This response was submitted to the consultation held by the Nuffield Council on Bioethics on *Dementia: ethical issues* between May 2008 and July 2008. The views expressed are solely those of the respondent(s) and not those of the Council.

Question 5

ANSWER:
Understanding the genetic basis of dementia still has the potential to pinpoint novel biological processes underlying disease development. Genetic studies of dementia have identified a over a dozen key genes (e.g., Alzheimer's(AD): amyloid precursor protein gene; APP; the presenilins:PSEN1 & 2 and apolipoprotein E: ApoE) the majority of which effect rare cases but in a devasting manner. The challenge for the future is to identify susceptibility genes for the common forms of dementia which effect a considerable proportion of our aging population. Recent technical advances and together with large sample collections of cases and controls, have laid the way to identifying these genes. The field of complex genetics is now able to test common variation in every human gene for a relationship with disease risk. This approach has already resulted in the identification of 140 independent DNA variants which contribute to genetically complex phenotypes such as Type II diabetes and Crone's disease. The future use of genome wide association studies on very large populations will reveal many more susceptibility genes for various dementias. There are most likely to be multiple genes each with small effects that co-act and interact with each other and with environmental factors. Trying to sort these effects out is a challenge but one that must be addressed. Understanding relationships with other health issues (e.g. vascular health, obesity & diabetes) is just part of this challenge. For such genetic breakthroughs very large studies are required, which are now becoming feasible. Most geneticists like myself, are motivated to use genetics to understand the biological components of disease development. However, we recognise that genetic information can be used for risk profiling. From an ethical perspective it is worth noting that people are and will increasingly be able to buy their own genetic profile/susceptibility and that this process has moved out of a controlled medical environment where counselling is available. Other key developments will be the creation of better animal models of dementia e.g. more complex models that capture known risk factors. While current transgenic mouse models recreate some aspects of the human condition, e.g. amyloid deposition, they are incomplete (e.g. they spare neurons in the neocortex and limbic pathways).

Question 6

ANSWER:
Benefits of early diagnosis – planning of finances, family provisions, wills, health care plan decisions made when the person is able to give reasoned input. Logically, pharmaceutical treatments should begin early (as early as possible) – yet current NICE guidelines do not support this. Rather, drug treatment is seen for people with more severe dementia. This seems an illogical stance given the nature of most dementias. Furthermore, this approach may penalise those with

higher levels of 'cognitive reserve' (people with higher IQ seem to develop AD at later ages, suggesting they are better able to resist the early stages). Risks – misdiagnosis (in fact diagnosis of AD in UK research programmes is about 90% accurate), leading to inappropriate concerns and provisions. Risk of depression (there are high rates in dementia). At present the dementias are incurable and so there may be an understandable temptation to not communicate an early diagnosis. This temptation is complicated by syndromes like Mild Cognitive Impairment, which is prodromal for dementia in about 50% of cases.

Question 18

ANSWER:
There is a concern that from a research perspective that the issue of legal liability remains unclear. While researchers standardly take informed assent from patients (where possible) and informed consent from next-of-kin or other appropriate persons, it is not clear how or whether this absolves researchers from legal liability.

Question 29

ANSWER:
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. Research should be progressing in parallel at the basic, translational and practice (quality of life) fronts. The priority must still be at the basic level and then getting that to a potentially translational level (i.e. the bottle neck is not doing clinical trials, but in finding genuine, novel candidates to test in clinical trials). There is real belief that research on dementia has been chronically under funded in light of its impact upon human health. Comparisons with cancer are invidious with a ratio of funding per patient at 11:293! Dementia is the main disease which causes burden in later life and the number of suffers will double in the next generation. This will have an enourous impact on our Health Service.

Question 31

ANSWER:
There are practical barriers, as there is now a lot of paperwork which could readily be either dispensed with or made much more manageable. The move from local ethical review committees to the MRECs (when appropriate) has been very helpful. There is, however, the parallel issue of drawing up agreements and monitoring progress with Health Trust R&D offices. There can be demands for a plethora of annual reports (of varying types) when a standard start of grant/trial end of grant/trial might be just as useful and reduce work all round.

Question 30

ANSWER:
While there are clearly issues here, the combined approach of assent and consent seems to steer the safest course. It would be illogical to stop research based on the dementia sufferer not being able to give full informed consent (all research would have to stop in many other areas e.g. studies of babies, people in comas etc). There is an issue about who is best placed as next of kin/carer/partner etc to give consent by proxy – and it would be very difficult to have rules that were rigid on this issue. The question is, what would the patient wish if they had their cognitive faculties intact. See also issues above re uncertainty over legal liability. Related issues that impact on research include the scarcity of post-mortem brain bank tissue.