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Human Genetics :Uncertainties and the Financial Implications Ahead

Report from The Royal Society and the Actuarial Profession Discussion Meeting, 25-26 September 1996

The Royal Society and the UK Actuarial Profession (the Faculty and Institute of Actuaries) held a joint meeting on *Human Genetics-Uncertainties and the Financial Implications Ahead* on 25 and 26 September 1996. The aim of the meeting was to bring together leading scientists, actuaries, and legal and social commentators to encourage professional debate and a further understanding of these issues. In giving their views the speakers and contributors from the floor gave personal opinions that did not necessarily represent their employer or any particular business sector.

This report provides a brief third party summary of the key points raised. Hopefully it will act as an easy prompt for those who attended and a useful indicator of the issues covered to others. The full text of the speakers will be published in *Philosophical Transactions of the Royal Society Biological Sciences*, early in 1997. (Contact: Sales and Marketing at the Royal Society. Tel: 0171-839 5561 ext 2645, http://www.pubs.royalsoc.ac.uk

This report, which summarises the themes and conclusions of the meeting, was prepared for the Royal Society and the Institute and Faculty of Actuaries by Wendy Barnaby.

Scientific and Medical Issues

The scientists explained the basics of human genetics and their current understanding of the impact they have on disease. They pointed to the exciting implications of this new area of medicine and some of the problems that need to be overcome before genetic information can be more reliably used as a predictor of predisposition to disease.

Sir Walter Bodmer explained that when sperm meets egg, a new genetic individual is created. Each parent donates one set of 23 chromosomes to the new cell. The chromosomes carry the DNA, which in its four letters (A,G,T,C) spells out the famous language of life: 120 million letters-worth on each chromosome, wound round and round in the double helical spiral. In its entirety, this language is called the genome; and it is this that geneticists have learned to read. Within perhaps five years, the Human Genome Project will have read the entire sequence of a representative individual and located the genes - the functional segments - on the long strings of the helix. Although the Project is being carried out mainly to satisfy scientific curiosity, it will also tell us a lot about the way the human body works and how we can intervene to put problems right, as well as about our own origins and evolution.

There are certain disorders that are associated with a fault in one gene. These are called monogenic diseases. Cystic fibrosis is one; Huntington's chorea another. Most disorders are likely to result from abnormalities in more than one gene and from additional effects created by environmental influences. These are called multifactorial diseases or, sometimes, polygenic diseases. Many disorders, including coronary heart disease, manic depressive psychoses and some cancers fall into this category. The picture is further complicated because a single disorder may result from faults in different genes - breast cancer is an example. Environmental factors can play an important role in triggering a genetic predisposition to certain diseases.

Professor John Bell pointed out that, although the present situation is unclear in many respects, genetics is a watershed in our understanding of disease because it will lead to an elucidation of the mechanisms of disease. Until recently, only the monogenic conditions, which affect relatively few people, were clearly identified with faulty genes; but in the last few years scientists have started to home in on genes associated with conditions that cause most sickness and death. Pharmaceutical companies are naturally keen to develop new drugs for such a large market, and genetics will enable them to design novel drugs. It will also allow doctors to discover which people are at risk of developing certain diseases. They can then advise preventative action or early treatment, where these are possible.

The mechanics of pinpointing people at risk are still being discussed, with no consensus yet on whether mass screening for certain conditions would be cost-effective for the Health Service or even worth while from the patientís point of view: many people would prefer not to know that they are predisposed to a condition if there is no treatment for it. The whole discussion about screening is largely conducted in a vacuum, however, because of the lack of data on which decisions could be based. This data will have to be collected by epidemiological studies to find out which predispositions lead to which diseases amongst which populations under what conditions. These studies are long-term and urgently needed, but there does not seem to be any enthusiasm for funding them at them moment.

Professor Christopher Higgins gave a glimpse of the way patients might be helped by genetics. One in 2000 live births in the UK is affected by cystic fibrosis, which causes - amongst other symptoms - the accumulation of mucus in the airways. The gene responsible for the disease was sequenced in 1989. Professor Higgins and his colleagues have conducted a preliminary trial in which they have delivered healthy copies of the gene to the airways of patients. They found that they could deliver the healthy gene and that it worked without putting the patients at any risk. This was not gene therapy but gene transfer. The treatment lasted for three weeks and then wore off; but it did establish that it is possible in principle to deliver genes safely. Work is now going on to improve ways of delivering the healthy gene. In the longer term the work will aim for permanent correction of the condition by treating the cells which give rise to the faulty ones, and to correcting the clinical condition. This would be the gene therapy. The future for it is bright but will need much more work before it can be realised.

Professor Peter Harper argued that the information genetic tests currently give us would have minimal impact on the life insurance industry. This is partly because some conditions show up very early in life, and also because much genetic testing is done for diagnostic purposes. In these cases, the person being tested may be healthy but the test shows whether the health of their siblings or children may be affected. Of all the different types of genetic disorders, only one could be relevant. This is a

group of monogenic conditions which are devastating and occur late in life: eg Huntington's and other rare degenerative diseases affecting the central nervous system. These are a real problem for insurance, but they are a small group. Other conditions in this category affect other systems: adult polycystic kidney disease, for example; but they can be picked up by careful clinical examination. Where genetic tests are done for them, early diagnosis and treatment can often reduce the death rate. Professor Harper forecast that if the industry continues to insist on the disclosure of the results of all genetic tests, people will stop having tests which could improve their chances of survival. Insurers will have to employ large numbers of people to interpret the results and keep up to date with the fast-moving science; over-the-counter testing, without the possibility of treatment or advice (and with the probability that the results will be withheld from insurance companies) will become the norm; and bad publicity for the insurance industry will continue.

Actuarial Issues

The actuaries set out the basic principles on which insurance operates and speculated about how genetic testing and screening might affect it.

Professor David Wilkie explained that actuaries are trained to deal with uncertainty, and they need uncertainty in order to operate. If we all knew when we were going to die, life insurance would be unnecessary. If people applying for life insurance knew their date of death but the insurance company did not, an open insurance industry would be killed off. Along with uncertainty, the other principle that allows the industry to operate is *uberrima fides* (utmost good faith): that each side should disclose all the relevant information available.

There are two basic sorts of insurance arrangements: mutuality and solidarity. Mutuality is the normal form of commercial insurance, in which the applicants voluntarily pool their risk on the basis of the perceived risk of each at the time they enter the pool. The funds then pay claimants either on the basis of their loss or the sum assured. Actuaries' main concern in relation to mutuality is to avoid adverse selection, i.e. adversely skewing the distribution of risk in the pool of insured people. This can happen if high-risk people find it worth while to take out insurance, which drives up the prices of premiums, so that the low-risk people are deterred from taking out policies and withdraw, making a vicious circle of worsening of the risk pool and increasing costs. Solidarity is completely different. It is not voluntary, but compulsory. Premiums are set according to ability to pay, or equally, and there is no direct relationship between the amount of people's contribution and the benefit they may draw. National insurance and social insurance are examples of solidarity. Both forms involve the sharing of loss, but only mutuality requires the sharing of risk.

Life insurers currently aim to include as many people as possible at the standard rate. Until recently, proposers (people who want to be insured) were rated only on age and sex. Smoking habit is now routinely included as well. Some UK insurers also ask about their income, socio-economic status, the region in the country in which they live, their family history (ie genetic information), and height/weight ratio. At the moment, a large majority of proposers are accepted on the information they supply on the initial form, and only 5-10% are asked to undergo medical examinations. If any genetic test has been carried out, the insurance company asks for the results of it. The outcome is that about 95% of applicants are accepted at ordinary rates; 4% are asked to pay more and 1% are effectively refused cover.

Mr Desmond Le Grys argued that widespread genetic testing, which would lead on to early diagnosis and treatment of disease, will improve population mortality. However, knowledge of the results of a genetic test may lead to a change in buying habits for life assurance. People with a poor profile rating would be likely to take out life assurance and so the mortality of assured lives could improve more slowly or even increase. However, the results of mathematical models indicate that the trends would not be so serious that insurers would need to know the results of genetic tests if sums assured were of average size and below an agreed limit. However, underwriters would need to impose tighter financial underwriting. Underwriters will need to be vigilant that the amount of cover granted is reasonable, given the proposer's income and financial status. Mr Le Grys also addressed fears that the 'super fit' - proposers who score very well on all rating factors, including genetic profiles - would be reluctant to take up life insurance at all, and only persuaded to do so by large discounts from insurers. He maintained that this would not happen because most UK insurers prefer to keep to the broad-brush approach of rating only age, sex and smoking habit; also because sufficiently precise genetic information would not be available for many years.

Dr Angus MacDonald asked what the costs would be if life insurers did not have any access at all to genetic information. He considered a number of different scenarios with different levels of assured sums and prevalence of genetic testing. His conclusion was that genetic testing would be largely irrelevant to life insurance. Adverse selection would only be costly where policies were taken out for large sums of money.

Mr Tom Ross considered whether employers would want to make use of genetic testing in deciding what benefits to give their employees. He concluded that genetic testing would not be directly relevant to employers, but that if it led to a healthier population, that would result in a better economy which could afford to pay for bigger pensions and better health services. He also pointed out that the biggest issue for the UK would not be employer-employee relations, but medical benefits and long-term care.

This theme was echoed by other speakers as well: life insurance was not the main issue. For example, genetic testing - say for Alzheimerís disease - is likely to become very important for long-term care policies, and the insurance industry would have to face up to this issue and work out a way to deal with it.

Social, Legal and Philosophical Issues

Several speakers considered genetic testing and screening in their social and legal context.

Professor Sally MacIntyre reported that there have been a few studies of the way genetics affects people in practice, but many more are needed before we will be able to predict how developments in the field will change social attitudes.

Different people react very differently to clinical genetics. Those who are positive look to better understanding of disease mechanisms, cheaper and more accurate diagnoses of common diseases, improved drug design, better understanding of environmental as well as genetic components of disease, targeting of people at risk, and tailoring prevention or treatment to take account of genetic factors.

Other people, however, treat the new developments with concern. Some worry that an increased emphasis on genetics may result in others ascribing the difference between people to differences in their DNA; that the social and cultural factors which help shape people may fall prey to assumptions of genetic determinism. This would have grave implications for health and social policy. Another concern is that, if genetic testing were to become a prerequisite for insurance cover, a new category of people would emerge: the asymptomatic ill. These would be people who, although healthy, would be treated as though they were disabled. This could be because of confusion between carrier status, which does not affect the individual's health, and actually having a condition. This has happened in the United States, where experience has also shown that where a genetic abnormality does exist, insurance companies have not always understood the severity of what it causes or whether it is relevant to the insurance being sought. In these circumstances, even deciding whether to be tested can present people with a double bind: a negative result would reveal some reason for taking the test at all, and discrimination; a positive result would result in discrimination; and refusing to take the test would mean foregoing any benefits the test could bring in the way of treatment or other intervention. Another worry - also intensified by US experience - is that, where a condition is found mainly amongst a particular racial group, the rest of the population could associate it with that group only. They could then refuse to accept diagnoses of it outside that group as such diagnoses would be thought to imply racial intermixing.

People who are concerned about where genetics is taking us point to the fact that those who have genetic tests may not benefit from the good news they can bring. People who are found not to carry serious illnesses which develop later in life, such as Huntington's, may experience depression and survivor guilt. Such results can change family dynamics in unexpected ways, and there have even been cases of families rejecting members whose test results have been negative. There is also uncertainty about whether people will modify their lifestyles as the result of a genetic test. If an individual is shown to be at high risk for a condition, he or she may either try to minimise that risk by making lifestyle changes, or assume that such changes are pointless.

Another worry is that our attitudes to parenthood may change. When 'perfect' designer babies may seem attainable, the onus may be put on parents to accept nothing less. Parents who knowingly give birth to children with genetic defects may be seen as irresponsible and blamed; and society may decide to withdraw resources and care from people with genetic disorders.

Professor Gerald Dworkin outlined the current legal position regarding property rights and genes. Although there have been some decisions on this in the USA, a lot is still unclear as far as Europe is concerned.

In the United States of America it has been ruled that people do not own their genetic material and therefore have no rights to it or to money made from it. This matter has not yet been considered by UK courts, but it is before the Council of Europe.

There has been more legal consideration of patenting genes. Opposition has lined up behind two arguments: technical and ethical. On the technical issue, opponents maintain that genes are not inventions in the patenting sense, but merely discoveries. US applications to patent DNA which made up partial gene sequences whose functions were unknown have been refused on the grounds that these were indeed

merely discoveries. Other genes whose functions have been known have been patented, but only, at present, with a definition of the function of the gene. The European Patent Office has taken the same line. It has decided that genes whose products were put to use outside the body were not merely discoveries because they had needed refinement, isolation and extraction before being able to be used in this way.

Opponents of patenting also argue that it is ethically abhorrent to allow life to be owned for commercial profit: that it erodes human rights and destroys reverence for life on which so many human values and institutions are built. As far as the US Supreme Court is concerned, ethical considerations lie outside its orbit. The European Patent Office initially worked on the same basis. European campaigners against patenting, however, have used an Article (53A) of the European Patent Convention which says that patents should not be granted if they would be contrary to public order or morality. This has caused confusion in Europe, with the Patent Office trying to decide whether it should weigh up the balance on the question of morality (which it is by no means trained or equipped to do). In 1988 the biotechnology industry introduced a Directive to the European Parliament to allow it to patent genetic material, but it was defeated in 1995. It has since been reintroduced and has not yet been decided on.

As far as gene therapy is concerned, the view expressed in the current draft Directive is that there are no problems with somatic therapy (which treats one individual only and has no effect on that individual's offspring), but prohibits germline therapy (which would affect offspring).

The meeting also raised ethical questions about the notion of fairness used by the insurance industry. Dr Onora OíNeill argued that actuarial fairness, which matches premiums to individual risk levels, may be acceptable for motor insurance, but could lead to unacceptable forms of discrimination (including racial discrimination) in life and health insurance. Larger premiums for risky drivers can encourage safer driving; these risk factors are avoidable. Larger premiums for those with genetic risk of disease or early death place additional costs on those with unalterable genetic characteristics. Actuarial fairness is ethically unfair in life and health insurance.

Conclusions

There was general agreement that, over the next few years, genetic testing and screening would have least impact on life insurance. Sufferers from monogenic disorders commonly show symptoms of the disorder at young ages, and often do not survive to an age where insurance becomes relevant. Where they do, their age at death can be estimated with quite a high degree of probability. The only cases which are relevant here are the very small group of people who have monogenic, late-onset disorders such as Huntington's or one of the breast cancer genes. Information about multifactorial disorders is as yet too imprecise to affect life insurance. There were several suggestions about how the insurance industry could cope with such risks as exist.

At the moment, people who have genetic tests are required to disclose the results when they apply for insurance. Because of fears about the use to which this information may be put, and that it might not be understood and treated appropriately, many people prefer to avoid a test if they know they will have to apply for insurance. This actually matters little as far as life insurance companies are

concerned, but it is not good for the proposer who is denied the possible benefits of being tested. Experience from the United States suggests that if the insurance industry does not draw up a voluntary code of conduct in relation to genetic testing, it will have one imposed on it by Parliament. The Members of Parliament at the meeting confirmed that the idea of legislation had attracted cross-party support. The meeting heard about self-regulation as practised in the Netherlands where, however, the government wants to legislate. Some doubts were expressed about whether self-regulation could be effective. The actuarial profession expressed the insurance industry's distaste for statutory regulation.

Discussants also raised the important question of whether or not genetic tests are in any way different from biochemical, physiological or immunological tests that relate to abnormalities in the products produced by specific genes or sets of genes. If the insurance industry has access to the latter (eg blood pressure measurements) at present, what is the difference between the two categories of tests? Both may be indicative of the presence of disease or possible predisposition to disease later in life.

The meeting discussed the security of genetic information in both medical and insurance spheres. There were alleged to be problems in both areas. Actuaries maintained that medical information given to insurance companies was utterly secure and could not be used to assess the risk of any person other than the one to whom it pertained. However the Assistant Registrar at the Data Protection Registrar pointed out that the fact that a proposer has had an HIV test is currently put onto a register to which all insurance companies have access; and he asked whether the same would not happen with genetic information. The point was made that genetic information is not only about specific people but about families, and that it would be of great interest for insurance companies to see it. In response, an actuary emphasised that the register only records if an individual had special terms applied or was refused insurance - the cause of those special terms is not noted. Furthermore only minimal details are recorded: date of birth, first name or initials, and the first three letters of the surname. These are not enough to identify the individual. Clinicians reported that some patients do not allow their GPs to see the results of genetic tests, fearing that they will have to pass this information on to insurance companies. GPs required by law to pass such information on maintained that this could undermine the trust between doctor and patient. The security of information is a difficult area that underlies many of the problems in discussions of genetics and insurance.

The meeting recognised the ethical importance of insurance which allows us to pool risk to the benefit of all, and that the industry's profitability is desirable not only for itself but for society at large. It was stressed that insurance companies want proposers to declare relevant facts - and they also want to see people take up life insurance. What sort of regulatory scheme might then be acceptable both to the industry and to applicants for insurance? It was suggested that healthy people whose genetic profile puts them at, say, between four and ten times the usual risk of death could be accepted by an insurance company and pay, for an endowment policy, a premium that would be only slightly higher than usual - provided the sum insured did not exceed a reasonable amount (say £100,000). Those policies could then be passed on to a statutory reassurance pool subsidised by the government and financed either through taxation or a levy on all insurance companies. This would spread the risks for those people across all taxpayers or all insured people. It would prevent adverse selection because it would involve an upper limit of risk and benefit; it would allow insurance companies to keep their requirement of full disclosure of relevant facts,

and it would prevent people from refusing genetic tests for fear of the insurance consequences.

Other suggestions for practical ways forward were for the insurance industry to adopt a voluntary code of practice which would exclude the use of genetic information, with the provision that payouts for deaths from certain listed genetically-related diseases would be limited by ceilings related to age and sex. Another suggestion was that people could be allowed to buy life and unemployment cover to an agreed limit before having any genetic test. The limit could be set by consultation with consumer groups and building societies who could determine how much cover is necessary to buy accommodation and protect dependants. It was also suggested that insurance companies could practise retrospective pricing - ie set premiums at a sufficiently high level to cover their worst expectations, and then distribute the profits back to the policy-holders. This has commonly been done in Europe for a very long time.

The life insurance industry expressed its fears that special treatment given to one group might be the beginning of a slippery slope on which exemptions would be extended to others. It sought an assurance from the Members of Parliament that, if it voluntarily imposed a moratorium on using the results of genetic tests for monogenic disorders, this would not create pressures to extend this type of agreement to other types of insurance or other special risk groups.

While putting forward these suggestions for life insurance, however, the meeting was agreed that it was not the main problem. Genetic testing would undoubtedly have an impact on health, critical illness and long-term care policies. Many speakers pointed to the value of the National Health Service in this context: solidarity which protects individual citizens from having to negotiate mutuality in these difficult areas. Many expressed fears that if the NHS were to be weakened, citizens would be very vulnerable. The meeting agreed that this very difficult area would have to be tackled, and it was argued that solidarity must be maintained in these categories of insurance.

While the discussions produced some heated argument, the general feeling was that the meeting had been very valuable for each professional group. It had established a frank dialogue, which all hoped would be continued with the aim of finding ways to further the legitimate interests of insurance companies and citizens alike.