

Chapter 9

Personal genetic profiling
for disease susceptibility

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Overview

What is new? Anyone who has a moderate amount of money can now pay companies to analyse their DNA and provide an assessment of their personal genetic susceptibility to a wide range of common health risks. Advances in genetics are improving scientific understanding of some of the links between genetics and predisposition to diseases, and the cost of genetic analysis has fallen enormously in the past few years. The availability of direct-to-consumer genetic profiling tests raises the potential for increasing personalisation in several of the senses identified in Chapter 1, although as we shall see, some of these tests have only limited predictive power and can therefore not provide accurate individualised predictions. But this method of providing testing certainly lends itself to a ‘consumerist’ approach to healthcare and potentially opens up new ways for people to take a responsible approach to their health and healthcare.

Which ethical values come into conflict as a result of this development? Many potential dilemmas arise among our ethical values in this domain. The value of individuals being able to pursue their own interests comes into conflict with the values of state action to reduce harm, safeguarding private information, fair and efficient use of public resources and social solidarity. The value of safeguarding private information also comes into conflict with those of state action to reduce harm and social solidarity. The value of fair and efficient use of public resources is already coming into conflict with that of social solidarity.

What is the existing pattern of interventions like? People who use genetics services and the services themselves if operating in the UK are subject to numerous laws and regulations, notably the provisions of the data protection regime and the more service-specific measures of the Human Tissue Act 2004 and Medical Devices Directives. But direct-to-consumer DNA profiling companies can offer their services to customers based anywhere in the world, meaning that such companies may be operating under a jurisdiction different from that applying where some or even all of their customers live.

What gaps or shortfalls are there in existing interventions? The existing system of interventions does not promote the provision of good information to consumers about the type of genetic profiling for susceptibility for common diseases offered directly to consumers. There is also a lack of evidence of potential harms and benefits that may result from taking these tests. In the absence of such evidence, we find it problematic that parents are able to order the type of profiling we focus upon for their children.

What types of intervention might possibly fill those gaps or remedy those shortfalls? Research on benefits and harms needs to be done to inform consideration of other appropriate interventions. Other possible interventions could range from encouragement of more comprehensive information to be provided about these tests, through a requirement that such information be provided, to the placing of restrictions on the sale of disease susceptibility tests that do not achieve a certain level of clinical validity and utility.

What types of intervention do we recommend, and why? The potential harms have not been quantified at this time, and indeed it may not be possible to quantify them precisely, but we think the harms do not appear sufficiently serious to justify restriction on sales. We therefore recommend independent research (to be periodically updated as scientific developments occur) on the impact and effects of multifactorial genetic testing on individuals. We also recommend that: (i) responsible authorities should request evidence for clinical claims made by companies; (ii) government health service websites should provide public information about genetic profiling services and companies should indicate to consumers where to find this information; (iii) companies should voluntarily adopt good practice; (iv) companies should not knowingly carry out for children DNA tests that do not meet the criteria of the UK National Screening Committee; and (v) professionals in the public healthcare system should adapt their practice in the light of the development of direct-to-consumer genetic testing.

Introduction

- 9.1 As noted in our opening chapters, advances in genetics are leading to improvements in the understanding of the factors relating to predisposition to different diseases, as well as to associations between genes, diet and the environment. A number of commercial services now offer genetic profiling for disease susceptibility directly to people who do not necessarily have any medical symptoms: analysing their DNA to give them information about their own personal risks of developing certain diseases or health conditions in the future. The cost of genetic analysis over the past decade has fallen to the point where genetic profiling services are readily affordable to middle-income people in developed countries (see Table 9.1). We therefore need to consider how these services are promoted, how accurate the tests are, how useful the results are, the associated benefits and harms, and the ethical dilemmas they raise.
- 9.2 More traditional routes of genetic testing recommended or initiated by healthcare professionals include diagnostic testing when a particular condition is suspected or a person is of particular risk due to their family history, and tests that are used in screening programmes (see Box 9.1).⁴¹⁵ Established clinical genetics services are offered by the National Health Service (NHS) in the UK and other countries' healthcare systems and are of proven value for analysing a person's risk of some more common conditions and detecting rare but collectively numerous genetic disorders. These genetic tests are usually offered with advice from genetic counsellors or clinical geneticists.

Box 9.1: UK National Screening Committee: criteria for genetic screening programmes

Countries vary substantially in the type of public screening programmes that are provided, and those differences often reflect cultural differences. In the UK, the UK National Screening Committee (UK NSC) advises the Government and the NHS about population screening programmes, including genetic screening. It assesses the evidence for introducing screening programmes against a set of standard criteria that cover the condition, the test, the treatment options and the effectiveness and acceptability of the screening programme. Assessing programmes in this way is aimed at ensuring that they "do more good than harm at a reasonable cost".⁴¹⁶

The NSC criteria include:

- the condition should be serious;
- the condition should be understood;
- psychological implications of carriers should be understood;
- the test should be simple, precise and validated;
- the programme should be acceptable to health professionals and the public;
- there should be an effective treatment or intervention available for people identified through early detection;
- the screening programme should be effective in reducing mortality or morbidity;
- evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice;
- the benefit should outweigh any physical and psychological harm caused;

⁴¹⁵ For further information see Nuffield Council on Bioethics (1993) *Genetic screening: Ethical issues* and (2006) *Genetic screening: A supplement to the 1993 report by the Nuffield Council on Bioethics*. See also Raffle AE and Gray JAM (2007) *Screening: Evidence and practice* (Oxford: Oxford University Press).

⁴¹⁶ UK National Screening Committee (2010) *About us*, available at: <http://www.screening.nhs.uk/about>.

- the programme should represent value for money; and
- all other options for managing the condition should have been considered.

There are population screening programmes in the UK and other countries for a number of genetic conditions. However, rather than using genetic profiling, most of the screening programmes operate indirectly, by looking for an indicator of the particular condition.

- 9.3 The particular focus of our discussion in this report is on commercial genetic services that seek to assess a person's genetic risk of a range of multifactorial conditions where the contribution from genetics is complex and often uncertain (as opposed to monogenic disorders, see Box 9.2), including age-related macular degeneration, breast cancer, coeliac disease, Crohn's disease, Parkinson's disease, prostate cancer, heart diseases, diabetes and Alzheimer's disease.⁴¹⁷ In the UK, the NHS does not offer genetic screening for most of these conditions, because they do not meet the NSC criteria described in Box 9.1.

Box 9.2: Monogenic and multifactorial genetic conditions

For some genetic conditions, a large part (or all) of predisposition is caused by variation in a specific section of the genetic code. These conditions are conventionally called 'single-gene' or monogenic disorders. Examples include Huntington's disease, cystic fibrosis and haemophilia. If a person's DNA is tested and they have certain variations in a particular gene or genes, they will be highly likely or even certain to develop that particular disorder. For example, almost everyone who carries the genetic variant for Huntington's disease will develop it at some point in adulthood. These conditions show clear patterns of inheritance within families, and may be dominant (one copy from one parent is sufficient to have an effect) or recessive (one copy from a parent can be carried, without being manifested; if two copies are inherited, that is, one from each parent, the condition will show). Many people are familiar with the concept of monogenic diseases, and much of the ethical and regulatory debate has focused on the implications of testing for them. The NHS and other public healthcare systems offer genetics services that provide testing, as well as genetic counselling to help people decide whether to take such tests and to help them interpret the results.

Other genetic conditions (generally relatively common ones) are multifactorial. Genes play a role in predisposition (and many sections of DNA may be involved), but so does a person's environment, lifestyle and other health factors. Whether or not these conditions will develop (and if so how serious they will be and at what age) depends on interaction between complex genetic factors and those other elements such as environment and lifestyle. Examples of such conditions include diabetes, heart disease and certain cancers.⁴¹⁸ The genetic susceptibility profiling tests that are the focus of our report offer risk predictions for this type of condition. As they are not a simple case of genetic determination, only risk predictions are able to be given, and these will be of varying clinical validity (see Paragraph 9.7).

- 9.4 The availability of personal genetic profiling for disease susceptibility relates to at least three of the four types of personalisation described in Paragraph 1.18. The marketing material for these profiling tests promise greater personalisation in our first sense, namely the delivery of highly individualised healthcare management tailored or customised to the individual involved. However, the extent to which these tests will actually be able to offer such 'personalised' information depends on their predictive power, an issue we discuss below. In addition, the results often allocate the person being tested into a 'risk group' rather than provide an individualised risk assessment. Moreover, even where personalised information is available, the

⁴¹⁷ Some companies also offer information on carrier status for monogenic diseases (see Box 9.2): providing information about whether a person is a carrier for a genetic condition they might pass onto a child if the child's other parent were also a carrier. Others offer paternity testing services, profiling for ancestry and sporting or musical potential. These other services are not the focus of our report.

⁴¹⁸ Within these more common multifactorial conditions there is often a small subgroup that have a 'single-gene' cause. For example: BRCA1/2 genes in breast cancer or the LDLR gene as a cause of high cholesterol.

availability of ‘personalised’ treatment is not guaranteed.⁴¹⁹ Even more strongly invoked is our third sense of personalisation in which healthcare services are provided as a good or commodity as a matter of consumer choice rather than on the basis of advice or action from a healthcare professional. It might also be that, with the increasing availability of the tests described in this chapter, people might see (or be encouraged to see) the taking of such tests as socially responsible behaviour, and thus use them to play a more active role in trying to predict and prevent disease or ill-health, the fourth sense of personalisation we identified in Chapter 1. Moreover, taking such tests confronts those who take them with the responsibility of trying to make sense of complex risk data, face the consequences for themselves or their families and make appropriate changes to their lifestyle. To the extent that such tests are predicatively accurate, they could lead to ‘unpooling’ of the financial risks associated with ill-health, notably through obligations to inform private insurers. We return to a discussion of these themes in Chapter 11.

Table 9.1: Examples of personal genetic profiling tests for disease susceptibility on offer in the UK and internationally at the time of writing

Company	Example product	Price	Details
23andMe	Health Edition	\$429	“Find out if you carry inheritable markers for diseases such as breast cancer, cystic fibrosis, and Tay-Sachs...Learn your genetic risk for type 2 diabetes, Parkinson’s disease, and other conditions.” ⁴²⁰
deCODEme	Complete Scan	\$2000	“Calculate your genetic risk for 51 conditions...” ⁴²¹
Genetic Health	Premium Male	£825	“These are our most comprehensive test and includes all the other tests in our range... Evaluates the risk of prostate cancer as well as the risk for thrombosis, osteoporosis, metabolic imbalances of detoxification and chronic inflammation. It also evaluates the risk profile of the most common cardiovascular diseases...” ⁴²²
Graceful Earth	Alzheimer’s genome test	\$280	“Check your future susceptibility BEFORE symptoms occur... Pre-emptive insight into one’s genetic predisposition can empower and allow for pro-active prevention.” ⁴²³
Navigenics	Health Compass	Varies	“Knowing your genetic predispositions for important health conditions and medication reactions can help motivate you to take steps towards a healthier life. By gaining insight into these risks, you can plan for what’s important.” ⁴²⁴

⁴¹⁹ For example, it has been argued that “In the absence of concomitant effective, affordable, and non-harmful interventions, prognosis alone, even if correct, is of questionable value”. Furthermore, although “many findings from genomic research are likely to provide new clues to disease biology by the identification of genes and biological pathways unexpectedly associated with the disease process” such a process can take decades from the point of understanding the molecular causes of a particular disease. See: Ioannidis JPA (2009) Limits to forecasting in personalized medicine: An overview *International Journal of Forecasting* 25: 773–83; Burke W and Psaty (2007) Personalized medicine in the era of genomics *Journal of the American Medical Association* 298(14): 1682–4.

⁴²⁰ 23andMe (2010) Store, available at: <https://www.23andme.com/store/>.

⁴²¹ deCODEme (2010) Store, available at: <https://www.decodeme.com/store>. See also footnote 448.

⁴²² Genetic Health (2010) Premium male, available at: <http://www.genetic-health.co.uk/dna-test-services/premium-male.htm>.

⁴²³ Graceful Earth (2010) Alzheimer’s genome test now available!, available at:

<http://www.gracefulearth.com/index.asp?PageAction=VIEWCATS&Category=3>.

⁴²⁴ Navigenics (2010) Clinically guided genetic analysis, available at:

http://www.navigenics.com/visitor/what_we_offer/our_tests/.

Benefits and harms

9.5 A number of potential advantages and disadvantages of personal genetic profiling for disease susceptibility were included in Table 3.1.

Potential advantages

- More information;
- allows early intervention;
- allows more personal control;
- possibility of saving public healthcare resources if testing and treatment conducted privately; and
- can alert relatives to important genetic conditions.

Potential disadvantages

- Costs to individuals of tests that yield little determinate information;
- social harms when private testing can undermine equal access to healthcare;
- costs of consequences of having information: a) for individual when inaccurate or hard to interpret, b) for individual when nothing can be done, c) for individual if inaccurate risk assessments lead to false reassurance or misplaced anxiety, d) for individual if results lead to stigma or information abuse (e.g. blackmail) or other effects that may be regretted, given that information once known cannot be ‘un-known’ (e.g. for insurance declarations), e) for taxpayers when unnecessary follow-up testing and treatment is carried out;
- costs and harms to third parties – when children or third parties are tested without consent, or when embryos are tested for conditions whose risks may be hard to determine; and
- can change perception of wellness and illness through medicalisation of normal variation, including for children.

9.6 Taking a personal genetic profiling test for genetic susceptibility can in principle help people who wish to do so to learn more about their health and become more involved in making decisions about their healthcare. The marketing material of the commercial providers of tests stresses this theme, suggesting that taking a proactive approach to health could result in being able to look out for, prevent, treat or simply know about any conditions for which the person is at risk. Examples of the types of tests available are included in Table 9.1. Two companies have given the following reasons for individuals to take up their services.⁴²⁵

“You'll learn what your genes say about your traits. And learn about your disease risks. So you can team up with your doctor to make better decisions about your health.” *23andMe*

“Based on your unique results we can advise you how to create your own individual plan for cardiac disease prevention” *Genetic Health*

It may be that simply taking tests and thinking about health encourages some people to take more interest in their health and live healthier lifestyles, though we are not aware of systematic evidence on this. But even so, the benefits and harms of such tests also depend on how predictive the tests are about individual susceptibility to disease.

Clinical validity

9.7 As noted in Chapter 1, clinical validity refers to how well test results detect or predict the associated disorder. We have also noted in Box 9.2 that many factors can influence whether a person will develop most conditions. Hence, the predictive value for the type of genetic profiling that offers a risk assessment for various, often relatively common, complex diseases is much

⁴²⁵ Information correct at time of going to print.

lower than testing for a particular monogenic disorder, where there is a clearer genetic link. In recent years some progress has been made in identifying the genetic variants relevant to different diseases, in particular using genome-wide association studies (see Box 9.3).⁴²⁶ In early 2008 it was reported that this approach had in total revealed around 50 disease-susceptibility loci.⁴²⁷ With a few exceptions, the increases in risk caused by variations at the newly identified loci are modest (see Box 9.3), and large sample sizes are required to identify them.⁴²⁸

Box 9.3: Genome-wide association studies

These studies involve large numbers of people with and without particular diseases, each of whom is genotyped at several hundred thousand markers throughout the genome. Comparisons are then made between these groups to identify genetic markers associated with the disease. Studies so far have included type 1 and type 2 diabetes, prostate cancer, inflammatory bowel disease and asthma.⁴²⁹ By 2010, approximately 400 studies of this kind had been performed.⁴³⁰ They have become possible since the completion of the sequencing of the human genome in 2003 and a map of human genetic variation (the International HapMap Project, completed in 2005), and as a result of technological developments.

The first results of one of the largest such studies, examining 500,000 different DNA sites in 17,000 individuals for associations with seven major diseases, were published in 2007.⁴³¹ This study found 24 sites at which there was strong statistical evidence for association with one or more diseases, and a larger number of sites with weaker evidence for association. Some of the associations confirmed earlier findings, while some were previously unidentified, and of those that were novel, the presence of a particular disease-associated genetic variation resulted in a modest increase (1.2- to 1.5-fold) in the risk of the disease.⁴³² In total, these studies have identified hundreds of genetic variants associated with complex human diseases and traits, but the size of the genetic effect of common variants associated with major diseases is mostly small.⁴³³

It is currently unclear whether the results obtained so far through genome-wide association studies are the “tip of the iceberg or the bottom of the barrel”.⁴³⁴ Also unclear is to what extent it is possible to utilise information derived from these studies in a clinical setting.⁴³⁵ In addition, this approach has so far mainly been used to uncover areas of the genome of interest using one particular type of genetic marker called a single nucleotide polymorphism (SNP). Using it to search for different types of genetic marker is likely to be more complex.⁴³⁶ Overall, the variants identified so far explain only a small proportion of individual variation in disease risk, limiting the immediate utility of genetic profiling to predict individual disease susceptibility.⁴³⁷ It is said to be

⁴²⁶ See Iles MM (2008) What can genome-wide association studies tell us about the genetics of common disease? *PLoS Genetics* **4**(2): e33.

⁴²⁷ Disease-susceptibility loci are locations in the genome associated with an increased risk of disease. See: Burke W and Psaty (2007) Personalized medicine in the era of genomics; McCarthy MI, Abecasis GR and Cardon LR et al. (2008) Genome-wide association studies for complex traits: Consensus, uncertainty and challenges *Nature Reviews Genetics* **9**: 356–69.

⁴²⁸ McCarthy MI, Abecasis GR and Cardon LR et al. (2008) Genome-wide association studies for complex traits: Consensus, uncertainty and challenges *Nature Reviews Genetics* **9**: 356–69.

⁴²⁹ *Ibid.*

⁴³⁰ Copperthwaite MC, Mohanty D and Burnett MG (2010) Genome-wide association studies: A powerful tool for neurogenomics *Neurosurgical Focus* **28**(1): E2.

⁴³¹ The Wellcome Trust Case Control Consortium (2007) Genome-wide association study of 14,000 cases of seven common diseases and 3,000 shared controls *Nature* **447**: 661–78; Bowcock AM (2007) Guilt by association *Nature* **447**: 645–6.

⁴³² Manolio TA, Collins FS, Cox NJ et al. (2009) Finding the missing heritability of complex diseases *Nature* **461**: 747–53.

⁴³³ Zeggini E and Ioannidis JP (2009) Meta-analysis in genome-wide association studies *Pharmacogenomics* **10**(2): 191–201.

⁴³⁴ Iles MM (2008) What can genome-wide association studies tell us about the genetics of common disease? *PLoS Genetics* **4**: e33.

⁴³⁵ Knight JC (2009) Genetics and the general physician: Insights, applications and future challenges *QJM: An International Journal of Medicine* **102**: 757–72.

⁴³⁶ McCarthy MI, Abecasis GR and Cardon LR et al. (2008) Genome-wide association studies for complex traits: Consensus, uncertainty and challenges *Nature Reviews Genetics* **9**: 356–69.

⁴³⁷ *Ibid*; see also: The Academy of Medical Sciences (2009) *Genome-wide association studies: Understanding the genetics of common disease – symposium report*, available at:

<http://www.acmedsci.ac.uk/download.php?file=/images/page/GWASWEBF.pdf>.

unlikely that it will be possible to give each individual a precise, individually tailored disease risk, but it may be possible to stratify them into groups with different levels of risk.⁴³⁸ Such stratification might lead to screening targeted at the most 'at-risk' group.

A recently announced NHS research study aims to sequence patients' entire genomes in order to investigate the underlying genetic links of cardiovascular disease in 10,000 patients over the age of 16 over a ten-year period.⁴³⁹ This aim is in line with the recommendations in the House of Lords 2009 *Genomic medicine* report that basic and clinical genomic research should be effectively translated into clinical practice.⁴⁴⁰

- 9.8 In short, much research is ongoing in this area but scientists commonly assert that it difficult to use the results that have emerged so far to make accurate predictions from a genome sequence alone about a person's risk of developing a disease that is caused by multiple genetic and other factors (see Box 9.2).⁴⁴¹ In addition, results from such studies are specific to the population upon which they were carried out (for example people designated 'Caucasian'), and therefore may not be relevant for people from outside such populations who have these tests. Problems of replicability are also commonly encountered with these studies.⁴⁴²
- 9.9 An optimistic view of these developments is given by Francis Collins, director of the National Human Genome Research Institute, stating: "The hope is that sometime within the next few years, healthcare providers will be able to scan each of our genomes to identify the most significant genetic variations that predispose each of us to certain diseases. Not only should this offer better opportunities for diagnosis and prevention, it should lead to the development of more individualized strategies for treating or managing the disease if it does occur."⁴⁴³ However, others are less convinced: "it could take years, if not decades, before lifestyle and medical interventions can be responsibly and effectively tailored to individual genomic profiles".⁴⁴⁴
- 9.10 Nonetheless, as we have seen, companies are already offering risk information for many multifactorial conditions to consumers based on the sequence of their DNA at specific points in their genome. Many of those companies acknowledge that environmental (lifestyle) factors have a large role to play in the development of the conditions for which they offer risk information, but their marketing information tends to highlight the clinical value of the genetic information from the tests. We return to this point in our recommendation in Paragraph 9.51.
- 9.11 There is little independent systematic research on the clinical validity of the types of genetic profiling tests under consideration here. One recent review concluded that "There [was] insufficient scientific evidence to conclude that genomic profiles are useful in measuring genetic risk for common diseases or in developing personalized diet and lifestyle recommendations for disease prevention."⁴⁴⁵ The authors examined previous meta-analyses and HuGE reviews,⁴⁴⁶ in

⁴³⁸ PHG Foundation (2008) *Evidence to the House of Lords Science and Technology Committee – genomic medicine*, available at: <http://www.phgfoundation.org/file/4070/>.

⁴³⁹ Royal Brompton and Harefield NHS Trust (2010) 'Next Generation' Gene Sequencer to determine the genetic links of heart disease, available at: <http://www.rbht.nhs.uk/media/press-releases/?assetid=2753237=342161&p=1>.

⁴⁴⁰ House of Lords Science and Technology Committee (2009) *Science and Technology Committee 2nd report of session 2008–2009: Genomic medicine – volume one: Report*, available at: <http://www.publications.parliament.uk/pa/l200809/ldselect/ldsctech/107/107i.pdf>.

⁴⁴¹ Edelman E and Eng C (2009) A practical guide to interpretation and clinical application of personal genomic screening *British Medical Journal* **339**: b4253.

⁴⁴² See, for example: Hirschhorn JN, Lohmueller K, Byrne E and Hirschhorn K (2002) A comprehensive review of genetic association studies *Genetics in Medicine* **4**(2): 45–61.

⁴⁴³ Quoted in Honey K (2008) GINA: Making it safe to know what's in your gene *Journal of Clinical Investigation* **118**(7): 2369.

⁴⁴⁴ Janssens ACJW, Gwinn M and Bradley LA *et al.* (2008) A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalised health interventions *American Journal of Human Genetics* **82**: 593–9.

⁴⁴⁵ Seven companies were identified which together provided tests for at least 69 different variations in 56 genes. Of the 56 genes tested, 24 were not reviewed in meta-analyses. For the remaining 32 genes, 260 meta-analyses were found that examined 160 unique variation-disease associations. Of these, only 60 were found to be statistically significant. The 60 associations involved 29 different polymorphisms and 28 different diseases, and were generally of modest quality. Genes in cardio-genomic profiles were more frequently associated with non-cardiovascular diseases than with cardiovascular diseases. While two of the five gene sequences of the osteo-genomic profiles (i.e. profiles relating to bone formation) did show significant associations with disease, the associations were not with bone diseases. Janssens ACJW, Gwinn M and

which the genetic sequences of people with a disease were compared with those of a healthy or general-population control group. They assessed the scientific evidence supporting purported gene-disease associations for genes included in profiling tests offered by private companies offering predictive testing over the internet. The review concluded that “the excess disease risk associated with many genetic variants included in genomic profiles [that the companies tested for] has not been investigated in meta-analyses or has been found to be minimal or not significant”, and, as such “scientific evidence for most associations between genetic variants and disease risk is insufficient to support useful applications.” As well as the danger of people being given misleading information suggesting they are at high risk, a further possible danger is also highlighted: “those with ‘low-risk’ profiles could be led to mistakenly believe that they have little need to make health lifestyle changes”.

- 9.12 In a newspaper article in 2008,⁴⁴⁷ a journalist described how he had approached several companies, including GeneticHealth (UK), deCODEme (Iceland)⁴⁴⁸ and 23andMe (USA), to compare their test results. There was considerable variation in the way in which information was presented, and specific risk predictions also differed considerably. For example, deCODEme stated that the risk of developing exfoliation glaucoma for the individual being profiled was 91% below average, while 23andMe claimed the risk was 3.6 times more likely than average. In the case of heart problems, deCODEme quoted a risk of a heart attack, angina or sudden cardiac death at 54.8% (6% above average), while 23andMe claimed the risk of a heart attack between the ages of 45 and 84 for the individual concerned was 17.5% below average.
- 9.13 It is also worth noting that when people make decisions about whether or not to take a predictive genetic test, they have been found not to pay attention to the uncertain nature of the information derived from the tests in their decision-making process. Thus the fact that the test does not give them a clear answer does not significantly inform their decision as to whether or not to take the test. Indeed, people have been found generally to approach the test as providing a binary result, even where it does not.⁴⁴⁹

Clinical utility

- 9.14 In addition to problems with clinical validity, further questions arise about whether the results of direct-to-consumer profiling for susceptibility to multifactorial diseases enable the person tested to do anything specifically useful to counteract the possible harm about which they have been warned. For example, are there any preventive measures or therapies they can take to remove, reduce or defer the risk of disease? The risk predictions given generally do not greatly differ from the average risk levels. They also relate to overall lifetime risk and give no indication of when any potential disease will develop, or how severe it might be. It is therefore not generally possible to take specific actions in response to direct-to-consumer predictive genetic profiling beyond those that would result in healthier lifestyles for anybody, such as to maintain a healthy

Bradley LA et al. (2008) A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalize health interventions *American Journal of Human Genetics* **82**(3): 593–9.

⁴⁴⁶ “A HuGE (Human Genome Epidemiology) review identifies human genetic variations at one or more loci, and describes what is known about the frequency of these variants in different populations, identifies diseases that these variants are associated with and summarises the magnitude of risks and associated risk factors, and evaluates associated genetic tests. Reviews point to gaps in existing epidemiologic and clinical knowledge, thus stimulating further research in these areas.” See: Centers for Disease Control and Prevention (2010) HuGENet™, available at: <http://www.cdc.gov/genomics/hugenet/reviews/index.htm>.

⁴⁴⁷ Fleming N (2008) Rival genetic tests leave buyers confused *The Times* 7 September, available at: <http://www.timesonline.co.uk/tol/news/science/article4692891.ece>.

⁴⁴⁸ deCODEme is a service provided by deCODE genetics, a company based in Iceland that filed for bankruptcy in 2009. The majority of deCODE's assets were subsequently purchased by Saga Investments LLC. deCODE genetics has since asserted its intention to continue all its previous product and service lines, including the deCODEme personal genome scans. See: deCODE genetics (2010) Announcing the new deCODE, available at: <http://decodeyou.com/announcing-the-new-decode/#more-843>.

⁴⁴⁹ Henderson BJ, Maguire BT, Gray J and Morrison V (2006) How people make decisions about predictive genetic testing: An analogue study *Psychology & Health* **21**(4): 513–39.

weight, eat healthily, take exercise and refrain from smoking or drinking excessive amounts of alcohol.

Psychological impact

- 9.15 Some of the risk predictions given as a result of the profiling tests available are for very serious conditions, including those that have no treatment or cure.⁴⁵⁰ Added to the fact that, as we have seen above, clinical validity is not clear for many of these tests (a fact acknowledged by some of the companies offering the tests), there is potential for concern about how people will react psychologically to the information they receive from tests. We recognise that genetic information can be delivered in different ways (for example, over the internet or through face-to-face consultation with a genetic counsellor) and these differences may well have an impact on the way people react to the information.⁴⁵¹ There have been some studies into people's psychological response to predictive genetic information, but it is not clear how the evidence should be interpreted. The 2004 REVEAL study suggested that most people did not suffer significant psychological harm from being informed that they carried the apolipoprotein E (*APOE*) gene, which is associated with an increased susceptibility to the development of Alzheimer's disease (although the predictive power is poor).⁴⁵² A further study, conducted by the same researchers in 2009, found that when 162 asymptomatic adults who had a parent with Alzheimer's disease were randomly assigned to two groups, one that would receive the results of their own *APOE* genotyping and one that would not, "there were no significant differences between the two groups in changes in time averaged measures of anxiety...depression...or test-related distress". The study concluded: "the disclosure of *APOE* genotyping results to adult children of patients with Alzheimer's disease did not result in significant short-term psychological risks."⁴⁵³ However, there has been some debate about the nature of the control group used in the second study; alternative analysis of the data indicated "significant increases in depression in eight of nine measures" for those who were informed of their *APOE* genotyping results.⁴⁵⁴
- 9.16 In 2010, Martin Richards, a professor at the University of Cambridge, published a paper describing his experiences when purchasing genetic profiling tests from two different companies: one from 23andMe and one from deCODEme.⁴⁵⁵ Similarly to the journalist's investigations mentioned in Paragraph 9.12, Professor Richards identified substantial differences in the disease risk profiles provided by the companies and also described differences in the types of information provided and the ways in which that information was presented to the user. He noted that most companies provide a 'package', rather than a specific set of customisable tests. Thus, the customer may be given information concerning a range of traits, such as disease risk, drug metabolism, hair/eye colour and even ear wax type: "a mixture of medical information (disease genetic risks and drug metabolism) and other rather different kinds of personal information". Professor Richards also drew attention to the heavy emphasis in some companies' "lengthy" terms of service agreements that customers should not treat the information supplied as 'medical' in nature. However, he questioned whether the average user would read these agreements in detail and suggested that it was "unlikely" that anyone who bought such tests would then approach the results as "a series of bits of information about their genome with no relevance at all for their health".⁴⁵⁶

⁴⁵⁰ Risks of additional conditions may also be revealed to customers some time after having genomic analysis as a result of further research.

⁴⁵¹ Of course, once some people have seen a genetic counsellor, they decide not to have genetic testing.

⁴⁵² Roberts JS, Barber M and Brown TM (2004) Who seeks genetic susceptibility testing for Alzheimer's disease? Findings from a multisite, randomized clinical trial *Genetics in Medicine* **6**(4): 197–203.

⁴⁵³ Green RC, Roberts JS, Cupples LA et al. (2009) Disclosure of *APOE* genotype for risk of Alzheimer's disease *New England Journal of Medicine* **361**(3): 245–54.

⁴⁵⁴ Gordon SC and Landa D (2010) Disclosure of the genetic risk of Alzheimer's disease *New England Journal of Medicine* **362**(2): 181–2.

⁴⁵⁵ Richards M (2010) Reading the runes of my genome: A personal exploration of retail genetics *New Genetics and Society*, forthcoming.

⁴⁵⁶ *Ibid.*

- 9.17 The providers of the types of profiling under discussion generally do not offer clinical assessment of symptoms and risk nor genetic counselling and we have noted that such tests can produce results that are unreliable or difficult to interpret. As already noted, even when results purport to be clear, false negatives can be produced which could lead to complacency and there is also the possibility of false positives which could create needless confusion or anxiety.⁴⁵⁷ There is also the possibility of people experiencing stigma as a result of the results they receive if those results are communicated to others, such as family members, teachers, employers or insurers. In the absence of evidence, such harms are speculative, but that does not mean they should be dismissed.

Impact on insurability

- 9.18 Since 2001 the Association of British Insurers (ABI) has operated a voluntary moratorium on the use of genetic tests by insurance companies which runs until 2014, having been extended on a number of occasions. It specifies that customers will not be required to disclose the results of predictive genetic tests for policies up to £500,000 of life insurance, or £300,000 for critical illness insurance, or paying annual benefits of £30,000 for income protection insurance. The relevant public advisory body (formerly the Genetics and Insurance Committee, whose functions are now performed by the Human Genetics Commission) has to date only approved one application for disclosure of test results, for Huntington's disease in life insurance applications over £500,000. This decision does not mean that everyone can be asked to have a genetic test for Huntington's disease before they can get insurance. What it means is that where people have already been tested as part of their medical care, there is nothing to prevent insurance companies asking for that information from customers.
- 9.19 We have been informed by the ABI that "insurers ask about tests and investigations carried out (or planned) and do not specifically refer to how the test or investigation was originated."⁴⁵⁸ It is for the insurer to decide whether the information provided is relevant and insurers require full and accurate answers to their direct questions. Different insurers vary as to the time period covered by their questions, and the time period will depend on how relevant the information could be to the product being purchased. Insurance companies have always been able to ask for details of a family history, from which genetic information may be gleaned; and other indirect genetic tests, such as clinical investigations which reveal particular features can be utilised as part of the actuarial decision making. We conclude that there may be questions as part of applications for various types of insurance that require the applicant to disclose information relating to genetic tests: not answering or hiding the existence of test results would constitute non-disclosure which can affect the payment of a claim. The ABI told us that neither they nor insurers have had many queries from consumers about whether or not they need to reveal the results of genetic tests or whether they should take such a test.

Extent of use

- 9.20 Genetic testing was previously an area in which patients were advised by healthcare professionals about tests that would be clinically useful, and has now shifted to one where people are also able to order tests directly. Direct-to-consumer genetic testing has come about owing to the availability of the technologies on which the tests are based and the decrease in cost to carry out the tests. Tests can be cheaply and easily marketed and sold online, and the

⁴⁵⁷ Although true negatives can also lead to complacency through a reduction in health-promoting behaviours, the complacency associated with false negatives has the additional risk of a patient also failing to undergo potentially effective interventions. See: Madlensky L, McLaughlin JR, Carroll JC, Goel V and Frank JW (2005) Risks and benefits of population-based genetic testing for Mendelian subsets of common diseases were examined using the example of colorectal cancer risk *Journal of Clinical Epidemiology* 58: 934–41.

⁴⁵⁸ Association of British Insurers, personal correspondence.

internet seems to be the predominant medium by which such tests are provided to the public.⁴⁵⁹ Commercial companies sell DNA collection kits via the internet, then mail the kit to the customer who uses it to collect a DNA sample (e.g. from inside the mouth) and then typically returns it in the post to the company involved for analysis.

- 9.21 We asked major companies operating in this field in the UK and overseas about the scale of their operations but none was willing to give us this information. There is one company based in the UK and it is registered as 'small'⁴⁶⁰ at Companies House.⁴⁶¹ A 2008 report from PriceWaterhouseCoopers notes that the overall global market for genetic tests is approximately \$730 million, but describes the direct-to-consumer element as a "relatively small portion" of the overall market (although it also notes that this section of the market is expected to grow rapidly).⁴⁶² An article in *The New York Times* asserts that uptake of personal genetic profiling for disease susceptibility has so far been limited: "Two and a half years after beginning its service, 23andMe has only 35,000 customers. And at least a quarter of them got the service free or for only \$25, instead of the hundreds of dollars on which the business model is based. Navigenics and DeCode have even fewer customers."⁴⁶³

Current system of interventions

- 9.22 There is no overarching system of interventions relating to personal genetic profiling. Where health professionals are involved they will be subject to their own codes of professional conduct (see Box 4.1). There are also several relevant laws and other forms of governance, relating to data protection, collecting DNA, advertising and the products themselves and we explore these below. But companies based anywhere in the world can offer their services to customers based locally or overseas online or by post, which means that some companies may be operating under a jurisdiction different from that applying where their customers live. In the UK, domestic law will apply to such services in some cases, and there are other cases in which it will not, and we consider this issue below.

Data protection

- 9.23 As noted earlier in this report, personal health data is commercially valuable and the entry and storage of such data on servers accessed via websites opens up opportunities for loss, theft and misuse. The different regulatory frameworks relating to privacy and confidentiality that various countries operate, and the lack of an overarching international policy on the subject, means that the legal protection afforded to an individual's data may vary significantly between service providers, depending on where they are based. For example, organisations and companies based in the UK and other European countries are subject to data protection legislation, as described in Chapter 5 (see Paragraphs 5.37–5.40), whereas the legislation or

⁴⁵⁹ Direct-to-consumer genetic tests are not exclusively provided via the internet. There have been instances of genetic tests being sold by 'bricks-and-mortar' establishments. For example, in 2007 Sorenson Genomics began selling paternity tests through Rite Aid pharmacies in parts of the USA (and, in 2008, the whole of the USA except New York State). In 2010, Pathway Genomics and Walgreens announced that Pathway's genetic testing service would be available in Walgreens stores (see also Paragraphs 9.33–9.39). See: Sorenson Genomics (2007) Sorenson genomics to bring the first-ever retail DNA test to market, available at: http://www.sorensongenomics.com/press_release_20071120.html; Sorenson Genomics (2008) Identigene begins nationwide over-the-counter retail sales of DNA paternity test kits in rite aid drug stores, available at: http://www.sorensongenomics.com/press_release_20080325.html.

⁴⁶⁰ Defined under s382 Companies Act 2006 as meeting two or more of the following requirements: having a turnover of less than £5.6 million, a balance sheet total of less than £2.8 million and fewer than 50 employees.

⁴⁶¹ As it was permitted to submit only 'abbreviated' accounts. Companies House performs a variety of functions, one of which is to "examine and store company information". Information regarding companies established in the UK are available for a fee. See: Companies House (2010) Our main functions, available at:

<http://www.companieshouse.gov.uk/about/functionsHistory.shtml> and Companies House (2010) WebCHheck – Select and Access Company Information, available at:

<http://wck2.companieshouse.gov.uk/c221d2b44f40d1871bd8f703b9ae2db7/wcframe?name=accessCompanyInfo>.

⁴⁶² PriceWaterhouseCoopers (2008) *The new science of personalized medicine: Translating the promise into practice*, p19, available at: <http://www.pwc.com/us/en/healthcare/publications/personalized-medicine.jhtml>.

⁴⁶³ Pollack A (2010) Consumers slow to embrace age of genomics *The New York Times* 19 March, available at: <http://www.nytimes.com/2010/03/20/business/20consumergene.html>.

the means to ensure compliance varies greatly in other countries. Even if a company guaranteed security, if it went into administration or changed hands, there is no guarantee that the data held would be used for the same purposes for which it was originally gathered. For example, following the bankruptcy filing of the company deCODE genetics in 2009 and the purchase of most of the assets by another organisation, it remains unclear what exactly will happen to the personal genetic data held by deCODE genetics. Although the company has stated that the data will be used in the manner that it was prior to their bankruptcy,⁴⁶⁴ it has been argued that “deCODE’s new owners remain (legally) free to alter or expand their use of genetic data within a range of allowable uses”.⁴⁶⁵ In Europe, if a company goes into administration or changes hands, the data should be used only in accordance with the original consents or other lawfully authorised purposes. But this obligation does not apply to all jurisdictions and consumers may find it difficult to enforce even in Europe. We return to this issue in our recommendation in Paragraph 9.60.

Collecting DNA

- 9.24 The Human Tissue Act 2004 requires that anyone in the UK procuring and analysing a biological sample to obtain scientific or medical information about a living or deceased person which may be relevant to any other person (including a future person) must have appropriate consent from the person from whom the sample was taken for the test to be lawful.⁴⁶⁶ This requirement means that sending someone else’s sample to one of these companies for analysis without their permission would be an offence, regardless of where the company was based. There is an exception for children,⁴⁶⁷ for whom consent may be given by a person who has parental responsibility. We return to this issue in our recommendation in Paragraph 9.53.
- 9.25 In the USA, a 2009 investigation found there was substantial variation among states in terms of how non-consensual DNA collection, analysis or disclosure were regulated. For example, no relevant regulation of such practices was identified in a total of 21 states and the District of Columbia while ten states restricted non-consensual collection and analysis (or disclosure) of DNA for both health and non-health related purposes.⁴⁶⁸

Provision of information by providers and advertising

- 9.26 As described earlier, NHS screening programmes are regulated by national standards that aim to ensure that, prior to screening, a patient is informed of the risks and benefits, the potential for diagnostic errors and the implications of any subsequent investigations or treatment (see Box 9.1).⁴⁶⁹ Given the complexity of all the information, the gaining of informed consent can often be problematic and the same goes for effective risk communication. The way people understand and interpret risk often depends on how it is presented. Transparent risk communication can reduce the likelihood that risks will be interpreted wrongly by the public, and such communication is especially important given wide differences in ‘health literacy’ within the population.⁴⁷⁰ But the information that is provided to customers about genetic tests performed outside the NHS is not overseen in any way. If companies meet the controls relating to advertising that we summarise below they will have met their regulatory obligations.

⁴⁶⁴ See, for example: Henderson M (2009) Privacy fears as DNA testing firm deCODE Genetics goes bust *The Times* 18 November, available at: <http://www.timesonline.co.uk/tol/news/science/genetics/article6920653.ece>; Stefánsson K (2010) Icelandic genetic database not at risk from bankruptcy *Nature* **463**: 25.

⁴⁶⁵ Vorhaus D (2010) Meet the new deCODE, same as the old deCODE? *Genomics Law Report* [internet blog] 25 January, available at: <http://www.genomicslawreport.com/index.php/2010/01/25/meet-the-new-decode-same-as-the-old-decode/>.

⁴⁶⁶ Human Tissue Act 2004, Section 45.

⁴⁶⁷ Human Tissue Act 2004, Schedule 4, Part 1 s.2(2)(a).

⁴⁶⁸ Genetics and Public Policy Center (2009) *Summary: Analysis of State laws on surreptitious testing*, available at: <http://www.dnapolicy.org/resources/SurreptitiousDNAtestingsummary.pdf>.

⁴⁶⁹ Austoker J (1999) Gaining informed consent for screening *British Medical Journal* **319**: 722–3.

⁴⁷⁰ Sihota S and Lennard L (2004) *Health literacy: Being able to make the most of health* (London: National Consumer Council).

- 9.27 There are measures relating to ‘truth-in-promotion’,⁴⁷¹ which are applied and enforced by a number of UK bodies, including: the Advertising Standards Authority (ASA), the Office of Fair Trading (OFT) and the Office of Communications. As noted in Chapter 5, the ASA deals with complaints about advertising in both broadcast and non-broadcast media. The Committee of Advertising Practice Code, which the ASA administers, requires advertisements to be “capable of objective substantiation”.⁴⁷² When the ASA receives a complaint, it first considers whether the case falls within the remit of the relevant advertising code and then whether the behaviour being complained about breaches any rules of the code. If a complaint passes both of those tests, there are a variety of sanctions available depending on the nature of the violation, and they were described in Chapter 5. Where complaints concern a device such as a genetic test, both the ASA and the OFT have said they would be likely to consult with the Medicines and Healthcare products Regulatory Agency (MHRA) for further advice.⁴⁷³
- 9.28 Concerns have been raised about the information contained in advertisements of genetic tests available directly to consumers. In its report *More genes direct*, the Human Genetics Commission noted:⁴⁷⁴

“We share the widespread concerns about the advertising of direct genetic tests and believe that it should be discouraged. We believe that the Advertising Standards Authority and the Office of Fair Trading should emphasise the need for responsible and accurate advertising of such products.”⁴⁷⁵

The Human Genetics Commission has since published *A common framework of principles for direct-to-consumer genetic testing services* which includes reference to the types of information that should be provided for prospective consumers (see also Paragraph 9.31).⁴⁷⁶ We return to this subject of the information supplied by providers in our recommendation in Paragraph 9.51.

Interventions related to the products provided

- 9.29 Medical genetic tests fall under the broader regulatory framework associated with medical devices in the UK (see also Paragraph 8.26–27),⁴⁷⁷ and are governed in the EU by the In Vitro Diagnostic Devices (IVDD) Directive (98/79/EC). This Directive came into force in the UK in 1998 and was implemented in the UK by the Medical Devices Regulations 2002.⁴⁷⁸ The MHRA is currently the UK body responsible for ensuring compliance with the IVDD Directive.⁴⁷⁹ The Directive requires that testing kits are safe and accurately measure what they say they do. The IVDD Directive applies only to devices for medical purposes,⁴⁸⁰ and works on the basis of risk-based regulation, in which the level of regulation applied to a specific test is intended to be proportional to the risk it poses to the user.⁴⁸¹

⁴⁷¹ Melzer D, Hogarth S, Liddell K et al. (2008) *Evidence and evaluation: Building public trust in genetic tests for common diseases – research report*, p9, available at: http://www.phgfoundation.org/file/redirect/?link_ID=4003.

⁴⁷² Committee of Advertising Practice (2009) The CAP Code – general rules: 3 Substantiation, available at: http://bcap.org.uk/The-Codes/CAP-Code/CAP-Code-Item.aspx?q=CAP+Code_General+Rules_3++Substantiation.

⁴⁷³ Human Genetics Commission (2007) *More genes direct*, p13, available at: <http://www.hgc.gov.uk/Client/document.asp?DocId=139&CACategoryId=10>.

⁴⁷⁴ The UK Government’s advisory body on new developments in human genetics.

⁴⁷⁵ Human Genetics Commission (2007) *More genes direct*, p25., available at: <http://www.hgc.gov.uk/Client/document.asp?DocId=139&CACategoryId=10>.

⁴⁷⁶ Human Genetics Commission (2010) *A common framework of principles for direct-to-consumer genetic testing services*, available at: <http://www.hgc.gov.uk/Client/Content.asp?ContentId=816>.

⁴⁷⁷ Hogarth S, Liddell K, Ling T et al. (2007) Closing the gaps – enhancing the regulation of genetic tests using response regulation *Food & Drug Law Journal* **62**: 833.

⁴⁷⁸ SI 2002/618.

⁴⁷⁹ Human Genetics Commission (2007) *More genes direct*, p11, available at: <http://www.hgc.gov.uk/Client/document.asp?DocId=139&CACategoryId=10>.

⁴⁸⁰ Articles 1 and 2(a) Directive 98/79/EC.

⁴⁸¹ Human Genetics Commission (2007) *More genes direct*, p11, available at: <http://www.hgc.gov.uk/Client/document.asp?DocId=139&CACategoryId=10>.

- 9.30 The remit of the MHRA does not extend to medical device regulations outside the European Union and consequently does not cover any tests performed outside the EU. However, the MHRA has stated that it expects that tests or products used in conjunction with any healthcare service offered in the UK be safe, effective and fit for purpose, and that such tests meet all of the relevant regulations covering *in vitro* diagnostic medical devices in the country within which the laboratory in question is based.⁴⁸² The MHRA has also stated that where samples are obtained within the EU, both the specimen receptacles and any equipment used to obtain the samples must be CE-marked (see description in Chapter 8, footnote 402).
- 9.31 As mentioned above, the Human Genetics Commission has recently published *A common framework of principles for direct-to-consumer genetic testing services*, with the aim of promoting “high standards and consistency in the provision of genetic tests amongst commercial providers at an international level in order to safeguard the interests of people seeking genetic testing and their families.”⁴⁸³ The Principles are provided as guidance for developing codes of practice.⁴⁸⁴ The European Society of Human Genetics (ESHG) has also recently published recommendations for the regulation of direct-to-consumer genetic testing for health purposes.⁴⁸⁵
- 9.32 Other states and countries have also responded to the availability of direct-to-consumer tests. For example, in February 2010, German legislation came into force that requires predictive genetic examinations to be conducted or commissioned only by doctors who specialise in human genetics, by other similarly qualified and specialised medical doctors.⁴⁸⁶ This legislation may have a significant impact on any direct-to-consumer genetic profiling company operating in Germany.

The changing situation in the USA

- 9.33 At the federal level, the Food and Drug Administration (FDA) is responsible for regulating *in vitro* diagnostic (IVD) tests performed in a laboratory. Medical devices are required to be safe and effective. In this context, a device is considered safe when the probable benefits to health from its use outweigh any probable risks,⁴⁸⁷ and effective where, for “a significant portion of the target population, the use of the device for its intended uses and conditions of use, when accompanied by adequate directions for use and warnings against unsafe use, will provide clinically significant results”.⁴⁸⁸
- 9.34 Despite the existence of this legislation, it has been claimed that the majority of new direct-to-consumer genetic tests are being developed as a different type of test, ‘laboratory developed tests’.⁴⁸⁹ although the FDA has stated that such tests are medical devices and therefore under FDA jurisdiction it has, so far, exercised a discretionary approach to their regulation (although this situation may change in the future: see below).⁴⁹⁰

⁴⁸² Information supplied by Medicines and Healthcare products Regulatory Agency.

⁴⁸³ Human Genetics Commission (2009) *A common framework of principles for direct-to-consumer genetic testing services – principles and consultation questions*, p4, available at: <http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Principles%20consultation%20final.pdf>.

⁴⁸⁴ *Ibid*, p2.

⁴⁸⁵ European Society of Human Genetics (2010) Statement of the ESHG on direct-to-consumer genetic testing for health-related purposes *European Journal of Human Genetics* advance online publication, 25 August 2010.

⁴⁸⁶ S.7 Gesetz über genetische Untersuchungen bei Menschen.

⁴⁸⁷ 21 US Code of Federal Regulations § 860.7(d)(1).

⁴⁸⁸ 21 US Code of Federal Regulations § 860.7(e)(1).

⁴⁸⁹ US Congress Committee on Energy and Commerce Staff (2010) *Memorandum re hearing on “direct-to-consumer genetic testing and the consequences to the public health”*, available at: <http://energycommerce.house.gov/documents/20100720/Briefing.Memo.oi.2010.7.20.pdf>.

⁴⁹⁰ *Ibid*.

- 9.35 The Clinical Laboratory Improvement Amendments (CLIA),⁴⁹¹ passed by the US Congress in 1998, defines and mandates quality standards for laboratory testing. The Centers for Medicare and Medicaid Services manage an accreditation and regulation system for clinical laboratories but exercise little supervision over companies that sell direct-to-consumer genetic testing kits.⁴⁹² CLIA is designed to “ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed”,⁴⁹³ but it has been noted that it does not require an assessment of the clinical utility or effectiveness of a test.⁴⁹⁴
- 9.36 In 2010, there were several developments at the federal level concerning the regulation of direct-to-consumer genetic tests: the US National Institutes of Health announced plans to create a Genetic Testing Registry (a database of genetic tests),⁴⁹⁵ the FDA contacted various direct-to-consumer genetic testing companies about whether those companies were fulfilling various regulatory requirements applicable to the provision of genetic tests; the FDA also held a meeting “to discuss the agency’s oversight of laboratory developed tests”;⁴⁹⁶ the US House of Representatives Committee on Energy and Commerce Subcommittee on Oversight and Investigations launched a hearing into the direct-to-consumer genetic testing industry;⁴⁹⁷ and the US Government Accountability Office published a report on the direct-to-consumer industry that criticised some direct-to-consumer genetics companies’ test results as being “misleading and of little or no practical use”.⁴⁹⁸
- 9.37 In May 2010, following the partnership between Walgreens and Pathway Genomics to provide a genetic testing kit in retail stores in the USA, the FDA informed Pathway Genomics that they considered the Pathway Genomics saliva collection kits as fulfilling the relevant “definition of a device”,⁴⁹⁹ and Walgreens withdrew the product.⁵⁰⁰ In June 2010, the FDA sent letters to other direct-to-consumer genetic testing companies advising them that the FDA viewed their testing kits as medical devices.⁵⁰¹ Following recent meetings, the FDA is considering its position, and no formal decision on the subject of the oversight of laboratory diagnostic tests had been made at the time of writing.⁵⁰²
- 9.38 At the state level, approximately half of the states in the USA specifically regulate direct-to-consumer genetic testing. What is defined as direct-to-consumer testing differs among states,

⁴⁹¹ See: http://www.access.gpo.gov/nara/cfr/waisidx_04/42cfr493_04.html.

⁴⁹² US Congress Committee on Energy and Commerce Staff (2010) *Memorandum re hearing on “direct-to-consumer genetic testing and the consequences to the public health”*, available at: <http://energycommerce.house.gov/documents/20100720/Briefing.Memo.oi.2010.7.20.pdf>.

⁴⁹³ Food and Drug Administration (2010) Clinical laboratory improvement amendments (CLIA), available at: <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/IVDRegulatoryAssistance/ucm124105.htm>.

⁴⁹⁴ Vorhous D (2010) Personal genomics follows pathway to corner drugstore; is regulation next? *Genomics Law Report* [internet blog] 11 May, available at: <http://www.genomicslawreport.com/index.php/2010/05/11/pathway-walgreens-and-dtc-regulation/>.

⁴⁹⁵ US National Institutes of Health (2010) NIH announces genetic testing registry, available at: http://www.nih.gov/news/health/mar2010/od-18.htm?utm_source=twitterfeed&utm_medium=twitter.

⁴⁹⁶ US Federal Register (2010) *Oversight of laboratory developed tests; public meeting; request for comments; notice of public meeting; request for comments* 75(116): 34463–4, available at: <http://edocket.access.gpo.gov/2010/2010-14654.htm>.

⁴⁹⁷ US House of Representatives Committee on Energy and Commerce (2010) Committee investigates personal genetic testing kits, available at: http://energycommerce.house.gov/index.php?option=com_content&view=article&id=2009:committee-investigates-personal-genetic-testing-kits&catid=122:media-advisories&Itemid=55; US House of Representatives Committee on Energy and Commerce (2010) Hearing on “direct-to-consumer genetic testing and the consequences to the public health”, available at: http://energycommerce.house.gov/index.php?option=com_content&view=article&id=2083:hearing-on-direct-to-consumer-genetic-testing-and-the-consequences-to-the-public-health&catid=133:subcommittee-on-oversight-and-investigations&Itemid=73.

⁴⁹⁸ US Government Accountability Office (2010) *Direct to consumer genetic tests: Misleading test results are further complicated by deceptive marketing and other questionable practices*, available at: <http://www.gao.gov/new.items/d10847t.pdf>.

⁴⁹⁹ Food and Drug Administration (2010) Letter to Pathway Genomics corporation concerning the pathway genomics genetic health report, available at: <http://www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM211875.pdf>.

⁵⁰⁰ Jaspen B and Jones MS (2010) Walgreens postpones carrying Pathway Genomics genetic test kit *Los Angeles Times* 13 May, available at: <http://articles.latimes.com/2010/may/13/business/la-fi-dna-kits-20100513>.

⁵⁰¹ The relevant letters are available directly from the FDA. See: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/default.htm>.

⁵⁰² Information supplied by Food and Drug Administration.

leading to differences in application and enforcement.⁵⁰³ In 2008, some states in the USA made moves towards stricter regulation of direct-to-consumer genetic tests. 'Cease and desist' notices were sent by the California Department of Public Health to 13 genetic testing companies, including 23andMe, Navigenics and deCode Genetics, explaining that the companies should not solicit business from residents in the state.⁵⁰⁴ The letters advised the companies that, as clinical laboratories, they needed to have state licences, and that genetic tests could be ordered only by a doctor, not by consumers. One of the companies responded by saying that a physician was involved in the approval of the test as well as the release of the results to the customer, and another questioned the legality of the claim that a physician was needed.⁵⁰⁵ In August 2008, 23andMe and Navigenics were granted state licences in California to continue to do business.⁵⁰⁶

- 9.39 New York State also took action similar to that of California by issuing warning letters to similar firms, such as Navigenics, instructing them to cease marketing their services directly to consumers and to obtain permits to operate in the state.⁵⁰⁷ In New York State, consumer genomics firms are regulated as clinical laboratories.⁵⁰⁸ In 2010, Navigenics was given permission to operate in New York State as a clinical laboratory and gave an undertaking not to market its genetic testing services directly to the public in that state. Rather, Navigenics will be required to "operate through physician's orders". This company may well adopt this approach for all its operations in the USA.⁵⁰⁹

Softening the ethical dilemmas

- 9.40 We conclude that, although personal genetic profiling for disease susceptibility to common multifactorial conditions has a number of benefits and offers people the freedom to access information about themselves, and the tests work as specified in terms of the data they produce,⁵¹⁰ they often offer low clinical validity and utility. Tests from different companies produce different information about the same person, perhaps because those companies use different research findings as their baseline. The way information is presented can be difficult to interpret. For many of the conditions to which the tests relate, there are no treatments available until clinical symptoms have appeared, or there may be none at all. The information that is provided by these test providers about preventing adverse health conditions from developing is generally no more specific than the usual healthy living messages applicable to everyone. It is possible, too, that if people are told their risk of a particular condition is below the population average, they might be complacent and continue to follow unhealthy lifestyles, which we know often play a considerable role in some of these conditions. Indeed, since the population average for some of these conditions is relatively high, any complacency based on a prediction of risk from a test that may not be clinically valid would seem to be unadvisable.

- 9.41 This mixture of benefits and harms means that some of our ethical values come into stark contrast within this case study: the value of individuals being able to pursue their own interests comes into conflict with the values of state action to reduce harm, safeguarding private information, fair and efficient use of public resources and social solidarity. And the value of

⁵⁰³ Vorhaus D (2010) *A lawyers guide to the personal genomics landscape*, available at: <http://www.genomicslawreport.com/wp-content/uploads/2010/07/Genomics-and-the-Consumer-23andMe-Forum-Vorhaus.pdf>.

⁵⁰⁴ Wadman M (2008) Gene-testing firms face legal battle *Nature* **453**: 1148–9.

⁵⁰⁵ *Ibid.*

⁵⁰⁶ Pollack A (2008) California licenses 2 companies to offer gene services *The New York Times* 19 August.

⁵⁰⁷ *Ibid.*; see also: Ray T (2010) Navigenics agrees not to market genetic testing services directly to NY residents *Pharmacogenomics Reporter* 20 January, available at: <http://www.genomeweb.com/dxpgx/navigenics-agrees-not-market-genetic-testing-services-directly-ny-residents>.

⁵⁰⁸ Ray T (2010) Navigenics agrees not to market genetic testing services directly to NY residents *Pharmacogenomics Reporter* 20 January, available at: <http://www.genomeweb.com/dxpgx/navigenics-agrees-not-market-genetic-testing-services-directly-ny-residents>.

⁵⁰⁹ Navigenics (2010) *Service FAQs*, available at: http://www.navigenics.com/visitor/what_we_offer/faqs/.

⁵¹⁰ A property sometimes referred to as 'analytic validity'.

safeguarding private information also comes into conflict with those of state action to reduce harm and social solidarity. The value of fair and efficient use of public resources is already coming into conflict with social solidarity.

- 9.42 Some have argued for tough curbs on these tests,⁵¹¹ but following the proportionality principle we set out in Chapter 4, we do not think it is currently justifiable to prevent individuals from buying these tests (and thus pursuing what they see as their own interests in their own way), without good evidence of actual harm beyond the administrative error occurring in a genetics laboratory in 2010 when 96 customers received results that were not their own and some expressed distress as a result.⁵¹² Such evidence has not yet been provided, even though, as we have noted, a number of potential harms could arise. And even if future evidence reveals harm that is sufficiently great to warrant some form of coercive government regulation, the genetic profiling analyses described in this chapter are sold over the internet by companies that could be located anywhere in the world, meaning that it would be expensive and difficult to enforce some forms of coercive regulation. In the light of these considerations, we consider it appropriate to make recommendations aimed at promoting our other ethical values but without restricting people's ability to pursue their own interests. First, we recommend independent research on the impact and effects of multifactorial genetic testing on individuals so the harms can be quantified. We also recommend that: (i) responsible authorities should request evidence for clinical claims made by companies; (ii) government health service websites should provide public information about genetic profiling services, and companies should indicate to consumers where to find this information; (iii) companies should voluntarily adopt good practice; (iv) companies should not knowingly carry out for children DNA tests that do not meet the criteria of the UK National Screening Committee; and (v) professionals in the public healthcare system should adapt their practice in the light of the development of direct-to-consumer genetic testing.

Claims made about genetic profiling tests

- 9.43 As noted above, we consider that the predictive value of many privately offered personal genetic susceptibility analyses for multifactorial conditions is unclear. That lack of clarity is problematic because people who receive these profiling results could misinterpret information about their health status, perhaps through giving too much weight to the clinical validity of the results. Inaccurate conclusions, either positive or negative, about a serious condition may have substantial implications for the people receiving test results (see Paragraph 9.15). There may also be financial risks associated with the insurance status of people taking tests (see the recommendations in Paragraphs 9.49 and 9.51). And, although we noted at the outset that the cost of genetic profiling tests is now easily within the means of middle-income consumers in developed countries and may well continue to fall, such tests nevertheless cost consumers money and those people are wasting their money if results are presented (either directly or by implication) as being medically valuable when they are not. Although, as we have said, we do not think it would be proportionate to ban the sale of these products until or unless systematic evidence of harm is produced, we do think that the potential seriousness of these harms makes it proportionate for regulatory and advertising authorities to assert their powers to request that the information provided by companies does not overstate the clinical validity of their products at this time.
- 9.44 Standards could be improved if regulators insisted that better data on clinical validity of tests be provided as a prerequisite for market authorisation. At present however, providers within the EU are required only to prove as a condition of market release that their test is medically valuable if they expressly claim it to be so. In other circumstances it suffices to prove analytic validity (i.e. that the biomarker of interest is correctly identified each time the test is used).

⁵¹¹ The Lancet (2010) New guidelines for genetic tests are welcome but insufficient *The Lancet* 376: 488.

⁵¹² Aldhous P (2010) Genome scan customers sent the wrong results *New Scientist* [internet blog] 7 June, available at: <http://www.newscientist.com/blogs/shortsharpscience/2010/06/personal-genome-customers-sent-1.html>.

9.45 We recommend that responsible authorities pay more attention to whether genetic test providers are making clinical claims for their products, even if implied rather than explicit (such as in their ‘customers’ testimonials’). If so, they should ask for evidence to be supplied. We direct this recommendation to authorities responsible for pre-market review and advertising standards, including the Medicines and Healthcare products Regulatory Agency and the Advertising Standards Authority in the UK.

Information available to consumers

Research and information provided by public healthcare systems

9.46 We have already noted that evidence on possibly harmful effects on people of undergoing predictive genetic profiling has not been clearly established for either their health behaviour or their psychological health (see Paragraph 9.15). In line with our belief that people should, as far as possible, be able to pursue their own interests in their own way, they need good, accurate and impartial information about the services they might consider purchasing. Such information is also needed for evidence-based policy making in this domain.

9.47 We recommend that independent research on the health and psychological impact and effects of multifactorial genetic susceptibility testing on individuals, including children, should be carried out by public healthcare systems. Such research should include investigation into how many people are purchasing this type of analysis, and the results of this research should be made easily accessible. We recognise this information might need updating periodically if scientific developments meant that more associations between genetics and predicting common diseases were discovered. Potential buyers could then better assess what kind of results they would receive and what impacts they could expect, whether positive or negative. In the UK the National Institute for Health Research could be best placed to fund and commission this research.

9.48 As noted in Paragraph 9.30, the specimen receptacles and any equipment used to obtain samples need to be CE-marked if sold in the UK and the EU. However, the interpretation of the results and the information that is provided to consumers is not regulated (except where advertising codes apply) in the UK and in many other countries. We are concerned that it is difficult for people to find out general information from an independent source about services offering genetic profiling for disease susceptibility (i.e. from somewhere other than the companies themselves). There are precedents for action in other commercial sectors, as in the case where non-company-specific information on credit cards and mortgages is provided by the UK and other governments.⁵¹³

9.49 We recommend that appropriate publicly-funded health service websites should include general information for the public about direct-to-consumer genetic profiling services provided by commercial companies. This information should include reference to:

- potential risks and benefits;
- any difficulties with establishing clinical validity;
- the possibility of finding out about conditions for which treatment is not available;
- the special case of children (see also recommendation in Paragraph 9.54); and

⁵¹³ See, for example: Financial Services Authority (2009) *No selling. No jargon. Just the facts about credit cards*, available at: http://www.moneymadeclear.org.uk/pdfs/credit_cards.pdf.

- whether it could be necessary for consumers to inform life, mortgage or travel insurance companies of the results of any tests, either at the time or in the future.

We further recommend that governments should require details about where to find this information to be included in the advertising and information provided by companies selling genetic profiling services in their countries (see also our recommendation in Paragraph 9.51).

Information provided by commercial providers

- 9.50 The information on some direct-to-consumer genetic test providers' websites gives the impression that only useful health and medical information can be gained from taking these tests. This is particularly true in the statements presented in the form of 'customer testimonials'. However, we think that such an impression can be misleading. As we have said, for the types of analysis that involve risk predictions for common multifactorial conditions, the predictions given about any individual's future health are of limited clinical validity. The best way to promote individuals being able to pursue their own interests in their own way is for these companies to provide better information both about how the services they offer can be useful and about their limitations. That is why we recommend a two-pronged approach: governments should provide independent general information about these services as set out above, and the providers themselves should also provide certain information about their services.
- 9.51 We recommend that all companies that provide genetic analysis for susceptibility to common multifactorial diseases should make the following information prominently available in lay language for the consumer before they buy:
- the operator of the services;
 - the location in which the operator is based;
 - the evidence on which interpretations of the test results are based;
 - the tests' limitations, including the fact that they are probabilistic and based on current research results which may change;
 - that the test results may require interpretation by a qualified medical practitioner or genetic counsellor;
 - the possibility of finding serious health problems and revealing family genetic relationships;
 - the nature of the risk being communicated to the consumer, i.e. absolute or relative risk;
 - advice about whether it might be necessary for consumers to declare any results they receive as a result of genetic tests to their life, mortgage or travel insurance companies;
 - which other third parties, if any, have access to the information/data;
 - that the results should not be used alone for medical decision making given their limited clinical validity;
 - that tests that do not meet the requirement of clinical validity should not be carried out for children (see recommendation in Paragraph 9.54);
 - arrangements for data security (including in case of any changes to the administration of the company);

- funding and advertising arrangements; and
- where to find independent information about this type of service on public healthcare service websites (see our recommendation in Paragraph 9.49).

We further recommend that all companies selling direct-to-consumer genetic tests follow the Common Framework of Principles intended for international use by genetic test providers developed by the Human Genetics Commission and approved by the Department of Health in England.

Testing third parties and children

- 9.52 Procuring a biological sample from someone else for DNA analysis without their knowledge is prohibited in the UK by the Human Tissue Act 2004.⁵¹⁴ Similar restrictions apply in some other countries and in some states in the USA (see Paragraph 9.25), and we consider such restrictions to be a sensible way of trying to safeguard information that many people would consider private. Nevertheless, services that rely on sending samples through the post make it possible (although it would be an offence) for a person to send someone else's sample and receive the results without their knowledge.
- 9.53 We recommend that genetic testing companies should require their customers at the point of sale to click on a statement confirming that they have the consent of the person whose DNA they intend to have analysed, or have parental responsibility in the case of children (see below). Where people live in countries such as the UK where procuring someone else's biological sample for DNA analysis without their knowledge is a legal offence, this statement should also require confirmation that the customer has understood this fact. This agreement should be stated in clear language and separated from other terms and conditions.
- 9.54 In the case of children, given our ethical value of the state striving to reduce harm, we recommend that companies should only analyse the DNA of children if (i) a genetic test meets the criteria of the UK National Screening Committee (see Box 9.1)⁵¹⁵ and (ii) valid parental consent has been given. For such testing to take place, a condition would need to be serious, the test would need to be precise and validated, and there would need to be an effective treatment or intervention available for children identified through early detection. As we have said, many companies are offering services that do not meet these criteria, although we recognise there are exceptions. The basis for this recommendation is that some individuals do not want to know susceptibility information, particularly where the clinical validity is unclear. Additionally: (i) any benefits of this type of analysis offering a risk profile of common multifactorial conditions do not seem particularly relevant to children at this time; (ii) the problems with clinical validity of this type of analysis at present need to be taken into account; and (iii) the potential harms involved, particularly those of stigma, also need to be considered, given that children and those responsible for their care would receive information that they cannot un-know, and yet the child did not decide himself or herself to take the DNA profiling test. We consider that this advice should be given to parents on appropriate publicly-funded health service websites (together with the other information we recommend above in Paragraph 9.49), as well as the information that companies provide to consumers that we recommend in Paragraph 9.51.
- 9.55 We believe this recommendation is the most feasible way to try to ensure that children have the opportunity to be able to pursue their own interests in their own way once they reach adulthood.

⁵¹⁴ Human Tissue Act 2004, Section 45. This section of the Act is applicable throughout the UK.

⁵¹⁵ Which we interpret as children who do not have a certain level of competence, such as the standard 'Gillick' test.

The recommendation would not prevent diagnostic genetic testing of the type usually carried out in conjunction with a genetic counsellor or clinical geneticist, for example by NHS clinical services. Such testing is covered by professional codes that involve a presumption of caution in response to parental requests for testing that has no immediate medical benefit so that a child's choices as an adult are preserved.

Impacts for the public healthcare system

- 9.56 One of our ethical values described in Chapter 3 is that of using public resources fairly and efficiently. That value implies that we need to consider whether the new developments considered here result in inefficiencies and unnecessary costs to public healthcare systems. We think that the availability of commercial genetic tests available to consumers on request could indeed have implications for publicly-funded healthcare systems. While there is a lack of peer-reviewed evidence on this point, we were told during our consultation and evidence collection that people do indeed attend their general practitioners after they have purchased such tests to seek help in interpreting their results or to discuss their concerns about the results. We were also told that these patients sometimes request further tests and referral provided by the public healthcare system, even though in many cases referral is unnecessary given the generality and lack of clinical validity of the results. That situation could become increasingly common if direct-to-consumer genetic profiling becomes widespread.
- 9.57 Considering this dilemma between ensuring that public resources are used fairly and efficiently and the value of social solidarity offered by a public healthcare system in the sense of treatment and health advice provided to everyone irrespective of their circumstances, we think it would not be appropriate for a public healthcare system to turn away people who were worried about their health as a result of a privately bought genetic profiling service. But the need for health professionals' time to be spent in this way might at least be somewhat reduced if the predictive test providers offered the types of information we recommend in Paragraph 9.51.
- 9.58 **To lessen the dilemma involved, we recommend that organisations responsible for the training of healthcare professionals and professional standards (such as medical schools, Royal Colleges and the General Medical Council in the UK) should train and advise healthcare professionals about best practice in the areas of giving advice about direct-to-consumer personal genetic profiling services: recognising their value as a tool for discussing healthier lifestyles, addressing their limitations, and taking a responsible position with regard to when to refer patients for specialist services.**

Safeguarding private information

- 9.59 Another of our ethical values is that of safeguarding private information. Many people consider their genetic data to be private information, and the data can reveal highly sensitive information about who they are and are not related to. We therefore consider it important that providers of these services take seriously their responsibilities relating to transferring and holding the private information to which they have access. Even if a company guaranteed security, if it went into administration or changed hands, there is no guarantee that the data held would be used for the same purposes for which it was originally gathered (see Paragraph 9.23).
- 9.60 **Genetic profiling companies should provide details about what would happen to personal genetic data and interpretations should the company go into administration or change hands. This information should be made available to consumers before they buy (see also our recommendation in Paragraph 9.51).**

Future impact

- 9.61 The cost of sequencing a person's DNA is decreasing dramatically as a result of technological developments.⁵¹⁶ This genetic analysis may take various forms, from genotyping small numbers of genetic markers relevant to a particular disease or trait, to full sequencing of a person's entire genome.⁵¹⁷ It is predicted that a person's entire genome could be sequenced for \$1,000 in the near future.⁵¹⁸ In the Human Genetics Commission's 2005 report *Profiling the newborn*, it concluded that genetic profiling could in the future have clinical potential but that its effectiveness could not be judged at that time and recommended research should be carried out to define the full costs and potential benefits of genetic profiling for the health of children and adults.⁵¹⁹ A recent study has suggested that some clinically relevant information may be derived from full genome sequencing.⁵²⁰
- 9.62 The reduction in costs mentioned above may lead to more people coming to take the types of test we have discussed in this chapter, and may also mean that instead of being sent simply risk information, or sequences of specific points in a person's genome, people may come to receive more and more sequence information or, in the future, their entire sequence at an affordable price. There are differences of opinion as to how fast our knowledge of the relationships between genetics and health conditions will develop, but what we do know is that more information will be available to consumers. That is why we think it is vital for more research to be conducted on the impact of testing, and for better information to be provided for the customers or potential customers of these tests to understand their implications and limitations.

⁵¹⁶ Robertson JA (2003) The \$1000 Genome: Ethical and legal issues in whole genome sequencing of individuals *American Journal of Bioethics* 3(3): W-IF1; Mardis ER (2006) Anticipating the \$1000 genome *Genome Biology* 7(7): 112; Service RF (2006) Gene sequencing: The race for the \$1000 genome *Science* 311 (5767): 1544–6.

⁵¹⁷ Sequencing a person's entire genome has recently been used in the genetic diagnosis. See: Lupski JR, Reid JG, Gonzaga-Jauregui C et al. (2010) Whole-genome sequencing in a patient with Charcot–Marie–Tooth neuropathy *New England Journal of Medicine* 362: 1181–91. See also: Lifton RP (2010) Individual genomes on the horizon *New England Journal of Medicine* 362: 1235–6.

⁵¹⁸ Wolinsky H (2007) The thousand-dollar genome: Genetic brinkmanship or personalized medicine? *EMBO reports* 8: 900–3.

⁵¹⁹ Joint Working Group of the Human Genetics Commission and the UK National Screening Committee (2005) *Profiling the newborn: A prospective gene technology?*, available at: <http://www.hgc.gov.uk/Client/document.asp?DocId=154&CCategoryId=10>.

⁵²⁰ The study aimed to "undertake an integrated analysis of a complete human genome in a clinical context" and was prompted by the authors' belief that the clinical translation of genetic risk estimates for common variants reported in genome-wide association studies was unclear. It was designed to assemble information regarding the patient's future health and potential response to various drugs and found that, while challenges remained, whole-genome sequencing could yield useful and clinically relevant information for individual patients. As a consequence of the sequencing, the individual whose genome was sequenced for the study was subsequently prescribed a statin, as he was identified as having a higher than normal risk of heart attack and being likely to respond well to lipid-lowering therapy. See: Ashley ES, Butte AL and Wheeler MT et al. (2010) Clinical assessment incorporating a personal genome *The Lancet* 375(9725): 1525–35.