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Direct-to-consumer genetic testing

Foreword

The European Academies Science Advisory Council (EASAC) and the Federation of European Academies of Medicine (FEAM) are composed respectively of the national science and medical academies of the European Union (EU). They offer European science a collective voice, enabling the academies to collaborate in providing advice to European policy makers.

Mindful that the advent of new consumer genetic services is raising a raft of difficult scientific, regulatory and ethical questions, EASAC and FEAM set up a joint Working Group – their first collaborative venture of this kind – to review them. The outcome of this work is a list of recommendations to policy-makers in the European Commission, European Parliament and Council of Ministers, and to Member States in which parallel action may be necessary.

The Working Group's report, *Direct-to-consumer genetic testing for health-related purposes in the European Union* is available at www.easac.eu and www.feam.com.eu. The present document, a summary of the full report, offers readers a non-technical account of its principal content and conclusions.

Introduction

Order a kit from our online store. Register your kit, spit into the tube, and send it to the lab. Our certified lab analyzes your DNA in 2-3 weeks. Log in and start exploring your genome.

Website of US online genetic testing service

Genetic tests that would once have been available in only a handful of elite research institutions are now accessible to all through the Web for as little as a few hundred Euros. Direct-to-consumer genetic testing (DTC GT) is not only a reality, but one of concern to many doctors who are wary of seeing tests of this kind passing into the marketplace without proper regulation and supervision.

The genetics research that has made these tests possible reached a high point in public consciousness with the publication of the first draft of the make-up of the human genome in June 2000. This event sparked interest around the world. Scientists, it was suggested, would soon be able to identify the genes responsible for many diseases and, as a consequence, devise new interventions for detecting and curing or even preventing them. Gene therapies of various kinds would become routine.

While the content of these hopes was justified, the timescales that characterised many public expectations was not. The past decade has witnessed the discovery of many genes that cause disease or increase its risk, and these discoveries have led to the development of molecular diagnostic tests of considerable importance in preventing or managing diseases such as hereditary breast cancer. Advances in gene sequencing have made DNA analysis cheaper and faster. However, although DTC GT has become a reality, the range of diseases for which it is available is still limited, and the number of users relatively small.

DTC GT poses a variety of practical and ethical issues that have yet to be considered in detail. Even in countries where the issues themselves have been considered in detail, necessary regulation or legislation has seldom been implemented. At present, there is wide variation among Member States in the regulation of genetic services.

Credit: iStockphoto

DTC GT may create uncertainty.

There is now an important opportunity for evaluating the risks and benefits of these tests before arrangements and practices that are sub-optimal or ill-advised have had a chance to gain a significant foothold in the member countries of the EU. This is important because, although DTC GT does allow individuals increased choice and control, there are concerns about accuracy and usefulness, and it creates several risks. These include unrealistic expectations, anxiety, the possibility of misuse and a loss of privacy.

The aim of the joint EASAC–FEAM report is to provide the evidence needed to inform policy development at the EU level, and to achieve a good balance between the increased use of sound testing, and protection against irresponsible testing.

How does direct-to-consumer genetic testing work?

When first developed, tests designed to identify people with relatively uncommon variants of certain potentially disease-causing genes were administered by, and only available through, doctors and other registered providers of healthcare. Direct-to-consumer tests, by contrast,

are sold through advertisements or the internet. No doctor or other healthcare professional is necessarily involved.

The test kit is posted to consumers who themselves collect their own sample for analysis. This normally takes the form of a small quantity of saliva or a cheek swab. These are posted back to the supplier's laboratory where the subject's DNA is extracted and analysed for potentially troublesome variants of certain genes. The results are sent out by post or may be available from the company through a password-protected website. Some companies also provide genetic counselling to help consumers understand the findings and their significance.

Many companies, mainly outside the EU, now advertise and sell genetic tests directly to the public through the internet. For those consumers who prefer health professionals to be involved in test procedures, some companies concentrate on advertising directly to consumers rather than DTC sales, and seek to have healthcare professionals order the test on behalf of the patient. The professional can then interpret the test findings.

How much is DTC GT used?

At the moment, that is difficult to say. But, although there are regional differences across Europe, use of the internet for health-related purposes of all kinds is on the increase, and this will almost certainly include DTC GT. For the moment, although precise figures are not available, usage seems to remain fairly low.

The emergence of DTC GT exemplifies some of the wider changes taking place within healthcare. These include the growth of globalised industries; a loss of public deference to professional forms of medical authority; a familiarity with the internet; the increasing desire of many people to have more health information; and various pressures to exercise more personal choice and responsibility. Within the context of health systems, genetic testing for well-defined but relatively uncommon single-gene disorders has already found rapid acceptance. All these factors might suggest that DTC GT would have taken off more rapidly than it has.

Although there is evidence of public interest in DTC GT, the slow uptake may not be altogether surprising. The disorders that most commonly afflict us, from heart disease to cancer, are usually the result of variation not in one but in many genes, with each contributing only a small amount of genetic susceptibility. Moreover, they do not act in isolation but in concert with environmental or other non-genetic factors. So, in these common but complex disorders, the predictive importance to an individual of a genetic test is usually, by itself, severely limited.

Credit: David Parker/Science Photo Library

DNA fingerprinting, X-ray autoradiograph.

What uses do genetic tests have?

Genetic tests as a group, undertaken in connection with health, have a variety of uses. These include the following.

- Diagnostic testing when a clinician suspects that a patient has a particular condition, but needs to be sure.
- Presymptomatic testing when the patient has no discernible symptoms, but is known to be at risk of a late-onset disease.
- Carrier testing, used by genetic counsellors to find out if someone without symptoms nonetheless carries the gene that can cause a particular disease.
- Prenatal and pre-implantation genetic diagnosis of disorders in a foetus or embryo.
- Susceptibility testing, for predispositions to common diseases in which genes are only one of several or many causative factors.
- Pharmacogenetic testing for predicting a patient's response – beneficial or otherwise – to a drug.
- As part of a genetic screening programme targeted at a population group such as pregnant women or people of a specific ethnicity.

Many of these tests are available through the health services of many EU countries. But, as will become clear, few of them are suitable for DTC GT.

Advantages and drawbacks of DTC GT

DTC GT, it is said, empowers people and gives them a feeling of personal control in improving the quality of their lives. It allows the rapid diagnosis of disorders when public or other private healthcare resources are in short supply. It allows earlier intervention. In addition, it alerts relatives to important genetic conditions of which they may be unaware.

Credit: Laguna Design/Science Photo Library

Model of a DNA double helix.

The disadvantages of DTC GT include users' lack of preparation for results and what to do about them if there is no individualised medical supervision and genetic counselling. The cost of testing is borne by the individual, and may therefore exacerbate social inequity. Scarce public health resources may be used in unnecessary follow-up. The information itself may be of little real use, or may induce anxiety, for example if no beneficial treatment or other intervention is possible. Relatives may find themselves alerted to health risks of which they would have preferred to have no knowledge. And test results may impart an unwarranted sense of reassurance.

On the whole, there is little empirical evidence to support either the advantages or disadvantages listed. However, clinical geneticists in the EU have expressed their concern that many consumers do not understand the test results they are given. A patient's own estimate of risk, for example, is often not what the clinician believes the patient to have understood.

Moreover, there is little evidence that information about health risks derived from DTC GT leads to changes in behaviour, although there may be some effect on peoples' intentions to make such a change. There is a clear need for more evidence about the impact on health outcomes of all genetic testing, whether in the clinic or at home.

How far are these tests already regulated?

The picture varies greatly across Europe, with Germany currently having the strictest national legislation. Its Genetic Diagnostics Act regulates both predictive and diagnostic genetic testing. It also requires an involvement of physicians that effectively rules out some DTC GT services. Several European bioethics groups have reviewed the issue of DTC GT, and so has the UK Government's advisory body, the Human Genetics Commission. Its *Common Framework of Principles for DTC Genetic Testing Services*, a system of voluntary regulation, sets out not only to inform UK policy but also to guide the development of other national codes of practice. It covers a broad range of issues from consent and data protection to truth in marketing, scientific rigour and balanced interpretation. However, until it is implemented, there is no way of knowing how effective it might prove.

At the regulatory level of the European Union, novel tests are governed by the Commission's Directive 98/79/EC on *In Vitro Diagnostic Medical Devices*. This requires a test provider to show evidence of laboratory validity, but not of clinical validity or usefulness. Most diagnostic tests are classified as low risk; as such, they are exempt from an independent pre-market review of the evidence on which they are based. Moreover, this Directive has been interpreted as covering only genetic tests that have a medical purpose; some putative DTC GT might be interpreted as outside its scope.

Calls have already been made for the Directive to be revised. In response, the EU Directorate-General for Health and Consumers (DG Sanco) organised a consultation on the issue. Most respondents backed the creation of additional restrictions for DTC GT, and many mentioned the importance of appropriate medical intervention and counselling. Some called for a ban on the direct sale of tests. Any revision of the Directive is likely to have a significant impact not only on DTC GT but on all genetic testing.

Active consideration of the regulations governing DTC GT is also underway in several non-EU countries. In June 2010, for example, the US Food and Drug Administration announced its intention to ensure analytical and clinical accuracy by treating DTC GT as medical devices

requiring pre-market review and approval. Australia will try to control DTC GT as part of a wider revision of its medical device regulations.

Before framing recommendations on regulation, the experts from EASAC and FEAM made a detailed examination of the value of each type of currently available test with a view to deciding which might safely be made available on a direct-to-consumers basis, and which might not.

Which tests should not be offered DTC GT?

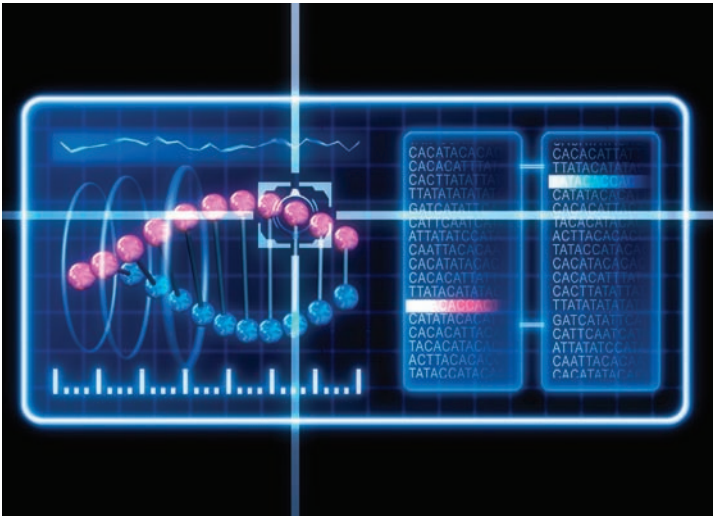
Monogenic and other high-penetrance gene disorders

Diseases resulting from abnormalities in a single gene are described as "monogenic". They include sickle cell anaemia, cystic fibrosis and Huntington's disease. A gene is said to be highly penetrant if most or all the people who possess it are likely to develop the condition for which it is responsible.

EASAC and FEAM recommend that testing individuals for high-penetrance genes associated with serious diseases, including monogenic disorders, should be excluded from the services offered by DTC GT companies. In practice it can be difficult to define the boundary between high- and low-penetrance genes. So, pragmatically, they suggest discouraging the direct-to-consumer use of any tests that health services currently use for investigating serious (including monogenic) disorders. This suggestion is based on the greater need for individual medical supervision and genetic counselling when using tests for this group of conditions.

Prenatal testing

Research on foetal genetic material found in maternal blood samples has opened up new options in prenatal screening and diagnosis. And the range of disorders in the foetus that may be detected by this means will continue to increase. However, there are some contentious issues including the relevance of such tests, and their implications for reproductive choice. They should therefore be offered only in the context of clinical obstetric and genetic services, and not as DTC GT.



Credit: Pasieka/Science Photo Library

Conceptual image of genetic screening.

Preconception carrier screening

It would be difficult for DTC GT services to provide the pre- and post-test information and counselling that should be part of preconception carrier testing. Ideally this should be conducted in the public sector; but if the range of carrier tests available there is insufficient, DTC GT services should follow the guidance on information and quality control that applies to tests used in healthcare. Carrier testing in children should not be included in DTC GT services.

Nutrigenomics

Nutrigenomics is the science of the interaction between genes and nutrients. It suggests that an individual's diet should be matched to their genetic make up. Although nutrigenomic tests can be categorised as providing health information, they are often poorly validated and may even be meaningless and misleading. One particular concern here is the sale by the test suppliers of nutrient products to tackle claimed deficiencies. These may be costly and of little or no value. Unless and until these tests can be properly validated, they should not be offered as part of DTC GT.

Pharmacogenetics

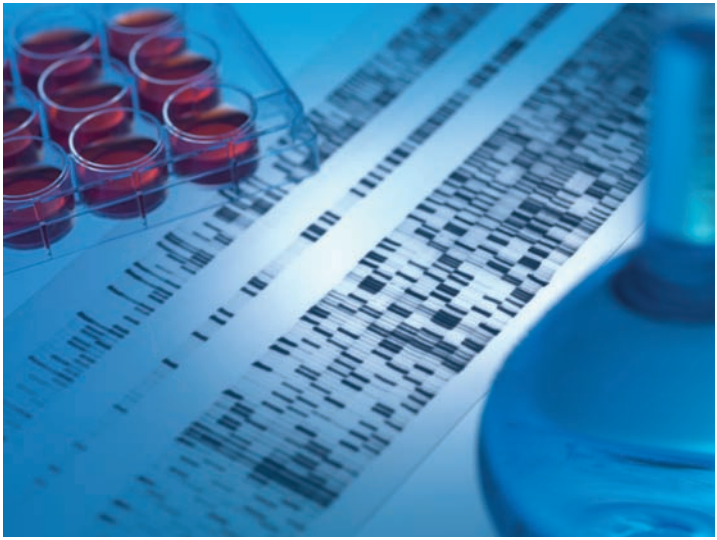
Pharmacogenetic testing identifies individual differences in how well or badly people respond to particular drugs. But reviews of ethical and social issues associated with pharmacogenetic testing have revealed that making them available through DTC GT services would create problems. Patients might be tempted, for example, to adjust their dose of a prescribed medicine without seeking medical supervision.

More generally, policy-makers should recognise that it would be inconsistent to introduce the regulation of gene testing if other tests that yield information on inherited disorders are not equivalently regulated. Any adverse consequences that may arise would stem from a test's findings, not from the fact that it relies on investigating genes as opposed to some other factor. That said, EASAC and FEAM acknowledge that gene testing is making rapid advances, and that some genetic information has attributes that merit special consideration. For example, findings may have implications for relatives who did not themselves wish to be tested; and because a genetic test need be performed only once in a lifetime, it must be of exceptionally high quality.

How should DTC GT be managed?

EASAC and FEAM have set out some general principles for managing the health-related uses of DTC GT. First, they believe that tests for high penetrance genes, including monogenic disorders, should generally be provided as part of a country's clinical genetic services. Where DTC GT is judged acceptable for health testing purposes, it should be regulated – as is genetic testing in other settings – by the EC Directive *In Vitro Diagnostic Medical Devices*. But they believe this Directive needs substantial change (see below).

Susceptibility testing for complex disorders should be based on scientifically validated claims about the link between the genes and the disease. Consumers will need to be provided with clear and honest information, including advice on who ought *not* to use DTC GT services. The quality assurance underpinning the test should apply not only to analytical work in the laboratory but also to the professional interpretation of results and the provision of appropriate counselling. This latter is especially important in the context of common disorders



Credit: Tek Image/Science Photo Library

Genetic research.

in which several or many genes and also other non-genetic factors may all play a part. Companies supplying the tests should have a named person taking responsibility for their service. DTC testing of samples from minors, pregnant women and third parties should not be allowed.

When DTC GT companies wish to use data for research, they should seek specific consent to do so, explain what the research is for, and say what will happen to samples and information about them in the event of a change of company ownership.

It would also be desirable to estimate any cost of DTC GT to health systems and to health insurers, and to anticipate any other implications that such a service might have for public health and health policy. Testing might, for example, require resources in interpreting and following up results. International discussion and collaboration will be required to ensure that global internet provision is regulated, and supported by cross-border co-operation.

How should the EC Directive on *In Vitro Diagnostic Medical Devices* be revised?

Extensively, say EASAC and FEAM. They see significant scope for improving the evidence-based assessment of benefit and risk underpinning the Directive. They add that this should apply to all genetic testing for medical purposes, not just DTC GT. They put forward many suggestions for reform. The Commission should, for example, consider introducing an independent review of the claims made for tests used at the upper end of the spectrum of risk to consumers. The Commission should also consider issues raised by the need for confidentiality of personal data.

EASAC and FEAM comment that the use of the internet to access DTC GT is often seen as creating practical difficulties for legal jurisdiction in terms of geographical location. However, they go on to argue that where the laboratory test originates does not matter; if a test is used in the EU it must conform to EU standards. If a company based abroad ignores these standards, then Member State authorities can still seize test kit material at their borders.

While waiting for the development of a public policy on all these matters it would be prudent for DTC GT companies to work together to develop and implement an industry-wide code of practice. The principles listed by the UK Human Genetics Commission (see above) would provide a suitable starting point for such a code.

What else?

EASAC and FEAM favour the creation of a registry of the availability, validity and usefulness of genetic tests. There is also a need for more education of medical and other health professionals. Many primary care physicians lack confidence in their ability to perform basic genetic health-related tasks. This should be accompanied by more education of the public in understanding what DTC systems have to offer. Of particular importance is the difference between testing for monogenic as opposed to complex disorders.

Technological advance may soon make it easier and cheaper to sequence an entire genome than to search out a particular group of genes. This may reveal information about, for example, future disease risks that was not requested by the consumer, and not anticipated. Arrangements will need to be in place for dealing with the possibly distressing consequences of this unexpected knowledge.

On a global scale, EU policy will need to be co-ordinated with that developed in other regions of the world. The World Health Organization would be the obvious body through which to pursue such co-ordination.

Conclusion

EASAC and FEAM conclude that, on the whole, DTC GT currently has little clinical value and may, on occasion, be harmful. At present, they would therefore not encourage EU citizens to use DTC GT, particularly if citizens have symptoms of any kind or know themselves to be at increased risk of a disease. All varieties of genetic testing require appropriate professional advice.

More generally, EASAC and FEAM would like to see the European Commission, the European Parliament and the Council of Ministers each play their role in bringing about an improvement in the current regulatory framework governing all genetic testing in the EU. Delay will serve only to exacerbate the existing problems.

FEAM, the Federation of European Academies of Medicine, promotes cooperation between the national Academies of Medicine and extends to the political and administrative authorities of the European Union the advisory role that the Academies exercise in their own countries on matters concerning medical sciences and public health. As an umbrella organization, it brings together national Academies of fourteen European member states (Austria, Belgium, Czech Republic, France, Germany, Greece, Hungary, Ireland, Italy, Portugal, the Netherlands, Romania, Spain and the United Kingdom) and aims to reflect the European diversity by seeking the involvement of additional Academies and experts in its scientific activities and by collaborating with other networks on scientific matters of common interest. FEAM is independent from vested interests (commercial, ideological, political) and provides collective and evidence-based advice on topical medical issues with a European dimension.

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EASAC – the European Academies Science Advisory Council – is formed by the national science academies of the EU Member States to enable them to collaborate with each other in providing advice to European policy-makers. It thus provides a means for the collective voice of European science to be heard.

Through EASAC, the academies work together to provide independent, expert, evidence-based advice about the scientific aspects of public policy to those who make or influence policy within the European institutions. Drawing on the memberships and networks of the academies, EASAC accesses the best of European science in carrying out its work. Its views are vigorously independent of commercial or political bias, and it is open and transparent in its processes. EASAC aims to deliver advice that is comprehensible, relevant and timely.

The EASAC Council has 28 individual members and is supported by a professional secretariat based at the Leopoldina, the German National Academy of Sciences, in Halle (Saale). EASAC also has an office in Brussels, at the Royal Belgian Academies of Science and the Arts.

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