Nuffield Council on Bioethics
Forward Look Seminar
10 May 2007

Note of meeting

Present:

Members of Council
Professor Sir Bob Hepple QC
Professor Roger Brownsword
Professor Sir Kenneth Calman
Professor Sian Harding
Professor Peter Harper
The Rt Rev Lord Harries of Pentregarth
Professor Søren Holm
Anatole Kaletsky
Dr Rhona Knight
Professor Peter Lipton
Professor Alison Murdoch
Professor Hugh Perry
Lord Plant of Highfield
Professor Nikolas Rose
Professor Peter Smith

Guests
Professor Martin Bobrow
Professor Allan Bradley
Dr Helen Firth
Dr Frances Flinter
Professor Peter Littlejohns
Professor Alan Maynard
Professor Stephen Oliver
Professor Karol Sikora
Professor Ann Sommerville

Secretariat
Hugh Whittall
Harald Schmidt
Katharine Wright
Catherine Joynson
Caroline Rogers
Julia Trusler

SESSION 1: THE IMPACT AND IMPLICATIONS OF THE HUMAN GENOME PROJECT

General overview

1 The Human Genome Project (HGP) has produced one million pages of text detailing three billion base pairs and 25,000 genes. This information was already beginning to change biomedical research and clinical practice. 'Second generation' genome projects included the Wellcome Trust Case Control Consortium project, which was sequencing the genes of 20,000 people to compare variations associated with common diseases.

2 The HGP and future related research was likely to lead to improved healthcare delivery. For example, genetic analysis may enable drugs to be tailored to individuals so they were more effective and had fewer side effects. Two cancer drugs, Glevec and Herceptin, had been developed

that were effective in people with a particular genetic characteristics. The genetic testing market was likely to increase.

3 However, the path from human disease gene identification to effective drug treatment was a difficult one. It was estimated that 20,000 strains of mutant mice would be required to fully 'mine' the human genome – an unacceptable number of animals. Pharmaceutical companies also may be reluctant to embrace the changes that genetic data would bring to drug development.

4 Further issues that may be raised by the HGP in general included:

- Problems may arise from the public perception that genes were 'for disease'. Determining gene function could be difficult and, even if gene function was known, it was uncertain how this would affect the individual. Factors such as environment, lifestyle and previous medication also had an influence on health. Education was important in raising awareness of the power of genetics, along with common misconceptions.
- Personalised medicines may be effective in only a small sub-set of the population and have higher development costs, reducing revenue for the pharmaceutical industry. This may have implications for rates of drug development.
- New treatments and services that arose from the HGP may be expensive for patients. This may increase inequalities in access to healthcare.
- There may be implications for individuals in obtaining information about their genetic makeup. Anxiety may be increased if abnormalities were found but the consequences were not fully known.
- Insurance companies in the UK had agreed until 2011, in a moratorium, not to take genetic information into account when providing insurance policies. Similarly, the use of genetic screening by employers did not appear to be a cause for concern at present. If this changes in future, confidentiality and access to genetic information would become serious issues.
- There was a great deal of interest in using genetic information to track down relatives and to find out about ancestry. Some companies were offering to provide information about family origins through genetic analysis, but the accuracy of this kind of information was uncertain. Such developments may have an effect on concepts of race and ethnicity, and may increase the incidence or fear of genetic discrimination.
- The HGP cost many millions of dollars. Considering the benefits likely to be derived from the project, was this the best use of resources?

And was directing further funds into genetic research a cost effective approach?

- The HGP sequenced the 'average' genome of several individuals. The results of the project may give a false idea of what it was to be normal, and may promote the view that anything that differs from this average was abnormal.
- The completion of the HGP may give the impression that scientists had discovered what it means 'to be human'. Many philosophers would disagree with this and would not want discussion in this area to cease.

The $1000 genome

5 Due to advances in technology over the past 20 years, the rate at which genes could be sequenced had increased dramatically, and the cost of sequencing had decreased. There were currently several different sequencing techniques being used and developed by different biotechnology companies, and many of these companies were working towards the goal of achieving complete genome sequencing for US$1000.

6 The possibility of complete genome sequencing being available for $1000 raised a number of issues and questions:

- Cheap genome sequencing would be very useful for research purposes, but the benefits for the health of individuals were not as certain. Benefits that could be identified currently included using genetic knowledge to guide how a person leads their life. For example, if a genetic susceptibility to cancer was discovered, that person could attend regular health checks and lead a low-risk lifestyle. There may be further health benefits by the time genome sequencing was available for $1000.
- Although $1000 was cheap in sequencing terms, it was still a significant amount of money for many people. Only wealthy people may have access to the potential benefits of the technology.
- Who should pay for personal genome sequencing – the individual, employers, governments or insurers? Also, who would own the information obtained from genome sequencing?
- Although the human genome had been sequenced, the functions of all genes and the causes of all diseases had not been uncovered. Knowledge about genotype did not necessarily lead to knowledge about phenotype. Caution should be exercised when using genetic data to make predictions about an individual's health.
- The relatively low quality data produced by genome sequencing may be better suited for use in population studies.

- Even if genome sequencing was available to individuals, it was unlikely that medicines would become completely 'personalised', but there may be some improvement in the 'one-drug-for-all' approach.
- As well as considering the right to know, it would be important to protect the patient's right *not* to know about their genetic makeup.
- Cheap genome sequencing might generate additional costs for the health service. For example, there would be costs in interpreting genetic information, providing that information to the patient and carrying out further tests on the patient and other members of their family. The burden on GPs may also be increased if patients were concerned about genetic abnormalities that had been found through private testing. In addition, there may be harms to consider in the misinterpretation of information.

Use of arrays for prenatal genetic diagnosis

7 Prenatal chromosome analysis was currently performed on selected high risk patients and accurately detected rare abnormalities which had serious clinical effects. However, the technique involved some uncertainty as it also detected variants that were clinically unimportant for some babies but significant for others. It was also time consuming, was not automatable, and required considerable training and skill.

8 Several new techniques had been developed, one of which was using diagnostic microarrays. This technique could be partially automated, and was less dependent on persons trained in pattern recognition. It was more sensitive than visual analysis and could test many sites on the genome at once. These sites must be deliberately chosen, which raised the question of how decisions should be made about which disorders to include or exclude from the test. Factors that may influence this decision included:

- severity of phenotype;
- treatment available;
- predictability of phenotype;
- proportion of the population affected by the genetic change; and
- prevalence of the condition.

9 Further questions to be considered included:

- Should the decision about which disorders to test for be made at the population level or should individual parents decide? Companies could be left to design and market the tests, or there may be a need for public consultation.

- If parents were to decide, how would information be provided to enable them to choose, given the hundreds of possible conditions and the variation in severity of the disease? Should couples be told about genetic abnormalities where the clinical significance was unknown?
- Pre- and post-test counselling is already offered to pregnant women and their partners. If complex tests are developed covering many conditions, should counselling place for every test, or for each condition that was being tested?
- Was there a need for statutory or professional regulation? Tests on foetal blood to determine the sex of a baby at six weeks of gestation were already being advertised on the Internet.

10 It was unclear whether any new ethical issues would be raised by the introduction of genetic techniques for prenatal diagnosis. It was thought that many of the issues were not new and had been examined by the Council in the past. However, this topic required urgent consideration as practical decisions about which abnormalities to test for would need to be made very soon. The Human Genetics Commission may an appropriate body to provide advice on this to the NHS, and it was agreed that the topic would be discussed with the Commission at the next joint meeting with the Council in October.

Conclusions

11 Many of these issues were not unique to the HGP and the Council had already produced a number of publications on the ethical issues raised by different areas of genetics research.

SESSION 2: RATIONING HEALTHCARE RESOURCES

12 Rationing could be described as 'depriving patients of interventions that were of benefit to them and they would like to have'. It could be said to have two, sometimes competing objectives: to achieve efficiency and to achieve equity:

- Efficiency – the UK currently spent around £90 billion on healthcare each year, which was one tenth of GDP. Economists tried to balance cost with benefit in order to prioritise where resources should be directed. The QALY, or quality adjusted life year, was a measure of the benefits gained from a health intervention, and could be used in comparisons of different treatments. The cost of drug treatments were set by industry and protected by the Pharmaceutical Price Regulation Scheme (PPRS). This was under review following an Office of Fair

Trading report in 2007, with industry now moving towards 'value based pricing'.

- Equity – most healthcare systems forego some level of efficiency in order to achieve equity goals. For example, although they may be seen a 'bad investment', resources were directed towards low birth weight babies and poor people.

13 Some principles for rationing had been suggested by Williams (1998)[1]:

- to treat equals equally and with dignity;
- to meet people's needs for health care as efficiently as possible (imposing the least sacrifice on others); and
- to minimise inequalities in the lifetime health of the population.

14 The National Institute for Health and Clinical Excellence (NICE) had carried out studies on the efficiency of around 100 treatments. NICE recommended that a treatment with a cost per QALY of more than £30,000 per year should not usually be available on the NHS. However, many rationing decisions took place at the Primary Care Trust (PCT) level, which was the cause of the current 'postcode lottery' in healthcare. There was uneven uptake of NICE guidance among the 152 PCTs in the UK, with each making independent decisions about the treatments offered to the people their region.

15 A major problem was that the evidence of clinical effectiveness on which rationing decisions must be made was often incomplete and of poor quality. Much of the research was funded by industry which may have led to a bias in the evidence that was available. There was public under-investment in the evaluation of treatments.

16 Rationing healthcare resources was complicated further by the fact that those with the financial means could buy medicines or treatments privately, or more cheaply on the internet or abroad, if they could not receive it on the NHS. These people were empowered to make decisions about their own health. However, if a patient could not afford to buy privately, would it be unethical for the doctor to tell that patient about effective treatments that were not available on the NHS?

17 A study recently published had found the UK to be one of the worst countries in Europe for access to new cancer drugs. There were six cancer drugs available in Belgium that were not available in the UK. Fast

[1] Unpublished.

access to diagnostic tests and radiotherapy were also important, but improvements in the treatment of cancer were likely to be driven by access to new drugs in the future. In the current climate, it was likely that patients in the UK would be denied many of the new drugs coming onto the market. However, there were no longer international barriers to healthcare: insurance was now available which guaranteed a patient access to any cancer drugs licensed in Europe if they were diagnosed with cancer.

18 There would always be top-level, expensive treatments that were not available on the NHS, but a core package of care should be available to all cancer patients. However, it was hard to define what that package should comprise.

19 Questions to be considered included:

- Should doctors use their time in the NHS to help wealthy people get medicines available in other countries?
- Should doctors tell poorer people about medicines they cannot afford?
- Should PCTs be making decisions on a patient-by-patient basis, which depended on doctors making a special case for some patients to get expensive medicines and not for others?

Ethical implications

20 The objective of rationing healthcare resources to achieve equity raised a number of ethical issues that needed to be considered. For example, should the wealthy and the poor, and the old and the young be treated the same? And what about people who chose to lead unhealthy lifestyles vs those who were healthy?

21 The debate on rationing had quietened in recent years due to two major developments: a significant increase in NHS funding, and the establishment of NICE in 1999. NICE was tasked with advising the NHS on the use of new and existing medicines and treatments. In its guidance on 'social value judgements', NICE subscribed to the following moral principles that underpin clinical and public health practice:

- respect for autonomy;
- nonmaleficence;
- beneficence; and
- distributive justice.

However, these could be contradictory. For example, maximising health benefits meant putting resources towards some people and not others, but the principles also advocated everyone getting the treatment they wanted and needed.

22 It was clear that NICE and the extra NHS funding had not solved the problem of rationing and debate on the issue had recently been reignited. A report by the BMA[2] published in May 2007 called for "an alternative, rational approach to health reform to secure the long-term future of the NHS in which Parliament would oversee the setting of national standards with health professionals, supported by managers, directing and operating the NHS within those standards. In doing so they would be answerable to locally elected representatives of the people." The report recommended that the NHS should provide a core set of services available nationally, but it did not provide guidance on how decisions should be made about which services should be included in the core.

23 Economists had debated whether healthcare could work in a market model. A number of reasons were put forward for why healthcare was different to other consumer commodities:

- Necessity: healthcare was a necessity, not a luxury.
- 'Externalities' and 'spill over effects': making someone healthy had benefits for society.
- Market failure: patients were better informed about healthcare than normal consumers.
- Uncertainty: people could not predict when they would need treatment (health insurance had helped here).
- Public good: collective action could be more effective than individuals looking after themselves.

However, these arguments were probably less valid now than they were 50 years ago due to a number of changes in society, including increases in personal income; public health improvements; better access to information and education; the growth of the private sector; rising expectations by patients; a non-deferential culture; and the advent of personalised medicines. It was suggested that a new system of rationing healthcare resources was required.

24 Further issues and questions to be considered included:

[2] British Medical Association (2007) *A rational way forward for the NHS in England* (London: BMA) Available at: http://www.bma.org.uk/rationalwayforward Accessed on 25 May 2007.

- Little was known about how current decisions about allocating resources were taken at the GP level. Decisions by PCTs were more transparent but it was likely that many decisions were a result of lobbying and campaigning by patients. Historical factors had also affected the services available, i.e. the number of beds in a hospital depended on decisions made when the hospital was built.
- There were many idiosyncrasies in the current system. For example, dental treatment was no longer considered part of the NHS. Also, NICE had a cut off point of £30,000 per QALY for the cost of treatments, but the Department of Health could override this and allow more expensive treatments if it decided this was appropriate.
- It was not only which services that were available on the NHS that needed to be considered, but how soon a patient would received treatment. A common reason for buying private healthcare was waiting times.
- A culture of consumerism was now prevalent in the UK. This had affected attitudes towards healthcare in that patients were more demanding about the services they were entitled to and sometimes had unrealistic expectations.
- It was important to remember that the NHS alone would not make society healthy. Many other factors also had an influence, such as education and a healthy economy.
- There was general consensus among the participants that the Council could make a useful contribution to the debate by setting out a framework within which rationing decisions could be made. In fact, the need for an ethical review in this the area had become quite urgent. Issues that could be considered included:

    - Who should make decisions about the allocation of resources and at what level?
    - What criteria would be used to decide which treatments should be included in a core NHS service package?
    - Would providing a core package mean giving people a 'right' to healthcare?
    - Could there be a consensus on social values?
    - How should decisions be communicated to patients and voters?
    - Should doctors continue to make rationing decisions?
    - How should the UK's different healthcare systems (England and Wales, Scotland and Northern Ireland) be considered?
    - What should be the role of health insurance and private healthcare and how should it be regulated?

- The work would be aimed at government, policy-makers, PCTs, healthcare professionals, and the private healthcare sector. Whether

the word 'rationing' would be used in any future work would need to be debated further.

SESSION 3: OTHER FUTURE TOPICS

25 The list of other future topics provided by the Secretariat was discussed by participants and the following were suggested to be of particular interest:

- Donation, volunteering and payment – the impact of payments on the doctor-patient relationship had not been properly examined.
- Global health inequities – this might include health tourism and internet drug sales, but it was difficult to envisage a single report on the topic as it was so broad. Health tourism might also be considered under the topic of rationing.
- Alternative medicine – this could be used as a case study in a report on rationing.
- Nanotechnology – despite several reports on this topic, there may still be a need to clarify the ethical issues.
- Synthetic biology – this area of research may be too far in the future at the moment, but should be monitored.
- Follow-up reports – there had been some interesting developments in the area of mental disorders and genetics, but it was unlikely the Council would have the capacity to conduct any follow-up studies in the near future.

Conclusion

26 At its next meeting in June, the Council would consider the discussions that had taken place and decide whether any of the topics should be explored further.