

GeneWatch UK is a not-for-profit organisation which aims to ensure that genetic science and technologies are used in the public interest. We welcome the opportunity to input to this review.

Background to the Review and problems with transparency

The Wellcome Trust is promoting a plan in which everyone in the UK has their whole genome sequenced and stored in their electronic medical records.¹ According to this plan, each individual will have a “variant file” (containing the difference between their Sanger Centre’s genome and the “reference genome”) attached to their electronic medical record. Up to 60 million variant genomes will be stored in the cloud by the European Bioinformatics Institute (EBI), amounting to 600 terabytes of data (10Mb per person). This will allow genomes to be linked to clinical data using the Scottish Health Informatics Programme (SHIP), GPRD (General Practice Research Database, now part of the Clinical Practice Research Database, CPRD), LSDBs (Locus-Specific Databases of mutations and common variants in different genes) and the Research Capability Programme (RCP).

The genome data and associated healthcare data will be made available as Open Data for data-mining via “cloud-based secure services” (a contradiction in terms?) using computer algorithms or “apps”, written by computer scientists or anyone with access to the data (including commercial companies). The proposed model for privacy protection is a “Secure Virtual Machine” (SVM), based on one or more “honest brokers” who will store the data on the cloud but allow it to be data-mined by others. Users will not gain access to the raw data but will be allowed to see the results of queries made by their computer algorithms or apps.

Individuals will not be asked for their consent to sequencing or sharing of their genomes or health record data but will receive feedback about their individual risks, via a “decision support system” for medical professionals. It is likely that individuals will be able to exercise some choice about the extent to which they want research results fed back on an individual basis.² Since doctors will be able to feedback results, the genome attached to an individual’s medical record will presumably become part of the information that is shared routinely with all medical professionals and will be available for the individual themselves to access online.

The rationale for abandoning the need for informed consent for genome sequencing and to take part in medical research is that: (1) genetic variants have small effects on risk for the big killer diseases, so larger databases are needed to quantify these small effects; (2) only a small percentage of people approached (reportedly 7%) volunteered to take part in UK Biobank, so if a bigger database is to be built it must be done without consent; (3) the market-leader in online genetic tests, Google’s 23andMe, has only about 150,000 users³ (despite record levels of publicity and giving tests away for free) and has not been able to establish a viable business model (especially for health-related tests, compared to ancestry-related ones).

This suggests that most people only want their genomes sequenced if and when it is actually useful for their health (i.e. not very often): and this creates a big problem for those who want to make a business out of it or have proclaimed a “vision” that everyone should be wandering around with their genome sequence on their mobile phone. The Wellcome Trust plan is therefore based on a “disruptive business model” in which specific genetic and genomic tests are not conducted as and when they are necessary for a person’s care: instead costs are sunk up-front in whole genome sequencing for everyone. This will be done as a public-private partnership i.e. by venture capital investors (probably including Google as

they have a major interest in this area) as well as taxpayers. Use of the data by individuals (with or without medical professionals) is then low cost (involving an electronic test of the person's existing stored variant file). This will allow this data to be mined for marketing, even when it is of no relevance to health.

It is currently unclear how people's DNA will be obtained. It is possible that "surplus" biological samples or "excess" blood (collected for tests during medical care or on registration with a healthcare provider) will be used without consent, as has been proposed by researchers in the USA⁴ and by the Human Genomics Strategy Group.⁵ Or, maybe samples will initially be obtained from people with consent (all employees at the Sanger Centre have been offered free tests to start things off) and others will be added later. It is also possible that the blood spots taken from every baby at birth (Guthrie tests) will be sequenced, perhaps with the consent of parents, perhaps not, but obviously not with the consent of the individual. These blood spots are taken for specific medical tests at birth and millions have been stored within the NHS.^{6,7}

It is not surprising that these plans will raise concerns about total surveillance of the whole population. Despite claims about "anonymisation", it is clear that such a database would allow every individual in the country to be tracked and their relatives identified.

Building a DNA database of the whole population within the NHS is not only a major threat to privacy but also the wrong priority for health research because differences between individuals' genomes are of limited value in predicting most diseases or adverse drug reactions. This means it is hard to justify the upfront expense of sequencing and storing everybody's genome (as well as the costs of collecting, storing, managing and analysing the data, there will be significant energy requirements to store the vast quantity of data). Further, most tests fed back to individuals will not meet medical screening criteria for the general population: meaning that, from a health perspective, they are likely to do more harm than good. This data will provide a gravy train for personalised marketing of healthcare products to the "worried well".

The framing of the Review (driven by advocates of this approach) is poor because it claims to be about how open we should be about sharing data within science. Decisions about what data should be collected, how money should be spent, and who really has power and control, are being hidden from proper public scrutiny. Important questions include:

- Is this a good use of resources? Why should this database be built?
- Do claims about "anonymisation" really stand up to proper scrutiny?
- Who will the researchers be, who will they be working for, and how will this data really be used?
- What will be the impacts on the NHS and public health?
- How will plans to build a DNA database in the NHS and undertake research without informed consent impact on public trust in the NHS and in medical research?

Benefits to health?

These proposals are part of a trend towards "data-driven" science, promoted by major funders such as the Wellcome Trust. Instead of scientific hypotheses driving what data is collected and what research is done, enormous expensive databases are created and data-mined for statistical correlations between different variables. Whilst often described as "hypothesis-free" there are hidden assumptions in this methodology, including the assumptions about how genes and environmental factors jointly lead to complex traits, adopted by the eugenicist Ronald Fisher in 1918; and the misleading deterministic idea that if all data points are known the future is perfectly predictable (given a new lease of life by the idea of medicine as an "information science" and the culture of Silicon Valley).⁸

Epidemiology has been transformed since the Human Genome Project. Instead of focusing on risk factors known broadly as “environmental”, with the aim of finding causal factors that can be amended or reduced, the focus has been on genetic epidemiology, with the much more difficult (and usually much less useful) aim of predicting people’s risk. The idea is that only a small group of people are genetically susceptible to common disease or adverse drug reactions and that they should be identified so that any intervention can be targeted at them.

This strategy was invented by the eugenicists who went to work for the tobacco industry in the 1950s and backed by leading scientists in the run up to the Human Genome Project in order to gain the necessary industrial and political support to get the project funded.⁹ They did this by making false claims about the predictive value of inherited genetic differences. The idea of genetic “prediction and prevention” of disease was also backed by the food, nuclear, chemical and pharmaceutical industries in order to undermine public health measures directed at their products or pollution and expand the drug market.¹⁰ As a result, an enormous gravy train has been created in which science has been redefined to mean “discovery” of genes linked to disease. Usually these discoveries are later refuted but not before they are hyped up in the press and claims are made that they will lead to the prediction of who will get cancer, heart disease or diabetes. In reality, however much research is done and even if all genetic variants are identified, they will still have poor predictive value for most diseases in most people and limited clinical utility.^{11,12,13,14}

The entire project is based on a false premise because the major differences in people’s health and life expectancy observed in Britain and throughout the world have little to do with individual differences in biology.^{15,16} The poor predictive value of genetic tests for common diseases is hardly a surprise.^{17,18,19,20,21,22} Inclusion of any gene-gene and gene-environment interactions (assuming they could be identified and even if an exact model of all interactions could be developed) will not improve this situation.²³ And much of the so-called “missing heritability” that future research is supposed to find is unlikely to exist.^{24,25,26}

The situation for predicting drug response is not any better. The way people metabolise some drugs and their risk of the relatively rare familial forms of some diseases can sometimes be deduced from analysing their DNA. But these limited, specific applications do not justify a roll-out of whole genome sequencing to the whole population. They should be used, as they are now, in high-risk families at risk of developing a disease, or before prescribing a specific drug.^{27,28,29}

There will of course be an infinite number of variables in the proposed database and an infinite number of models (i.e. computer algorithms) that could be fitted to the data: thus even a database of infinite size will lead to multiple possible interpretations and misinterpretations.^{30,31} Like the computer algorithms used to predict financial risk (which are blamed for the self-destruction of the global financial system) these computer models will not be reliable: it is simply not correct to assume that models with no theoretical basis will have any predictive value. The focus will remain on risk due to differences in biology (even if other biomarkers, not just genes, are introduced): this is a poor (and expensive) health strategy for prevention of disease.

The proposed model of individual feedback amounts to the abandonment of medical screening criteria for both diagnostic and prognostic tests. This will be combined with the blurring of the line between what are research findings and what are clinically validated findings: and with a meaningless process of extrapolation from potentially valid group level findings (e.g. that the group of people with genetic variant A have a higher risk of hypertension than the group of people with variant B) to meaningless claims about individual risk. All data will be regarded as “information” even though what will be fed back will in fact

be statistical interpretations, most of which will be invalid and therefore better described as “misinformation”. Screening which does not meet screening criteria will be bad for health.

Vested interests

“... through Connecting for Health (CfH), the UK is already in an enviable position to take advantage of the opportunities it offers. In the future, the ability to mine the data taken from this environment will bring about a true revolution in the practice of medicine, opening new industrial as well as healthcare horizons”. Industry ‘early health’ paper to MMTSG, 2008.

"This is not the genetic community saying here's something important that you should pay attention to. This is the Web 2.0 community looking for a market." Venture Capitalist firm Farnbrough, 2008.³²

The Wellcome Trust plan to build a DNA database of everybody in the NHS is also being promoted by the Human Genomics Strategy Group based on misleading claims about the likely benefits.³³ This is just the latest in a long history of attempts to build a database of everybody's DNA within the NHS, which has been promoted by a small group of government advisors since at least 1999.^{34,35}

There are many vested interests who wish to profit from “prediction and prevention” of disease. In 2000, Richard Sykes (then at GSK) argued that genetic testing combined with “pre-symptomatic” medication would massively expand the drug market for healthy people, leading to a transformation in the NHS which would allow patients to pay for extra medicines outside NHS funding, whilst keeping the NHS only as a basic service for people who are ill.^{36,37}

When the Government set up its Ministerial Medical Technology Strategy Group (MMTSG) in October 2007, the meetings were co-chaired by the US company GE Healthcare, which states on its website: “Our vision for the future is to enable a new “early health” model of care focused on earlier diagnosis, pre-symptomatic disease detection and disease prevention”.³⁸ The idea of ‘early health’ is described in a 2008 paper from the industry side of the MMTSG.³⁹ In this vision of the future, screening people's genomes will routinely be applied to identify high risk individuals and populations, and it is claimed that “tailored prevention programmes” will improve personal and public health. Industry will communicate more directly with patients and there will be “more innovation that will blur the regulatory boundary between drugs, biologics, devices, cosmetics and nutritionals”. There will be increasing consumerism, including ordering directly over the internet, bypassing medical professionals, and more suppliers will be engaged in “nurse-led care”.

The same idea is being promoted in North America by a coalition of ‘life science’ companies, as described in a presentation by Burrill & Co, a specialist venture capital company for such companies.⁴⁰ It envisages:

- routine genetic screening – using whole or partial genome scans conducted by gene testing companies - delivered by nurse-staffed pharmaceutical outlets in Wal-mart and other stores;
- widespread use of home diagnostics and remote health monitoring, with blood samples collected via Blackberrys and iPods;
- smart cards including electronic health records and DNA;
- consumer-driven personal health planning;
- tools to monitor medication regimens to drive compliance, and tools to measure physical activity and diet, linked to online work-outs and incentive programmes (such as paying people to lose weight);

- roaming nano-devices in blood vessels to diagnose and fix problems, and nano-particles to add nutrients to food;
- a shift from 'one size fits all' healthcare to personalisation, prediction, prevention/disease pre-emption and patient responsibility.

The Burrill presentation claims that people will be empowered and live longer lives, and that this approach will be cost-effective. However, it also predicts a near-doubling of the pharmaceuticals market by 2020, including the creation of big new markets in 'wellness' (the 'prediction and prevention' of disease) and obesity. The presentation highlights the ability for healthcare companies to "*generate value*" throughout people's lives, from 'wellness' to terminal illness.

In 2009, the Chief Executive of the US gene sequencing company Illumina advocated sequencing every baby's genome, using the blood spots collected at birth in the NHS, and claimed that the benefits will outweigh the harms.⁴¹ Illumina is now involved in a pilot project in the Faroe Islands which has been established to test the practicalities of integrating whole genome sequences into electronic medical records.⁴² In the UK, the sequencing is more likely to be done by Oxford Nanopore, which was spun-out from Oxford University in 2005. Its venture capital investors include IP Group^{43,44}, whose CEO (Alan Aubrey, a Director of Oxford Nanopore⁴⁵) was until recently on the audit committee of the Department of Business, Innovation and Skills (BIS).⁴⁶ Oxford University is also an investor in the company and will profit from any future income.

The genome data sent to the "Genome Campus" is likely to be processed in batches using a method developed and patented by a Cambridge-based company, Population Genetics Technologies.⁴⁷ The company was co-founded by Nobel prizewinner Sydney Brenner (the same person who had a secret meeting with British American Tobacco before setting up the Human Genome Organisation). Its investors include the Wellcome Trust.⁴⁸ The Trust has significant venture capital investments,⁴⁹ is about to launch a £200 million investment business⁵⁰ and has recently appointed a new Venture Capital investor to its Board⁵¹.

Whose data, open to whom, and for what purposes?

The Panel must be careful not to dress up commercial data-mining, aimed at personalised marketing, as scientific research, conducted in the public interest.

If this proposal goes ahead, who decides what data is collected and what research is done will be driven, even more than it is today, by who has the money to invest i.e. by vested interests rather than the public interest.

In this context it is important to think about the definition of "research" and about who is a "researcher". This will be dominated by those who have the money to do the analysis (or pay others, perhaps in universities or other public institutions, to do the analysis). It is likely to include:

- Researchers working for Web 2.0 companies, such as Google, which aims to use personal data for personalised marketing;
- Researchers working for private healthcare companies, such as GE Healthcare, who wish to sell more healthcare products and services to people deemed to be at risk of becoming ill in future;
- Researchers working for companies with products to sell based on personalised marketing using individual risk assessments, such as: pharmaceuticals, nutraceuticals, functional foods, supplements or other products.

It is disingenuous to claim that the above researchers will have no vested interests in using people's data in ways which lead to monetary gain: some of these uses will be harmful to individuals and the general population, particularly when they lead to overtreatment or false reassurance about the risk of a disease. Overall, this will not be of benefit to health. As originally envisaged by the tobacco, food, nuclear and chemical industries, this personalised approach to disease prevention will also continue to act as a massive distraction from public health measures designed to tackle their unhealthy products or pollution. The same is true of adverse drug reactions, which are not rising because of an increase in genes for adverse drug reactions but because of a variety of factors including weaker regulation and greater use of over-the-counter and off-label medicines (a trend that will be exacerbated along with over-treatment).

Anyone who agrees to "feedback" is likely to be bombarded with personalised advertising based on the data-mining of their medical records and genetic information. It is questionable whether the public will regard this as legitimate medical research.

The idea of Open Data is all very well, but in the context of healthcare it means ordinary people, including some of the most vulnerable (such as newborn babies and the mentally ill), giving up control over very private information. They will then be open to commercial exploitation. Instead of their medical information being shared only with people directly involved in their care, it will be shared with private healthcare companies and Google and used for data-mining to make predictive algorithms about their risks. This will then be used to establish a new market in personal health predictions and personalised marketing (or "personalised medicine" as it is erroneously called). A massive increase in the drug market is expected, because everyone will be classified as at high risk for something (although risk predictions will not usually correctly identify the disease or diseases they are going to get).

Everyone's electronic medical records are due to be posted on the internet by 2015 as part of the Government's new NHS Information Strategy.⁵² Plans are already underway to share these records with private companies.⁵³ But no one is being told about the commercial motivation to expand the healthcare market, or the implications for the NHS. The additional costs of all this extra (mostly unnecessary) treatment will require a privatised "top up" healthcare system for rich, healthy people (who make a better market), whilst the NHS will remain responsible for treating people who actually are ill.⁵⁴ Yet, the costs of building and maintaining the massive databases required, and following up on much of the unnecessary screening that results, will fall on the taxpayer.

Privacy, surveillance and the state

"Someday we'll have a complete pedigree of the entire human population, and everybody will be connected to everybody on a huge family tree that looks like Google Maps".
Professor George Church, co-founder of the Human Genome Project, 2009.⁵⁵

"There will be no secrets about paternity anymore". Professor Sir John Sulston, 2008.⁵⁶

Even advocates of whole genome sequencing acknowledge that privacy can no longer be protected if a universal genetic database exists. A DNA sequence acts as a biometric (an identifier for an individual, linked to their name and other details) and can also be used to identify relatives (including paternity and non-paternity). A genetic database within the NHS could therefore allow every individual to be tracked and their relatives to be identified: forming a system of surveillance with serious negative implications for privacy and rights.

Genetic information can also be used to categorise individuals, which can lead to stigma or discrimination. There is currently a voluntary agreement between insurers and the

government not to use most genetic test results in deciding who gets insurance or setting premiums, but no law to prevent this happening in future.

It is important to remember that although records are likely to be “de-identified” for research purposes (for example, by removing names, NHS numbers, and perhaps by restricting location data to sector postcodes or doctor’s practice) this will not mean that data cannot be linked back to individuals, either directly (by someone authorised to link the data and feedback information to an individual or their doctor) or indirectly (by ‘researchers’ with access to the data in the cloud). It seems likely that people with direct access to linked data (i.e. genomes associated with names and other personally identifying information) will include all the NHS staff who are currently allowed to access individuals’ medical records.

Perhaps some scenarios will help the Panel to realise what this could mean in practice:

- A person’s employer or a pharmaceutical company could be classified as a “researcher” and thus gain access to data about individuals who suffer from a workplace-related illness or an adverse drug reaction: they are likely to be able to use “deductive identification” (based on the occurrence of a rare event with other information) to work out who these individuals are. They could try to look for data that might allow them to blame the condition on a person’s genes, or for unrelated personal data (e.g. sexual health or use of drug rehabilitation services) that might be used to discredit that individual should they make a claim against the company.
- A person’s DNA can be obtained easily from a beer glass, coffee cup or toothbrush. Anyone who could get that DNA sequenced could search it against stored variant files and identify the individual, either directly (if they have access to the medical record in the NHS or the de-identifying system) or indirectly by the clues stored in their public records. They could also look for partial matches to identify that person’s relatives (including paternity and non-paternity). This process could be used by the police or state to track individuals who have not committed any crime (creating a “surveillance society”) or it could be used by criminals to track undercover police officers, witnesses on protection schemes, and potential victims (including women and children fleeing abuse).
- The same process could be used to find out what personal medical information is linked to a particular genome, including e.g. use of medical services, including sexual health, or specific information about a disease or carrier status for a genetic disorder. This might be of interest to the press, private detectives, parents, neighbours, or insurance companies. Unscrupulous charities might even use the data to seek donations from the relatives of anyone with cancer.

Consent and decision-making

The language of openness and empowerment being used in this debate is seriously misleading. The proposal involves completely removing people’s choices about what data about them is collected and stored, with the intention of creating a vast database including everybody’s whole genome and their entire medical records. Instead of deciding whether or not to have their genome sequenced, people will be asked what “information” (actually interpretations of their data which will include a lot of misinformation) they want to be fed back. They will not be told who is accessing their data or what it is being used to do.

Storing genetic data and biological samples without people’s knowledge or consent is likely to breach their right to privacy under the European Convention on Human Rights. Storage and use of babies’ blood spots without consent has proved highly controversial in other countries and it is not clear on what legal basis data-sharing of babies’ genomes and medical information could take place if the recipient of the information does not need it for the baby’s care.^{57,58,59,60}

People who opt-out may also be at risk of being denied proper care: for example, babies' blood spots are required for important medical tests but there is a danger that anyone who refuses to have their baby's genome sequenced may struggle to get access to these tests.

Public trust

The Wellcome Trust's plans are a recipe for a major loss of public trust. A previous attempt to introduce data-sharing without consent (following from the Walport-Thomas report commissioned by Gordon Brown) was introduced but rapidly dropped by the New Labour government in 2009, following massive opposition from the public and the medical profession.^{61,62}

Even if these latest proposals do not suffer the same fate, it will only be a matter of time before data-breaches and abuses lead to growing public concern: perhaps only after huge amounts of money has been wasted.

Legitimate researchers will then suffer a backlash and instead of finding it easier to access data they may find nobody trusts researchers any more.

What should happen

There is no medical justification for building a database of everybody's DNA within the NHS and this proposal should be abandoned.

None of the above means that medical data should not be stored electronically, nor that its use for research should be prevented. But enforceable rules are required, not only to protect people's privacy but to re-align the health research agenda with the public interest. It is no longer acceptable (if it ever was) for powerful vested interests to determine research priorities and to use information and misinformation as a means to control markets and mislead the general public. It is certainly wrong to claim that people have a "duty" to take part in sharing of their data with people that they do not know for purposes that will not always be in the public interest.

The increased capacity to store and share information on computers and mobile devices and via the internet means that **people should have more control, not less** over what is stored, who has access to their data, and what research is done. This requires the opposite approach to what the Wellcome Trust is proposing. It means recognising that power is money and that people with money need to be accountable: particularly when they spend taxpayers' money rather than their own.

Although this submission has focused on the problems associated with linking whole genomes with electronic medical records, this does not mean that simply omitting genetic data from the plan will be sufficient to allay concerns. Problems with "deductive identification", security breaches, sharing of linked information with large numbers of NHS staff, and misuse of data for personalised marketing by private companies will exist, even before people's genomes are added to the database. The Panel must consider how and where to draw the line so this does not happen. They must also identify and address the reality that open data-mining means that research conducted in the public interest is likely to be swamped by research conducted for commercial gain: with no quality control on what is invalid or misleading.

The current decision-making system is not bad for research: it requires informed consent with some exceptions. Whilst this can be frustrating for some researchers, the alternative of a free-for-all for commercial data-mining isn't going to make things easier for legitimate

research. The Wellcome Trust's own research shows clearly that people are keen to take part in medical research, but only when they have been asked.^{63, 64} This is an important safeguard to protect not only individual privacy but the broader public interest.

A shift to presumed consent with widespread data-sharing is a recipe for disaster. There is no problem with removing red tape (streamlining procedures): but only if this does not weaken accountability, undermine the public interest, or expose members of the public to unnecessary risks to privacy without their knowledge or consent.

Conclusions

The Panel should be open about the plan that is driving the call for "Open data".

The main concerns about this plan are:

- Storing people's DNA sequences in their medical record would allow a DNA database of the whole population to be built by stealth. Anyone with access to this database could track any individual using their DNA and identify their relatives.
- A DNA database of the whole population cannot be made anonymous: anyone with access to the data will be able to work out the identity of individuals and find out personal, private information, even if they are not given names and addresses.
- Legitimate medical research involves seeking people's informed consent, so they know what research is being done by whom and why.
- There are many ways in which private companies could misuse this data for marketing purposes rather than legitimate medical research, including making misleading predictions about people's risk of future illness (based on genetic or other data).
- Building and maintaining such a database and expanding the number of healthy people who receive medication based on their claimed genetic risks will be extremely expensive. The costs could bankrupt the NHS, without delivering any net benefit to health.

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