

Medical profiling and online medicine: the ethics of ‘personalised’ healthcare in a consumer age
Public consultation: Nuffield Council on Bioethics

Response prepared July 2009 on behalf of the ESRC Genomics Policy and Research Forum by:

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The Genomics Policy and Research Forum is a novel ESRC-funded initiative dedicated to the development of links between social scientists and scientists working in the contemporary life sciences, and the connection of research in this area to policymakers, business, the media and civil society. The Genomics Forum is based at the University of Edinburgh and is part of the ESRC Genomics Network (EGN), a major ESRC investment spanning five of the UK’s leading universities examining the development and use of the science and technologies of genomics.

Summary of response

- In the absence of further research, personal genetic data should not be treated differently for regulatory purposes from other sources of health information. (Q2)
- The predictive value and clinical utility of genomic screening is currently limited for most common conditions. Little could be gained by encouraging or obliging people to undergo DNA profiling. (Q3)
- DNA profiling services should not be required to fund follow-up care that is provided by public health services. Indeed, such a requirement might prove counterproductive if it reinforced the view that commercial profiling provides legitimate and valuable health information, rather than an arguably recreational service. (Q4)
- We report the experiences of Professor Martin Richards, University of Cambridge, who purchased personal genome scans from deCODE and 23andMe. (Q11)
- Until we know more about why people undergo personal genome profiling, and how they react to and use the results, it would be premature to regulate in this area. (Q12)
- Any efforts to improve the quality and usefulness of DNA profiling services by regulatory or other means will need to deal separately with the analytical validity of the genomic screening process itself, and the interpretation and advice provided to customers on the basis of that data. (Q14)
- Health care providers must be equipped to deal with growing public awareness of genetic risk, including but not confined to anxieties resulting from commercial testing. (Q15)

Framework for response

This response addresses those parts of the consultation relating to direct-to-consumer DNA profiling. It has been prepared with reference to the recent public and panel debate (14 May 2009, Murray Edward College, Cambridge) entitled ‘Personal genetic data: do we need to know?’, organised by Dr Simone Rödder on behalf of the Genomics Forum, in collaboration with the Institute for Science and Technology Studies (IWT), University of Bielefeld, Germany.

The event was chaired by Dr Frances Flinter, Consultant in Clinical Genetics at Guy’s Hospital, London, and Chair of the Human Genetics Commission (HGC) working group to develop a common framework of principles for direct genetic tests. The three speakers were:

- Dr Richard Durbin, Co-Chair of the 1000 Genomes Project, Wellcome Trust Sanger Institute, Hinxton
- Dr Barbara Prainsack, Senior Lecturer, Medicine, Science & Society, Kings College, London
- Professor Martin Richards, Emeritus Professor of Family Research, University of Cambridge.

This event considered the following questions in relation to direct-to-consumer DNA profiling:

- Why do we need to know our personal genetic information?
- What data is currently available and what does it tell us?
- What are the risks, benefits and legal implications of providing public access to personal genetic data?
- What are the consequences of accessing our genetic data through commercial organisations?

This response draws on the discussions at that event, plus additional information provided by the participants and by the present authors.

Section 1: Introduction

Question 2. Validity of information

Discussion at the public meeting on ‘Personal genetic data: do we need to know?’ included consideration of whether and how personal genetic data differs from the plethora of sources of health information already in the public domain. Speakers at the meeting were in no doubt about the dubious reliability and usefulness of much genetic information – particularly such information as is provided by commercial direct-to-consumer providers – for personal health care. In this respect, genetic data is no different from much of the non-genetic health information that is available in the public domain, which also varies widely in reliability or usefulness, and is generally unregulated. It is a moot question whether consumers regard genetic information differently from how they treat other kinds of health information; it is sometimes suggested, for instance, that the public tend to think of genetic information as a peculiarly reliable or trustworthy guide to future health prospects. However, more research needs to be conducted on just how far this is the case; on whether public perceptions vary depending on whether genetic information is provided by public or commercial providers;

and on whether perceptions are changing as a result of growing public experience of public and commercial genetic testing. In the absence of further research, it is difficult to argue that personal genetic data should be treated differently, for regulatory purposes, from other sources of health information.

In another respect, the kind of information provided by many commercial providers of genetic and genomic information differs significantly from much publicly available non-genetic health information. As the consultation document observes, and as all three of the speakers at the Cambridge event made clear, much of the genetic information provided by companies such as 23andMe is non-medical and largely recreational in character. But as Dr Prainsack went on to argue, the attention that health regulators have paid to the issue of direct-to-consumer personal genomics to date has framed the issue almost exclusively in terms of medical information. This is unhelpful insofar as it reinforces the view that DNA profiling is primarily a source of health information. We therefore recommend that regulatory bodies should be careful to avoid any action which increases the extent to which companies offering personal genome tests and scans are seen as providers of serious medical information.

Question 3. Prevention

A basic distinction needs to be drawn between genetic tests – usually for single-gene disorders – of demonstrated analytic and clinical validity and clinical utility, and other kinds of genetic tests and genomic profiling – often for complex multi-factorial conditions – the predictive value and clinical utility of which may be highly uncertain.

In the former case, where tests are judged to be of genuine clinical utility, they are generally provided by the NHS. Such provision is accompanied by counselling and various forms of follow-up, including referral to specialist services where appropriate. The provision of genetic tests and related services in this setting is subject to strict ethical oversight and governance. This is undoubtedly an appropriate model for simultaneously promoting the interests both of individuals and of society. Questions of expectation, encouragement or obligation therefore do not – or at least should not – arise.

In the latter case, where genetic or genomic tests are of doubtful or limited clinical utility, the issues are less clear cut. Genomic research is proving particularly fruitful in identifying genes that confer an increased risk of disease in a range of common complex disorders. As pointed out by Dr Richard Durbin at the ‘Personal genetic data’ debate, we now know many of the different variants in the genome that affect, for example, how tall we are or whether we are likely to develop type II diabetes. Such findings are of genuine scientific value for understanding disease progression and the identification of avenues for further research. Consequently, there is clear public benefit to be gained from encouraging individuals to undergo DNA profiling for the purposes of legitimate, well-governed research such as that undertaken by UK Biobank and Generation Scotland.

However, participation in such research is unlikely to be of direct benefit to the individual, and the same is true of testing for the susceptibility genes so identified. In most such cases, susceptibility genes confer only a

relatively small increase in the risk of developing symptomatic disease, while a wide range of environmental, social and lifestyle factors may contribute to the development of disease in the presence or absence of any genetic predisposition. To take an example cited by Dr Durbin at the event on ‘Personal genetic data’, the likelihood of developing type II diabetes is far more effectively predicted by looking at a patient’s body weight, diet and exercise than by looking at their genome sequence. Consequently, the meaning and utility of this kind of genomic information will depend upon a wide range of variables, including the size of the genetic contribution to risk and the availability of effective preventive or therapeutic interventions. Moreover, as Professor Martin Richards added, even where genetic data indicate a clearly elevated risk for a common disease, individuals rarely make significant lifestyle changes (see also Saukko et al. 2006). Rather than providing genetic data of ‘unclear predictive value’, to quote Professor Richards, the challenge for public health is therefore to find effective ways of changing people’s behaviour and encouraging healthier lifestyles.

It is for this reason that genome-wide scans for increased genetic risk are not provided by the NHS. Rather, such provision is undertaken almost exclusively by commercial direct-to-consumer providers. There is little to be gained for individual or public health by expecting, encouraging or obliging individuals to undergo genomic profiling of this kind. Indeed, even to hint at such an obligation would tend to reinforce the view that commercial providers offer valuable health information rather than information of primarily recreational value. Consequently, we strongly oppose any suggestion that such an obligation should be written into policy.

Questions of obligation in relation to genetic testing are not simply a matter of explicit policy, however. As is clear from the wording of Question 3, individuals are increasingly under pressure to take responsibility for their own health. Official discourses of individual responsibility and ‘health citizenship’ are reinforced by wider cultural pressure – from family and friends, as well as commercial media and advertising – to monitor and regulate one’s own behaviour in the interest of health (eg, Rose 2006). Genetic testing as a means of identifying elevated risk and triggering preventive or prophylactic action is often framed in such terms, both in discourse around medical policy and by commercial direct-to-consumer providers (Prainsack, ‘Personal genetic data’ event). There thus exists a subtle and pervasive cultural pressure for individuals to seek information about genetic risk as part of their responsibility to manage their own health. The availability and marketing of direct-to-consumer testing for susceptibility genes undoubtedly contributes to that pressure, but is by no means the only source of it. Moreover, where individuals actually purchase such information, their understandings of and responses to that information may vary. In some cases, knowledge of a genetic predisposition may relieve feelings of guilt or responsibility for an illness, even when someone is unable to do anything about it. In other cases, however, identification of a genetic risk may entail an additional burden of responsibility on the affected individual. Overall, however, it appears that the marketing of direct-to-consumer genetic risk evaluation plays a significant though not necessarily central role in increasing the number of individuals seeking medical advice, support and monitoring around matters of genetic risk, even in the absence of any overt policy initiatives intended to oblige individuals to undergo genetic testing or profiling (Bharadwaj et al. 2006, Lock et al. 2007).

Question 4. Who pays?

Any such increase will obviously have resource implications for health service providers. Where clinically appropriate, it will be necessary to offer follow-up diagnosis and treatment, and to provide training for medical practitioners to meet these follow-up needs. Moreover, with increasing knowledge of the genetic dimensions of common complex diseases, and expanding public awareness of those factors, a much wider spread of practitioners – not just specialists, but also general practitioners – will likely find themselves called on to offer advice on genetic matters. There will therefore be a need not only to expand specialist training, but also to integrate appropriate training in providing genetic health care into the core medical curriculum.

It is doubtful whether commercial providers of direct-to-consumer genetic tests should or indeed could be held financially accountable for any of the costs associated with such measures, however. As noted in our response to Question 3 above, the availability and marketing of genetic tests is only one element in a much larger set of cultural processes leading individuals to seek medical advice around genetic risk. Knowledge of family history, for instance, is a much more important source of genetic anxiety around conditions such as breast cancer and dementia than genetic testing. Appropriate medical care and training would therefore need to be provided even in the absence of commercial genetic testing. Insofar as commercial tests may help to identify opportunities for genuinely beneficial medical interventions, public health services surely have a duty to provide under the normal funding arrangements, irrespective of how patients came to seek assistance. And insofar as commercial testing may be a cause of unfounded anxiety, or may identify risks that cannot be ameliorated by medical means, we would suggest that the health services can best address the issue, not by seeking to reclaim costs from commercial providers, but by helping patients to appreciate the limited utility of such tests.

We therefore recommend that there is little to be gained by proposing that DNA profiling services be required to fund such follow-up care as is provided by the public health services. On the contrary, any such requirement might prove counterproductive in reinforcing the view that commercial profiling services are legitimate providers of valuable health information.

Section 8: Body imaging and DNA profiling services: cross-cutting issues

Question 11. Your experiences

Professor Martin Richards, the final speaker at the Genomics Forum's 'Personal genetic data' event, recently purchased personal genome scans from two different commercial companies, deCODE and 23andMe, at a cost of US\$985 and \$439 respectively, for research purposes. Professor Richards provided an overview of his experience of the process, as well as what he learned from the extensive information provided by both companies. Professor Richards reported the following:

- There were numerous differences between the reports of the two companies. In about one-third of cases, both his absolute and relative risk values for certain diseases were different between the two reports,

leading him to be assigned to different risk categories for the same condition. This also applied to the pharmacogenetic assessment relating to Warfarin dosing.

- The basis for the two risk assessments was not clear, nor was it clear how certain the assessment was. In particular, within 2 days of receiving his test results Professor Richards was emailed by deCODE to advise that two of his risk predictions had now been revised on the basis of new research. This combined with the differences in risk assessment between the two companies very seriously undermines confidence in the predictions.
- Ancestry and ethnicity information provided by deCODE illustrated the dependence of test results on the data that are already present in a company's database and the occurrence of 'small n' artefacts with regard to data interpretation. The company identified Professor Richards as sharing most genetic material with people from Orkney, Iceland, France and the Basque region, based on their database of '1000 reference individuals from 50 different populations world wide'. However, these were the only populations represented from northern or western Europe, making the rankings effectively meaningless for someone of general European origin.
- Professor Richards felt that he did not learn anything significant for his health. Virtually all his relative disease risks were around 1, and many of the other traits measured were either self-evident or had nothing to do with health (for example, eye colour, ear wax type, height, hair thickness and freckling). In the case of deCODE this directly contradicts their claim that results will focus on conditions for which the individual has some control over risk factors.
- In Professor Richards's case, there was no preventive health action that could be taken on the basis of the information produced by the tests. He therefore concluded that the tests had been a 'waste of time and money'.

Question 12. Regulation

As we noted in our response to Question 1 above, it is debatable whether commercial direct-to-consumer genetic profiling services should even be regarded, for regulatory purposes, in the same light as medical services. At the 'Personal genetic data' event, Dr Durbin pointed out that while much genome research funding is medical, and while genomic information is often applicable to medicine, genomic information is not *inherently* medical. As such, this type of data should not be seen by society 'as being owned or controlled by the medical profession'. Professor Richards confirmed that, in his own experiences of direct-to-consumer genomic profiling, many of the results reported were non-medical, relating instead to appearance or genealogy (for example). As Dr Prainsack observed, commercial genetic profiling companies themselves acknowledge this. The three main companies offering direct-to-consumer genome testing variously target themselves at people with health concerns, those who are 'intellectually curious', and those whose interest is more 'recreational', while their websites carry disclaimers advising potential customers that the information they offer is neither a clinical diagnosis nor a therapy ('Personal genetic testing'). Whether consumers pay attention to these disclaimers is a moot point, but there are indications that at least some people obtain genetic profiles for recreational rather than medical purposes. However, as Dr Prainsack stressed, we know little about what actually motivates people to undertake and pay for DNA testing, about

how individuals use the results of such tests, or about how these may affect ‘understandings of disease risks and life styles’. In the absence of such knowledge, it is not clear what the purpose or effects of efforts to regulate direct-to-consumer DNA profiling might be. One possible outcome, for instance, might be to reinforce the view that such tests are not simply recreational, but yield information of serious medical import; such an outcome would, paradoxically, serve to legitimise such tests in the public mind. Consequently, we recommend that it would be unwise to pursue legislation until we know more about people’s motivations for testing and what they do with the information they receive. Additionally, we join Dr Prainsack and her co-authors in a recent commentary in *Nature* (2008) in recommending ‘that public authorities make it a priority to fund empirical research exploring what individuals expect from personal genomics, and in what way genetic-susceptibility information is likely to affect practices and lifestyle choices’ (p. 35).

In this respect, it is encouraging to note that there is some evidence that consumers of personal genetic tests are already becoming disillusioned with the commercial products sold to them. According to Prainsack and co-authors (2008):

Personal-genomics customers are already going through a process of disenchantment: it is increasingly clear how little power SNP-based readouts of a person’s ‘genotype’ offer for predicting future ailments in an individual. Reported frustrations of ‘early adopters’ with the kind of information they’ve received show that the fascination may be fading. (p. 35)

If this is true, and if the process of public disenchantment continues, market failure may pre-empt many of the issues that regulation would be intended to address.

Question 14. Quality of information

It is important to distinguish between the generation of basic genomic data through the identification of specific biomarkers, and the interpretation of that data. This issue emerged strongly from discussions at the ‘Personal Genetic Data’ event in Cambridge. Much of the variation in the risk information provided by different genome-testing companies is due, not to differences in the generation of basic data, but to differences in interpretation. Discussing Professor Richards’s experiences with deCODE and 23andMe, for instance, Dr Durbin pointed out that both companies use very similar DNA chips to derive genomic data, but employ different datasets and different methods to derive risk information from that data – hence the strikingly different risk profiles produced by the two companies. Data production and data interpretation will also develop along different trajectories in future. Basic genome-scanning technology is likely to become cheaper, increasingly standardised and increasingly reliable. Interpretation of the genomic data, by contrast, will remain subject to variation both between companies and over time since, as Dr Prainsack pointed out, genome-based risk profiles are not fixed, but are subject to constant recalculation ‘whenever a new correlation between a genetic locus and a phenotype is found’ (‘Personal genetic data’ event).

Consequently, any efforts to improve the quality and usefulness of DNA profiling services by regulatory or other means will need to deal separately with the analytical validity of the genomic screening process itself, and with the interpretation and advice provided to customers on the basis of that data. In view of the nature and likely trajectories of the technologies involved, moreover, questions of quality and usefulness arise principally in relation to the interpretation, not the generation of basic genomic data.

Ultimately, the question that arises is whether the problems associated with the commercial provision of genomic risk information are radically irremediable. These problems include the issues just noted, of local and temporal variation in the methods and datasets used to derive risk information from genetic data. But as we observed in response to Question 3, they also include fundamental constraints on the predictive value of this kind of risk information when applied to individuals, and on the utility of that information for guiding preventive or prophylactic interventions. In this respect, even if methods of evaluating genetic risk were to be standardised, it is unclear whether this could ever provide a basis for generating information of real clinical value for individual consumers. As Dr Durbin put it at the Cambridge event, DNA profiling for common diseases might best be regarded – at least for the present – as analogous to Sunday supplement health advice. Indeed, it may be in the nature of the information itself that in most cases it will only ever have limited clinical utility. If so, there may be little that can be done to improve it.

Question 15. Any other issues

In its current state, commercial direct-to-consumer provision of personal genome data raises more questions than it answers. For reasons that we have outlined above, it is very unclear whether any kind of regulatory intervention would serve at present to address those questions. Little is known as yet about how consumers regard such tests and what they do with the information they provide. Moreover, consumer attitudes to genetic testing are inevitably conditioned by a wider social context of pressure for individuals to take responsibility for their own health, of the expansion of private health care services of one sort and another, and of the valorisation of genetic information more generally. Questions about how best to respond to the growth of direct-to-consumer genetic testing thus need to be thought of not just in terms of the quality of the information provided and its impact on individual health behaviour, including recourse to state medical services. We also need to understand how regulatory intervention might impact on the wider dynamics of geneticisation and health citizenship.

Social research is already under way to cast light on such issues, and more is undoubtedly needed. But in the absence of the information that such research will yield, it is difficult to say with any confidence what might be the impact of efforts to regulate the commercial provision of personal genomic information. We have indicated above that one possible outcome might be the unintended legitimisation of commercial testing as a medical rather than just a recreational procedure. At a time when it appears that public disillusion with commercial genomic profiling may already be setting in, any moves towards regulation should therefore proceed with caution.

Far more urgent, in our view, is to ensure that health care providers are equipped to deal with growing public awareness of genetic risk, including but not confined to anxieties resulting from commercial testing. Equally, much might be gained by supporting and enlarging public discussion around this issue, including listening to the views of those who have first-hand experience of personal genetic profiling, as a means of sharing information about both the appeal and limitations of genetic data.

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References

- Bharadwaj, Aditya, Lindsey Prior, Paul Atkinson, and Angus Clarke. 'Genetic Iceberg: Risk and Uncertainty in Cancer Genetics and Haemochromatosis.' *Innovative Health Technologies: Meaning, Context and Change*. Ed. Andrew Webster. Palgrave Macmillan, 2006.
- Lock, Margaret, Janalyn Prest, and Stephanie Lloyd. 'Genetic Susceptibility and Alzheimer's Disease: The Penetrance and Uptake of Genetic Knowledge.' *Thinking About Dementia: Culture, Loss, and the Anthropology of Sensibility*. Ed. Annette Leibing and Laurence Cohen. New Jersey: Rutgers UP, 2006.
- Prainsack, Barbara, Jenny Reardon, Richard Hindmarsh, Herbert Gottweis, Ursula Naue, and Jeantine E. Lunshof. 'Misdirected Precaution.' *Nature* 456 (6 November 2008): 34-35.
- Rose, Nikolas. *The Politics of Life Itself: Biomedicine, Power and Subjectivity in the Twenty-First Century*. Princeton UP, 2006.
- Saukko, Paula, S. Richards, M. Shepherd, and John Campbell. 'Are Genetic Tests Exceptional? Lessons from a Qualitative Study on Thrombophilia.' *Social Science and Medicine* 63.7 (2006): 1947-59.