The Science and Technology Committee inquiry into commercial genomics

Response from the Christian Medical Fellowship

The Christian Medical Fellowship (CMF) was founded in 1949 and is an interdenominational organisation with over 5,000 British doctor members in all branches of medicine, and around 1,000 medical student members. We are the UK's largest faith-based group of health professionals. A registered charity, we are linked to about 80 similar national bodies in other countries throughout the world.

1. The health or other benefits that consumers can derive from using commercially available genomic testing

Commercial genomic testing is limited in the benefits it can provide; arguably, those benefits are outweighed by the confusion and anxiety the tests may provoke in this setting.

Unlike the 100,000 Genomes Project, an NHS initiative run by Genomics England, in which a person's genome is fully sequenced, commercial genomic testing generally looks at only short lengths of a person's DNA. If that person's interest is simply to understand their personal ancestry, then such testing may not disappoint. But if they were seduced by the hyperbole used in promotional advertising into thinking that the test would provide a reliable indicator of present and future health, they may well be disappointed and possibly confused, alarmed or misled.

In a medical setting, genetic tests can be carried out for various reasons (see amplified list under point number 3. below), including:

- To help diagnose a suspected genetic condition;
- To identify the specific underlying genetic change causing a genetic condition;
- To help determine the chance of developing a genetic condition in the future;
- To determine whether someone is a carrier of a genetic condition;
- To clarify the chance of passing a genetic condition on to children;
- To find out whether a developing baby or embryo has a specific genetic condition.[1]

However, expert health care professionals and laboratories are essential to the carrying out, reporting and interpreting of these tests. CMF's concern is that commercial genomic testing companies may purport to be fit for such purposes but lack the necessary expertise to be able to deliver.

Big Business exploits the 'worried well'

Home-testing kits are easy to acquire through a host of websites, and easy to use. They are proving to be very big business, with a global market estimated to be worth around £7.7bn by 2022. They appeal to the increasingly health and fitness conscious, not to say narcissistic, populations of the developed world. As such, they are most likely to be bought by those already fitter than average

[1] http://www.geneticdisordersuk.org/aboutgeneticdisorders/genetictesting

people, looking to track the results of their dietary and exercise regimes – the latest fad to feed their obsession.

The tests may also appeal to those who are starting to worry about their long-term health prospects, having never made 'wellness' a priority in earlier years. The advertising manipulates their anxiety towards the purchase of the test. Depending on the 'package' they have bought, when the results come back they may be faced with a bewildering array of information about genetic variants and risk factors that, individually, have a very low chance of predicting specific health risks, as there are too many variables. The science is too immature to make these results of any clinical use but, without access to experts to interpret the data many are left perplexed, anxious and fearful.

Some companies have genetic counsellors or other health care professionals available to answer questions but for the most part clients are encouraged to 'seek further advice from your GP if you are concerned'.

Of course, the tests come with all sorts of disclaimers and caveats, among them that the tests are 'not diagnostic'. The 'helpful and reassuring advice' that the products promise is little more than generic advice about sensible eating, sufficient exercise, weight control and the like, information available freely from GP surgeries up and down the land.

Dr Margaret McCartney, a GP and author of *The Patient Paradox,* is quoted by the Guardian's Barbara Ellen[2]: *'People are given very dramatic reasons to have these tests – it could help save your life, it could help improve the quality of your life – but where is the evidence –base to support such claims? There's no evidence that says doing these tests makes people become healthier.'* Dr McCartney goes on to say that anxious people often contact her, saying they wished they hadn't done the tests. *'These companies often say that it's worth it for the helpful advice. But I can give you really good advice right now without seeing a single test result: be active, have lots of social networks, do work you enjoy, try not to smoke or drink too much, don't be overweight or underweight, eat lots of fresh fruit and vegetables. Nobody needs to get tests done to get that kind of basic lifestyle advice.'*

CMF believes there is a risk that the 'worried well' may receive a mass of complex data they cannot understand and possibly suffer unfounded anxieties, or a mass of data amounting to little more than common sense for which they have paid generously.

2. The industrial strategy opportunity for genomics within the UK biotechnology sector, and how the Government could support UK growth (including for exports)

No Comment

3. The extent to which currently available genomic sequencing and interpretation can provide accurate and unambiguous health results, for healthy and ill sections of the population

[2] https://www.theguardian.com/science/2017/jul/23/what-i-learned-from-home-dna-test-kits-are-they-accurate-or-worthwhile

It is accepted that genomic sequencing and its interpretation is a branch of science still in its infancy, though with immense potential. In the hands of medical specialists, it can be used:

- to identify or exclude a specific genetic diagnosis when a genetic condition is suspected;
- to see whether a healthy individual with a family history of a certain genetic condition is a carrier of that condition;
- to test if someone with a genetic condition in their family, for example Huntington's disease, is likely to develop it themselves later in life;
- to carry out prenatal genetic tests, either by amniocentesis or by chorionic villus sampling, or by examining fragments of fetal DNA that are present in the mother's circulation, to determine the likelihood of chromosomal trisomies such as Down Syndrome (NIPT), or diagnose some single gene disorders inherited from the father or arising *de novo* (NIPD);
- to exclude a sex-linked genetic condition through examination of circulating fetal DNA for Y chromosome material;
- to undertake preimplantation genetic diagnosis (PGD) in IVF to avoid implanting an embryo with a genetic condition

Diagnostic genetic tests are not yet available for all genetic conditions, nor is it yet possible to do carrier testing for all genetic conditions. However, the range of testing is constantly enlarging. This is a complex field and interpreting the results is a highly nuanced skill even in the hands of trained personnel. Distributors of commercial testing-kits should neither over-simplify their benefits nor over-promise their clients through online advertising. CMF would like to see such kits clearly distinguished from legitimate science and medicine; they belong in the lifestyle-extra zone.

One example of blurred boundaries between the medical and the commercial zones concerns telomeres. Shortening in the length of telomeres - the protective fragments at each end of a chromosome – is associated with age. Telomere measurement is sometimes offered as part of the package on commercial genomic test sites but, says Bill Newman, professor of translational genomic medicine in the Manchester Centre for Genomic Medicine at the University of Manchester, '*there's no evidence whatsoever that measuring a person's telomeres gives any indication about their health – or beauty, intelligence, or anything else that might be listed on these sites*.'[3]

Newman goes on to say that '*there's a basic lack of 'literacy' and understanding about genetic testing, among the public and even among other health professionals. People are given false reassurances or made to panic (just because you have certain genetic variants, it doesn't mean that you will develop a particular condition).'* Most people will not know how to interpret phrases like 'higher risk' or 'probability factor' and are left to imagine the worst without someone to interpret their results.

4. The counselling or other support offered for those receiving, or considering asking for, commercial genomic test results, and whether this is to the standard required;

As mentioned above, some commercial sites offer access to genetic 'counselling' or other healthcare professionals, though presumably at a price. We cannot comment on the standard of support or advice that might be given in such settings. In practice, most commercial sites do not provide such backup and customers are left to navigate their way through technical and often confusion language

[3] https://www.theguardian.com/science/2017/jul/23/what-i-learned-from-home-dna-test-kits-are-they-accurate-or-worthwhile

without help. 'If you have concerns, please seek the help of your GP' is a commonly-used get-out clause.

In the case of NIPT (see below, under point 5) the Nuffield Council on Bioethics, in their 2017 report,[4] highlighted the need for trained counsellors, but they remain few and far between even in the NHS. Some courses to train already stretched midwives have been offered,[5] but this has hardly plugged the gap. ARC, Antenatal Results and Choices, are offered as a solution. The Nuffield report profiled them as non-directive in the counsel they provide. However, the facts call this into question. They have not collaborated with Down syndrome charities. Previously known as SAFTA, Support After Termination for Abnormality,[6] they received donations from manufacturers of NIPT totalling £11,500 from 2014-2017 and offer no support groups for women who decide to continue their pregnancy.

There continues to be no national care pathway for women wishing to continue their pregnancy following a high chance or positive result from testing (6.20, Nuffield Report). This represents a form of 'coercion by omission' – the assumption is that women carrying affected children will choose to abort and resources are applied accordingly. But some women will choose to continue their pregnancies and neither NICE nor the Royal College of Obstetricians and Gynaecologists (RCOG) have prioritised this in the last two years. What little guidance there is remains buried in RCOG guidelines entitled Termination of Pregnancy for Fetal abnormality, published in 2010.[7] Nuffield strongly suggested that the name of this guidance should be changed immediately to reflect the inclusion of continuation of pregnancy guidance and that that section should be substantially expanded or separate guidelines should be produced. CMF strongly concurs.

We draw attention to the findings of the Parliamentary Inquiry into Abortion on the Grounds of Disability[8] that *'there should be best practice guidelines for training and practice for professionals in counselling families facing a diagnosis of fetal disability'* (recommendation 9) and also that *'there needs to be improved, positive and consistent care and support for parents who choose to continue with their pregnancy from across the medical profession'* (recommendation 13).

CMF calls for an NHS helpline staffed by trained genetic counsellors to help patients process all the prenatal genetic information that is now available, as called for by the Down Syndrome Association.[9] The need was recently demonstrated, by a case[10] in which a woman was given a high chance result from a private clinic for Turners syndrome, with all the associated worry and suggestions of invasive testing, only for it to emerge after much research that her result was approximately only 40 percent likely to be correct. A trained counsellor, able to interpret results and explain options in a non-directive way, would save a great deal of anguish.

Many commentators on 'direct-to-consumer' genetic risk information have raised concerns that giving results to individuals with insufficient knowledge and training in genomics may harm consumers, the health care system, and society. In response, several commercial laboratories have shifted to more traditional 'direct-to-provider' (DTP) marketing strategies, repositioning clinicians as

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[4] http://nuffieldbioethics.org/wp-content/uploads/NIPT-ethical-issues-full-report.pdf:6,30, 6.36

[5] https://phescreening.blog.gov.uk/2018/01/15/genetic-counselling-training-for-screening-midwives-at-cambridge-university/

[6] https://www.arc-uk.org/about-arc/history

[7] https://www.rcog.org.uk/en/guidelines-research-services/guidelines/termination-of-pregnancy-for-fetal-abnormality-in-england-scotland-and-wales/

[8] https://dontscreenusout.org/wp-content/uploads/2016/02/Abortion-and-Disability-Report-17-7-13.pdf

[9] https://www.downs-syndrome.org.uk/news/dsaupdatenovember2018/.

[10] https://www.bbc.co.uk/news/stories-47150878

the intended recipients of advertising of laboratory services and as gatekeepers to personal genomic information. However, a 2014 study[11] by McGowan *et al* in North America found that these clinicians relied on the expertise of the commercial laboratories, not having the ability to critically evaluate the knowledge or assess risks themselves. The study concluded that, because commercial laboratories are the entities with the most 'skin in the game' financially, these laboratories are not the most appropriate entities to hold and control genomic information and its interpretation.

5. The potential benefits and risks for the NHS that arise from the increasing availability of commercial genomic testing;

It is hard to see any benefits for the NHS arising from commercial genomic testing apart from the reinforcement of general advice on healthy lifestyles. At present, the people most likely to invest in commercial testing are those who already take their health and fitness very seriously, and so any extra benefit to the overall health of the nation is likely to be marginal.

The downside for the NHS is very much clearer to see. The fundamental problem is that the reports generated by commercial testing raise more questions than they answer. Results are frequently vague; terms are technical and lack adequate explanation; clients are left uncertain as to the implications of their various genetic variants and disease predispositions. At the very least, people may be confused; frequently they may be needlessly frightened and worried; at worst, they may be seriously misled. Naturally, people need to talk to someone they trust, someone who can interpret the results for them. For most people, that 'someone' will be their GP. The additional load on NHS resources is not hard to predict.

Dr McCartney again: *'The companies make their profits and walk away, letting the NHS sort out all the fallout, the push-back, from the test results, in a way I find absurd. Why should the NHS have to prop up the problems that these companies create?'*

NIPT

As the scope of commercial testing widens, we are particularly concerned about it being used as non-invasive prenatal testing (NIPT) to screen maternal blood for foetal DNA (cfDNA analysis). We see several potential dangers in this:

- Misinformation continues to abound around what NIPT is and what it can do (6.8, Nuffield report). NIPT is a *screening* test, more accurate than the so-called combined teat in suggesting risk but not a replacement for an invasive *diagnostic* test such as amniocentesis. Further, tests are evaluated by different measures and the difference between these appears to elude manufacturers, clinics, midwives, and the media. 'Sensitivity' measures the percentage of all affected fetuses in a population that the test will pick up. But it is the Positive Predictive Value (PPV) of a result that indicates the accuracy of the statistical result, ie, how likely a high chance result is to be correct.
  It is claimed that NIPT will pick up 99% of babies in some populations, although the bias of available studies has been questioned by the Warwick systematic reviewers.[12] However, a

[11] PLoS One. 2014; 9(9): e108484.
[12] http://wrap.warwick.ac.uk/76523/.

pregnant woman with a high chance risk result may have a PPV ('true positive') as low as 46%, depending on her age and combined screening test results.
CMF is concerned that without skilled personnel available to interpret the results of commercial NIPT testing, needless anxiety will be generated and lead to knee-jerk decisions to abort, with the loss, sometimes, of normal foetuses.

- Sex selection. The International Bioethics Committee of UNESCO (IBC), sounding their concerns over the test, has said that: *'Another risk lies in the cultural prejudices of preferring a child of the male sex, the sex of the baby being one of the characteristics that can obviously be discovered by NIPT. As this test can be carried out at a very early stage of the pregnancy it would be difficult, even impossible for doctors to forbid the communicating of sex to the parents, and especially at a time when many countries have liberalised abortion. This could lead to a selection based on sex, which is against ethical values of equality and non-discrimination.'*[13]
- In theory, a positive NIPT screening result, followed by a diagnostic invasive test that confirms trisomy (Down, Patau or Edwards Syndromes), enables parents to prepare for the arrival of a child with special needs. The availability of time for reflection, qualified counselling and support, written and online resources and the opportunity to meet with parents of children with trisomy-related disabilities as well as the children themselves, are all helpful in this.[14] In reality, however, such parents are unlikely to receive pre-test information and counselling in a commercial setting. They receive results outlining all manner of variable predictive risks faced by their babies but do not have the context in which to discuss, assess and weigh the relevance of those results. This increases anxiety further and makes abortion a more likely outcome, sometimes even without confirmatory evidence of trisomy. Inevitably, it increases increase pressure on NHS resources as those with positive cfDNA results seek confirmatory invasive tests (amniocentesis or chorionic villus sampling), not offered as part of the commercial package.
- The intention is for the NHS gradually to roll out NIPT as a screening procedure. Even without the added number of positive cfDNA tests from the commercial sector, the resulting increased rate of discovery of babies affected by Down Syndrome and other trisomies is predicted to lead to an overall increase in abortion numbers and a projected decline of 13% reported live births of babies with trisomies,[15] – a figure that can only increase if referrals from the commercial sector are added in. Healthcare professionals will be enabling a kind of informal eugenics, which will raise issues of conscience for many.
- Commercial NIPT testing serves to foster in society the notion that only the (genetically) perfect, or those who reach a certain arbitrary minimal standard, are acceptable and that it is socially desirable to prevent people with some or all disabilities from being born. The International Bioethics Committee comments: *'The widespread use of genetic screening and in particular of NIPT may foster a culture of "perfectionism" or "zero defect" and even renew some eugenic trends, with the consequence that it could become more and more difficult to accept imperfection and disability as a part of normal human life and a component of the*

[13] 'Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights', October 02nd 2015: http://unesdoc.unesco.org/images/0023/002332/233258e.pdf
[14] Parens E and Asch A. The Disability Rights Critique of Prenatal Genetic Testing: Reflections and Recommendations. Hastings Center Report 1999; 29(5): S1-S22
[15] http://www.binocar.org/content/annrep2013_FINAL_nologo.pdf

diversity we are all called on to acknowledge and respect.'[16] CMF believes that every human person has equal intrinsic value and is worthy of respect and protection in law, regardless of disability.

- WHO criteria governing screening protocols include the requirement that: 'there should be treatment for the condition being screened'.[17] With cases of trisomies, prenatal screening tests are carried out not to identify individuals with special needs, in order that they may be more effectively treated, but with the expectation of eliminating them from the population. This type of screening offers no benefit to the foetus being screened and results in collateral damage in that unaffected foetuses may also die from inadvertent miscarriage. We submit that this is contrary to the Hippocratic Oath,[18] the Declaration of Geneva[19] and to the general strategy of medicine. This is true, whether the tests are part of NHS strategy or provided in a commercial setting.

6. What data obtained from genomic testing could be used for and if sufficient protection is in place for consumers using commercial genomic tests

At present, the personal data, or 'bioinformatics', emerging from most direct-to-consumer commercial genomic testing is limited because only short stretches of DNA are examined. Greater scope and depth of testing will follow quickly and so it is important to put in place now safeguards to protect such data from being 'sold on' to other interested bodies, such as insurance companies, mortgage providers, marketing companies and the like.

Indefinite retention or 'recycling' of genetic data and 'profiling' should be unlawful. Current loopholes in the law that permit the feedback of profiling for 'research' purposes, without the knowledge and permission of the client, to be used for commercial purposes, must be closed. Failure to do so provides a back-door route to health screening of whole populations by commercial companies without medical justification. The law must protect privacy, allow people a say over how their data is used and who has access to it, and prevent excessive government surveillance or commercial exploitation. These rights are enshrined in Article 8 of the European Convention on Human Rights, which prevents the indefinite retention of biometrics such as genomes (genetic 'fingerprints') without an individual's knowledge or consent, unless they have been convicted of a crime.

It should be protected in law that the information 'belongs' to the client buying the service from the commercial genomics company and cannot be shared, even for research purposes, without the specific permission of the client. Where commercial genomics websites subcontract the testing of clients' samples to commercial laboratories, then those laboratories must respect similar data protection constraints.

Last year the UK government helpfully updated the Code on Genetic Testing and Insurance to prevent life insurance companies from forcing customers to disclose their genomic data when taking out policies with them.

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[16] http://unesdoc.unesco.org/images/0023/002332/233258e.pdf, section IV, para 125

[17] Wilson JMG, Jungner G. (1968) Principles and practice of screening for disease (large pdf). WHO Chronicle Geneva:World Health Organization. 22(11):473. Public Health Papers, #34.

[18] http://www.pbs.org/wgbh/nova/body/hippocratic-oath-today.html

[19] http://www.wma.net/en/30publications/10policies/g1/

7. The regulations or standards that commercial genomic tests are currently subject to, and if any new or strengthened regulations or standards should be introduced to mitigate any perceived risks associated with commercial genomic testing

Laboratories offering genetic testing in the UK are subject to quality assurance and accreditation. Genetic laboratories in the UK should be accredited with Clinical Pathology Accreditation (CPA) (UK) Ltd - the national accreditation body for Medical Laboratories in the UK. The company offering the test should be registered with the Care Quality Commission (CQC) when in England, or with equivalent bodies in other parts of the UK.

Those persons considering a commercial genomics test should therefore enquire whether the testing company is registered with CQC, and if the testing laboratory is appropriately accredited.

Nuffield recommended that private companies be regulated and their advertising controlled by the Committee for Advertising Practice (6.39, Nuffield report). There are now CQC inspections[20] but misleading information is still being given in the advertisements.[21]

Patients enrolled in the NHS initiative 100,000 Genomes Project have their entire genome sequenced and data from this are kept in an NHS data centre in pseudonymised form. Those patients are told that their data are unlikely to offer them any personal health benefits, but that a better understanding of disease, accumulated from the 100,000 individuals tested, it is hoped will help patients of the future.

CMF believes strong privacy rules are vital, but also recognises it is important that anonymised data, donated by the public, can be used for research purposes and not blocked by overly-strict data rules.

8. The potential benefits and risks, for individuals and for the NHS, and the ethical implications of the NHS offering genomic testing to healthy individuals willing to pay and share their data anonymously

This proposal seems no different in principle to the 100,000 Genomes Project, except that payment is included.

If whole genome testing is in view, then the ethical issues are more significant. Will full disclosure to the individual be made? Some of the information might potentially be harmful if the results include a high risk of serious or life-threatening disease. Some individuals would opt not to know such information. Effective pre-test and post-test assessment and counselling would be a necessity. Would the information be shared automatically with the individual's other health care providers, such as their GP?

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[20] http://nuffieldbioethics.org/news/2019/care-quality-commission-regulate-private-providers-noninvasive-prenatal

[21] https://www.gynae-centre.co.uk/our-services/harmony-prenatal-test/

The offer of payment might tempt some people to volunteer who would be considered inappropriately vulnerable at pre-test assessment. Discrimination legislation could then be recruited as leverage to proceed with the test, with harmful results.

If payment is simply an inducement to participate and the data are legally safe-guarded as the sole property of the individual concerned, that cannot be shared without their explicit knowledge and permission, then many concerns would be alleviated. However, in general 'he who pays the piper calls the tune' and it is likely that in practice the state would consider itself the owner of the data purchased, not the individual. That data could indeed be useful for genuine research purposes and help to build a better picture of diseases and their prevention/management. But the same data in the hands of the state could be used to qualify an individual's entitlement to state benefits, government employment opportunities etc. The data could also be a lucrative source of income if shared with insurance companies, banks and mortgage providers, marketing companies and so on. Data protection issues have already been referred to in Sections 6 and 7. Confidence that the state could effectively 'police' its own affairs in these areas would be open to question.

We are sceptical of promises assuring data protection, and for these reasons CMF is opposed to a system in which healthy individuals are offered financial inducements to provide genetic data.