cancer and 17.6 per cent with cardiovascular diseases, only 1.4 per cent focused on dementia.⁴¹⁷ In June 2009, the UK Clinical Research Network listed 104 trials for dementias or other neurodegenerative diseases being set up or currently recruiting, compared with 218 for cardiovascular diseases and 383 for cancer.⁴¹⁸ Similar differences are found in the levels of public funding for medical research: figures on combined research funding by the English Department of Health and Medical Research Council published in response to parliamentary questions cited a total of £32.4 million spent in 2007–8 on dementia, compared with £248.2 million the same year on cancer⁴¹⁹ – a distinction much criticised by organisations such as the Alzheimer’s Research Trust.⁴²⁰

8.3 Before commenting further on the implications of these figures, however, we would first like to consider what research into dementia should be trying to achieve. We identify below six broad areas of potential research into dementia, all of which received considerable support in our public consultation.

8.4 **Basic science research:** working to understand both the mechanisms of normal ageing and the mechanisms which lead to the death of brain cells and hence brain atrophy. As the Academy of Medical Sciences highlighted in their response to us, the precise mechanisms causing neurodegeneration are still unclear, despite identification that a number of proteins, such as

⁴¹⁷ Knapp M and Prince M (King’s College London and London School of Economics) (2007) *Dementia UK* (London: Alzheimer’s Society), p xv.

⁴¹⁸ Figures correct as at 9 July 2009, see: <http://public.ukcrn.org.uk/Search/Portfolio.aspx>.

⁴¹⁹ House of Commons *Hansard*, 16 December 2008, c677W, available at: www.publications.parliament.uk/pa/cm200809/cmhansrd/cm081216/text/81216w0033.htm#08121714000065.

⁴²⁰ Alzheimer’s Research Trust website, available at: www.alzheimers-research.org.uk/info/statistics/.

amyloid, tau and the presenilins, and the gene ApoE4 all have important roles.⁴²¹ Until we have a better understanding of what role these particular hallmarks of the different dementias play in the development of the disease, we will be limited in our ability to identify new targets for possible drug treatments. Basic science research is also required to understand the reason why ageing of the brain leads to dementia in some people and not in others, especially given that Alzheimer-type pathology has been found in the post-mortem examination of brains of people who exhibited no symptoms of dementia during their lifetime.⁴²² Basic science research in other areas involved in normal ageing, such as sensory impairments, is of particular relevance for people with dementia: we currently know very little either about how these impairments contribute to the effect of the person's dementia on their mood and behaviour or about how the pathology of the dementia itself may itself compound sensory losses.⁴²³

- 8.5 Development of treatments.** The primary aim of much current research into dementia treatments is to find strategies which will limit, and ultimately halt, the damage to the brain, for example by research into techniques to reverse the accumulation of amyloid in the brain. We have already noted in Chapter 1 that, given the way our brains 'age' even without dementia, the idea of a simple 'cure' for dementia is misleading (see paragraph 1.30). Moreover, for people living with dementia, the most important aspect of their condition will generally be the effect of the dementia on their day-to-day life (both in terms of cognitive and behavioural changes) and the rate at which their difficulties increase. Research therefore needs to focus on possible treatments to delay or limit the effects of the underlying pathology on daily life, as well as tackling the pathology, such as the accumulation of amyloid, itself. One of the criticisms levelled against NICE's decision to recommend only limited NHS access to the cholinesterase inhibitors in England and Wales, for example, is NICE's alleged failure to pay sufficient attention to the personal experiences of many people with dementia and their carers, who reported significant improvements, albeit for a temporary period, in their quality of life.⁴²⁴ Moreover, it is important that research addresses drug development for all the various different types of dementia: the UK Age Research Forum, for example, highlighted the lack of work in this area for several diseases leading to dementia, including vascular dementia.⁴²⁵
- 8.6 Prevention,** or at least strategies to delay the onset of dementia. Work in this area would include research into genetic predispositions to dementia; long-term cohort studies (drawing from across all ethnic groups) which aim to increase understanding of the influence of lifetime risk factors such as environmental influences, diet and lifestyle; and research into 'neuroprotective' strategies and treatments, such as the effect of cognitive activity earlier in life on developing a 'cognitive reserve' against dementia.
- 8.7 Social science research** seeking a better understanding of issues such as:
- the experience of living with dementia, both as a person with a diagnosis of dementia and as a family member or carer;
 - how quality of life is affected throughout the course of a person's dementia;

⁴²¹ Academy of Medical Sciences, responding to the Working Party's consultation.

⁴²² Neuropathology Group of the Medical Research Council Cognitive Function and Ageing Study (2001) Pathological correlates of late-onset dementia in a multicentre, community-based population in England and Wales *The Lancet* **357**: 169–75.

⁴²³ Uhlmann RF, Larson EB, Koepsell TD, Rees TS and Duckert LG (1991) Visual impairment and cognitive dysfunction in Alzheimer's Disease *Journal of General Internal Medicine* **6**: 126–32; Pham TQ, Kifley A, Mitchell P and Wang JJ (2006) Relation of age-related macular degeneration and cognitive impairment in an older population *Gerontology* **52**: 353–8.

⁴²⁴ Alzheimer's Society statement *Access to drugs*, available at: <http://62.216.236.229/site/scripts/documents.php?categoryID=200264>; see also Foresight (2008) *Mental Capital and Well-being: Making the most of ourselves in the 21st century – final project report* (London: Government Office for Science), p212, where it is argued that the indirect effect on carers, in terms of their well-being and productivity, is not properly considered in the current process for determining the cost-effectiveness of drugs.

⁴²⁵ The UK Age Research Forum, responding to the Working Party's consultation.

- the role of stigma in affecting how people with dementia cope with their condition, and how stigma can best be challenged;
- how people can best be supported to 'live well' with their dementia, including the effect of the 'small things' of life such as the courtesy and respect with which others treat them in everyday matters;
- the most effective approaches to educating and supporting professionals and care workers in their understanding of and response to people with dementia;
- how best to educate and support those providing paid or unpaid care in responding to the ethical challenges they face on a daily basis; and
- the potential effect of wider environmental and social changes, such as attempts to make buildings and services more 'dementia-friendly', on the daily lives of people with dementia and those close to them.

8.8 Care to improve the lives of people with dementia now, including:

- comparative health services research on what is effective in caring for and supporting people with dementia; what forms of support are most cost-effective; the factors that affect the transferability of existing models of good practice; and the factors affecting the speed with which developments in the evidence base spread into day-to-day practice;
- nursing research on how to manage physical care needs appropriately in dementia;
- the use of technology to help people retain independence for longer; and
- development of more non-drug treatments and strategies to help people with dementia and their carers cope with difficult moods and behaviours.⁴²⁶

8.9 A sixth category, that of '**translational research**', aims to support the outcomes of one or more of the research targets above: for example the encouragement of early trials to enable swifter transfer from laboratory to clinical practice; the development of biomarkers, with the long-term aim of distinguishing between different dementias at an earlier stage and improving clinical trials by providing more reliable markers of how the disease is progressing; the creation of 'clinical cohorts' to facilitate longitudinal research; and the development of models to investigate the drivers of disease.

8.10 In their responses to our public consultation, major research funding bodies, such as the UK Age Research Forum (representing the views of almost 30 funding bodies), the Wellcome Trust, the Medical Research Council and the Economic and Social Research Council were in agreement that all of these broad research areas were important and required attention. It was noted that, in general, preventative research receives a relatively small proportion of research funding, and that this holds true for dementia.⁴²⁷ Indeed, analysis carried out by UK Clinical Research Collaboration in 2006 suggested that just 0.3 per cent of all neurological research related to prevention.⁴²⁸ The importance of work in this field was underlined to us by the UK Age Research Forum, who commented that it will "not be sustainable" in the future simply to try to ameliorate symptoms and provide long-term care: if the average onset of dementia is not delayed, there will simply be too many people with dementia for the system to cope. As we have already noted (see paragraph 1.29), 'preventative' strategies that result overall in people living longer may not reduce the numbers experiencing dementia, as increased age itself is a significant risk factor for dementia.

⁴²⁶ The guidelines published in 2006 by SIGN highlighted a number of areas in this category where the research base is currently far from adequate, including research on alternatives to drug treatment, the role of physical exercise in maintaining independent living, how to treat pain in dementia, effective interventions for "repetitive vocalisations" and the most effective way to prevent falls in dementia: SIGN (2006) *Management of Patients with Dementia: A national clinical guideline* (Edinburgh: SIGN), paragraph 6.4.

⁴²⁷ The UK Age Research Forum, responding to the Working Party's consultation.

⁴²⁸ UK Clinical Research Collaboration (2006) *UK Health Research Analysis* (London: UK Clinical Research Collaboration), p28.

However, such strategies may still be effective if, overall, they reduce the number of years of living with the more disabling aspects of dementia, even if the total number of people developing dementia before they die increases.⁴²⁹

- 8.11 While direct figures as to the amount spent on research into care models in dementia are not readily available, the UK Clinical Research Collaboration research cited above demonstrated that for the larger category of neurological research as a whole, only 0.3 per cent of expenditure was devoted to health services research.⁴³⁰ The British Geriatrics Society suggested to us that one cause of the low levels of funding in this area of research is the emphasis placed in the Research Assessment Exercise (on which government funding for universities is partly based) on publications in high-impact journals. This may make it difficult for departments of gerontology or old age psychiatry to compete on equal terms with those concerned with basic science research; indeed, the Society argues that it is “difficult for academic departments of geriatric medicine or old age psychiatry to survive let alone flourish” in this funding environment.⁴³¹
- 8.12 It was clear from our public consultation that many people, especially those with direct first-hand experience of dementia, felt that more research effort needed to be focused on different models of care with the aim of improving the quality of life of people who are living with dementia now.⁴³² Indeed, it has been noted in the context of the English dementia strategy that a key gap in current research evidence is research relating to longer-term outcomes of particular types of care models.⁴³³ Some of the key elements in the strategy itself, such as dementia care advisers and improved end of life care for people with dementia, are in fact recommendations for ‘demonstrator projects’, subject to future evaluation. Concern was also expressed to us, for example by members of the Bradford Dementia Group, that even where research evidence *does* exist that particular forms of care and therapy are beneficial for people with dementia, there appears to be little impetus to ensure that they are implemented.⁴³⁴ Exploring why this is the case, and what models of care are readily transferable between different geographical areas and services, is a further important research question.
- 8.13 It should also be noted that different types of research have the capacity to benefit different groups. Prevention and cure both seek primarily to benefit future generations, while research focused on quality of care has the potential to benefit people with dementia in the near future. There are also very different degrees of uncertainty involved: while research relating to quality of life and care is likely to produce some benefit (even if hard to measure), no-one can at present predict whether current research targets within basic science will turn out to be blind alleys or, alternatively, may transform the research landscape. Do we ‘bet’ on the enormous benefits to be obtained by developing either effective preventative strategies or a cure, or do we prioritise readily achievable improvements in day-to-day care and support?

⁴²⁹ Brayne C, Gao Lu, Dewey M and Matthews FE (2006) Dementia before death in ageing societies: the promise of prevention and the reality *PLoS Medicine* **3**(10): e397; Jagger C, Matthews R, Lindesay J *et al.* (2009) The effect of dementia trends and treatments on longevity and disability: a simulation model based on the MRC Cognitive Function and Ageing Study (MRC CFAS) *Age and Ageing* **38**: 319–25.

⁴³⁰ UK Clinical Research Collaboration (2006) *UK Health Research Analysis* (London: UK Clinical Research Collaboration), p28.

⁴³¹ British Geriatrics Society, responding to the Working Party's consultation. The House of Commons Science and Technology Committee has raised similar concerns about the perceived impact of particular journals within the Research Assessment Exercise (RAE) process, and reminded RAE panels that they are obliged to judge the quality of individual articles, not the reputation of the journal in which they are published: House of Commons Science and Technology Committee (2004) *Tenth report*, part 9, paragraph 210, available at: www.publications.parliament.uk/pa/cm200304/cmselect/cmsctech/399/39912.htm#a54.

⁴³² Nuffield Council on Bioethics (2009) *Dementia: Ethical issues – summary of public consultation* (London: Nuffield Council on Bioethics), Q29.

⁴³³ Burns A and Robert P (2009) The National Dementia strategy in England: a ‘smorgasbord’ of evidence, economics and obligation *British Medical Journal* **338**: 614.

⁴³⁴ Working Party's fact-finding meeting with the Bradford Dementia Group, 29 July 2008.

8.14 A final important issue in connection with research into both treatment and care is the outcome measures used. We have noted in paragraphs 1.5 and 8.5 that the availability of medicines within the NHS is linked with their cost-effectiveness, and that this calculation in turn will be strongly dependent on the way that the effectiveness of the medicine is measured. A European taskforce recently reviewed the various outcomes or endpoints used in research into mild, moderate and severe Alzheimer's disease, and recommended that "cognition and function" should be the two primary outcomes in research into symptomatic treatment of mild and moderate disease, while factors such as "time to reach a specified incapacity scale, entry to institutional care, number of admissions to hospital, need for home help, level of satisfaction, lack of a basic ADL [activity of daily living] and onset of behavioural disorders" are all relevant outcomes in severe Alzheimer's disease.⁴³⁵ While the increasing focus on factors such as levels of satisfaction and the person's ability to function in everyday life is strongly to be welcomed, further research is needed in this area into how outcome measures can reflect, as accurately as possible, the extent to which both medicines and non-pharmacological treatments and services genuinely help the person to live well with their dementia. Such research also needs to go beyond Alzheimer's disease to cover all dementias.

Our approach to research priorities

8.15 A constant theme running throughout this Report has been the impact, worldwide, of the growing prevalence of dementia. As more people in both developed and developing countries live to greater ages, so the likelihood of developing dementia at the end of life increases. Dementia, as currently experienced, imposes a significant economic burden both on families and the state, and we have cited above the view of the UK Age Research Forum that the systems currently in place to support people with dementia (imperfect as they are) will simply not be able to cope in the future. In our own ethical framework, set out in Chapter 2, we argue that an appropriate, and ethical, response to the increasing challenge posed by dementia is that of solidarity: accepting a mutual responsibility for supporting people with dementia. A key aspect of this solidarity must also be a commitment to supporting research into dementia, with the aim of minimising the effect of dementia on all concerned.

8.16 We are aware of the difficulties inherent in making comparisons between the funding available for research into dementia and funding available for other conditions. Funding comes from many different sources, including charitable funding, which in some cases will be heavily dependent on individuals' willingness to donate; research does not take place in 'silos', and a breakthrough in one area of science may turn out to have major implications for another apparently unconnected area; the value of putting large resources into an area of research depends on the current state of knowledge and techniques; and thus the quality of research is not related solely to levels of funding. Nevertheless, the low levels of funding for dementia research in comparison with many other conditions is striking in the light of the numbers affected, the extent of disability resulting from the condition and the economic impact of the condition.⁴³⁶ It seems unlikely that dementia research is receiving a fair or appropriate proportion of funding in medical research.

⁴³⁵ Vellas B, Andrieu S, Sampaio C, Coley N and Wilcock G (2008) Endpoints for trials in Alzheimer's disease: a European taskforce consensus *Lancet Neurology* 7: 436–50.

⁴³⁶ See, for example, Lowin A, Knapp M and McCrone P (2001) Alzheimer's disease in the UK: comparative evidence on cost of illness and volume of health services research funding *International Journal of Geriatric Psychiatry* 16: 1143–8. See also World Health Organization (2008) *Global Burden of Disease 2004* (Geneva: WHO Press), table 13, where dementia is cited as the fourth highest cause of 'burden of disease' (measured in terms of lost years of full health) in high-income countries, after unipolar depressive disorders, ischaemic heart disease and cerebrovascular disease.

8.17 We are struck by the fact that the major research funding bodies within the UK do not appear to have explicit policies according to which they allocate funds between different conditions, focusing rather on research excellence and the ‘importance’ of the topic.⁴³⁷ While it is clearly appropriate that funding bodies support important and high-quality research, criteria such as these do not, alone, ensure a just distribution between the needs of different parts of the population. **We believe that major research funders should be more explicit as to how they divide their research funds between areas of research that have the capacity to benefit very different groups of the population. Given the social and economic impact of dementia, we believe that a more explicit approach to research priorities would be likely to lead to significant increases in research funding for dementia. If such an increase were not to be matched by research applications of the necessary high standard, then active steps should be taken to develop and promote research capacity in the relevant areas.**

Recommendation 15: We recommend that the major research funders develop, and articulate, a reasoned basis for the division of their research funds between areas of research which have the capacity to benefit very different groups of the population. We further recommend that, if necessary, they take active steps to promote and sustain the creation of research communities capable of carrying out high-quality research.

8.18 On the question of how funding should be prioritised *within* dementia research, we agree with the major funding bodies that all the types of research into dementia outlined in paragraphs 8.4–8.9 above are important and no one type of research can be highlighted as having priority over others. We would, however, make the following observations:

- There appears to be widespread agreement that research into the effectiveness and transferability of different models of care and support for people with dementia is relatively neglected. Yet research into these areas is crucial if people are to be supported to live well with dementia. This is particularly important given that the prospect of a real cure for dementia is highly elusive (see paragraphs 1.30, 1.31 and 8.5).
- There are also widespread concerns about the outcome measures used when assessing the effectiveness or cost-effectiveness of a particular treatment or service, as evidenced, for example, by the challenges to the NICE decision on cholinesterase inhibitors.
- It is crucial to understand better how people with dementia and their carers live with dementia, how dementia affects them throughout the course of the disease, and how their quality of life could be improved throughout those stages. Social research in this area is an essential starting point for both the research into care models and the development of sensitive outcome measures described above. More research into the effects of stigma and how stigma can best be challenged would also be highly valuable.
- We highlight throughout this Report how all those involved in caring for people with dementia need better access to ethical education and support in order to respond to the ethical problems they encounter on a daily basis. Further research is required on how best to achieve this aim, encompassing both research into the content of the teaching, and appropriate educational teaching methods.
- Research into non-Alzheimer’s dementias lags far behind that into Alzheimer’s disease.
- Research into preventative strategies appears to receive too low a priority.

⁴³⁷ The Medical Research Council, for example, states that “The main factors in funding decisions are research excellence – i.e. the likelihood of major advances in knowledge – and the importance of the topic”, see: www.mrc.ac.uk/About/Strategy/Principles/index.htm.

Recommendation 16: We recommend that relevant research funders consider ways in which the level of funding for dementia research could be increased in the following areas: health services research into how people with dementia and their carers can best be supported to live well, how mainstream services can best be adapted to their needs, and how good practice can more readily be implemented; more meaningful outcome measures for assessing the effect of particular forms of treatment or service; research into how best to improve the provision of support for ethical decision making; all forms of research for the non-Alzheimer's dementias; and research into preventative strategies.

Recommendation 17: We particularly highlight the importance of social research in providing an evidence base to underpin better ways of supporting people with dementia and their carers. We recommend that funding bodies such as the Economic and Social Research Council, in partnership with others, take active steps to encourage further research into issues such as how people live with dementia, the nature of their experience and the quality of their lives; how stigma can best be challenged; and how those working in health and social care can best be supported in providing care which genuinely respects the personhood of everyone with dementia.

- 8.19 We also note, and welcome, a number of recent developments throughout the UK, which seek to promote research into dementia and encourage closer links between research and clinical practice. These include: the 'research summit' promised for July 2009 by the English dementia strategy; the development of clinical networks such as the National Institute for Health Research's Dementias and Neurodegenerative Diseases Research Network (DeNDRoN), the Scottish Dementia Research Network, the Dementias and Neurodegenerative Diseases Research Network in Wales (NEURODEM Cymru) and the Northern Ireland Clinical Research Network in dementia;⁴³⁸ and the funding by the National Institute of Health Research of dementia-specific programmes such as 'EviDem' (Evidence Based Interventions in Dementia)⁴³⁹ and SHIELD (Support at Home – Interventions to Enhance Life with Dementia).⁴⁴⁰

Who should be involved in research?

Choosing to be involved in research

"I feel like I'm doing something not only interesting but I think something that's needed."⁴⁴¹

"People with dementia, sometimes even quite moderately severe dementia, often have an idea as to whether or not they wish to participate in research, and it is very important that they are consulted." Professor Gordon Wilcock, consultation respondent

- 8.20 Individuals with the capacity to make their own decisions as to whether or not to be involved in research may be involved only if they give consent. As with consent to treatment, consent to research participation must be sufficiently informed and given voluntarily if it is to be legally valid. Research participants are entitled to withdraw from research at any time, with no obligation to give a reason.
- 8.21 People choose to participate in research, including research related to dementia, for a wide range of reasons. They may wish to access an experimental treatment before it is generally available in the hope that they will benefit. They may have altruistic reasons for participating, even where they do not expect to benefit personally. They may also find that the process of taking part in research

⁴³⁸ For more information, see: www.dendron.org.uk/about/index.html; www.ukcrn.org.uk/index/networks/uk_wide.html; www.wales.nhs.uk/sites3/page.cfm?orgid=580&pid=14713; www.nicrn.hscni.net/themednetworks.aspx.

⁴³⁹ See: www.evidem.org.uk/.

⁴⁴⁰ See: www.nelft-rd.co.uk/research/current_research/shield/index.php.

⁴⁴¹ Henderson CS (1998) *Partial View: An Alzheimer's journal* (Dallas: Southern Methodist University Press), p63, on participating in research.

(such as extra attention from health professionals and the sense of being involved) is enjoyable or beneficial.

- 8.22 The ability of people with dementia to make their own decisions (if necessary with plenty of support) as to whether or not they wish to participate in research should not be underestimated. Nor should it be forgotten that a person's capacity may fluctuate significantly: for example, people with dementia may have 'good' and 'bad' times of day and may be able to make their own decision if approached at the right time and in the right way. A person with dementia should receive all possible support to help them make their own decision about involvement in a particular piece of research, at the time the decision is required. We will return to this point in paragraphs 8.39 and 8.45, when we consider the way information about research is presented.

The aims of research

- 8.23 The main aim of medical research is to gain knowledge that, it is hoped, will benefit people in the future. There is a distinction between research that has the potential to benefit those who take part and that which does not. An example of research that may benefit those taking part is a trial comparing current treatment with a novel treatment. An example of research which does not have the potential to benefit those taking part is basic science research concerned with a better understanding of dementia that is unlikely to result in any improvement in management for many years.
- 8.24 One concern which is often raised when considering the consent requirements for research (whether or not the person has capacity to consent for themselves) is the extent to which people participating in research may not properly understand these distinctions and hence may participate primarily in the hope of personal benefit where this is inappropriate.⁴⁴² This may be a problem particularly where the two paradigms of research described above have the potential to become intertwined: for example in the case of early research into new treatments, where participants are bound to hope there is some chance the treatment will help them directly, even when they understand that the outcome is unknown and that in any case they may unknowingly receive a placebo or an existing treatment rather than the new treatment.

Involving people with impaired capacity in research

- 8.25 Where individuals do not have the capacity to make their own decision about participating in research, and where the research is not likely to benefit the participant, several different approaches have been suggested:

Prohibition on involvement in research

"Avoiding research on participants who lack capacity through dementia is prejudicial to the elderly and to the mentally and neurologically unwell and is in our view unethical."
Alzheimer's Research Trust, consultation respondent

"I don't think it is right to involve anyone in research without their informed consent."
Hazel Simpson, consultation respondent

- 8.26 At one end of the spectrum, it could be argued that people should *never* be involved in research if they lack the capacity to make this decision for themselves. Concerns, for example, are expressed about people being made to participate in research when it simply cannot be known whether they

⁴⁴² Appelbaum PS, Roth LH, Lidz CW, Benson P and Winslade W (1987) False hopes and best data: consent to research and the therapeutic misconception *Hastings Center Report* 17(2): 20–4.

wish to do so or not.⁴⁴³ Critics of this position argue that such an approach, if applied more widely, would prevent much beneficial research in other areas where participants cannot give consent for themselves, preventing improvements in the care of babies, emergency treatment in Accident and Emergency departments and care for people in comas. It is also argued that it is positively unethical to exclude people from research who are not able to give valid consent, as whole sections of the population may thus be excluded from the benefits that research may bring.

- 8.27 Moreover, as highlighted above, many people with dementia do show positive willingness and enthusiasm for being involved in research, even if their understanding of the precise details of the research project concerned may not be sufficient for a legally valid consent to be obtained. As one carer commented: “[My mother] would be quite cross to think that she could not take part, because she could no longer consent herself.”

Giving consent in advance

“I think the government should promote a campaign to get people (during ages 40–50) to consent to such research.” *Lukas Kalinke, consultation respondent*

“When he still had capacity, my husband consented to take part in lots of research, but he actually became traumatised by over-testing.” *Barbara Poynton, consultation respondent*

- 8.28 A second position is the principle that people should only be involved in research if they had, in the past, expressed a positive desire to participate, for example through some form of advance decision or statement of values. Such a decision might be specific (for example limited to observational research, or research on treatment which has reached a particular stage of testing), or it might be quite general, expressing a general altruistic willingness to participate in any relevant research that has been approved by the appropriate authorities. This approach found significant support in our consultation responses, a number of which highlighted the possible benefits of open discussion of attitudes to research around the time of diagnosis, with the person’s opinions about research being clearly documented at the time.⁴⁴⁴ It was noted, though, that such advance consent should not automatically give a ‘green light’ to research, as it may be hard to predict the effect of the research on the person and may cause unforeseen distress. Clearly, our discussion in Chapter 5 as to the way past and present wishes should be balanced (see paragraphs 5.24–5.32) is highly relevant also in relation to research.

Various forms of proxy consent

“[Research should be allowed] only after careful consideration and if it was in accordance with past wishes in an advance directive or they had appointed a person such as a spouse, son or daughter to make that decision for them.” *Falkirk Branch – Alzheimer Scotland, consultation respondent*

“Patients are more likely to agree to non-therapeutic research than their carers who I think are naturally defensive. Conversely, carers are more likely to be enthusiastic about intervention and treatment studies, whereas patients are often more reluctant because of fear of adverse effects, or simply ‘being changed’ by the treatment.” *Anonymous consultation respondent*

⁴⁴³ Nuffield Council on Bioethics (2009) *Dementia: Ethical issues – summary of public consultation* (London: Nuffield Council on Bioethics), Q30.

⁴⁴⁴ *Ibid.*

- 8.29 A third option is that of proxy consent. A proxy might be named by the individual in advance of any loss of capacity, or by others at the time the decision is needed. Alternatively, it has also been suggested that a proxy could be named by the individual at the time the consent is required, in circumstances where the individual no longer has capacity to give valid consent to the research proposal but does have the capacity to nominate a trusted person to make the decision.⁴⁴⁵ Where a proxy approach is adopted, much will depend on the constraints (if any) placed on the proxy decision maker. Those respondents who commented on the role of a proxy decision maker generally saw it as a positive safeguard, based both on the proxy's prior knowledge of the person's likely approach to research and on the trusted nature of the relationship. It was also highlighted that at present a welfare attorney in England and Wales does not have specific power to give or withhold consent to research (see paragraph 8.34 for a summary of the legal position).⁴⁴⁶
- 8.30 This positive attitude to proxy consent was not universal, with at least one respondent to our consultation expressing concerns about a proxy's ability to second-guess the wishes of the person with dementia.⁴⁴⁷ As we discuss in Chapter 5, however, while there is some evidence to suggest that proxies do not always correctly predict what a person would choose in a particular situation,⁴⁴⁸ for many this may not be the key factor. Rather, in nominating a welfare attorney, the person is trusting the nominated individual to make a decision on their behalf in the context of that trusting relationship.

Current legal safeguards

- 8.31 The law in the UK broadly adopts a proxy-based approach, but imposes varying constraints on the proxy decision maker depending both on the type of research and on where in the UK the research is taking place. A distinction is made between a 'clinical trial' (which aims to test the safety and the effectiveness of a new medicinal product) and other types of research. Clinical trials are regulated by the Clinical Trials Regulations⁴⁴⁹ (which apply to the whole of the UK), while other forms of research are regulated in England and Wales by the Mental Capacity Act and in Scotland by the Adults with Incapacity (Scotland) Act. There is as yet no equivalent Act in Northern Ireland (although one is promised for 2011),⁴⁵⁰ and hence research in Northern Ireland which does not count as a clinical trial is currently subject to the common law. All medical research involving human participants in the UK must also be approved by an independent research ethics committee.
- 8.32 All three sets of statutory requirements (the Clinical Trials Regulations, the Mental Capacity Act and the Adults with Incapacity (Scotland) Act) specify criteria that aim to protect people who lack capacity from undue risks in research. All three also require some form of consent from, or consultation with, a proxy. However, there are some differences both in language and in approach between the three pieces of legislation.

⁴⁴⁵ See, for example, Kim SYH and Appelbaum PS (2006) The capacity to appoint a proxy and the possibility of concurrent proxy directives *Behavioural Sciences and the Law* 24: 469–78.

⁴⁴⁶ Nuffield Council on Bioethics (2009) *Dementia: Ethical issues – summary of public consultation* (London: Nuffield Council on Bioethics), Q30.

⁴⁴⁷ John Shore, responding to the Working Party's consultation.

⁴⁴⁸ Ditto PH, Danks JH, Smucker WD *et al.* (2001) Advance directives as acts of communication *Archives of Internal Medicine* 161: 421–30.

⁴⁴⁹ Full title: Medicines for Human Use (Clinical Trials) Regulations 2004, SI 1031, as amended.

⁴⁵⁰ Northern Ireland Department of Health, Social Services and Public Safety (2009) *Legislative Framework for Mental Capacity and Mental Health Legislation in Northern Ireland: A policy consultation document* (Belfast: Northern Ireland Department of Health, Social Services and Public Safety), paragraphs 1.4 and 5.3.

8.33 On protecting the individual from harm:

- The Clinical Trials Regulations specify that there must be grounds to expect that administering the product to a person who lacks capacity will produce a benefit to the person that “outweighs” the risks, or will result in no risk at all.
- The Mental Capacity Act requires that research involving incapacitated adults must *either* have the potential to benefit the person without exposing them to “disproportionate” risks, *or*, if no direct personal benefit is expected, the risks must be “negligible” and anything done to the person must not be “unduly invasive or restrictive” or interfere significantly with their freedom of action or privacy.
- The Adults with Incapacity (Scotland) Act requires that the research should involve “only a minimal foreseeable risk” and only “minimal discomfort.” The Adults with Incapacity (Scotland) Act adds a further proviso that if the research is not likely to benefit the individual directly, it can go ahead only if it is likely substantially to further scientific understanding, and hence improve care for others (in the future) with the same incapacity. Unlike the Mental Capacity Act, the Adults with Incapacity (Scotland) Act thus sets the same threshold for risk regardless of whether or not the research is likely to benefit the individual.

8.34 On seeking consent:

- In research governed by the Clinical Trials Regulations, consent must be given, either by individuals themselves before loss of capacity, or by a “legal representative.” In England, Wales and Northern Ireland, the legal representative may be a suitable relative or friend of the individual, or, if no such person is available, the individual’s own doctor as long as he or she is not involved in the research. In Scotland, the first choice of representative is the welfare attorney or guardian, if one has been appointed; if not, it would be the nearest relative, or the individual’s own doctor as long as he or she is not involved in the research.
- Under the Mental Capacity Act, however, formal consent is not sought from a proxy: instead, a carer (or other unpaid person interested in the welfare of the person with dementia) must be consulted for advice as to whether the person should take part in the project. If the carer’s advice is that the person would not have wished to be involved in the research project, then the person should not be involved. If there is no appropriate unpaid carer to consult, then a person unconnected with the research must be nominated to take on this role. The person’s welfare attorney (where one has been appointed) does not have any special role in research decisions, although it is likely that such an attorney would be an obvious choice as the person to be consulted as the ‘carer.’
- Under the Adults with Incapacity (Scotland) Act, consent must be obtained from the individual’s guardian or welfare attorney or (if no such person has been appointed) from the nearest relative.

8.35 The ethical difficulties inherent in carrying out research among participants with impaired capacity to consent to their involvement has also been addressed by member states of the Council of Europe, through an additional protocol to the ‘Oviedo Convention’ on human rights and biomedicine (see Box 8.1).⁴⁵¹

⁴⁵¹ Council of Europe (2005) *Additional Protocol to the Convention on Human Rights and Biomedicine, Concerning Biomedical Research* 25 Jan (Strasbourg: Council of Europe) available at: <http://conventions.coe.int/Treaty/en/Treaties/Html/195.htm>.

Box 8.1: Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research – Article 15

1. Research on a person without the capacity to consent to research may be undertaken only if all the following specific conditions are met:
 - i. the results of the research have the potential to produce real and direct benefit to his or her health;
 - ii. research of comparable effectiveness cannot be carried out on individuals capable of giving consent;
 - iii. the person undergoing research has been informed of his or her rights and the safeguards prescribed by law for his or her protection, unless this person is not in a state to receive the information;
 - iv. the necessary authorisation has been given specifically and in writing by the legal representative or an authority, person or body provided for by law, and after having received the information required by Article 16, taking into account the person's previously expressed wishes or objections. An adult not able to consent shall as far as possible take part in the authorisation procedure. The opinion of a minor shall be taken into consideration as an increasingly determining factor in proportion to age and degree of maturity;
 - v. the person does not object.
2. Exceptionally and under the protective conditions prescribed by law, where the research has not the potential to produce results of direct benefit to the health of the person concerned, such research may be authorised subject to the conditions laid down in paragraph 1, sub-paragraphs ii, iii, iv, and v above, and to the following additional conditions:
 - i. the research has the aim of contributing, through significant improvement in the scientific understanding of the individual's condition, disease or disorder, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition;
 - ii. the research entails only minimal risk and minimal burden for the individual concerned; and any consideration of additional potential benefits of the research shall not be used to justify an increased level of risk or burden.
3. Objection to participation, refusal to give authorisation or the withdrawal of authorisation to participate in research shall not lead to any form of discrimination against the person concerned, in particular regarding the right to medical care.

Are these safeguards appropriate?

- 8.36 We sought views through our various consultative activities as to whether the current safeguards, described above, are sufficient to protect the individual, or whether, on the contrary, they are seen as unnecessarily hindering research which could be of positive benefit to people with dementia both now and in the future. While the self-selected nature of our consultation respondents prevents the outcomes of the consultation from being presented as fully representative research, we did receive responses from a large number of funding bodies and of individual academics with personal experience of carrying out research. Despite the differences in language between the systems in England and Wales, in Scotland and in Northern Ireland, it was not suggested to us that any particular system was superior to any other, although the practical point was noted that the different systems do not facilitate UK-wide research.⁴⁵² Given the current political pressure for more collaboration at European level, this concern may have wider resonance.⁴⁵³
- 8.37 Perhaps unsurprisingly, a number of academic respondents highlighted what they saw as the 'cumbersome' elements of research review, suggesting that increasing requirements for 'form filling and red tape' may be slowing progress and discouraging researchers from developing new models of research.⁴⁵⁴ Procedures exist in order to protect and promote the welfare of those with impaired capacity and not for the convenience of researchers; but at the same time it must be recognised that procedures created with the best of intentions may have undesirable consequences and may even defeat their own purposes. Three aspects of the current regulatory position seemed to us to be worthy of particular consideration.
- 8.38 First, a number of people drew to our attention the fact that research which carries almost no risk of harm to the individual, such as observational research carried out in care homes with the aim of

⁴⁵² Medical Research Council, and Economic and Social Research Council, responding to the Working Party's consultation.

⁴⁵³ European Commission press release (2009) *Commission steps up action on Alzheimer's disease and other neurodegenerative conditions* 22 July, available at: <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/09/1171&format=HTML&aged=0&language=EN&guiLanguage=en>.

⁴⁵⁴ Nuffield Council on Bioethics (2009) *Dementia: Ethical issues – summary of public consultation* (London: Nuffield Council on Bioethics), Q31.

improving quality of care, is subject to exactly the same procedures as much more interventionist research.⁴⁵⁵ Thus researchers are required to justify to research ethics committees why they wish to amend standard procedures, such as the ‘cooling off’ period before the research can start, which may be inappropriate in more advanced dementia, where potential participants may have little recall of discussions several days earlier.

- 8.39 Secondly, there is the question of the *detail* required when providing information to potential participants. It is clearly important in any kind of research that people being invited to take part and those concerned with their welfare have sufficient information on which to make their decision. However, the provision of complex and detailed information, relating not only to the clinical aspects of the research but also to the requirements of data protection legislation, may simply become an intimidating barrier to research and disempower people with dementia altogether from the process. Working Party members’ own experience suggests that people with dementia who do not have a keen and committed carer may simply be excluded from the opportunity to participate in research. Moreover, the nature of the material produced may itself determine whether the person with dementia is considered to have capacity to make their own decision (if necessary with support). The detailed information currently required by research ethics committees can exclude people with dementia who are in fact quite capable of understanding the broad concept of a study and of giving their own consent.
- 8.40 Thirdly, it is of concern that, at present, there is a lack of clarity about the procedures to be followed if a person gradually loses capacity to consent to their ongoing involvement in a research project during that project. In a clinical trial governed by the Clinical Trial Regulations, a person’s consent to participate in the trial remains valid after loss of capacity, as long as the trial is not significantly altered.⁴⁵⁶ However, the position is more complicated in research which is not a clinical trial.
- 8.41 In its guidance to researchers, the Medical Research Council notes that neither the Mental Capacity Act nor the Adults with Incapacity (Scotland) Act explicitly set out what should happen if a person loses capacity to consent to their continuing involvement in a research project, with the exception of special provisions governing research that had already begun at the point when the Mental Capacity Act first came into force.⁴⁵⁷ The Medical Research Council therefore suggests that, when designing studies, researchers should discuss the possibility of loss of capacity with research participants and include an option to consent to remain within the study in the event of incapacity. This consent would not, however, be absolute, as the person’s continued participation would be subject to the Mental Capacity Act or Adults with Incapacity (Scotland) Act safeguards described above (see paragraph 8.34).
- 8.42 This lack of legal clarity (and hence the increased risk that people who have given consent to take part in research may have to drop out of the project) is of particular concern in dementia, given the degenerative nature of the condition and the risk that the results of studies may be seriously distorted by the withdrawal of participants as they lose the capacity to consent to ongoing participation. If a person who lacks capacity to decide for themselves on their involvement in research shows distress at possible involvement, there is a strong justification, in terms of respecting both their autonomy and well-being, in withdrawing that person from the research. If, on the other hand, the person does *not* appear to experience any distress at the involvement, and had in the past actively chosen to participate, then respect for their autonomy interests would suggest that they should be enabled to continue.

⁴⁵⁵ See, for example, consultation responses by Alzheimer’s Research Trust and the Ethox Centre. The same point arose in the Working Party’s fact-finding meeting with Professor Dawn Brooker of the Bradford Dementia Group, 30 Sept 2008.

⁴⁵⁶ Schedule 1, Parts 1 and 3, The Medicines for Human Use (Clinical Trials) Regulations, SI 2004/1031, as amended; Medical Research Council (2007) *MRC Ethics Guide: Medical research involving adults who cannot consent* (London: MRC), p15.

⁴⁵⁷ Medical Research Council (2007) *MRC Ethics Guide: Medical research involving adults who cannot consent* (London: MRC), pp15–7.

Our approach

8.43 We have argued above that a key way in which solidarity for those with dementia can be expressed is in the promotion of research which seeks to minimise the negative effects of dementia (see paragraph 8.15). Much dementia research requires participants who themselves have dementia, and dementia can affect the ability of people to give valid consent to take part in research. For this reason, dementia research can be held back through the lack of an adequate number of people who are able to consent to take part in research.

8.44 There are clearly good ethical reasons, based on concern for people's autonomy and well-being, for ensuring that strong safeguards are in place to protect people who lack capacity from being harmed by research. Even where a person has expressed an interest in participating in research in the past, concern about their current well-being may in some circumstances make it quite inappropriate for them to be included in a particular research project. However, at the same time there is a risk that, if the procedural bar is set too high, people with dementia will be excluded altogether from research. This, in turn, would be discriminatory: it would prevent people with dementia from acting altruistically when they have autonomously expressed a wish to do so, and would reduce the chance of better treatment and care both now and in the future. **We believe that the current legal safeguards set out in paragraphs 8.31–8.35 above are an appropriate way of protecting people with dementia from harm. However, we believe that action should be taken to make it easier to allow those who have expressed a wish to take part in research to do so.** In particular, we highlight the following:

- The importance of good clinical trial networks. We have been impressed by networks such as DeNDRoN (see paragraph 8.19) which bring together both clinicians and people with dementia who are interested in helping with clinical trials of promising interventions. Ways of involving more clinicians and patients in these and related networks should be sought.
- We also emphasise the importance of researchers carefully considering the possible effects of the trial on the person with dementia *beyond* the end of the trial period. Participation in a trial has the potential significantly to affect a person's future well-being or options: for example, those who participated in research on a possible vaccine for Alzheimer's disease will no longer be able to participate in trials of other new medicines. Other examples cited to us of post-trial problems included a case where the person with dementia benefited from a lower dose of the trial drug, but had to be withdrawn from the trial (with adverse effects on his cognition) because he could not tolerate the higher dose being tested.⁴⁵⁸
- Advance decisions and advance care planning have been given a clear legal status in England and Wales in the Mental Capacity Act. We believe that this focus on future planning also provides a way in which people, while they have the capacity to do so, can state their views and wishes regarding their participation in research at a time in the future when they may lack capacity. Such views and wishes could, with appropriate safeguards, provide a basis for participation in research at a time when the person lacks capacity to consent.
- While welfare attorneys in Scotland have the power to consent to research on behalf of the person for whom they hold the power of attorney, those in England and Wales do not; instead a carer must be 'consulted' (see paragraph 8.34). It is not clear to us why the power of welfare attorney is restricted in this way in England and Wales.

⁴⁵⁸ Example cited by one of our peer reviewers.

Recommendation 18: We recommend that the UK Departments of Health should commission research on the feasibility of developing some form of (non-binding) advance statement on research participation which could influence decisions on research participation after loss of capacity.

Recommendation 19: We recommend that serious consideration be given to enable the role of the welfare attorney in England and Wales to be explicitly extended to include decisions over research, both within the Mental Capacity Act and the Clinical Trials Regulations. In the meantime we recommend that the Mental Capacity Act Code of Practice should provide guidance on the role of the welfare attorney in decisions about participation in research governed by the Mental Capacity Act.

Recommendation 20: We further recommend that the mental capacity Codes of Practice should include clear guidance on the procedures to be followed when capacity is lost during involvement in a research project covered by the Act, to minimise the risk of research results being compromised as a result of people dropping out of research despite their initial wish to participate.

8.45 The general *principles* of research governance and consent are, we believe, broadly correct. The *practice*, however, can place unnecessary barriers in the way of research in dementia. In particular:

- The bureaucratic procedures around research ethics approval can be cumbersome for researchers. We encourage current attempts by the Department of Health to simplify the procedures particularly in the context of low-risk research.⁴⁵⁹
- The ability of people with dementia to give, or withhold, valid consent to research should not be underestimated. The information provided both in written and verbal form, however, may need to be provided in a different form for people with some cognitive impairment compared with people without such impairment. Both researchers and ethics committees should adapt the informing process in a way to enable, rather than to exclude, people with dementia in making a valid decision as to whether or not to participate in research.

⁴⁵⁹ Department of Health (2006) *Best Research for Best Health: A new national health research strategy* (London: Department of Health), paragraph 1.6.