

**Nuffield Council on Bioethics: Dementia: ethical issues****Response by the Wellcome Trust**

July 2008

1. The Wellcome Trust is the largest charity in the UK. It funds innovative biomedical research, in the UK and internationally, spending over £600 million each year to support the brightest scientists with the best ideas. The Wellcome Trust supports public debate about biomedical research and its impact on health and wellbeing.
2. The Wellcome Trust is pleased to respond to the Nuffield Council on Bioethics consultation on dementia. Over the last five years, the Trust has awarded over £20 million in project awards, studentships and fellowships that relate to dementia research.
3. Our response is focused on the consultation questions on scientific research and public engagement, and has been developed with reference to the Trust's Neuroscience and Mental Health Strategy Committee, the Biomedical Ethics grants programme, and direct consultation with researchers.

**What current developments in scientific understandings of dementia, or developments that are on the horizon, do you consider the most significant for the care and treatment of people with dementia? (Question 5)**

4. It is important to maintain and strengthen underpinning basic research, including animal models, to improve understanding of dementia and encourage developments in treatment options, early diagnosis and drug development.
5. **Improvements in animal modelling and neurogenetics:** developments in animal modelling of neurodegenerative diseases play a key role in gaining insight into dementia. Although mice are most commonly used in animal modelling studies, there are concerns about the scientific value of mouse models in certain types of dementia research. Dementias are varied and have different (sometimes multiple) causes, and therefore some researchers have expressed a need to develop and refine the animal models currently in use, and to explore possibilities for new, more complete modelling techniques. The use of non-human primates in dementia research is discussed in response to question 32 below.
6. The UK is particularly strong in the field of neurogenetics, and it is likely that further understanding into dementia will be gained from genome-wide studies, combining large datasets which require powerful bioinformatics and biocomputing research tools.
7. **Improvements in early diagnosis:** early diagnosis of dementia is important as it can present opportunities for treatments that change the course of the disease, and potentially delay or reduce symptoms. Improvements in imaging technology ranging from molecular imaging to gene and protein-based studies, have led to the development of biomarkers that allow earlier diagnosis. Continued progress in imaging techniques, and better understanding of the underlying biological mechanisms, could catalyse the further development of biomarkers to improve early diagnosis of dementia.
8. **Discovery of drug targets:** current treatments focus on symptom mitigation. The advent of therapies that address biomedical causes of dementia is likely to be a major imminent development. There are however concerns that current research is unduly focused on a small number of therapy targets. Given the high failure rates associated with the drug development

process, it is vital to maintain basic research in order to uncover new potential drug targets, and conditions for the optimal efficacy of existing treatments. Stem cell research is one area that is being explored with reference to new approaches in the study of dementia.

**In your experience, how do you think society perceives dementia? Do we need to promote a better understanding of dementia and if so, how? (Question 7)**

9. There are approximately 700,000 people with dementia in the UK, and yet the stigmatisation of people with neurodegenerative disease unfortunately still occurs. In some cases, this may prevent people with dementia and their carers from accessing diagnosis and treatment<sup>1</sup>. The Trust has engaged with the issue of mental illness and stigma, and considers it essential to raise awareness through public understanding and education initiatives. And in doing so, it is important to ensure an accurate portrayal of the effects of diseases such as dementia at all levels – from personal to societal - in a way that raises appropriate questions for debate.
10. The Trust is pleased to note the Department of Health recommendation to increase public and professional awareness of dementia, as part of the proposed national dementia strategy.
11. The Trust supports a range of public engagement activities to improve understanding of science and health, and to encourage discussion of the way research affects people and society. An example of the awareness-raising work supported through our 'Engaging Science' awards is a 2006 film project produced by Missing in Action Films in 2006. The film, entitled "Ex Memoria"<sup>2</sup> addresses the subject of dementia. The script was developed in collaboration with academics at the Bradford Dementia Group at the University of Bradford. DVDs of the film and accompanying guidance notes have been distributed to care homes across the UK for training purposes, as well as to the Alzheimer's society, specialist media and other sector academics and professionals.
12. The forthcoming Wellcome Collection event programme includes a public discussion entitled 'The Myths of Dementia: Who am I if I can't remember?' as part of series of events this year that explore aspects of identity.

**What should research into dementia be trying to achieve? On what basis should funding be allocated? (Question 29)**

13. The aim of dementia research should be to improve understanding across the full research spectrum from the basic biological process, through treatment discovery and development, to delivery of health services and dementia management support resources for people with dementia and their carers. The UK Clinical Research Collaboration has conducted a Health research analysis<sup>3</sup>, which illustrates the funding profiles of government, research council and charity funders for neurological research, including dementias. The profiles illustrate the range of research types that are currently funded.
14. Research funding should recognise the breadth of disciplines involved in dementia research, and the particular importance of collaborative approaches which pool the resources and expertise necessary for large scale, high cost, or long term projects. An example of a high cost project would be the development of a preventative treatment for dementia, which is a chronic

<sup>1</sup> Department of Health: consultation on a National Dementia Strategy, June 2008

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_085569](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085569)

<sup>2</sup> <http://www.exmemoriafilm.co.uk/>

<sup>3</sup> UKCRC 'UK health research analysis' May 2006

[http://www.ukcrc.org/PDF/UKCRC\\_Health\\_Research\\_Analysis\\_Report.pdf](http://www.ukcrc.org/PDF/UKCRC_Health_Research_Analysis_Report.pdf)

UKCRC 'From donation to Innovation' October 2007

[http://www.ukcrc.org/PDF/From\\_Donation\\_to\\_Innovation\\_Report\\_07.pdf](http://www.ukcrc.org/PDF/From_Donation_to_Innovation_Report_07.pdf)

condition. It should be recognised that proving efficacy would necessitate a long trial phase with asymptomatic participants.

15. As with all areas of research, the Trust considers the primary criteria for research funding to be the importance of the research question, and scientific excellence. In recognition that many dementias are underpinned by neurodegeneration, a new call for strategic awards proposals is being launched later this year to encourage research that focuses on this area. The scheme will be designed to encourage cross-discipline, collaborative approaches.
16. It is important that funders consider the potential outcomes of dementia research on a global scale. Only ten per cent of the population-based dementia research has been directed towards the approximately 66 per cent of people with dementia, who live in developing parts of the world. This is particularly true of studies into causes of dementia, which are most likely to be conducted within Europe and North America. Research findings from developed countries may not be applicable globally, as differences in population-specific genetics, culture (behaviour and lifestyles) and physical environment may all impact on the prevalence and effects of dementia.
17. The 10/66 Dementia Research Group is an international collaboration led by Professor Martin Prince at the Institute of Psychiatry, King's College London and partly funded by the Wellcome Trust. The group have just published results from an assessment of almost 15,000 people over the age of 65 in eleven countries, including India, China, Cuba and Peru<sup>4</sup>. According to the study, prevalence of dementia in urban settings in Latin America is comparable with rates in Europe and the US.

**What is your view on involving people in research if they lack capacity to give consent themselves? Under what circumstances, if any, should such research be permitted? What safeguards would you choose and why? (Question 30)**

18. In all research involving people, an appropriate balance must be struck between the interests of participants (and, where relevant, the communities to which they belong) and the interests of society or the advance of knowledge. In planning any research a careful risk-benefit assessment should always be carried out so that participants or communities are not exploited or disadvantaged by their inclusion in the research.
19. The Trust along with others in the medical research community, explored issues of consent during the development of the Mental Capacity Act, 2005. We are broadly supportive of the research provisions in the Act and consider them to take a balanced approach, imposing strict safeguards to protect vulnerable individuals whilst ensuring that research of potential benefit to people with mental incapacity can continue. For the first time in law, the Act makes clear that under certain conditions, non-therapeutic research is lawful.
20. Subject to relevant ethics committee approval, the Wellcome Trust considers that it is acceptable to enrol adults incapable of providing consent in research if all of the conditions below have been met:
  - a. the participation of such adults is necessary to answer the research question
  - b. the participants' interests are safeguarded or promoted
  - c. discussions have been carried out with an appropriate legal authority responsible for the care of a mentally incapacitated adult (where such a body exists)
  - d. the research complies with relevant laws.

<sup>4</sup> Llibre Rodriguez, J. et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey (The Lancet Early Online Publication, 28 July 2008)  
<http://www.thelancet.com/journals/lancet/article/PIIS0140673608610028/abstract?iseop=true>

**Does the current legal position, together with the requirements for independent ethical review of research projects, prevent any research which you believe would be valuable? If so, could any changes in the regulatory framework be ethically justified? (Question 31)**

21. The UK framework for ethical review is considered to be robust, affording the necessary guidance and protection for researchers and research participants without directly preventing valuable research. There are however continued concerns centred around the administrative burden and time delays associated with compliance. For example, particular concerns have been raised that the level of bureaucracy involved to gain permission for animal experiments may deter some researchers.
22. In order to maintain the strengths of the UK research base, it is crucial that the regulatory framework facilitates research while maintaining public trust and confidence. If regulations are seen to be unduly restrictive in an international context, it could prevent potential collaborations and funding opportunities.
23. An example of UK regulation that may compare unfavourably with other countries is that applied to the use of human tissues in research (Human Tissue Act, 2004). Investigators in many countries outside the UK are able to keep research samples beyond the term of a single research grant, for ongoing work on a topic for which consent has already been given. In the UK it is necessary to seek permission to keep the tissue already used for research, if consent has not been given for secondary uses.
24. The Trust notes that the availability of control brains is an ongoing problem in dementia research. It is important therefore to assess the balance of regulation that relates to organ donation procedures, ensuring that barriers to brain supply for research are identified and minimised. The Trust is aware of the Medical Research Council (MRC) work to improve co-ordination of brain banks, and is pleased to note the Government's proposed investment in DeNDRoN (The Dementias & Neurodegenerative Diseases Research Network) which will also aid coordination in this research field.
25. As with all studies, researchers should ensure the confidentiality of personal information relating to participants in research. It is crucial that the public trust that data will be handled securely and with appropriate safeguards. However, some uncertainty remains as to when researchers can have access to information in medical records, and there are concerns this is restricting research. We hope that the recent statement in the Handbook to the draft NHS constitution (July 2008)<sup>5</sup> that "*Patients can therefore expect that a health professional or a research professional who owes the same duty of confidentiality as a health professional may use care records, in confidence, to identify whether they are suitable to participate in approved clinical trials*" will be a useful first step to clarifying the situation.
26. In relation to the EU legal framework, concerns have been raised that the EU Physical Agents (electromagnetic fields) Directive 2004/40/EC could limit the use of interventional Magnetic Resonance Imaging (MRI) by preventing workers from standing near an MRI scanner during operation. This could potentially restrict research and clinical treatment for neurodegenerative diseases and dementia. The Directive, which was due to be implemented in 2008, has now been postponed until 2012. It will be important to continue raising awareness of the potential impact on research and treatment, both at UK and EU level. A main criticism is that the legislation does not include a risk-benefit analysis, unlike regulation regarding ionising radiation. If such analysis were included, it should consider not only the benefits of MRI to research, patient diagnosis, and treatment, but also the risk that if the use of MRI is reduced, the use of X-rays is likely to increase. This would put researchers, patients and staff at greater risk by exposure to ionising radiation with known adverse effects. The Directive must be

<sup>5</sup> Handbook to the draft NHS Constitution (July 2008)

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_085814](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_085814)

revised in a flexible way to achieve a balance between the needs of research and the safety of researchers.

### **Are there any other ethical issues relating to dementia that we should consider? (Question 32)**

#### **Non-Human Primates**

27. The Weatherall report<sup>6</sup> noted that non-human primate research “has contributed to progress in understanding the causes of common neurological diseases such as Alzheimer’s diseases, Parkinson’s disease and stroke”, and concluded that “there is a strong case for their continued use in some aspects of fundamental neuroscience research” as non-human primates are “the only group of animals with brain circuits and networks that are really similar to those of humans”. We would welcome the development of a national primate strategy, as suggested in the Weatherall report, in order to provide a national framework in which such research and training can move forward. The Trust considers it essential to retain the UK expertise in non-human primate research through maintenance of a permissive regulatory environment, and is undertaking a joint 10 year review with the MRC and the Biotechnology and Biological Sciences Research Council, to assess the scientific outputs of such research.

#### **Early diagnosis and treatment**

28. It should be noted that if early diagnosis techniques such as biomarkers were to become available in the short term, the treatment options currently on offer would be limited. The ethical issues around disclosing diagnosis need to be fully considered - particularly in the case of asymptomatic people with dementia.
29. In the case of dementia, one person may require multiple treatments to treat different aspects of the disease. It is necessary to carefully consider who would be eligible to receive new treatments as they are developed. This is particularly true of preventative medicine and treatment of asymptomatic people with disease. Decisions about eligibility for treatment are in part ethical, practical, and economic.

#### **The importance of biomedical ethics research**

30. The nature of biomedical research means that it is constantly challenging our ideas about the world, society and health. This is particularly true for the neurosciences. Research into ethical issues must keep pace with scientific developments in dementia, if society is to make informed decisions about research.
31. The Trust funds research into ethical issues that arise in the development and delivery of healthcare, and seeks to pass the findings of biomedical ethics research to policymakers, public health experts and healthcare practitioners, to help inform their decisions.
32. Examples of Trust funded research in this area include:
- a. Professor Jonathan Glover of King's College London's conceptual, empirical and policy study of antisocial personality disorder and front-temporal dementias
  - b. Professor Julian Savulescu at the University of Oxford has recently received a Strategic Award to set up an interdisciplinary Centre for Neuroethics, which will focus on the ethical issues arising in four areas of neuroscience. One of these areas is borderline consciousness and severe neurological impairment.

<sup>6</sup> The use of non-human primates in research, December 2006  
[http://www.nhpstudy.com/NHP\\_Study-Final\\_report.pdf](http://www.nhpstudy.com/NHP_Study-Final_report.pdf)