

# GENETICS AND 'PREDICTIVE MEDICINE': Selling Pills, Ignoring Causes



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Genetic testing is being proposed as a way of identifying individuals who are 'genetically susceptible' to future disease. These 'high risk' individuals would then be encouraged to change unhealthy lifestyles, reduce their exposure to environmental hazards, or take medication before they become ill. This predictive/preventive approach sounds sensible but there are some important questions about the accuracy and negative effects of genetic testing:

- Will genetic tests really allow us to predict an individual's risk of common, complex illnesses like heart disease, cancer and diabetes?
- Will these predictions really help prevent disease and be of benefit to individuals, or could they lead to unnecessary medication and neglect of the socio-economic and environmental causes of disease?
- Could predictions of ill health based on a person's genetic make-up be misused by others and lead to stigma and discrimination?
- What are the broader implications for society of widespread genetic testing?

## What is predictive medicine?

*"The genetics revolution is already underway...In time we should be able to assess the risk an individual has of developing disease – not just for single gene disorders like cystic fibrosis but for our country's biggest killers – cancer and coronary heart disease – as well as those like diabetes which limit people's lives."*

The Rt Hon Alan Milburn, MP, Secretary of State for Health, January 2002<sup>1</sup>.

Several of the major pharmaceutical and biotechnology companies are promoting the idea of 'predictive medicine' or 'predisposition profiling'. This means using genetic tests to predict the chances that someone will contract

serious illnesses like heart disease, cancer or mental illness, and then offering either lifestyle advice or medication with the aim of preventing the predicted illness. The benefits for the companies are that they can not only sell genetic tests but also expand the drug market (to those whom they have predicted as being at high risk of future illness).

Many claim that knowledge of genetic predisposition or susceptibility to major diseases heralds the prospect of shifting medical practice from its current emphasis on diagnosis and treatment to an exciting new era of prediction and prevention. For example, the European Commission has stated that: "A *[genetic] revolution in health-care is anticipated through a move towards more prevention rather than cure...*"<sup>2</sup>.

However, there are concerns that for many people predictive medicine could do more harm than good - by worrying them and giving them medicines that they do not need - perhaps with unpleasant or even fatal side effects. This marketing strategy is sometimes known as 'pills for the healthy ill'. It could also take resources away from treating the sick and from preventing the underlying causes of many diseases (such as poor diets, lack of exercise, smoking and pollution).

## How accurate will the predictions be?

If used with care, genetic tests can help diagnose inherited genetic diseases caused by problems with a single gene (such as cystic fibrosis) and help early treatment. Some forms of heart disease and cancer are inherited as single-gene diseases and some people in these high-risk families may also benefit from access to genetic tests. Around 5% of cancers are thought to be of this type, although having the faulty gene still does not necessarily mean someone will get the disease<sup>3</sup>. However, more tests for genetic susceptibility to the common

forms of complex diseases such as cancer, heart disease and diabetes are being developed and an increased range of such tests is anticipated.

Common, complex diseases in the wider population are not usually inherited. They have many different causes including lifestyle and environment. A genetic test can only indicate a susceptibility to the disease with no certainty of the illness developing. Despite much research, genetic susceptibility to complex diseases such as heart disease, cancer and obesity has proved difficult to identify, with many poorly reproducible results. Except in a small percentage of cases, genes are poor predictors of future health<sup>4</sup>. Many people with the 'high risk' form of the gene will not get the disease and many people without it will. For complex diseases, there is a real prospect of statistical studies identifying false associations between genes and the risk of future illness. A spurious link between a gene and a disease is often found in the first scientific study published, or the importance of the gene is exaggerated<sup>5</sup>.

For both heart disease and cancer, many different genetic mutations in many different genes may each play a minor role, and a single genetic trait may predispose to one disease whilst being protective for another. Multiple environmental factors – particularly smoking, diet and exercise, and often infection and pollution – will also play a role and are usually more important than genetic make-up<sup>6</sup>. This makes it extremely difficult to quantify the risk using a genetic test. In addition, the more tests an individual undergoes, the more likely it is that some results will be false negatives or false positives<sup>7</sup>. In contrast, a single environmental exposure may contribute to many diseases and eliminating one exposure - such as smoking - can therefore reduce a large proportion of disease.

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### **Which companies are involved?**

*“Other [genetic] screens are in development... Next year, we want to introduce one focused on the skin, which would tell customers how sensitive their skin is to sunlight, chemicals and oxidative stress, how prone they are to skin cancer, and what they can do about it. We're also looking at metabolisms important for people with depression, and how they can be affected by diet and medicines.”*

Chris Martin, Chief Executive, Sciona Ltd<sup>8</sup>.

Large pharmaceutical companies and small biotechnology companies are both researching and developing genetic tests (see Table 1). Alliances between the two types of company are common.

GlaxoSmithKline has described the integration of diagnostics and pharmaceuticals - including genetic prediction as well as diagnosis of disease - as an area of significant added value for healthcare companies<sup>13</sup>. In 1997, it set up a joint venture with Incyte to develop and market genetic tests. Each still has a 20% stake in the company, Diadexus, that has inherited SmithKline's exclusive rights to diagnostic patents for a protein which has been associated with an increased risk of heart disease.

Abbott Laboratories, Roche and Millennium are also pursuing new genetic tests in the hope of transforming the stagnant \$20 billion diagnostics business into a growth industry. In 1997, Roche paid \$11 billion to become the world leader in diagnostic test kits, with 17% of the market. In July 2001, Roche signed a five-year alliance with DeCode Genetics to develop and market genetic tests for major diseases. DeCode Genetics is using its Icelandic biobank (a genetic

database) to focus on tests for genetic susceptibility to a range of diseases as a means of generating near-term revenue. DeCode Genetics already claims to have identified genes contributing to obesity, stroke and schizophrenia.

**Table 1: The main companies involved in developing and marketing genetic tests**<sup>9,10,11,12</sup>

Planning to sell genetic test kits	Identifying genes	Selling genetic tests via the Internet
Roche	Orchid Biosciences	Sciona
Abbott	DiaDexus	DNA Dynamics Inc
Bayer	Sequenom	D-FWMall.com
Johnson & Johnson	Quest Diagnostics	GeneLex Corp
Beckman Dickinson	Axis Shield	HealthScreen America
Qiagen	Promega	GeneLink Inc
Digene	Myriad Genetics	Bioheart Inc
Cytocell	Millenium	
Visible Genetics	Genomics Collaborative	
Celera Diagnostics	Exact Laboratories	
Gen-Probe	Virologic	
	Applied Biosystems	
	Affymetrix	
	DeCode	
	Genset	
	Third Wave Technologies	
	Oxagen	

**Companies are already selling genetic tests directly to the public but such sales are not regulated**

Genetic tests are expected to reach the market much more quickly than new medicines<sup>14</sup>. The US company, Myriad Genetics, is already generating revenue from genetic tests for the BRCA1 and BRCA2 genes that have been associated with genetic susceptibility to familial breast cancer. These tests have generated considerable controversy because of the patenting of these genes by Myriad and the high costs of the tests (around \$2500). Many argue that the patents create a monopoly, seriously impede or prevent the further use of existing and more effective tests, and impede research and development<sup>15</sup>.

Other companies are already selling genetic tests directly to the public but such sales are not regulated. The UK company Sciona describes itself as: *“the first company in the world to offer genetic screening that will empower the individual to take actions to improve their health and well-being”* by combining genetic testing with advice on diet<sup>16</sup>. The tests are now being sold on the high street via eleven Body Shop stores, as well as on the Internet. Sciona’s tests have been criticised as meaningless and unethical by leading scientists<sup>17</sup> and GeneWatch UK has called on the Body Shop to withdraw them from sale.

**Sciona’s genetic tests have been criticised as meaningless and unethical by leading scientists**

**Will genetic predictions lead to benefits to health?**

The pharmaceutical company, GlaxoSmithKline has identified predisposition profiling - *“the ability to assess an individual’s risk for a disease or diseases so that medicine can be given to prevent illness”* – as one key area of the new ‘predictive medicine’ and has argued that integrating genetic testing and pharmaceutical products will increase market size for pharmaceutical products and services<sup>13</sup>.

However, it is questionable whether targeting medicines at people who are genetically susceptible but do not yet show any symptoms (the ‘healthy ill’) in

this way would be safe and effective, except in high-risk families where the gene may be a good predictor of disease. In the wider population, one concern is that most of the people taking preventative medication on this basis would never have developed the disease. Most medications carry undesirable side-effects, some of which are serious or even potentially fatal. In contrast, population-based prevention measures (such as banning tobacco advertising or encouraging more healthy diets) carry a low likelihood of adverse effects and are also less expensive.

***People taking preventative medication may never have developed the disease***

Unlike most medicines, lifestyle changes such as stopping smoking, eating healthily and taking regular exercise have many benefits and protect against many different diseases. Some authors have suggested that a likely outcome of the genetic approach to disease prevention is that 'rich kids' will take large quantities of pills to try to avoid genetically predisposing risks without having to change their lifestyle<sup>18</sup>. This scenario would certainly be consistent with the strategies of the pharmaceutical companies who are seeking to increase the market for their products. However, by avoiding the need to change unhealthy lifestyles, this approach would lead to poorer health, even if there are no adverse side-effects from the medication.

The psychological impacts of genetic testing are also important and have been studied for single-gene inherited diseases, where counselling and the right to refuse a test (the right 'not to know') have been found to be important<sup>19</sup>. However, it is difficult to see how adequate, individual counselling can be given to the large proportion of the population likely to be identified as at high risk of common complex diseases, and how the highly uncertain risk predictions will be explained. Some people may be highly vulnerable to adverse psychological reactions to genetic predictions of stigmatised or feared conditions, such as mental illness and cancer.

There is also no current evidence to suggest that genetic information increases motivation or ability to change behaviour. Genetic information may even reduce motivation for some people, with some evidence that genetic tests can make a problem seem more worrying and less preventable than other types of test<sup>20</sup>. In other cases, motivation may increase, but the ability to address the problem may still be insufficient (for example, a genetic test may not help somebody to avoid pollution or overcome nicotine addiction). There is the potential to create a sense of fatalism in those who fail genetic tests and a sense of invulnerability in those who pass them.

***Many people who are not identified as genetically susceptible may be misled into believing they can safely adopt unhealthy lifestyles***

Focusing help and advice on those identified as genetically susceptible is also likely to mean that the majority of cases of common diseases will not be diagnosed. Many people at risk of heart disease or cancer who are not identified as genetically susceptible may be misled into believing they can safely adopt unhealthy lifestyles. Where medical interventions are appropriate and widely beneficial (such as using nicotine replacement therapy to stop smoking or providing folic acid supplements to prevent spina bifida), there is no evidence to suggest that limiting access to those identified as genetically susceptible would increase health benefits overall.

**Ignoring causes**

There is a danger that the underlying socio-economic or environmental causes of disease will be ignored in favour of a genetic approach to disease prevention. Some epidemiologists have argued that the genetic approach diverts limited resources, blames the victim and seldom assesses the relative importance of

modifiable social and behavioural factors. This can result in using more and more advanced technology to study more and more trivial issues while the major population causes of disease are ignored<sup>21</sup>.

Poverty is responsible for the most deaths worldwide and health inequalities are also of major significance within the UK and other European countries. Fatal heart disease in the UK is more than twice as common in Social Class V (the lowest class) as it is in Social Class I. Heart disease and cancer are strongly associated with the aggressive marketing of unhealthy diets, tobacco and alcohol and with reduced physical activity<sup>22</sup>. The variation in cancer incidence observed between different populations in the world is mainly a consequence of different lifestyle and environmental factors, which should be amenable to preventative interventions<sup>23</sup>. However, poorer groups are explicitly targeted by those marketing unhealthy products and are least likely to be reached by preventative measures<sup>24</sup>. Poor families are also more likely than those with higher incomes to live near polluting factories<sup>25</sup>.

Nearly two thirds of men and over half of women in England are now overweight or obese, and obesity is continuing to rise faster than in most other European countries. At the current rate of increase, more than one in four adults will be obese by 2010 and at a higher risk of a range of major health problems including heart disease and adult-onset diabetes. The cause is obviously not an increase in 'genes for obesity', but unhealthy diets and lack of exercise – problems which need tackling across Government departments, using measures to integrate healthy eating and exercise into daily life, particularly in schools<sup>26</sup>. Too much emphasis on susceptibility genes for obesity could lead to the underlying causes of the epidemic being ignored, and the growing sale of diet or anti-cholesterol pills to the genetically susceptible instead.

Asthma is the most common chronic disease in children and has been increasing in developed countries in the past few decades. Although the causes are disputed, environmental or lifestyle factors - outdoors or in the home - must underlie the increase. One recent study found a link between children playing sport outdoors in areas of high air pollution and the development of asthma<sup>27</sup>. Such problems cannot be tackled by hunting for susceptibility genes for asthma but require Government policies to cut pollution<sup>28</sup>.

Smokers are at an increased risk of more than 50 illnesses, of which 20 can be fatal. In countries where cigarette smoking has been common for several decades, such as the UK, about 90% of lung cancer, 15-20% of other cancers, 75% of chronic bronchitis and emphysema, and 25% of deaths from cardiovascular diseases at ages 35-69 years are attributable to tobacco<sup>29</sup>. Although genetic susceptibility may play a role in the development of some of these diseases, population-based measures to control tobacco marketing are likely to be both cheaper and more effective prevention measures than individual genetic testing for each smoking-related disease.

***Too much emphasis on susceptibility genes for obesity could lead to the underlying causes of the epidemic being ignored***

## The potential for stigma and genetic discrimination

*"Ethical considerations, and legal, are fundamental to the whole issue of genetic testing... The consequences for individuals with regard to insurance and employment are also of the greatest importance, together with the implications for stigma and discrimination."*

Expert Working Group to the NHS Executive and the Human Genetics Commission<sup>30</sup>.

**There are no laws in the UK to prevent employers from refusing someone a job because of poor genetic test results**

In the future, people may be required to reveal genetic predictions about their health to their insurers or employers, or even to their school. There is the real prospect of discrimination based on a person's genetic make-up. A 'genetic underclass' could develop, which is excluded from insurance and employment<sup>31</sup>.

A major concern is that genetic testing could be used to exclude those identified as genetically susceptible to hazardous substances from the workplace or from compensation rather than reducing or removing the hazard and improving the environment for all. This is a particular concern for diseases like cancer, which can be caused by many industrial chemicals and radiation, as employers may perceive genetic screening as a means of reducing liability<sup>32</sup>.

Although genetic testing is not currently widespread, dozens of cases of exclusion from insurance or employment on the grounds of genetic test results have already been reported in the US<sup>33,34</sup>. There are no laws in the UK to prevent employers from refusing someone a job because of poor genetic test results, and there is only a temporary moratorium on the use of most genetic test results to set insurance premiums. The Government has also not signed the Council of Europe's Convention on Human Rights and Biomedicine, which prohibits discrimination against people because of their genetic make-up.

### **The broader implications of widespread genetic testing**

*"The linkage of genetic and health information and the potential for using the [Biobank UK] database for a wide variety of analyses aimed at determining susceptibility to disease raises important issues about confidentiality, security of data and informed consent. These concerns were raised as recently as Monday by GeneWatch, and they were the subject of a debate in the House of Lords yesterday. The Government takes these concerns seriously and will not allow the work to proceed until they have been satisfactorily addressed."*

The Rt Hon Alan Milburn, Secretary of State for Health<sup>1</sup>.

**Companies undertaking genetic tests could patent people's genetic information without their knowledge or consent**

Any company, government or institution undertaking genetic tests can create a database that links people's samples, genetic make-up and lifestyle information (known as 'biobanks'). Biobanks raise many additional ethical issues, which the Government is currently considering in relation to the proposed national research project, Biobank UK<sup>35,36,37</sup>.

As well as the potential for genetic discrimination, issues include:

- the possibility that companies undertaking genetic tests will patent people's genetic information without their knowledge or consent;
- the possibility that companies will use genetic information to undertake research that people disagree with without their knowledge or consent;
- potential failures of strict privacy and confidentiality for genetic information, including potential access to the information by the police or the courts.

If biobanks are owned by commercial companies, genetic and lifestyle information may also be used to direct-market vitamin supplements, skin creams and medication, potentially to vulnerable individuals identified by the company as being at high risk following genetic testing.

## Conclusions

Without proper controls, genetic testing could be used to massively expand the drug market to healthy people identified as at high genetic risk. Many people could receive unnecessary medication and suffer the associated side effects. The underlying causes of heart disease and cancer, and current increases in obesity, asthma and adult-onset diabetes could be ignored, with serious implications for future health.

Genetic testing should only be used in carefully controlled circumstances where it is of proven benefit to health. Tests should not be sold over-the-counter in high street stores. It is essential that people are:

- fully informed about the implications of taking a genetic test before they do so;
- given accurate and up-to-date medical and scientific information about the results and their reliability, and proper medical advice;
- protected from potential misuse of their genetic information.

Genetic tests need urgent regulation by a statutory body to ensure their validity and usefulness, and laws must be put in place to ban genetic discrimination and control access to genetic information.

Genetic determinism (the over-emphasis of genetic factors in disease) must not detract from tackling the underlying causes of many major diseases, including health inequalities, poor diets, lack of exercise, smoking and pollution.

More detailed information on these issues is available in a recent report written by GeneWatch UK for the World Health Organisation<sup>38</sup>.

**Genetic tests need urgent regulation to ensure their validity and usefulness**

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