

A DNA database in the NHS: Your freedom up for sale?



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In April 2013, the Caldicott Committee, including Government Chief Scientist Sir Mark Walport, proposed new rules for data-sharing which would allow the Government to build a DNA database of the whole population of England in the NHS by stealth.¹

The plan is to make NHS medical records and people's genetic information available to commercial companies and to use public-private partnerships to build a system where all private information about every citizen is also accessible to the police, social workers, security services and Government.

The Wellcome Trust, which was involved in the Human Genome Project and was led by Walport for ten years, has produced a plan which involves including a variant file, containing the whole genome of every person minus the reference genome, as an attachment to every medical record in the NHS in England.² This data would be made available to 'researchers' (including commercial companies) for data-mining in the cloud and personalised risk assessments would be returned to individuals. The aim is to transform the NHS in line with proposals developed more than a decade ago by former GlaxoSmithKline Chairman Sir Richard Sykes. This is expected to massively expand the market for medicines, medical tests and other products, such as supplements and cholesterol-lowering margarines, by allowing products to be marketed to individuals based on personal risk assessments, created using statistical analysis of genetic data, medical records and other health information.

The proposal to build a DNA database in the NHS was endorsed by the Human Genomics Strategy Group in 2012^{3,4} and the Government (led by Prime Minister David Cameron) has quietly adopted this recommendation without telling members of the public. Those proposing the plan are well aware that only a small minority of individuals are likely to give their fully informed consent to the storage and use of their DNA and genetic information in this way. The intention is therefore to implement the proposal without informed consent.

Under this proposal, everyone's NHS medical records and genomes will be shared with companies such as Google without people's knowledge or consent. Data-sharing will be global, with Asia's richest man, Sir Li Ka Shing, already involved in the proposals.

The Government plan as it is envisaged creates a searchable DNA database of the entire genomes and medical data of the whole population in the cloud. This would allow:

1. The tracking of every individual and their relatives, due to the role of DNA sequences as biometrics and as a means to identify relatedness (including paternity and non-paternity);
2. Feedback of calculated risks to individual patients in a way which undermines medical screening criteria and is likely to be used for commercial marketing of health-related products;

3. The categorisation of individuals according to these calculated risks, which may lead to “personalised marketing” and probably also to discrimination e.g. by insurers or employers.

Other personal information, from any source, will be linked to individuals in the future, including social care and education records. No information will ever be deleted from the system, although people will have a right to see their own records and request corrections. DNA and genetic profiles will be collected from birth where possible and retained until long after a person’s death.

The data-sharing plans

“As you are aware, the report from the Human Genomics Strategy Group recommended that the Department of Health, in partnership with the Department for Business, Innovation and Skills and other relevant partners, should develop proposals to establish a central repository for storing genomic and genetic data, and relevant phenotypic data from patients, with the capacity to provide biomedical informatics services. The Group concluded this in recognition that sequencing technologies are developing rapidly and there is now a need to interpret genomic data in a clinically relevant way. The report has been welcomed by the Secretary of State for Health and the Minister for Universities and Science, who have asked for the recommendations to be implemented through a shared strategic framework”. Reply from the Department of Health to a Freedom of Information request by research group Ethics and Genetics, 2012.⁵

“What we are all trying to do is to get comprehensive electronic records with genomics attached to them, because, as I understand it, what the biopharma industry wants is not to do everything but to have very specialised interests of care. Once the research is conducted, we offer personalised care to the patients who are engaged in this. Particularly, Imperial, University College, Oxford and Cambridge are very focused on that, but all of the academic centres are striving in that direction”. Dr Gareth Goodier, Chair, Shelford Group (which represents England’s leading Academic Medical Centres), 2012.⁶

The Health and Social Care Act 2012 transferred control of medical records in the NHS from doctors to the Government, creating the Health and Social Care Information Centre (HSCIC), which has the power to require information, including individual patient records, to be sent to it.⁷ The Government intends to order the transfer of all medical records in England from GPs to the HSCIC using a loophole in the law called Section 251 (see Box A). This is the first step in implementing the Prime Minister’s plans for health data to be shared with commercial companies, without the knowledge or consent of individuals.^{8,9} Once these transfers have been made, individuals will no longer have any control over what happens to their medical records and a Government-controlled database of the private medical records of everyone in England will have been created. Scotland, Wales and Northern Ireland will make their own decisions because health powers are devolved.

By May 2013, four private firms including private health insurer Bupa had been approved to access England’s patient data, housed centrally by the HSIC.¹⁰ More companies are likely to be registered as “researchers” in the future. NHS England is to start extracting data from GP practice records in June 2013.¹¹

Box A: Section 251 and sharing patient identifiable information

Section 251 of the Health and Social Care Act 2006 contains a clause first adopted in Section 60 of the Health and Social Care Act 2001. Section 251 allows the Secretary of State for health to regulate the processing of patient information without consent in some

cases, when it is deemed to be in the public interest. The Patient Interest Advisory Group (PIAG) was set up to advise the Secretary of State on the use of these powers, but has recently been replaced by a new Confidentiality Advisory Group (CAG) under the Health Research Authority (HRA).

In March 2013, the NHS Commissioning Board applied to the CAG for an exemption under Section 251 to upload all electronic medical records currently held by GPs to the Information Centre (HSCIC).¹² If approved, this would allow a blanket approach to transfer of all medical records in England to the Centre, where they can be made available for research use without people's knowledge or consent. Although some data released onwards from the Information Centre for use in research will be anonymised (see Box B), the existence of Section 251 (and proposals to weaken Data Protection laws, Box E) means that identifiable data might also be released to other organisations in the future.

The Wellcome Trust's proposal to build a DNA database in the NHS is shown in Figures 1 & 2. The healthcare professional will test the individual, collecting a sample of their DNA for analysis. The full genome sequence (all the chemical letters in a person's DNA) will be compared with the "reference genome" (the single genome published by the Human Genome Project) at the Wellcome Trust's Sanger Centre, and the differences will be stored in a "variant file", attached to the individual's electronic health record. Figure 1 says the data will be "anonymised" before being sent to NHS databases (under the new arrangements, these will now all be managed by the Health and Social Care Information Centre, HSCIC). However, Figure 2 makes clear that the data is in fact "pseudo-anonymised" i.e. information derived from it is de-linked for research purposes but expected to be re-linked back to the individual using the NHS number by their health professional later on (see Box B). Once the pseudo-anonymised data has been transferred, the European Bioinformatics Institute (EBI) and the Wellcome Trust Sanger Centre, both based at the Genome Campus at Hinxton near Cambridge, will add further information from their databases about how genotypes and phenotypes (a person's physical characteristics) are related. Additional clinical information will be added by the Biomedical Informatics Institute (BII) and then all the information will be uploaded to the cloud (i.e. the internet), where it will be made available for data-mining by commercial companies. According to Figure 2, personal risk predictions will be fed back to individuals using computerised decision support systems for medical professionals. Up to sixty million people (the entire population of the UK) are expected to be included in this system, although the initial proposals apply only in England.

Box B: Anonymisation and pseudo-anonymisation

Anonymised data, which cannot be re-identified, is not covered by Data Protection laws. This means it is treated differently from personal (identifiable) data. A further category of data is now being discussed. Often referred to as "pseudo-anonymised" or "de-linked" data it is stored with a unique identifier, but with the individual's name (and perhaps some other identifying information) removed from the record. In some cases the NHS number will be the unique identifier but in other cases a more secure system can be used which barcodes the data so it can only be connected back to the NHS number by a small number of people. The Government expects that medical records with the names of individuals removed will count as "anonymised" or (more likely) as "pseudo-anonymised" data. However, as databases become larger it has become clear that individuals' identities can often be deduced from combining information such as age, postcode, medical history and occupation, even if the names have been stripped off. Genetic information alone, especially whole genomes, can be sufficient to identify an individual and the idea of "anonymised" data can therefore rapidly become meaningless.¹³ Several studies have shown that whole genomes cannot be reliably anonymised and individuals' identities and those of their families can be deduced either from their genome alone or from other stored data, such as details about medications, diseases, age and postcode.^{14,15,16}

The use of “pseudo-anonymised” data adds to the risks (in comparison to using anonymised data) because data stored with the NHS number can be re-identified by matching it back to personal details (including name and contact details) stored in the NHS Personal Demographic Service (PDS), to which more than 800,000 NHS staff have access. Because genomes are biometrics (Box E) this adds further risks, since data could also be retrieved by matching all or parts of a person’s DNA sequence (obtained from their coffee cup or toothbrush, for example) to the one stored in the record.

The Information Commissioner’s Office (ICO) has published guidelines on anonymisation¹⁷, but there are concerns these are too weak because they are based on deciding whether or not re-identification of individuals from their data is “reasonably likely”. This risks creating a loophole which could allow vast amounts of personal data to be processed without proper safeguards.

In order to create the proposed databases, the Government is planning to remove people’s right to be asked to give consent to how their medical records and other information is used by researchers. Informed consent has been the cornerstone of conducting medical research ethically since serious abuses by doctors conducting medical experiments were uncovered, particularly in Nazi Germany (Box C).

Box C: Informed consent

The 1947 Nuremberg Code followed the trial of Nazi doctors. It stated that every individual must have the right to give or withhold their informed consent to medical research. The Code was followed by the Helsinki Declaration, a set of principles for medical professionals conducting research.¹⁸ The Helsinki Declaration includes requirements to protect the “*dignity, integrity, right to self-determination, privacy and confidentiality of personal information of research subjects*”. Research participants must be informed of “*the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study*” before giving their consent, preferably in writing. For consent to valid it must be fully informed and freely given.

Special protections must be accorded to people who lack capacity to give consent and account must be taken of the changing capacity of children as they grow up.¹⁹

The European Convention on Biomedicine states (Article 16): Research on a person may only be undertaken if all the following conditions are met²⁰:

- (i) there is no alternative of comparable effectiveness to research on humans;
- (ii) the risks which may be incurred by that person are not disproportionate to the potential benefits of the research;
- (iii) the research project has been approved by the competent body after independent examination of its scientific merit, including assessment of the importance of the aim of the research, and multidisciplinary review of its ethical acceptability;
- (iv) the persons undergoing research have been informed of their rights and the safeguards prescribed by law for their protection;
- (v) the necessary consent as provided for under Article 5 has been given expressly, specifically and is documented. Such consent may be freely withdrawn at any time.

Lobbyists, including the Wellcome Trust, are trying to use two different mechanisms to remove people’s right to be asked for their consent for the sharing and use of their medical records and genetic data in non-interventional research (i.e. research which does not involve medical interventions such as taking drugs). One is the Caldicott Review (Box D) and the other is the revision of data protection laws in the European Union (Box E). The Government has not yet formally responded in detail to the Caldicott Review but Secretary of State Jeremy Hunt has stated that people will be able to opt out of having their data uploaded to the HSCIC. However, this is a significant shift from an “opt in” to an “opt out” system and

severely restricts patient choice because decisions to allow some sharing for some purposes will no longer be allowed: the choice will be an “all or nothing” choice in which opting in means everything is shared with any accredited researcher.

These data-sharing plans are similar to those introduced but rapidly dropped by the New Labour government in 2009, following massive public opposition (including from the Conservatives and Liberal Democrats).^{21,22} The main difference will be that much of the data will be stored on the internet, rather than on government computers. In addition, rather than introducing new legislation in parliament, the Government appears to be planning to exploit loopholes in existing laws and lobby for changes within the EU, thus avoiding public and political debate.

Box D: The Caldicott Review²³

The Caldicott Committee is led by Dame Fiona Caldicott and its members include the Government Chief Scientist Sir Mark Walport, former Director of the Wellcome Trust. In May 2013, the Committee published a blueprint for new data-sharing rules (known as “Caldicott2”) in which everyone’s medical records and genomes can be widely shared without their knowledge or consent.

The report recommends a shift to a default approach of data-sharing for research using “pseudo-anonymised” health data in the NHS, based on presumed consent. In other words, use of the NHS would be taken to imply consent to sharing of medical records and genetic information widely for research purposes. Rather than seeking informed consent for use of people’s medical records and other data, the legal basis for sharing and processing data would be contractual agreements with commercial companies and others (Section 6.3). The report states that genetic information should not be treated any differently from other forms of information (Section 5.8).

According to the report (Section 7.4), individuals will have a right to request that their data is not shared but no automatic right to opt-out, unless they can prove that sharing would cause them substantial damage or distress. A “Catch 22” scenario is described in which people who are insane can be considered at serious risk of self-harm due to their irrational belief that Government might misuse their data: but insane people lack the capacity to consent so these individuals will be dependent on their doctors to take them seriously. Health Secretary Jeremy Hunt stated that the government would provide a genuine “opt-out” option when he responded to the report at its launch.²⁴ However, this still falls far short of fully informed consent (Box C) and has the added downside that people will not be able to opt-in to legitimate and useful medical research without agreeing to relinquish all control of all of their medical information.

Under the proposals, so called “accredited safe havens” (with restricted access) will be used to link additional data sets from more than one source about an individual (such as information from social care and education) and this data will then also be made available to researchers on a “pseudo-anonymised” basis (Section 6.5).

A “Hotel California” clause in Section 5.6 (you can check out any time you like, but you can never leave) allows people to change their consent at any time, but “*withdrawal of consent cannot be reliably made retrospectively, as information may already have been shared...*”. Section 6.7 explains how Section 251 (Box A) will be used to release personally identifiable information when this is deemed to be in the public interest, for example when the size of a study is too large for it to be reasonable to expect researchers to contact all the participants. The report also expects health and social care records to be integrated and the information used to target individuals and families for early intervention (Section 10.8) in some cases including the unborn (Section 12.8). Access to records by insurers and mortgage providers is expected, provided this is “not excessive” (Section 12.12).

Current Department of Health advice is that all electronic records should be retained indefinitely (footnote 96).

Box E: The EU Data Protection Regulation

A single set of rules on data protection, valid across the EU, was published in draft form in January 2012 in the Data Protection Regulation.²⁵ The Regulation has been subject to an unprecedented level of lobbying from commercial companies and a vote by the European Parliament's LIBE Committee has been delayed due to more than 4,000 amendments having been submitted.²⁶

A coalition of consumer rights groups has launched a campaign calling on the European Parliament to stop corporations from weakening the Regulation, including requirements for informed consent.²⁷

Lobbyists include the Wellcome Trust and many proposed amendments applying to health data are similar to the Caldicott proposals (Box D). If adopted, these amendments could allow use of health data (including genetic data) by any "researcher" for any research or statistical purpose without consent, and would allow indefinite storage of all data, including whole genomes. There is particular pressure on MEPs to exempt "pseudo-anonymised" data from data protection controls, including from consent requirements.²⁸

The EU-US Free Trade Agreement, currently under discussion, is also likely to include data protection regulation.²⁹ US companies can use their customers' personal data with almost no restrictions and the aim of the FTA is to harmonise trade rules by adopting the lowest standard of protection: it is therefore possible that data protection will be weakened further during these negotiations.

The creation of a national DNA database within the NHS also requires samples (blood, tissue or saliva) taken from individual patients to be analysed to sequence of all or parts of each individual's genome (the string of chemical letters in their DNA which comprises each person's own unique genetic make-up). A pilot project for linking DNA and medical records already exists, called UK Biobank (see Box F), which is about to begin genotyping samples from half a million people. Implementing the plan to put everyone in England on a DNA database depends on not asking people for consent because only a small percentage of people approached (reportedly 7%) volunteered to take part in UK Biobank.

Box F: UK Biobank³⁰

UK Biobank, based near Manchester, contains blood and urine samples from half a million people, linked to their electronic medical records and other information (such as lifestyle questionnaires and blood pressure measurements) collected when people signed up to the study. Participants were recruited via their GPs and gave "broad consent" to the use of their stored samples and data in medical research. The study is funded by the Wellcome Trust, Medical Research Council (MRC) and Department of Health and was established as a pilot study for a DNA database of the whole population under the New Labour government. Whole genome sequencing of all participants is still too expensive to be used on all the samples stored in UK Biobank (costing more than £1,000 per genome) but parts of the genome can be sampled much more cheaply (known as 'genotyping'). Genotypes typically consist of hundreds or thousands of single nucleotide polymorphisms (SNPs, pronounced "snips"), which can be identified using DNA chips or arrays sold by commercial companies. SNPs are single chemical letters in the DNA sequence which differ between individuals and more than 10 million common SNPs have been catalogued in the human genome. US company Affymetrix announced in March 2013 that it would begin genotyping of multiple SNPs in all 500,000 UK Biobank participants by the end of 2013.³¹

A pilot project to sequence 100,000 genomes over 3 to 5 years was announced by the prime Minister in late 2012, as part of a £100 million project focused on people with genetic disorders and cancer, rather than the healthy population.³² The Government announcement stated: "*Genome sequencing is entirely voluntary. Patients will be able to opt out of having*

their genome sequenced without affecting their NHS care” and “*Whole genome sequence data will be completely anonymised apart from when it is used for an individual’s own care*”. However, an “opt out” system is completely different from an opt-in system, which requires people to be fully informed about who will use their data and for what purposes.

Anonymisation of whole genomes and medical data is also likely to be impossible (Box B) and the stated intention to re-link the genome and its interpretation back to the patient for their individual care suggests that it could become part of their electronic medical record once the analysis is done (see Figures 1 & 2). If this were to be the case, it is possible that such information could be widely shared on an identifiable basis within the NHS, as well as on a pseudo-anonymised basis with any accredited researchers.

It is currently unclear how the DNA of people who have not volunteered to take part in UK Biobank will be obtained to create a DNA database of the whole population in the future. 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 USA.³³ Processing and storage of DNA without consent is unlawful under the Human Tissue Act (HTA) 2004, but there are exemptions for research.³⁴ If the DNA comes from a living person, paragraph 10(b) of Schedule 4 of the HTA, and regulations adopted in 2006³⁵, mean research can be undertaken without consent provided it is approved by a research ethics committee and the person carrying it out is not in possession, or likely to come into possession, of information from which the individual from whose body the material has come can be identified. This is a loophole that could be used to sequence de-linked (or “pseudo-anonymised”) samples for research without consent, allowing the findings to be linked back to the individual later on. It is also possible that the HTA could be amended by further legislation. The Academy of Medical Sciences (then led by Professor Sir John Bell) proposed in 2011 that human saliva and some blood products should be exempt from the Human Tissue Act.³⁶ The Human Genomics Strategy Group (also led by Bell) subsequently lobbied the Government’s former advisory body the Human Genetics Commission to allow the sequencing of samples of blood or saliva taken as part of routine care in the NHS on the basis of opt-out consent.³⁷

The idea of using an “opt out”, instead of fully informed opt-in consent, for whole genome sequencing (WGS) is particularly problematic because it will not be possible to inform people in advance of the kind of findings that might be fed back to them. So-called “incidental findings” can include highly uncertain estimates of risks for a wide variety of common or rare diseases, which it may be impossible to do anything about. This means it is important that people not only give their fully informed consent to take part in research but also have a say about (or are at least made aware of) whether or not research findings will be fed back to them in future.³⁸

Another possible source of DNA is the blood spots taken from every baby 5 days after birth to perform a few specific health tests. These blood spots could be genotyped or sequenced, perhaps with the consent of parents, or perhaps not, but obviously not with the consent of the individual baby. Millions of babies’ blood spots have been stored within the NHS.^{39,40} All newborn blood spots collected in the NHS are retained for a minimum of five years as part of quality management, but some hospitals have policies to retain the bloodspots indefinitely or until adulthood. There is no explicit national policy for destruction of the blood spots.

Guidelines were published in 2005 and incorporated into a Code of Practice which states the blood spots can be used for research where the samples have been anonymised and the research project has ethical approval, as outlined in the Human Tissue Act.^{41,42} Under current guidelines, parents can be re-contacted and asked to allow the use of the blood spots for research, provided they agreed to this when the blood spot was taken (the blood spots are stored with a barcode so they can be linked back to the individual child). Currently, newborn screening laboratories may not sell, or grant exclusive access to, residual newborn

blood spots to commercial organisations. However, the Code of Practice is now under review and the new version has not yet been published for public consultation. Storage and use of babies' blood spots without consent has proved highly controversial in other countries.^{43,44,45,46}

Even when samples are obtained from people with consent (for example, all employees at the Wellcome Trust Sanger Centre have been offered free genotyping) "broad consent" is likely to be used, as for UK Biobank, so people will not be told which companies or organisations will gain access to their data, for what purposes.

Construction of the necessary infrastructure to build a DNA database in the NHS is already underway.

Samples are likely to be collected at the five centres in England awarded Academic Health Science Centre (AHSC) status in 2009: one in Cambridge (Cambridge University Health Partners⁴⁷), three in London (Imperial Academic Health Science Centre⁴⁸, King's Health Partners⁴⁹ and UCL Partners⁵⁰) and one in Manchester (Manchester Academic Health Science Centre, where the genetic research project UK Biobank is based⁵¹).

At Oxford University, a Big Data Institute at the new Li Ka Shing Centre for Health Information and Discovery will analyse electronic medical records and whole genomes. Using the UK Research Partnership Investment Fund, £10 million in Government funding will be matched by a £20 million donation from Chinese entrepreneur and philanthropist Li Ka-shing.⁵²

At Addenbrooke's Hospital in Cambridge, a major expansion is planned as part of creating a new Cambridge Biomedical Campus, which will also host a private hospital and hotel facilities, close to Junction 11 of the M11.⁵³ The Francis Crick Institute (a new consortium of the Medical Research Council, Cancer Research UK, the Wellcome Trust, University College, Imperial College and King's College, led by the Royal Society's Professor Sir Paul Nurse⁵⁴) is also likely to play a role in the research.

For the purposes of data-sharing, the intention is to treat genomes and genetic information in exactly the same way as other health data, on the grounds that, although the information content may be sensitive, it is no more sensitive than some other health data. However, this ignores the important role of DNA as a biometric (Box G), which can be used as a tool to identify and track individuals and their relatives.

Box G: Biometrics

Biometric systems, such as fingerprints, DNA and iris scans use a certain unique property of an individual for identification and/or authentication. Often, the biometric itself is not unique because it is based on a digitised representation of the relevant biological characteristic. However, the chances of the biometric matching another person is expected to be low. Unlike stored data, a biometric cannot be altered because it is linked to a person's body. The EU's Article 29 Data Protection Working Group has warned that biometrics allow for automated tracking, tracing or profiling of persons and as such their potential impact on the privacy and the right to data protection of individuals is high.⁵⁵ Biometrics that can be derived from DNA include: forensic DNA profiles (a string of numbers based on parts of the DNA called Short Tandem Repeats); genotypes based on multiple Single Nucleotide Polymorphisms (SNPs) which are single chemical letters which differ between individuals; and whole genomes (the entire string of chemical letters which makes up a person's DNA). Forensic DNA profiles are not unique identifiers but have sufficiently low probability of being shared by chance with another person to be useful to the police;

individual SNPs have low power to discriminate between individuals, but panels of multiple SNPs are sufficient (and are often used to identify body parts after disasters); whole genomes are thought to be unique. If whole genomes, or sufficiently detailed genotypes, are stored with other information this allows all that information to be connected to that individual.

Since DNA can be obtained from a person's coffee cup, for example, a DNA database allows individuals to be tracked by the police, security services or anyone who can gain access to the system. If DNA is linked to other information such as medical records, all this personal information can also be identified. In addition, relatives can be identified by searching databases for partial matches with the DNA of an individual (known as 'familial searching'). Non-paternity can be revealed if the records of a child and its supposed father can be identified and the child's DNA does not match half of the father's sequence. Under the EU Data Protection Directive (95/46/EC) biometric data are in most cases personal data. Therefore they may only be processed if there is a legal basis and the processing is adequate, relevant and not excessive in relation to the purposes for which they are collected and/or further processed. The EU's Article 29 Data Protection Working Group states that a prerequisite to using biometrics is a clear definition of the purpose for which the biometric data are collected and processed, taking into account the risks for the protection of fundamental rights and freedoms of individuals, and: "*It must be clear that such consent cannot be obtained freely through mandatory acceptance of general terms and conditions, or through opt-out possibilities*". Valid alternatives must exist for consent to be regarded as freely given (e.g. people must not be forced to seek care outside the NHS or go without treatment if they do not want their genomes sequenced). However, proposals to treat whole genomes as health data (Box D) – including the proposed use of "presumed" or opt-out consent and the indefinite storage of genetic data by the Government – threaten to undermine these important safeguards.

Thus the Government plan involves two aspects:

- (1) Routine sharing of personal medical records containing all the data collected during the course of an individual's care.
- (2) Collection, storage and sharing of genomic data which is largely irrelevant to the individual's care and which also acts as a biometric.

For research (and perhaps other purposes) it is also likely that additional data will be collected or obtained by linking to other information (e.g. the individual's employment record, social care records and education records) in so-called "safe havens". According to the Caldicott2 report (Box D) there are plans for at least 20 accredited safe havens. These include safe havens within Royal Colleges, National Clinical Audit contract holders, approximately ten Data Management Integration Centres, Public Health England, and the Clinical Practice Research Datalink service of the Medicines and Healthcare Regulatory Agency (MHRA).

One of the most controversial aspects is that all information, including whole genomes, will be retained indefinitely (Box H).

Box: H: Indefinite retention of all data: a DNA database by stealth

The Data Protection Act's section 33 exemption allows personal data held for research purposes to be retained indefinitely. "Research purposes" includes statistical or historical purposes, provided the data are not processed to support measures or decisions with respect to particular individuals and that the data are not processed in such a way that substantial damage or substantial distress is, or is likely to be, caused to any data subject.⁵⁶

Whilst retaining data for research often makes sense, under the proposed plans this would allow a DNA database of the whole population to be built by stealth, with no possibility of removal of any of the records.

Storage of genomes collected in the NHS would allow every individual and their relatives to be tracked, because genomes are biometrics (Box G). This would include babies whose DNA will have been collected without them giving their own consent to the collection or retention of their genomes. This gives enormous power over individual citizens to the government, which could easily be abused (for example, to track down dissidents and political opponents using their DNA, and even to identify their children). For this reason, the Government's proposal might be regarded as breaching Article 8 of the European Convention on Human Rights (the right to privacy).

In an unanimous judgment by the Grand Chamber in December 2008 in the case of *S. and Marper v. the UK*, the European Court of Human Rights found that the indefinite retention of two innocent persons' biological samples, forensic DNA profiles and fingerprints by the police in England "*constitutes a disproportionate interference with the applicants' right to respect for private life and cannot be regarded as necessary in a democratic society*".⁵⁷ It is therefore hard to see how building a DNA database in the NHS can be regarded as compatible with human rights. However, such legal cases can take many years to be decided.

Good for freedom?

The proposals in the Caldicott2 report (Box D) completely remove any right of patients in the NHS in England to have any say over who sees their medical records and how they are used. It is possible that consent will be sought to collect DNA samples, but it appears more likely that for most people this will also be undertaken on an "opt out" (or "presumed consent") basis. Once sequenced or genotyped this genetic information will be stored forever in government databases and shared without the knowledge or consent of individuals. This includes genetic information collected from babies at birth.

To date, approved registered researchers for UK Biobank include commercial researchers in the USA's Silicon Valley (probably the Google-funded gene test company 23andMe) and Europe, and public institutions across the world, including in several in China.⁵⁸ Approved researchers to be given access to NHS medical records for research already include private healthcare company Bupa. Thus, data will be sold globally to both governments and commercial companies.

Quite apart from any value attached to the content of people's genomes (their genetic information) having a unique biometric identifier (a 'genetic fingerprint') is a gold mine to commercial companies who may wish to link separate data sets to a single individual to monitor their behaviour in detail, and to totalitarian governments who will then be able to track every individual and their relatives. This is similar to the New Labour Government's proposed ID card scheme, except that genomes, rather than fingerprints and iris scans, will be the biometrics, allowing a person's relatives to also be identified.

Even advocates of whole genome sequencing acknowledge that privacy can no longer be protected if a person's whole genome is stored.⁵⁹

Storing an individual's DNA sequence linked to their name and other identifying information allows a form of biological tagging or "biosurveillance" which can be used to track them or their relatives.⁶⁰ There is widespread agreement that the creation of such databases raises human rights concerns. Because of these concerns, the Coalition Government has adopted the Protection of Freedoms Act and deleted more than one million DNA profiles belonging to

innocent individuals from the police National DNA Database and destroyed more than 6 million DNA samples containing sensitive biological material.⁶¹ However, under the Wellcome Trust's plan for the NHS, a searchable genetic database would be created in which the individual genome of each person in the NHS is stored as an attachment to their electronic medical record. Once complete, this would allow anyone who can obtain a DNA sample from an individual to search their genetic profile against the database and use biometric matching (or partial matching with close relatives) to:

- identify that individual and their relatives, if they can obtain access to the linked identifying information;
- obtain linked personal health information that has made available for research purposes, even if they cannot access identifying information. This may or may not be sufficient to identify the individual (and/or their relatives) via "deductive identification".

This proposal differs significantly from the current situation in which genetic test results focused on a specific gene or genes are stored in the health records of a relatively small number of patients. Whilst such relatively limited genetic data can lead to the deductive identification of an individual (e.g. based on knowledge that they have a rare disease, combined with other information), its collection and storage in specific cases based on clinical need does not amount to the creation of a biometric database. In addition, medical records are currently shared mainly for a person's care or for research which they have consented to take part in, for which a single named researcher is responsible. This will be transformed under the new plan into a system where pseudo-anonymised data will be made readily available to any approved organisation wanting to perform any statistical analysis.

An access order granted by a court can allow police access to samples from existing collections held by other parties, including the NHS.⁶² But until, now this power has been used only in rare cases. If a searchable database of genomes existed in the NHS this could be used to identify individuals from their DNA routinely, in the same way that the police National DNA Database is used now. The National DNA Database is based on data from parts of people's genomes, but the planned NHS database would contain the whole sequence, once this becomes affordable, or individuals' genotypes consisting of thousands of SNPs. Searching for partial matches with relatives could also allow the police or security services to identify relatives of a suspect (a process known as 'familial searching'). There would be a danger of misuse because the police or government could use such a system to track down political opponents or other 'undesirables' in exactly the same way (for example, by taking DNA from coffee cups left at a political meeting and looking for a match on the DNA database, which then reveals the name and medical details of the individual). Anyone who can infiltrate the system (for example, organised criminal gangs) might also use the database, perhaps to track down victims or expose witnesses on protection schemes or undercover police officers. Unlike the National DNA Database, which is accessible by a small number of people, an NHS database would be accessible to large numbers of NHS workers and researchers all over the world, and would be much harder to keep secure.

Impacts on medical confidentiality and the right to choose

"For decades medical confidentiality has been central to patients' relationships with their doctors, but this right is about to be removed. Quite aside from the serious security concerns, the creation of a system designed to harvest and pass on the medical details of potentially every person in the country is an unacceptable encroachment on the privileged nature of the GP/patient relationship that will undoubtedly deter those with sensitive conditions from seeking help, putting both individual and public health at risk".
MedConfidential Briefing, 2013⁶³.

"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, 2009.⁶⁴

"It is becoming impossible for medical researchers to guarantee privacy to the research participants they recruit – especially with the pressure from funding agencies who insist upon open-access archiving of genomic sequence data, as these data inevitably contain potentially identifying information. Indeed, it would now be misleading to promise privacy of personal genome information to research participants in exchange for consent to donate samples". Cesagen Round-Table Discussion, 2009.⁶⁵

The Government plan has major implications for the doctor-patient relationship and for vulnerable people who may be frightened to seek medical care if their privacy cannot be guaranteed.

Under the Government's plans, doctors will be required to consent on behalf of their patients to transfer of their practice's data to the Health and Social Care Information Centre (HSCIC). But they will have no idea where their patient's medical records will end up or how they are going to be used. The Caldicott Review (Section 7.4) suggests that GPs will be required to explain to anyone who objects to sharing of their medical records that they will only be used for research to improve medicine and the health service and identities will be protected. This is despite the fact that GPs themselves will not be fully informed of how the data will be used and cannot realistically make any guarantees about anonymity. Further, passing data to the Information Centre is likely to be necessary in order for the GP to obtain payments under the Government's Quality and Outcomes Framework (QOFs)⁶⁶ and for commissioning purposes. Thus, the GP's advice may not be disinterested and the consent of the practice to data-sharing cannot be regarded as freely given, since there will be no option to opt-in to selected data uses and out of others.

Some possible scenarios show what loss of medical confidentiality 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.

An individual inherits half their DNA from their mother and half from their father. Hence DNA can be used to identify familial relationships, including non-paternity. Identification of non-paternity can already occur in some NHS screening programmes for recessive genetic disorders (disorders which require two copies of a mutation to be inherited, one from the mother and one from the father)⁶⁷, such as the Sickle Cell and Thalassaemia screening programme. Current guidance states that the risk of non-paternity needs to be handled carefully if relationships and families are not to be disrupted. The Guidance states it is not in the interests of anyone to cause a division in the relationship by revealing this information, that the situation must be discussed with the mother alone (but only when necessary) and the possibility of errors fully considered, and that results must be carefully documented and communicated only to those professionals who need the information to support the family.⁶⁸ It is difficult for physicians to know the consequences of their actions (which may go way beyond issues related to a diagnosis) if they reveal such information. Apart from family breakdown (which may not be in the best interests of the child or other members of the family) there is a risk that routine exposure of such information might drive some women away from seeking appropriate care for themselves or their children, or, in some cases, could put the woman and/or child at risk of domestic violence or even so-called “honour killings”. Whilst such situations are always difficult, they will not be made any easier by breaching confidentiality.

The number of families in this situation will be significantly increased if sequencing of the whole population’s DNA is allowed to go ahead. In addition, the possibility for revelations about non-paternity to disrupt family relationships, or for health related information to have implications for other members of the family, cannot be discussed prior to testing if such testing is conducted on the basis of “presumed consent”. As Professor Sir John Sulston has noted, if everyone has their whole genome sequenced and stored in the NHS “*There will be no secrets about paternity anymore*”.⁶⁹ Even if an individual’s name is removed from data made available for research in the cloud, it is likely that relationships will be identifiable using a process of “deductive identification” based on information that is accessible.⁷⁰ Anyone who has access to linked data (i.e. genomes associated with names and personal identifying information) will be able to identify paternity and non-paternity with a simple search. This adds significantly to the concerns outlined above that collecting, storing and sharing such data when it is not necessary for a person’s care may not be in the best interests of them or their families.

There has already been a sharp increase concerns reported by GPs about separated parents seeking children's medical records.⁷¹ Although this is often well-intentioned, in some cases men are thought to have been seeking access to the information as a way to find out where their former partner is living or whether she has a new partner, which can be a major concern if the mother has been physically abused and living in a place of safety. The NHS Personal Demographic Service (PDS) has already raised concerns because contact details and addresses have been made widely available to NHS staff.⁷² These concerns would be exacerbated by the creation of a DNA database in the NHS because a child’s DNA can often be obtained quite easily e.g. from their toothbrush or hairbrush. Anyone with access to the database could search for a match and find the child’s address and medical records, even if they have changed their name. This means that vulnerable people who have been abused, victims on witness protection schemes, and even undercover police or security officers will have no place to hide, because they cannot change their DNA.

If the Wellcome Trust’s plan is implemented, large numbers of people (including vulnerable women and children) may be forced to seek care outside the NHS to avoid being identified or to keep hidden family relationships from being exposed. Examples of particularly private information that people (including young people) may not wish to be revealed to family

members, employers or others is likely to include: treatment for sexually transmitted diseases, sexual abuse, drug addiction, alcoholism, stress and psychiatric disorders. There will be a danger that some people do not seek care when it is needed because of fears that this will lead to stigma or discrimination in the future, particularly as all records will be retained indefinitely and there will be no possibility of erasing records at a later date.

International transfers of data also raise concerns because data that is sent overseas may not be secure. For example, in the US, medical data can be bought and sold and there is increasing concern about the implications for people's civil rights.⁷³ In other countries, such as China, it is unclear how personal and genetic data might be used, including whether the government or police might be able to gain access. In some countries, particularly in the Middle East, discovery of non-paternity could have very serious consequences for women and their families.⁷⁴ Discovery of other personal medical information, such as use of sexual health or drug rehabilitation services, or HIV status, might also have more serious consequences in some countries, or lead to travel restrictions such as the refusal of visas.

Undermining ethical standards such as those in the Helsinki Declaration means medical professionals might in future be put under pressure to build a DNA database for a dictatorial regime, by undertaking similar analysis of "spare" biological samples without seeking fully informed consent. The surreptitious collection and/or analysis of DNA from adults and babies at birth by medical professionals could readily be abused to build databases allowing the police or security services to track individual political opponents and their relatives. Identification and exposure of linked health data could also be used to target dissidents or other minorities (e.g. homosexuals or particular ethnic groups).

Implications for science and researchers

"Demolition of informed consent is unlikely to remedy the strained relationship between science and common citizens. We should foster the prototype of the citizen-scientist who indeed volunteers for any and all types of research. But that citizen is likely to be not ignorant of what is happening to his or her data; conversely, he or she should be extremely cognizant, in other words, extremely well-informed".⁷⁵ Professor John Ioannidis, Stanford University, 2013.

The Government's plan removes the right for individuals to decide who uses their medical records for research and for what purposes and may even allow whole genomes to be sequenced and shared without an individual's knowledge or consent. Even if an opt-out is allowed, this is likely to be a blanket out-out from any medical research. This means that individuals will not be able to decide whether some research projects are more legitimate and useful than others, or whether they trust some researchers, but not others, to maintain confidentiality and act in the public interest. This could be highly damaging for medical research because people will not be able to opt-in to a specific study without also allowing all their data to be shared with Google, Bupa and other companies or governments. Researchers will no longer be able to make promises regarding how people's information will be used or guarantees about its confidentiality.

Although most researchers dislike red-tape and some approval processes could be streamlined, some statisticians have argued strongly against abandoning informed consent and questioned the value of data-mining large data sets without consent as a means to do research.⁷⁶

One important consequence will be that people will no longer be able to check whether there are conflicts-of-interest involved in research being undertaken using their stored medical

records and genetic data, before deciding whether to take part. Commercial data-mining, aimed at personalised marketing, is not the same as scientific research, conducted in the public interest. In this context it is important to think about the definition of “research” – which according to the Data Protection Act includes any statistical analysis (including, for example, market research) - and about who is a “researcher”. This will be dominated by those who have the money to do the statistical analysis of stored data (or who can pay others, perhaps in universities or other public institutions, to do it). It is likely to include:

- Researchers working for Web 2.0 companies, such as Google (and the Google-funded gene testing company 23andMe) which aims to use personal data for personalised marketing;
- Researchers working for private healthcare companies, such as Bupa and 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;
- Researchers based overseas, in any commercial or government-funded institution in any country.

Making data widely available is unlikely to remove problems with bias in medical research, which can arise from many different sources, including commercial bias caused by conflicts-of-interest in the outcomes of the study.^{77,78,79,80,81,82,83} The history of genetic research is riddled with conflicts of interest involving industries seeking to blame diseases on individuals’ genes rather than their products or pollution (see Boxes I and J). Whilst it is possible that the tobacco industry might not be granted legitimate researcher status needed to gain access to NHS data, other companies – including pharmaceutical, food, chemical, nuclear and private healthcare companies - are unlikely to face restrictions. A major area of interest will be the personalised marketing of products and services based on unregulated predictions of people’s future health.

Box I: History of the Human Genome Project

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 aim of calculating individual risk. The idea is that only a small group of people are genetically susceptible to common diseases or adverse drug reactions and that they should be identified so that any intervention can be targeted at them. However, the individual approach has also been criticised for ignoring the major causes of disease, blaming the victim and producing interventions that can be harmful.⁸⁴

This strategy for public health was invented by the eugenicists who went to work for the tobacco industry in the 1950s and was promoted 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 in the late 1980s (Box J). The idea of genetic “prediction and prevention” of disease was 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.⁸⁵ As a result, medical research was redefined to mean “discovery” of genes linked to disease and looking for risk factors inside people’s bodies rather than in social or environmental conditions or in products such as processed foods. Individual risk factors could then be treated with medical products or functional foods (such as cholesterol-lowering margarines), rather than by tackling poverty or implementing controls on unhealthy products or pollution.

Repeated false claims have been made to support the idea of a “genetic revolution” in the NHS (for example by former Prime Minister Tony Blair): stating that in future scientists will be

able to predict and prevent the diseases people are likely to develop by sequencing their genomes and treating them before they develop any symptoms.⁸⁶

BOX J: Genetic research and the tobacco industry

Sydney Brenner (then based at the Medical Research Council, MRC), now a Nobel Prizewinner and co-founder of Population Genetics Technologies, is credited with persuading Margaret Thatcher to fund the Human Genome Project, following a secret meeting with British American Tobacco (BAT) in which he endorsed the idea of genetically screening smokers in order to predict which of them would get lung cancer.⁸⁷ The idea, based entirely on false findings by tobacco-funded scientists, was to target smoking cessation at a minority of genetically susceptible individuals and tell the rest of the population they could smoke “with impunity”. This approach to public health was promoted for many years as a key justification for the Human Genome Project, with much of the research jointly funded by the MRC and some by the Wellcome Trust. It was based on a theory published by the eugenicist Ronald Fisher (whose former student Sir Walter Bodmer co-founded the Human Genome Organisation with Brenner, to lobby governments for funding).

In order to support the spurious argument that genetic screening could lead to a significant reduction in cases of lung cancer, a Pharmacogenetics Unit was set up at the University of Newcastle, led by tobacco-funded researcher Professor Jeffrey Idle, which analysed samples taken from lung cancer patients and healthy controls. At that time, conflicts-of-interest were not required to be declared to research participants. Many of the misleading findings were published in a journal edited by Idle and widely promoted in the press. Myths promoted by the industry – such as the idea that it must be possible to predict who gets lung cancer by testing their genes – persist today, because they have never been publicly corrected (in reality, lung cancer does not have a significant inherited component). Tobacco-funded researchers are also responsible for misleading claims that genetic tests can predict the likelihood of smoking.⁸⁸

Another issue for researchers is the extent to which the idea of collecting and storing such vast amounts of data is really a good research priority. The proposal relies on data-mining (the computational process of discovering patterns in large data sets), a sub-discipline of computer science, and collection and storage of very large amounts of data (known as “Big Data”). Enthusiasts of Big Data in healthcare see the main objective as identifying correlations between genotype and phenotype (the physical characteristics of a person).⁸⁹ The use of large data sets and sophisticated statistical techniques increases the statistical power to detect weak correlations such as those between SNPs and common, complex diseases. However, predictions based on multiple correlations can have low predictive value and can be misleading for a variety of reasons, particularly when the effect size of each SNP is expected to be small. Risk assessments may be difficult to validate and/or may not be useful to improve people’s health. Researchers from disciplines such as evolutionary theory and psychiatry have highlighted the enormous difficulties in making sense of all the information.^{90,91}

Like all science, Big Data or “hypothesis free” science is based on hidden assumptions that define a paradigm: for example, an emphasis on using biological data (particularly genomic data) to predict individual risks, rather than environmental or social data (although the latter may be integrated at some stage in the future); the treatment of genetic variants such as SNPs as fixed risk factors, rather than context-dependent ones; an assumption that identification of future genetic variants will increase the utility of personalised risk assessments sufficiently for their use to improve health outcomes; and a focus on individuals and individual actions (lifestyle changes or medical interventions) rather than population-

level policy responses to improve public health (such as stricter regulation of medicines to prevent adverse drug reactions; or measures to restrict the marketing of unhealthy foods).

Ideas promoted in Silicon Valley, which assume that everything can be predicted by computers⁹², underlie the concept of Big Data. Companies are expected to extract commercial value by data-mining large sets of data, often using the results for personalised marketing. Science itself is being re-defined to fit this idea with concepts such as “hypothesis-free” science and “4th paradigm science”. This allows companies to pretend they never need to check whether the assumptions they make when analysing the data are correct, or to show the predictions they make are fit for the claimed purpose (known as “validation”). This is the same approach that led to the collapse of the financial markets.⁹³ Further, it remains rooted in the assumptions made by the eugenicists that free will does not exist and all human characteristics and behaviours can be predicted from a complete knowledge of all the relevant environmental and genetic factors (determinism).

There will, in effect, 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 could lead to multiple possible interpretations and misinterpretations.^{94,95} Lack of any prior hypothesis appears to undermine the scientific value of this type of approach.⁹⁶ Unlike search engine algorithms, which can be improved by feedback about the information people want and whether or not their search has been successful, algorithms predicting individual health risks will be impossible for the recipient to verify.

Good for health?

“In addition to the (currently largely hypothetical) advantages of analysing the personal genome, there are all too real disadvantages to obtaining information that could be burdensome or even harmful. Disadvantages include worry caused by (still) unclear findings and the resulting – often unnecessary – contacts with healthcare. As long as there is no clear positive balance of advantages and disadvantages, there can be no responsible implementation of whole genome population screening within public healthcare. However as soon as WGS/WGA [Whole Genome Sequencing/Whole Genome Analysis] becomes cheap enough, commercial parties will likely see a market.” Ethicists at the University of Maastricht, 2013.⁹⁷

“... many of these studies show that adding polygenic [multiple gene] information to risk-prediction models, when available, provide no or little additional discrimination... to current risk-prediction models based on traditional risk factors such as age, body mass index, and lipid levels”. Professor Muin Khoury, Director, Office of Public Health Genomics, US Centers for Disease Control and Prevention, and co-authors, 2013.⁹⁸

“Ten to 15 years ago we thought that we would be using genetic tests to predict all sorts of diseases. It turns out to have been wishful thinking. We used to think there might be five to 10 genes involved in a disease, but we now know there may be thousands that only contribute a tiny amount and interact with each other.” Professor Tim Spector, King’s College London, 2013.⁹⁹

“There are likely to be fundamental limits on precise [genetic risk] prediction due to the complex architecture of common traits, including common variants of tiny effect, rare variants that cannot be fully enumerated and complex epistatic [gene-gene] interactions, as well as many non-genetic factors”. Human Genome scientist Professor Eric Lander, MIT, 2011.¹⁰⁰

GeneWatch UK
May 2013

There are many different types of genetic testing which can be useful in specific circumstances. Currently, clinical use of genetic testing in the NHS is restricted to tests of specific genes in specific circumstances, which include: diagnosis of genetic disorders (often in babies and children); carrier testing (identifying rare mutations which must be present in both parents before a child develops a particular disease) for specific diseases within screening programmes or specific families with affected members; testing for predisposition to the relatively rare familial forms of some disorders (particularly breast cancer) in members of high risk families (an example is the mutation in the BRCA1 gene recently identified in actor Angelina Jolie); cascade screening of family members already diagnosed with a genetic condition or predisposition; and pharmacogenetic testing (genetic tests to predict drug response) for a few specific drugs and conditions. Pre-natal testing and screening is also available for a small number of conditions. Cancer patients may also be given somatic (non-inherited) pharmacogenetic tests designed to identify specific genetic mutations or gene expression patterns in cancer tumours. A few cancer drugs are available which are given to specific groups of patients based on these test results.

All these applications make a clear distinction between genetic testing (for people who have symptoms or a strong family history of a particular disease) and screening (for the general population). Criteria for the use of screening exist which are intended to ensure that the overall benefits to the population outweigh the harms. However, the “Number Needed to Treat” to prevent one case of a disease in screening programmes is nearly always high: many people identified as at risk will not have developed the condition (known as “false-positive” results) and may be treated unnecessarily (as a result of “over-diagnosis”). Use of genetic tests – especially whole genome scans - in population screening will increase false-positive and ambiguous test results, over-diagnosis, and incidental findings.¹⁰¹ As more independent tests are added to screening panels, the overall number of false positives (people informed they are at risk of a disease they are never going to get) inevitably goes up.

Implementation of the Wellcome Trust plan means abandoning any attempt to weigh up the benefits and risks to an individual or to the population, in favour of screening the whole genomes of the whole population. This idea involves the “creative destruction” of health services, to create new systems which revolve around information stored in electronic medical records, with the addition of genotypes or whole genomes. Under this scenario, each patient would receive a personalised risk assessment based on the information stored about them and this would form the basis of their future care. The primary commercial purpose of screening everyone’s whole genome is to make each person in the population a patient “from the cradle to the grave”, instead of only when they develop symptoms or regard themselves as ill. This allows people to buy health products – or be prescribed them by the NHS - based on their (or their baby’s) predicted risks. In the pharmaceutical industry’s view patient care would be improved by earlier treatment which would at the same time expand the market.¹⁰² However, others have expressed concern about the creation and treatment of a new type of patient, i.e. the person ‘genetically at risk’, and the resulting ‘biomedicalization’ of health and illness, which involves the privatisation of research and a focus on health surveillance as a moral obligation.¹⁰³ Earlier treatment of more people has the potential to significantly expand the market for medication and other health products such as functional foods because the “at risk” group is always significantly larger than the number of people who actually develop a disease.

One of the drivers behind the Wellcome Trust’s plan is to create a market for whole genome sequencing (WGS) by claiming that genomic research is ready to be translated into clinical practice. This involves blurring the line between researchers’ interpretations of an individual’s data (including those made by commercial companies) and clinical

interpretations (which normally require a process of assessment to determine how reliable and useful they are for improving people's health).

The Caldicott 2 report (Box D) defines **data** as “*qualitative or quantitative statements or numbers that are assumed to be factual, and not the product of analysis or interpretation*” and **information** as “*the output of some process that summarises interprets or otherwise represents data to convey meaning*”. However, it does not discuss the difficulties in interpreting data or conveying meaning, nor does it define **misinformation**, which can also result from (mis-)interpreting data. Whole Genome Analysis (WGA) is the term often used to describe the interpretation of whole genome sequencing (WGS), but WGA is not a simple process of reading out the meaning of the genetic code.

To date, sales of genetic tests by commercial companies have been controversial for several different reasons. Firstly, investigations (including by the US Government Accountability Office (GAO);^{104,105} academic researchers¹⁰⁶; and GeneWatch UK¹⁰⁷) have uncovered numerous examples where false or misleading claims have been made about genetic risk, in some cases accompanied by incorrect health advice or attempts to market products (usually supplements). These problems often arise due to the inclusion of SNPs that are not actually related to the risk of the disease (usually due to the large number of false statistical associations in the published scientific literature). Secondly, there is no definitive method to interpret an individual's genetic risk from pieces of information about the risk associated with different SNPs in different studies: these risks may depend on the context (both environmental and biological) and may combine in complex ways, which are not yet fully understood and may not always be predictable.¹⁰⁸ These two problems mean that different companies may give very different interpretations of a person's risk based on the same DNA.¹⁰⁹ Thirdly, there is growing evidence that the predictive value of genetic information for most diseases in most people is (and will remain) rather poor (even when more research is done), meaning that many genetic tests do not provide useful information for a person's care (and the usefulness is often exaggerated in marketing materials).¹¹⁰ This is also the case for many (but not all) genetic tests which aim to predict drug response (pharmacogenetic tests).¹¹¹ Finally, because rare mutations can sometimes have unexpected serious consequences (even though most tests have poor predictive value) there is the potential for nasty surprises which people may not be prepared for unless they have pre-test counselling to explain the pros and cons.¹¹² These problems are compounded by weak regulation of genetic tests and other predictive health information (Box K).

Box K: Weak regulation of genetic tests and computer-based health risk assessments

Commercial companies have repeatedly made misleading claims about genetic test results, including those sold direct to consumer (DTC) online and via private doctors. The EU's new IVD (In-Vitro Diagnostics) draft Regulation is supposed to regulate predictive genetic tests and software but is effectively meaningless as it provides no regulatory check of the companies' claims.¹¹³ If adopted by the European Parliament, the new Regulation is likely to be used by commercial lobbyists in US-EU Free-trade negotiations to undermine attempts by the FDA to regulate genetic tests in the United States, including those sold by Google's gene test company 23andMe.^{114,115,116}

Importantly, there are inherent limitations to the predictive value of genetic tests (and indeed, of any risk predictions) due to the complexity of natural systems, including interactions between environment and biology and the roles of choice and chance. Links between genetic factors and common diseases can provide useful clues about biology and how diseases develop.¹¹⁷ But most genetic factors seem to change a person's risk of common diseases only very slightly. Rather than a single gene predisposing someone to disease, it now seems likely that everyone possesses hundreds, perhaps thousands, of genetic

variants some of which slightly increase their risk, whilst others slightly decrease it.^{118,119} In reality, genetic variants do not have a property called risk, they act through their effects on complex biological pathways, and the risk of a particular genetic variant depends on the rest of biology and on the environment.^{120,121} This means that the idea that an individual's genetic risk of common diseases can be predicted has become increasingly controversial amongst scientists.^{122,123}

In general, common genetic differences are not more but less predictive than most other types of test, and no common genetic variants exist – either singly or in combination - that meet medical screening criteria for the general population.¹²⁴

Many geneticists are puzzled at the lack of success in finding the expected inherited component of common diseases.^{125,126} However, whilst many believe that more genes will be discovered which explain this 'missing heritability', others have long criticised the calculations (usually made from twin studies), and claim that the assumptions used inevitably exaggerate and oversimplify the role of genes.¹²⁷ This means that some or all of the so-called "missing heritability" that future research is supposed to find may not actually exist.^{128,129,130}

In reality, much research suggests that 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 (i.e. little prospect of bringing any benefit to health).^{131,132,133,134} 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.¹³⁵

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.^{136,137} Although some enthusiasts have tried to argue that the complexity of biology was unexpected, the poor predictive value of genetic tests for common diseases is not really a surprise.^{138,139,140,141,142,143}

Some examples of genetic associations with common diseases are given in Boxes L, K and M.

Box L: Breast Cancer

Rare mutations in specific genes cause 'familial' cancers. The best known examples are mutations in the BRCA1 and BRCA2 genes, which significantly increase the lifetime risk of breast cancer, to between about 50%-90%. However, these mutations account for only about 5% of breast cancer cases and are not recommended for screening in the general population due to uncertainties in their interpretation outside high risk families. The most effective action that a woman can take to reduce her risk is to have a prophylactic double mastectomy, although more frequent screening to try to catch any cancer early is another option. The National Institute for Health and Care Excellence (NICE) is currently updating its clinical guideline on familial breast cancer, which includes new, provisional recommendations on the use of the drug tamoxifen as an alternative approach to prevention of breast cancer in women at high risk. Although the drug appears to reduce risk a new study suggests 42 women would need to be treated with this drug to prevent one breast cancer event in the first 10 years of follow-up. Side effects include increased risk of cancer of the uterus and blood clots.^{144,145}

The hunt for the remaining genes, thought to increase people's risk of 'sporadic' (non-familial) cancers has been disappointing. For example, a study in 2008 found that combining all the common genes linked to breast cancer did not improve risk predictions compared to

existing models using non-genetic risk factors.¹⁴⁶ Some scientists have argued that spending more resources searching for such small genetic factors is a waste of money.¹⁴⁷ A series of papers published recently as part of the iCOGs study have found more SNPs with links to breast, ovarian and prostate cancer.¹⁴⁸ The top 1% of women at risk in this study were estimated to have about a 1 in 3 risk of breast cancer. This means if 10,000 women were screened, 100 would be in the highest risk group, about 33 of whom would be expected to get breast cancer. Giving all 100 high risk women tamoxifen would significantly expand the market for this drug and might prevent one woman getting breast cancer, but all the women taking it would be at risk of side effects. If lower risk groups were given preventive medication, even more women would be unnecessarily treated. In addition, the risk genetic assessments might not be reliable because the calculations assume the risk of carrying each SNP is fixed and that the statistical findings of the study are correct. Many of the iCOGs scientists have proposed that genetic screening should be used to implement a stratified breast screening programme, rather than giving preventive medication: this means all women would be screened genetically and then invited for mammography at different ages depending on their calculated genetic risk. However, other scientists are more sceptical about the complexity of this approach.¹⁴⁹ If individual risk predictions are fed back to patients these might also be used in other ways, for example for personalised marketing by private health or pharmaceutical companies. A new Wellcome Trust-funded study has just been announced to study whether testing cancer patients for breast cancer genes might help to make better decisions about their care: but the results of this are not yet known.¹⁵⁰ Testing cancer patients for specific mutations or SNPs is in any case very different from screening large numbers of healthy people for all genetic variants. Other research studies involve testing the genetic mutations that arise in cancer cells: again these are not relevant to healthy people.

Box K: Diet-related conditions

Type 2 diabetes (adult-onset diabetes) is strongly linked with being overweight. A total of 18 genes have been linked with type 2 diabetes but they do not improve risk predictions compared with measuring existing risk factors (such as body mass index, waist size and blood glucose levels).¹⁵¹ Calculating genetic risk alone and updating risk factors may produce contradictory information about an individual's risk status over time, with some people changing from low risk to high risk and vice versa.¹⁵² In a study of tests for genetic risk of type 2 diabetes sold directly to consumers, the addition of genetic factors to the clinical risk factors either did not change or only marginally improved predictions beyond the clinical risk models.¹⁵³

Susceptibility genes for **hypertension** have been very difficult to detect.¹⁵⁴ Studies have found genetic variants with individually small effects and with only partial overlap between study findings.¹⁵⁵ These genes explain only about 1% of the observed differences between individuals.¹⁵⁶ More recent Genome Wide Association studies (GWAS) have found more SNPs which may be linked to hypertension but added little to the predictive value of the tests.^{157,158}

A rare inherited form of high **cholesterol levels**, called familial hypercholesterolemia (FH) affects about 1 in 500 people.¹⁵⁹ But attempts to find more common genetic variants have been disappointing. Variability in cholesterol levels between individuals does not seem to be strongly influenced by genetic factors in most people.¹⁶⁰ A 2008 study of nine common genetic variants associated with cholesterol levels found that they did not improve clinical risk prediction in 5000 subjects.¹⁶¹

About 600 genes have been linked with increased risk of **obesity** but only two or three of these have been confirmed as more studies have been done. Together they account for less than 1% of the observed differences in body mass index (BMI) between individuals.¹⁶² More

recently GWAS have found more SNPs associated with obesity but including these new genetic variants only explains an estimated 1.45% of the inter-individual variation.¹⁶³ The genes identified are thought to influence appetite, not metabolism: they do not mean that some people can eat more than others without getting fat, or that only a minority of people need to eat healthily.¹⁶⁴ The Government's own Foresight programme recognises that tackling obesity requires a diversity of measures to create a healthier environment and better diets for everyone.¹⁶⁵

Box M: Other examples of diseases and conditions

Diseases and conditions vary greatly in complexity but all common conditions remain poorly predictable from people's DNA.

Analysis of genetic risk predictions of **Type 1 Diabetes** has shown that the (limited) predictive value of an early link with a gene involved in immunity has not been significantly improved by adding new links with SNPs and, importantly, is unlikely to be improved by adding any new discoveries.¹⁶⁶

Genetic tests for complex **cardiovascular disease** also have minimal predictive ability and no clear benefits and overall screening performance is poor.^{167,168}

In 2009, three published studies identified 30,000 genetic variants that may be linked with **schizophrenia**.^{169,170,171} However, most were not individually significant and their claimed causal roles have yet to be confirmed. Each genetic variant appears to marginally increase the risk and scientists do not know how these small differences in individual risk might be combined to attempt to predict who might develop schizophrenia. There is no overlap between genes identified using genome-wide association studies (GWAS) and genes previously thought to be linked to schizophrenia.^{172,173}

Age-related macular degeneration (AMD), which causes loss of vision with age, is one of the best predicted medical conditions based on known genetic risk factors. However, for age groups of over 80, over 65 and over 40, only 30%, 12% and 3% of the group classified as high genetic risk actually develop AMD.¹²⁴

The way people metabolise some drugs can sometimes be deduced from analysing their DNA: these tests are known as pharmacogenetic tests. However, these limited, specific applications also do not appear to justify a roll-out of whole genome sequencing to the whole population. They should be used, as they are now before prescribing a specific drug, if and when evidence from trials indicates improved health outcomes.^{174,175} Adverse drug reactions have been rising¹⁷⁶ but this is not because of an increase in genes for adverse drug reactions but because of a variety of factors including more older patients, possibly combined with weaker regulation and greater use of over-the-counter and off-label medicines (a trend that will be exacerbated along with over-treatment). For example, if drug use doubles as a result of treating healthy people based on their genetic risk (as some predictions suggest), adverse drug reactions and side effects will also increase significantly, even if pharmacogenetic tests are useful in some circumstances.

Rejecting the Wellcome Trust's proposal would not mean rejecting medical research or the use of genetic testing altogether. The alternative is to continue to recruit people to research studies which are separate from their care, with their fully informed consent, and to implement specific tests in healthcare as and when their benefits outweigh the risks. In this scenario, new tests will be introduced more gradually for specific groups of people, mainly those who are already ill or who have a strong family history of a particular disease. Whole genome sequencing would remain relatively rare and used mainly for children with undiagnosed genetic disorders and perhaps also for cancer tumours, if and when trials show that this can lead to better treatment. A more measured approach to the introduction of genetic and genomic tests would affect much smaller numbers of people and provide much

less of a challenge to existing systems for assessing risks and benefits and for obtaining informed consent and protecting privacy.

At the same time, traditional public health approaches should be used to reduce the incidence of common diseases by tackling health inequalities, poor diets, smoking and pollution.

Potential for stigma and discrimination

The Caldicott2 report proposes that multiple data sets will be linked in so-called “safe havens” and this information to be made available for research. This means employment, education, social care, tax and police records could all be connected. Since de-identification is unlikely to be preventable, and some use by insurers is anyway expected, there is a possibility that people may be refused insurance, visas or a job based on this information. There is potential for stigma and discrimination based on stored medical information (e.g. past use of drug rehabilitation or sexual health services, or unhealthy habits such as poor diets or smoking); other unrelated data (such as employment or tax histories); or genetic make-up. Fear of stigma or discrimination might make some groups of people less willing to seek medical care, especially if they fear losing their job or benefits, or having their children taken into care.

Most genetic variants are poor predictors of most diseases in most people, however this will not necessarily prevent genetic discrimination. The idea that genetic variants would be used in workplace screening was first promoted by tobacco-funded researcher Jeffrey Idle (see also Box I), who was a co-author, with US National Cancer Institute researchers, of an early (1989) study of susceptibility to lung cancer in workers exposed to occupational carcinogens, which advocates screening and targeting of susceptible workers.^{177,178} This idea is questionable on both ethical and scientific grounds (because genetic tests are poor predictors of who will develop most workplace illnesses)¹⁷⁹ and is opposed by a large number of organisations and individuals.¹⁸⁰ It implies that rather than taking measures to make the workplace safe, workers calculated to be genetically susceptible to workplace-related illness will simply be excluded from employment.

The Equality Act 2010 restricts what employers can ask about in pre-employment medical checks, so they can only ask for information that is directly relevant to the applicant's ability to carry out the work, or needed to make 'reasonable adjustments' to the workplace to enable a particular person to work there (as required by law). This largely allays fears about genetic discrimination in the workplace, and discrimination based on other medical information, because it tightly restricts the circumstances in which employers could access job applicants' or employees' medical and genetic information. However, this protection would be undermined by the plan to create a DNA database in the NHS because employers can become researchers. For example, an employer could conduct a study on their own employees by data-mining the genomes and associated medical data stored in the cloud. Because of the high potential for “deductive identification” individual workers' data is likely to be identified and could be misused e.g. to dispute a compensation claim¹⁸¹.

There is currently a voluntary agreement between the insurance industry and government which means the industry does not use predictive genetic test results to determine insurance premiums, with one exception for high value policies.¹⁸² However, there is no legislation to prevent genetic discrimination by insurers in the future. Insurers might be able to access data surreptitiously whilst working as researchers but more likely they would simply require the release of genomes or genetic risk information as a prerequisite to obtaining coverage. Although most diseases in most people are poorly predictable from people's genes, there are exceptions (such as mutations in the BRCA1/2 genes and breast cancer risk) which

could be of interest to insurers. It is also likely that this requirement would apply to all individual risk assessments, whether they are based only on a person's medical records or also on their genome.

Health risks are not the only risks that might be calculated from a person's genome. Although studies of genetics and behaviour have to date delivered very little (none of the many statistical associations made between genes and intelligence¹⁸³ or personality¹⁸⁴ have been definitively confirmed) it is also possible that people might be treated differently in future based on studies linking their genes with high or low intelligence or criminality, even if these links are spurious.

Who decides?

"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, 2008.¹⁸⁵

"The problem, for Morozov, is that this new open government - the thing that Silicon Valley types would love to inject into our actually existing government - wouldn't be about accountability to its citizens and political transparency. It would be about making government data available to companies that will mine it for profit". Review of Evgeny Morozov's essay *The Meme Hustlers*, 2013.^{186,187}

Many aspects of the Health and Social Care Act have been criticised for not having been spelt out in the coalition parties' manifestos. Failure to consult or inform the public about data-sharing plans is yet another failure to be open with the electorate.

The latest Government plan 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, including the Wellcome Trust, since at least 1999, with the support of the New Labour Government.¹⁸⁸ The Department of Trade and Industry (DTI) 1999 report "*Genome Valley*" endorsed claims that genomics would revolutionise healthcare by allowing predictive profiling, without making any assessment of the likely costs, or of the claimed benefits to health or the economy.¹⁸⁹ The report also highlighted the value of making NHS data available to industry for research as Britain's 'unique selling point' (USP) in the knowledge-based economy. This same plan – changed only by storing the data in the cloud rather than on a single government database - is now being promoted by Prime Minister David Cameron and Conservative ministers, as a result of being lobbied by many of the same vested interests as before. This raises important questions about the role of democracy and its relationship to science and technology. In practice a small circle of advisers is promoting what they claim will be a technical solution to rising healthcare costs and lack of economic growth, in the absence of any public scrutiny or debate about the pros and cons of their vision of the future.

The **Wellcome Trust** was a major player in the Human Genome Project and has lobbied persistently for a DNA database of the whole population to be set up.^{190,191} It is Britain's second largest registered charity (after the Big Lottery Fund) and has a £13.8 billion fund. The Trust has significant venture capital investments,¹⁹² and recently launched a £200 million investment business¹⁹³ and appointed a new Venture Capital investor to its Board¹⁹⁴. The Wellcome Trust, then the Wellcome pharmaceutical company's largest shareholder, supported the 1995 merger which created Glaxo-Wellcome (later to become Glaxo-SmithKline) by backing a hostile bid from Chariman and CEO Sir Richard Sykes without consulting the company's board.¹⁹⁵ Gordon Brown's Comprehensive Spending Review in

1998 created a public-private partnership between the Government and the Wellcome Trust¹⁹⁶, which allowed it to control research priorities and hence how public money as well as its own fund would be invested. The Trust also increased its funding for the Human Genome Project to allow its Sanger Centre to decode one third of the genome.

When Tony Blair and President Bill Clinton announced the completed draft of the human genome, on 26th June 2000, a packed press conference was held at the Wellcome Trust (which was thanked by Blair in his speech).¹⁹⁷ The Trust has played a major role in how stories about genetics and genomics are reported in the media ever since. The Science Media Centre (SMC, which has been criticised for its industry funding and control of the science media¹⁹⁸) is housed in the Wellcome Trust and part-funded by it.¹⁹⁹ Genetic scientists and ethicists who feel uncomfortable about the Wellcome Trust's claims and proposals rarely challenge their funders in public (because they do not wish to "bite the hand that feeds them"^{200,201}) and access to policy makers and the media to talk about the human genome is largely driven and facilitated by the Trust.

Since the Coalition Government came to power to end June 2011, the Wellcome Trust has had 26 government meetings (including one with Chancellor George Osborne, eight with Science Minister David Willetts, three with the Prime Minister's Permanent Secretary Jeremy Heywood, three with Chief Medical Officer Sally Davies and a meeting to discuss data-sharing with Minister for the Cabinet Office Francis Maude)²⁰²; Google has had a further 26 government meetings (including three with Chancellor George Osborne and one with the Prime Minister)²⁰³ and the Academy of Medical Sciences has had 12.²⁰⁴ Private healthcare company GE Healthcare has had four government meetings, three of them with Willetts.²⁰⁵ It is clear that lobbying has focused on Conservative ministers, rather than the Liberal Democrats.

Professor **Sir Mark Walport** led the Wellcome Trust for ten years before being appointed as Government Chief Scientist from 1st April 2013. A previous attempt, led by Walport, 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 (including the Conservatives and Liberal Democrats).^{206,207} Amongst many critics, the British Medical Association (BMA) warned that "*This Bill strips patients and doctors of any rights in relation to the control of sensitive health information*" and opposed the adoption of the data-sharing legislation, which had been hidden in Clause 152 of the Coroners and Justice Bill by the then Justice Minister Jack Straw.²⁰⁸

Former GlaxoSmithKline Chairman **Sir Richard Sykes** had a 30-year career in the pharmaceutical industry. He served on many task forces under the previous government and, as Rector of Imperial College, proposed the introduction of student fees to Tony Blair. In 2000, Sykes wrote a book on the future of the NHS which 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. Sykes argued that a new model for the NHS should allow patients to pay for extra medicines outside NHS funding, whilst keeping the NHS only as a basic service for people who are ill, thus allowing the pharmaceutical industry to increase its profits.²⁰⁹ The first Academic Health Science Centre (AHSC) was created by Sykes in 2007 by bringing Imperial College Healthcare NHS Trust and Imperial College London together.^{210,211} He was made head of NHS London in 2008 but resigned in 2010 after a row with then Health Secretary Andrew Lansley.²¹² Since December 2011, Sykes has been Chair of Imperial College Healthcare NHS Trust.²¹³

A more recent major influence is **Sir Li Ka Shing**, a Hong Kong business magnate, investor, and philanthropist considered to be the richest person in Asia, with an estimated wealth of **GeneWatch UK**
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\$31 billion. He is the world's largest operator of container terminals and the world's largest health and beauty retailer and his venture capital firm Horizons Ventures has stakes in Facebook and a number of new internet and technology startup firms.²¹⁴ In May 2013, Prime Minister David Cameron launched the new Li Ka Shing Centre for Health Information and Discovery at Oxford University, supported by a £20m gift from the Li Ka Shing Foundation and £10m for big data research from the Higher Education Funding Council for England.^{215,216} The launch was attended by **Lord Patten**, former Chairman of the Conservative Party and the last Governor of Hong Kong, who is currently both chairman of the BBC Trust and Chancellor of the University of Oxford.²¹⁷ The Li Ka Shing Centre, through its Big Data Institute, will develop approaches for generating, storing and analysing large datasets in medical science including electronic patient records and DNA sequencing for personalised medicine.

The Chair of the Human Genomics Strategy Group (HGSG), **Professor Sir John Bell** (who founded the Wellcome Trust Centre for Human Genetics at Oxford University in 1993), has been a long-term advocate of sequencing and storing the DNA of every individual in the NHS, based on misleading claims about the likely benefits to health.^{218, 219} Bell is one of the Prime Minister's Life Sciences Champions (advising on its Life Sciences Strategy), chairs the Office for the Strategic Coordination of Health Research, and is a former President and founder of the Academy of Medical Sciences. He is now the co-chair of the Centre for the Advancement of Sustainable Medical Innovation (CASMI), a partnership between Oxford University and UCL.²²⁰

Google is one of the commercial companies with an interest in the plan. The company has invested almost \$12 million to date in a gene testing company called 23andMe, which sells gene tests online.²²¹ **23andMe** was founded by Ann Wojcici, who is married to Google-founder Sergei Brin: both are also personal investors in the company. In 2008, 23andMe held a "spit-party" in New York, attended by Rupert Murdoch, and revealed that his wife Wendi is a financial backer: enthusiastic stories about the company were later run in the Murdoch press.^{222,223} In 2008, John Bell told the House of Lords Science and Technology Committee that Google had already been involved in discussions at the Department of Health about analysing genome data in the NHS.²²⁴ 23andMe met Cameron's advisor **Steve Hilton**, who has close links to Google (his wife Rachel Wetstone is global head of communications and public policy), in 2009.²²⁵ Hilton, who left to take a sabbatical, has recently been invited back into No.10, but has chosen to stay in California and fly in to London just a few times a year to join a new Conservative Party Advisory Board.^{226,227} In 2011, Google invested in a company that plans to use cloud computing to store DNA data.²²⁸ Google is developing a new £1 billion headquarters in London at King's Cross, near the Francis Crick Institute.²²⁹ Although it is the market-leader in online genetic tests, 23andMe has only about 250,000 users²³⁰ (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). Accessing all data in the NHS would provide a major route to expand its market, especially if the company could simultaneously undermine the FDA's gene test regulation plans and EU data protection laws, via the EU-US Free Trade Agreement which is currently under negotiation.

When the New Labour 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 was an advocate of the idea of 'early health' as described in a 2008 paper from the industry side of the MMTSG.²³¹ 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*

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nutritionals". The paper states that there will be increasing consumerism, including ordering directly over the internet, bypassing medical professionals, and more suppliers will be engaged in "nurse-led care". Sir William Castell, Chair of the Wellcome Trust since 2006, is a former CEO of GE Healthcare.²³² Other private healthcare companies also favour this approach because screening healthy people is a way to make more profits: rich, healthy people have more disposable income than poor sick people do.

A major incentive for investors is the potential to expand the healthcare market to large numbers of healthy people, perhaps including whole populations from birth, and to capture data which allows personalised marketing. Burrill & Co, a specialist venture capital company for biotech companies envisages.²³³

- routine genetic screening – using whole or partial genome scans conducted by gene testing companies - delivered by nurse-staffed pharmaceutical outlets in supermarkets 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;
- a near-doubling of the pharmaceuticals market by 2020, including the creation of big new markets in 'wellness' and obesity, allowing healthcare companies to "generate value" throughout people's lives.

Gene sequencing companies and their investors also stand to gain significantly from the roll out of whole genome sequencing.

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.²³⁴ Illumina is now involved in a pilot project in the Faeroe Islands which has been established to test the practicalities of integrating whole genome sequences into electronic medical records.²³⁵ In the UK, sequencing company Oxford Nanopore, which was spun-out from Oxford University in 2005, has investment from Illumina as well as a licencing deal,²³⁶ although there are technical problems with its sequencing technology.²³⁷ Its venture capital investors include IP Group^{238,239}, whose CEO (Alan Aubrey, a Director of Oxford Nanopore²⁴⁰) was until recently on the audit committee of the Department of Business, Innovation and Skills (BIS).²⁴¹ Oxford University is also an investor in the company and will profit from any future income.²⁴²

The genome data sent to the Wellcome Trust "Genome Campus" in Hinxton, Cambridgeshire, is likely to be processed in batches using a method developed and patented by a Cambridge-based company, Population Genetics Technologies.²⁴³ 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, Box J). Its investors include the Wellcome Trust.²⁴⁴

Other industries, including the food industry and computer companies, expect to benefit from an individualised approach to public health and from involvement in the storage and sharing of vast amounts of data expected to be generated.

Implications for the NHS

“Future health services will not revolve around consultants in hospitals. Instead, they will facilitate the active involvement of users themselves in providing their own care, drawing on a detailed understanding of a personalised risk profile, working with nurses, pharmacists, nutritionists, fitness experts and other advisers more often than with the specialist doctors of today”. Lord Darzi, 2013.²⁴⁵

“We’ll get a group of patients and do what I call data-driven segmented interventions. This means identifying a group more likely to be admitted to hospital, develop diabetes, at risk of developing hospital acquired infections. And targeting your interventions more than you would across the general populations.”
“So we’ll be linking data, doing risk profiles on the data then feeding it back to GPs to adapt their care. That’ll be OK because we’re feeding data back to the people who gave it to us for it to be used in direct patient care.” Dr Mark Davies, the HSCIC’s Executive Medical Director, 2013.²⁴⁶

The plan to create a DNA database of everyone in England within the NHS involves:

- A significant increase in the amount of personal information collected and stored about every individual (including babies and children);
- Sharing of personal data and genomes with large numbers of researchers, many involving public-private partnerships, including overseas;
- Major up-front investment in transforming infrastructure in the absence of evidence of significant health benefit for common diseases;
- A shift away from hypothesis-driven science to data-driven science (data-mining);
- A blurring of the line between research and clinical application, as interpretations of much of the stored data may be preliminary and uncertain;
- A significant shift in resources away from people who are sick (i.e. present with symptoms) towards people who are healthy (based on their personalised risk assessments);
- Major changes in the roles of individuals, families, medical professionals and commercial companies in medicine, involving increased use of computer algorithms, decision-support systems and online services in the diagnosis and prediction of disease.

The Prime Minister appears to have been persuaded to adopt the Wellcome Trust’s plan because it will attract significant capital investment. There is little doubt that venture capitalists like Li Ka Shing and companies like Google, GE Healthcare, Bupa and GlaxoSmithKline see NHS medical records as a gold mine that they would like to data-mine. But it is less clear that this will bring economic benefits, beyond employing a few hundred scientists and technicians. It is also unclear to what extent even these jobs will be based in Britain, since much of the data-mining could be done offshore. Further, if tax avoidance schemes continue, any profits are likely to be declared elsewhere and limited taxes paid in Britain.²⁴⁷

The Wellcome Trust plan is 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. The purpose of this approach is to change the business model: by first sinking the costs (with the public sector paying for much of the infrastructure and for collecting and storing people’s electronic health records and DNA) and then feeding back predictions made about risk of disease or

drug response. This will lead to a massive increase in the market for whole genome sequencing and data storage and analysis services, making a few venture capital investors (subsidised by R&D tax credits) very rich, whether or not any benefit to health is actually delivered. This is problematic because these investments are not accountable to customers (the people who have their DNA sequenced), because they have no choice, or to taxpayers (the people subsidising the public-private partnerships), because the plan has not been democratically debated and decided. Thus, the proposal fits neither a free-market nor a democratic-socialist economic model for investment and fails to be accountable to either the market or the general public. Further, seemingly independent institutions such as Oxford University benefit financially via their spin-out companies (such as Oxford Nanopore), in which they are investors, and from capital investments (such as the public-private infrastructure funding for Oxford University's Li Ka Shing Centre for Health Information). Thus claims of future benefit (used to justify the costs and other downsides such as loss of privacy) originate almost entirely from those with vested interests in the plan.

Once all the data has been collected and stored, its use by individuals (with or without medical professionals) is then low cost (involving an electronic test of the person's existing stored variant file, containing their whole genome minus the reference genome). This will allow this data to be mined for marketing, even when it is of no relevance to health, and also overcome the lack of interest of customers in purchasing gene tests from companies like 23andMe online. However, this plan requires enormous resources to be sunk in collecting and storing data which is likely to be of limited value to most people's health. This is the opposite of the Future Forum's recommendation that the NHS should be: "*Moving from a focus on collecting data (often too much data) to a focus on using data to generate intelligence to inform action*".²⁴⁸ Clinically useful data is likely to be swamped with clinically useless data which requires significant financial and energy resources to collect and store. Private sector investment will expect a high rate of return, whilst the return for taxpayers is only the claimed (but highly speculative) future benefit to health.

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 additional costs of all the expected 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. Health systems which prioritise rich, healthy people over poor sick people – such as the US system²⁴⁹ - are not generally cost-effective. 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.

Even life-long enthusiasts for whole genome sequencing remain sceptical of an early transition to providing genomes as part of electronic medical records, raising concerns about safe storage and access, incomplete information, and the need for informed consent.²⁵⁰ Others argue that currently, whole genome sequencing in healthy individuals has nothing to offer clinically because most of the data generated are meaningless.²⁵¹

Google and 23andMe, and other gene testing companies, have stated that they want the power of information to be wrested from the medical profession.²⁵² But companies like theirs

will write the algorithms which interpret people's genomes to tell each individual their supposed genetic risks. This means control over risk predictions will shift to commercial companies, not individuals or their doctors. The content of such algorithms is likely to remain commercially confidential, and there are ongoing debates about the extent to which patents will be allowed on software, including in the US and via the new European unitary patent, which is shortly to be implemented in UK law.^{253,254,255} Increased use of algorithms to calculate health risks (which it will be impossible for doctors or regulators – under the proposed new IVD Regulation - to check) has major implications for jobs and staffing in the NHS.

One study in the USA found that primary care physicians already perceive and experience the use of electronic medical records (EMRs) and clinical guidelines in ways that indicate “deskilling” of their jobs.²⁵⁶ The outcomes identified in the study include decreased clinical knowledge, decreased patient trust, increased stereotyping of patients, and decreased confidence in making clinical decisions. A majority of doctors in the study believed that the EMR encouraged them to change actively the manner in which they fed their clinical thought processes into a patient's record, losing important information and encouraging a “cut and paste” approach to recording consultations. Other problems included difficulties fitting a patient's circumstances into a standard template. In effect, these medical innovations were found to de-personalise rather than to personalise care. Whilst clinical guidelines generally been found to improve health outcomes, studies of the use of electronic health records in the USA have reported mixed results, with a large US study finding a significant increase in the per-patient rates of visits and phone calls to doctors' clinics, including out-of-hours visits, and increased use of emergency departments and hospitals, for users of electronic healthcare records.^{257,258} Although computer-assisted decision-making could improve outcomes in some circumstances, the opposite could also be the case in other circumstances, particularly because screening healthy people significantly increases false positive results.

It is currently unclear whether feedback of genetic risk predictions will occur mainly via doctors or directly to individuals (or to children via their parents) online. Everyone's electronic medical records are due to be posted on the internet by 2015 as part of the Government's new NHS Information Strategy²⁵⁹ and the Wellcome Trust Sanger Centre has run a consultation on how people might access their own genetic data.²⁶⁰ Since doctors may in any case be reduced to running a computer algorithm the content of which is unknown to them, it is likely that the role of medical professionals will increasingly be by-passed, especially by companies such as Google-funded 23andMe which already market gene tests direct to consumers online. There is a risk that anyone who agrees to “feedback” of healthcare risks (including genetic risks) calculated using their data in the NHS is bombarded with personalised advertising based on the data-mining of their medical records and genetic information.

In reality, rather than creating jobs, building a database of everybody's whole genome linked to their electronic medical records in the NHS could lead to more jobs for computers and less jobs for people, as computer algorithms replace doctors in deciding people's care, including ‘early treatment’ of people who are healthy.²⁶¹ The aim is less face-to-face contact with physicians (cutting healthcare costs) but more remote prescribing and increased use of medication (boosting private profits). However, it is currently unclear to what extent the NHS will face increased costs and burdens due to misleading risk predictions, unnecessary follow-up, over-treatment and adverse side effects.

Public trust

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.^{262, 263} This is an important safeguard to protect not only individual privacy but the broader public interest.

In December 2008, Connecting for Health held a consultation about the sharing of medical data for research without consent.²⁶⁴ The consultation did not mention that this would include sharing of genetic information, however the Human Genetics Commission (HGC)'s response included a large number of concerns raised by the HGC's Consultative Panel of members of the public, including concerns about sharing of data in "sealed envelopes" and the fact that "anonymisation" of data in a way that made individuals unidentifiable was likely to be impossible for rare disorders.²⁶⁵ In its response to the consultation the Wellcome Trust Sanger Centre "*encouraged the NHS Care Records Service to prepare for the integration of significant amounts of genetic and genomic information into patient records*" and argued that: "*If robust systems are in place.....the benefits of research will outweigh the risks associated with the use of identifiable information*" (including information that patients have requested to be kept confidential in 'sealed' and 'locked' envelopes).²⁶⁶ However, a quarter (25%) of the members of the public stated that they did not believe that it was possible to effectively anonymise data and some people were adamant that "their data" should not be shared for any purposes. There was wide concern amongst participants in the general public about the ability of the NHS to protect personal data. Concerns included risks of data loss by NHS staff, hacking and selling of data to third parties for commercial purposes, especially insurance companies and employers. The consultation revealed widely divergent views between the general public and researchers.

In 2007, the Science Horizons project (funded by GE Healthcare)^{267,268} highlighted public anxieties about privacy and surveillance, erosion of the human dimension in services and relationship building, future employment, trustworthiness of authorities, safety, fair access to technology and the potential for technologies to be misused. The concern that technology is being developed by industry and/or government in order to make profits, rather than in response to societal needs was "*a fairly common theme*" and it was also "*widely assumed that policy-makers in government and big business are not candid with citizens*". Overarching issues raised by the Deliberative Panel²⁶⁹ included:

- trust in expertise - who can be trusted?;
- concerns about the security, privacy and integrity of personal information (IT- or genetically-based);
- concerns about safeguards against abuse of technologies by authorities or by criminals;
- and fears about loss of the 'human touch' in everyday interactions, for example in relation to health, and in work.

There was a "*striking trust deficit*" and some people saw expert priorities for research investments as inevitably not the same as those of the average citizen.

Even if the latest proposals do not suffer the same fate as data-sharing under former Prime Minister Gordon Brown, it could 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. If public trust is lost, this might damage both the healthcare system and people's willingness to volunteer to take part in legitimate medical research.

Conclusions

A powerful group of lobbyists have convinced the government to sell the NHS medical records of everyone in England in return for capital investment in IT infrastructure and DNA sequencing machines, mainly in London, Oxford and Cambridge. If their plan goes ahead, people's genetic information, including whole genomes, will be included in their medical

records in future and will also be available for sale worldwide. Promises that this data will be effectively anonymised are completely meaningless. Ultimately, a DNA database of the whole population of England will be created in the NHS, allowing every individual and their relatives to be identified and tracked.

Genomes are poor predictors of most diseases in most people and plans to replace doctors with computer algorithms will allow commercial exploitation of their patients. This is unlikely to lead to better health but will lead to over-treatment with many people offered tests and treatments that they do not need, through personalised marketing. The resulting loss of privacy and the threat of stigma and discrimination will impact badly on vulnerable people's access to health and social care. Social, environmental and regulatory changes to improve public health will be neglected in favour of an individualised approach. The complete removal of people's right to choose who has access to their records could also lead to a massive loss of public trust in medical research.

The British people have never voted for this plan and its adoption by successive governments shows total contempt for any kind of democratic process and for individual choice. Support for the idea by former Prime Ministers Tony Blair and Gordon Brown led to public outcry about the growth of a Big Brother state.²⁷⁰ The Coalition Government should think again and abandon this proposal.

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Figure 1: From a presentation by Tim Hubbard, Wellcome Trust Sanger Centre, 22nd February 2012

Informatics for Genomic Medicine – 2012?

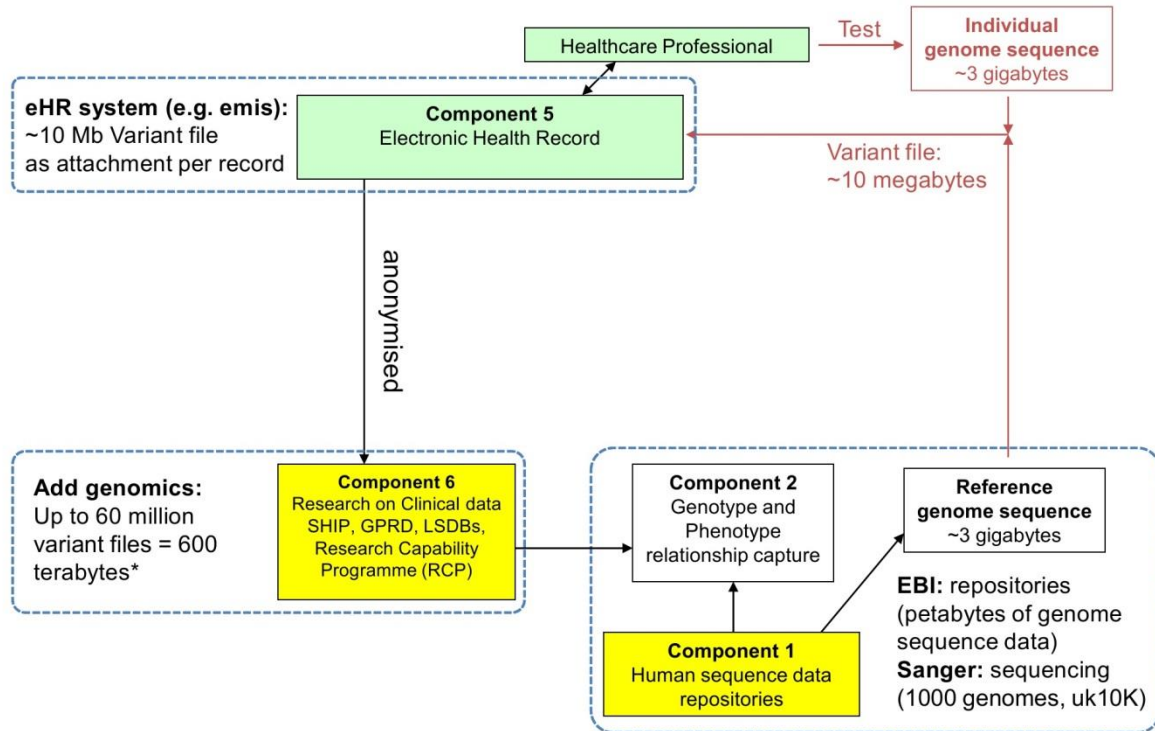
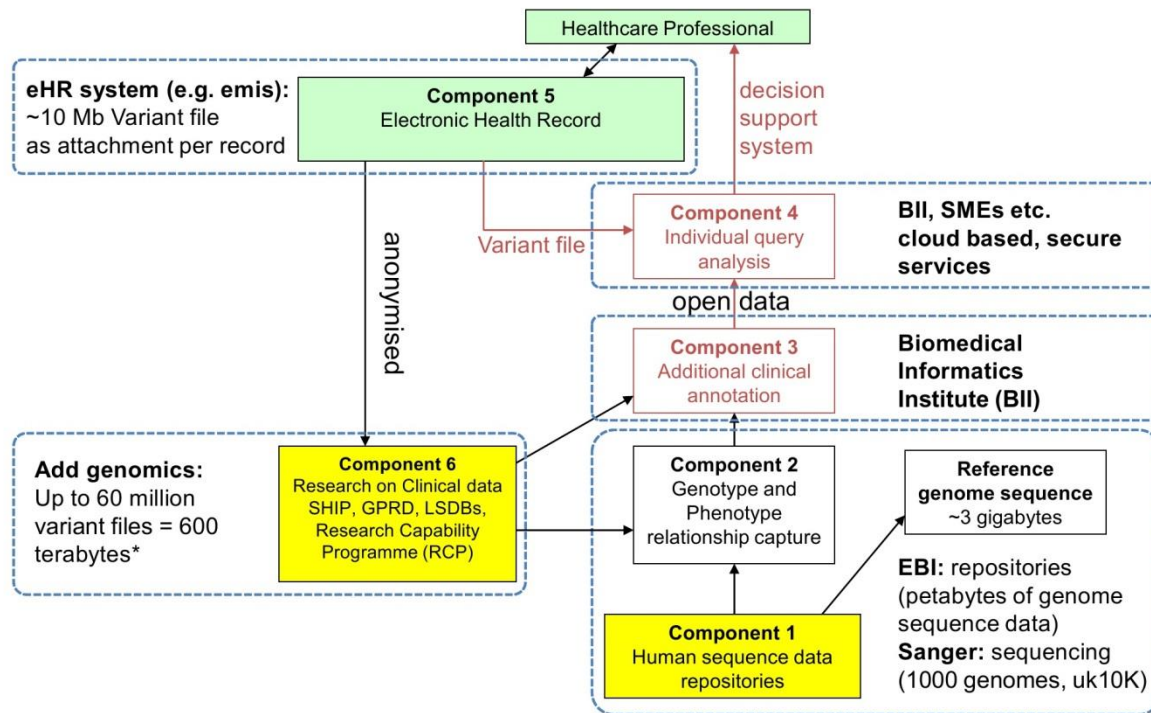


Figure 2: From a presentation by Tim Hubbard, Wellcome Trust Sanger Centre, 22nd February 2012

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