SCIENCE IN SOCIETY

Solidarity and equity: new ethical frameworks for genetic databases

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Genetic database initiatives have given rise to considerable debate about their potential harms and benefits. The question arises as to whether existing ethical frameworks are sufficient to mediate between the competing interests at stake. One approach is to strengthen mechanisms for obtaining informed consent and for protecting confidentiality. However, there is increasing interest in other ethical frameworks, involving solidarity — participation in research for the common good — and the sharing of the benefits of research.

Medical registers have existed for a very long time, with various motivations. For example, registers of people with tuberculosis were started in many countries in the first half of the last century. Their motivation was to monitor the extent of this health problem, but probably also to keep track of potential sources of infection.

Genetic registers have also existed for many decades. The reason for their establishment in the early part of the twentieth century might have been less than ideal, but registers started well after the Second World War were created for research purposes or for the detection and prevention of genetic disease, for example by identifying cases where genetic counselling might be offered[1]. As late as the 1970s, registers were run in several countries without any societal opposition[1–4]. However, there was awareness among people working in the field that genetic information could be misused, and ways to prevent this were discussed[5].

The aims of the early genetic registers were to provide genetic services to families with specific genetic diseases. For example, on the basis of information in the Register for the Ascertainment and Prevention of Inherited Disease (RAPID) in Edinburgh, members of families with genetic diseases were actively offered genetic counselling as they reached adulthood[1]. Similarly, workers at the University of Utah[6] used the family register of the Mormon Church to find people with autosomal dominant hypercholesterolaemia, a disorder with a high risk of early myocardial infarction and death. Individuals who were at risk could then take advantage of available therapeutic modalities (such as statins), which have totally changed the picture with respect to treatment and prevention of this serious disorder[7].

There can be no doubt that these early genetic registers have generally benefited individuals, families and societies. To abstain from informing a person with a high risk of a genetic disorder, to protect her or him from unpleasant information, seems difficult to defend when the alternative is premature death. But it is also the case that the early registers were relatively small — they contained only limited amounts of medical, biochemical or molecular data. More recently, the availability of innumerable genetic polymorphisms and the increased power of modern computers have facilitated the creation of much larger and more efficient genetic registers than before — the 'genetic databases' of today that have given rise to considerable ethical debate. In this article, we consider whether the existing ethical principle of informed consent is adequate to deal with the issues raised by the new genetic databases, and propose instead that alternative ethical frameworks, based on solidarity (participation in research for the benefit of others) and equity (sharing the benefits of research), provide a relevant and valuable perspective.

Modern genetic databases

Although it might not always be clear what is meant in contemporary debate by the terms 'genetic databases', 'DNA banking' or 'gene banking', there are at least two sets of issues — those concerned with DNA sample collections and those concerned with information collections. There is overlap between these sets of issues, but they are not identical.

As far as information databases are concerned, current research in the biological sciences is facilitating a new scientific paradigm, offering new possibilities to generate and test hypotheses. In parallel, there are new developments in ethics. This is not surprising, as developments in science and technology have a 'value impact' — they can change the way we look at things and call for new principles to mediate between competing interests. In the developments underway in the biological sciences, the interests at stake include those of research participants (individuals and groups), academic science, commercial organizations and the community, such as in public health.

In this article, we are concerned with collections of DNA samples, although some of the most complex ethical issues arise when these are linked with health records. It has become clear that some principles of biomedical ethics, such as individual informed consent, that have been highly regarded for some time, might not be ideally equipped to deal with the issues that arise in large-scale population-genetic research. Indeed, in the course of collecting samples for such research it might be appropriate to seek the consent of a community rather than of individuals, although issues of definition of both 'community' and 'consent' might be problematic[8].

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Harms and benefits

There has been considerable debate about proposals to set up genetic databases in different countries[9–12], and some of the main points of comparison of three such databases are summarized in BOX 1. The desirability and value of the databases is hotly contested, but discussions have for the most part focused on the potential harms to the individual[13]. Because it is known that there are risks arising from access to genetic information, both by individuals and by third parties, much attention has been paid to confidentiality and privacy issues. Also, for the databases that are going to be used for research purposes, the individuals who donate samples become research subjects. This raises issues concerning research ethics, in which the concept of informed consent is regarded as central[14–16] to the protection of human subjects. Although other considerations, such as the

Box 1 | Features of three genetic databases and points of controversy*

Aims

- Icelandic Health Sector Database — the aim is to link health records (ideally of the whole population) with genealogical information and information about genotype. This will facilitate research on the genetic factors in common diseases.
- UK Population Biomedical Collection — the proposal to establish this collection (with samples and data from 500,000 adults between 45 and 60 years of age) will help researchers to establish the genetic and environmental factors in cancer and cardiovascular disease.
- North Cumbria Community Genetics Project (NCCGP[10]) — aims to collect samples from newborn babies (10,000 over 10 years from 1993), together with personal information, as a resource for genetic epidemiological research.

Informed consent

- Iceland — DNA samples are collected with informed consent, whereas entry into the health records database is by presumed consent[24].
- United Kingdom — informed consent of volunteers to be sought for data and samples.
- NCCGP — maternal consent.

Protection of confidentiality

- Iceland — this is to be handled by 'third-party encryption'[25], where the third party is the government-appointed Data Protection Commission (DPC). Officers at the DPC strip data of all personal identifiers and encrypt patients' social security numbers using an encryption algorithm.
- United Kingdom — the data will be stored in a form that will not allow researchers to identify individuals.
- NCCGP — the DNA samples and the personal information are stored separately. The two data sets are linked by a coding system.

Commercial involvement

- Iceland — involves a single company, deCode Genetics, giving rise to controversy about the strong position of one commercial organization.
- United Kingdom — proposals indicate that no single company should be granted exclusive access. Information and samples are to be held in public ownership.
- NCCGP — research collaboration between Westlakes Research Institute and the University of Newcastle.

Social context

- Different social contexts affect the setting up of, regulation of and ethical debates about databases, for example, the long-standing interest in genealogy and the homogeneous population in Iceland, in contrast to the heterogeneous population in the United Kingdom. In North Cumbria, the relative lack of population movement facilitates follow-up studies.

*(See also table in REF. 23.)

concept of minimal risk, have also been important in the history of research ethics[17], the idea of informed consent has had not only practical but also symbolic value in both protecting and respecting the individual subject.

In addition to the potential harms to individuals, however, there are worries about the implications for groups and communities. It has been claimed that genetic research could characterize whole groups (such as Icelanders) in ways that might not be advantageous to them[18]. Where profit-making companies stand to gain considerable commercial advantage, there are concerns that groups or communities could be 'exploited' without adequate compensation. Potential harms have also been identified in relation to particular social institutions or practices. The practice of science as an institution depends on freedom of access to samples and information for research. Finally, the effects of genetic databases on the doctor–patient relationship and the ethics of medical practice more generally are difficult to predict.

Benefits. In contrast to the opinions above, there are suggestions that genetic databases might become the basis of 'smart' healthcare in the future[12]. By linking genetic information with healthcare records and patterns of disease, researchers hope to establish the genetic bases of common diseases, such as diabetes and heart disease. Beyond that, it is argued that information about the genetic basis of drug response should open the way to more effective and safer prescribing and to the genetically informed development of therapeutic products.

Increased knowledge concerning the molecular basis of human disease is in itself a benefit and this knowledge could, at a later stage, result in new therapeutic modalities. Progress in diagnostics and the prevention or treatment of disease is another benefit to society at large, as well as to patients and their families. Finally, genomic research that results in new therapeutic modalities could create substantial revenues for the pharmaceutical industry.

These points give rise to a question, however, about who the interested parties are, and to whom these benefits are most likely to accrue. There are clearly considerable commercial interests at stake and, in the Icelandic case, the potential profit of the single company involved (deCode Genetics) has been one of the points of contention. It is argued by deCode, however, that Icelanders as a whole also stand to benefit from the availability of free drugs, the provision of jobs and better healthcare. Arguably, scientific progress is also served by such initiatives.

Informed consent

In the light of the debates about potential harms and benefits, to what extent can traditional approaches to informed consent be applied to participants in these databases? Although it might be the community that needs protection and that should be asked for consent[8], an alternative view is that the community can approve, but that it cannot legally consent on behalf of individuals[18]. So the key issues remain focused on the individual, and there are several that need to be considered. One is the extent to which individual subjects whose samples are to be stored should have information about the type of research that might be done on their samples. This affects, for example, the extent to which it is possible to opt out of particular studies with which individuals might not be in sympathy. If someone supports research on the genetic basis of heart disease, but not on the genetic factors involved in alcoholism, they might want to limit the use of their sample, or they might want to withdraw from the database as a whole. Another issue concerns the extent to which individuals should be given feedback about what has been discovered concerning their individual samples and the nature of the information that should be provided[15]. The possibility of feedback, however, is clearly in tension with the preservation of anonymity, which is a safeguard against the potential harm arising from misuse of genetic information.

Box 2 | Risks commonly associated with genetic research

- Fear that genomic research could lead to discrimination against and stigmatization of individuals and populations, and could be misused to promote racism.
- Loss of access to discoveries for research purposes, especially through patenting and commercialization.
- Reduction of human beings to their DNA sequences, and attribution of social and other human problems to genetic causes.
- Lack of respect for the values, traditions and integrity of populations, families and individuals.
- Inadequate engagement of the scientific community with the public in the planning and conduct of genetic research.

(See also REF. 21.)

A more general concern is whether it is possible to be genuinely informed of all the risks and benefits in genetic research. Strictly speaking, no-one can be adequately informed, because it is not possible to foresee the full range of uses to which genetic information might be put, especially given that the ethical and regulatory framework is still evolving, nationally and internationally[14]. It is necessary, however, to address specifically an important difference between 'narrow' consent related to a specific condition and 'broad' consent to research on an unspecified range of conditions. It is possible to inform research participants of the type of research to be conducted and of the particular risks to them. It might be argued that it is only broad consent that is new and problematic. Conversely, even in the case of narrow consent to genetic research on a specific condition, individuals are making choices about their samples in an uncertain situation.

Several concerns have been expressed about genetic research (BOX 2), some of which might seem far removed from the case of an individual being asked to consent to provide a DNA sample. Arguably, however, it is because of these wider implications that the issue of informed consent might be particularly problematic in the genetic context[14]. It is to a large extent because of the potential for stigmatization and discrimination, such as from insurers and employers, that the informed consent issues involved in genetic research have been so concerned with privacy and confidentiality. The question of racism is also important because, for example, a research project might result in information that reveals predispositions to particular conditions that are prevalent in certain minority ethnic groups. Nevertheless, there is, at present, little evidence of discrimination against whole population groups because of genetic diseases or predispositions.

Alternative ethical approaches

One approach to the issues raised by databases is to look at how informed consent can be managed in the light of these complicating factors. For example, different stages of consent could be introduced, such as consent to entry into a sample collection, to specific research on the samples and to further (more general) research[15]. Instead of increasing the complexity of the process of informed consent, and the amount of information given, another approach is to consider alternative ethical principles that might apply, such as solidarity and equity[19]. In the remainder of the article, we consider these principles in turn.

> "… it could be argued that one has a duty to facilitate research progress and to provide knowledge that could be crucial to the health of others."

Solidarity and duties. In recent years, there has been a very strong emphasis on the individual's rights, for example, to refuse to participate in genetic research or to refuse to have health information recorded in medical or genetic databases. It is considered a right of people participating in medical research to withdraw from a study at any time and to demand that one's sample is given back, regardless of the damage to research or researchers. It is not obvious, however, why a right to refuse to participate in genetic research, when it could be to the benefit of others, should be overriding. On the contrary, it could be argued that one has a duty to facilitate research progress and to provide knowledge that could be crucial to the health of others. This principle of solidarity[20] would strongly contradict a view that no research should be conducted if it would not directly benefit those participating in a study[18].

With respect to genetic diseases, the basis for a principle of solidarity is particularly strong, provided that adequate protection against discrimination is in place. Family members share genes, their fates are intertwined and there are moral considerations in favour of sharing information that could benefit the whole group (one's family), even if the people providing information or samples cannot themselves benefit. Some genetic diseases are so rare that the only way to new knowledge is through examination of a handful of families across the world. If these families all refused to participate in research, there would be no way to move forward scientifically or to develop new therapeutic modalities. The time might be ripe to re-think at least some of the attitudes that concern informed consent and the right to refuse, or to withdraw, once one has agreed to participate in research. Present thinking in this area is at least in part the result of a response to crimes against humanity in totalitarian states, which occurred more than half a century ago — a situation with little similarity to present research or the medical uses of databases. There might be reasons to question the transferability of rules and principles developed in one context, to the problems of today and tomorrow.

Benefit sharing. In recent years, in response to concerns voiced around the world, a strong sentiment has developed that pharmaceutical companies should share benefits with the communities and families who have made their financial success possible[21]. Intuitively, sharing of economic benefits seems morally desirable, but it is also difficult to identify any specific reason why the pharmaceutical industry should be obliged to share their revenue from genomic research. The populations, families and individuals, whose samples have formed the basis for new products and revenue, have not themselves done anything to make their samples 'valuable'. So, they do not have a right comparable to a holder of intellectual property or a patent. If anything, their samples have become valuable because of work conducted by scientists. Accordingly, the right of scientists, universities or hospitals could be as strong as any right of the person from whom the sample originates.

Rather than any reason specific to genetics, we suggest that it is the duty of those who are well off to share with the poor that is the central element in the moral duty of the pharmaceutical industry to share benefits — in the same way that responsible rich countries assist developing countries. This duty is based on an ethically strong ideal of equal opportunities. It could be argued that the pharmaceutical industry has an added moral duty to help promote health and healthcare systems because they are making their income from patients and these systems, and because they have first-hand knowledge of medical and social needs.

However, there are practical problems raised by the sharing of benefits. For example, many years might elapse between the original research and the development of a marketable drug, and the people who contributed samples might no longer be reachable. It would then be difficult to decide which specific people or families should share benefits instead of the individuals originally studied. Bearing this in mind, the HUGO Ethics Committee proposed that pharmaceutical industries should set aside a certain proportion of their net income to give for healthcare development or as broad humanitarian assistance to developing countries[21].

Another problem is that the emphasis on distribution of benefits might be seen not as an exercise in distributive justice, but as an attempt to buy people off. The harms therefore need to be explicitly addressed — we cannot simply replace the harm-centred approach with the benefit-sharing model, especially as findings from public consultation have shown that adherence to informed consent is of central importance.

It is increasingly recognized that an informed consent process that is lengthy and complex might be more burdensome than protective[22]. We suggest that there might be a case for an attempt to balance the protection of real and important interests of individuals against likely humanitarian benefits. However, we do not advocate a full swing towards community — even democratic — control. This might be too great a restriction on individual freedom. Individuals need to be protected and respected, and there needs to be adequate data protection to safeguard against misuse, discrimination and stigmatization. It is arguably neither morally nor practically feasible to expect individuals to show solidarity in the absence of such protections. Moreover, to be as useful as possible for research, while respecting individuals, consent should be broad rather than narrow.

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Conclusion

We have argued that it might not always be feasible to obtain competent, informed and understanding individual consent, especially when there is the possibility of future (at present unforeseeable in detail) use of samples for research. This might be the case not only with special groups such as children but also with adults.

We also contend that the benefits of research could be shared more widely by those who profit, and that there is a duty to participate in research that could move medicine forwards on the basis of solidarity. It is questionable whether individuals should be free, from an ethical point of view, to refuse to help in an effort to relieve suffering for what could be regarded as trivial reasons, such as refusing to allow samples to be reused for research on drug abuse because of the disapproval of drug users. The rules that govern informed consent evolved from a very different situation from the one that now pertains, and now might be the time for a fresh ethical perspective.

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Links

FURTHER INFORMATION HUGO Statement on Benefit-Sharing | Icelandic Health Sector Database | UK Population Biomedical Collection | Association of Icelanders for Ethics in Science and Medicine | DeCode Genetics | Westlakes Research Institute | Estonian Genome Foundation | US National Bioethics Advisory Commission (NBAC) Report on Research Involving Human Biological Materials: Ethical Issues and Policy Guidance

1. Emery, A. E. H. in *Registers for the Detection and Prevention of Genetic Disease* (eds Emery, A. E. H. & Miller, J. R.) 53–63 (Stratton, New York, 1976).
2. Merritt, A. D., Kang, K. W., Conneally, P. M., Gersting, J. M. & Rigo, T. in *Registers for the Detection and Prevention of Genetic Disease* (eds Emery, A. E. H. & Miller, J. R.) 31–51 (Stratton, New York, 1976).
3. Vlietinck, R. F. & Van den Berghe, H. in *Registers for the Detection and Prevention of Genetic Disease* (eds Emery, A. E. H. & Miller, J. R.) 65–71 (Stratton, New York, 1976).
4. Hecht, F. in *Registers for the Detection and Prevention of Genetic Disease* (eds Emery, A. E. H. & Miller, J. R.) 73–86 (Stratton, New York, 1976).
5. Hook, E. B. in *Registers for the Detection and Prevention of Genetic Disease* (eds Emery, A. E. H. & Miller, J. R.) 9–29 (Stratton, New York, 1976).
6. Williams, R. R. *et al.* in *Genetic Approaches to Coronary Heart Disease and Hypertension* (eds Berg, K., Bulyzhenkov, V., Christen, Y. & Corvol, P.) 8–19 (Springer, Berlin, 1991).
7. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* **344**, 1383–1389 (1994).
8. Weijer, C. Protecting communities in research: philosophical and pragmatic challenges. *Cambr. Quart. Hlthcare Ethics* **8**, 501–513 (1999).
9. Norges Offentlige Utredninger in *Pseudonyme helseregistre* (Statens Forvaltningstjeneste, Seksjon Statens Trykning, Oslo, 1993).
10. North Cumbria Community Genetics Project. *Report 1996–2000* (Westlakes Research Institute, Cumbria, 2000).
11. Farrar, S. UK considers national gene database. *Times Higher Education Suppl.* 11 February (2000).
12. Fears, R. & Poste, G. Building population genetics resources using the U.K. NHS. *Science* **284**, 267–268 (1999).
13. Chadwick, R. The Iceland database: do modern times need modern sagas? *Br. Med. J.* **319**, 441–444 (1999).
14. Chadwick, R. in *Informed Consent in Medical Research* (eds Doyal, L. & Tobias J. S.) 203–210 (BMJ Books, London, 2001).
15. Medical Research Council. in *Human Tissue and Biological Samples for Use in Research: Report of the Medical Research Council Working Group to Develop Operational and Ethical Guidelines* (MRC, London, 1999).
16. National Bioethics Advisory Commission. *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance* (National Bioethics Advisory Commission, Rockville, Maryland, 1999).
17. Chadwick, R. in *Essential Practice in Patient-Centred Care* (eds Fulford, K. W. M., Ersser, S. & Hope, T.) 40–49 (Blackwell Science, Oxford, 1996).
18. Annas, G. J. Rules for research on human genetic variation — lessons from Iceland. *N. Engl. J. Med.* **342**, 1830–1833 (2000).
19. Knoppers, B. M. *Presentation to the Bordeaux Colloquium on Science, Ethics and the Life Sciences* (23 June 2000) (in the press).
20. Berg, K. in *Proceedings of the 2nd Symposium of the Council of Europe on Bioethics* 122–143 (Council of Europe Press, Strasbourg, 1994).
21. Human Genome Organisation (HUGO) Ethics Committee. *Statement on Benefit-Sharing* (Human Genome Organisation, London, 2000).
22. O'Neill, O. *Presentation (Greenwall Lecture) to the American Society for Bioethics and Humanities* October 1999 (in the press).
23. Kaye, J. & Martin, P. Safeguards for research using large scale DNA collections. *Br. Med. J.* **321**, 1146–1149 (2000).
24. Gulcher, J. R. & Stefansson, K. The Icelandic healthcare database and informed consent. *N. Engl. J. Med.* **342**, 1827–1830 (2000).
25. Gulcher, J. R., Kristjansson, K., Gudbjartsson, H. & Stefansson, K. Protection of privacy by third-party encryption in genetic research in Iceland. *Euro. J. Hum. Genet.* **8**, 739–742 (2000).
26. Human Genome Organisation (HUGO) Ethics Committee. Statement on the principled conduct of genetic research. *Genome Digest* **3**, 2–3 (1996).