History of the Human Genome

GeneWatch UK

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This briefing is based on a timeline of key events in the history of the Human Genome Project (HGP) and subsequent attempts to integrate scans of people's genomes into healthcare in Britain and the USA.

The history shows that:

- Claims that human genome sequencing will be useful to predict who develops common diseases are false and originate from spurious findings published by tobacco-funded scientists. Nobel Prizewinner Sydney Brenner had secret meetings with British American Tobacco (BAT) in 1988 and 1990, in an attempt to secure funding for the Human Genome Project, and the Medical Research Council (MRC) jointly funded much of the spurious research. Leading scientists at the US National Institutes of Health (NIH) also endorsed the false findings in journals and the press.
- Other scientists who received tobacco industry research funding (for unrelated projects) included Nobel Prizewinner Harold Varmus – recently reappointed by President Obama to run the US National Cancer Institute – and Kari Stefansson, the President of pioneering gene test company DeCode Genetics.
- The food and pharmaceutical industries have also promoted false claims that human genome sequencing will predict big killer diseases, in an effort to expand the market for healthcare products to large numbers of healthy people and to confuse people about the role of unhealthy processed foods in hypertension, type 2 diabetes and obesity.
- False claims about health benefits from sequencing the genomes of whole populations led to the £12 billion decision by Tony Blair to centralise electronic medical records in the NHS.
- Billions in taxpayers' money has been wasted in both Britain and the USA, and medical privacy has been jeopardised, in an attempt to create the vast databases of electronic medical records linked to DNA that will supposedly allow scientists to 'predict and prevent' disease. A massive expansion in the drug market is predicted if everyone is tested.
- Systems are being developed in both Britain and the USA to allow the sequencing of stored blood samples, including millions of babies' blood spots taken for medical tests at birth, without consent. Google and its gene testing company 23andMe is seeking access to samples in both countries.

Role of the tobacco industry

In the run-up to the Human Genome Project, the MRC, British American Tobacco (BAT) and the German pharmaceutical and chemical company Bayer set up a jointly-funded research unit at Newcastle University which published numerous spurious results linking

genes to lung cancer in a journal edited by its Director, Jeffrey Idle. The tobacco industry also infiltrated the US National Institutes of Health (NIH), where leading scientists endorsed its false claims that genetic tests would in future predict which smokers would get lung cancer, arguing that smoking cessation efforts could be targeted at them so the rest of the population could continue to smoke. There is no significant inherited component to lung cancer, so a test which predicts which smokers will get lung cancer cannot possibly exist. However, this spurious evidence laid the groundwork for a string of unsubstantiated claims that genome sequencing would lead to the 'prediction and prevention' of big killer diseases in the general population.

There is no evidence that tobacco-funded scientists falsified results. The false claims resulted from poor science and a process by which tobacco-funded scientists benefited from fast-tracked careers, financial and political support, and access to the media to promote the industry's messages: that cancer is a genetic disease and prevention depends on screening people's genomes so that lifestyle and medical advice can be targeted at those at high genetic risk.

Role of the pharmaceutical industry

In 1998, key funders of the Human Genome Project, such as the Wellcome Trust, distanced themselves from the tobacco industry and stopped co-funding research.

Beginning in 1999, GlaxoSmithKline – led by its former Chair Sir Richard Sykes and then Director of Science Sir George Poste – lobbied to build a database of everyone's medical records and DNA in the NHS. GSK wished to massively expand the drug market for healthy people, who would be told they were at high genetic risk of getting common diseases in the future. The database was intended to compete with the one set up by DeCode Genetics, led by Kari Stefansson, in Iceland.

The plan – which involves the creation of the £12 billion database of electronic medical records known as the Spine; the new GP Extraction Service now being developed to mine data from people's medical records without consent; and the storage of millions of babies' blood spots by NHS hospitals so their genomes can be sequenced when this becomes affordable – has yet to be abandoned by the new Coalition Government.

The food industry and Google

Mirroring the tobacco industry's genetic research strategy, the food industry has long argued that only a minority of people are salt sensitive, and that these individuals should be identified and targeted with advice and medication to reduce their blood pressure, as an alternative to reducing levels of salt in processed foods. The industry has invested heavily in studying the genetics of obesity and type 2 diabetes and, more recently, in developing premium-priced functional foods, such as cholesterol-lowering margarines and pro-biotic yoghurts.

Google and its gene test company 23andMe are now lobbying both the UK and US Governments to use DNA and medical records for personalised marketing. The private healthcare and food industries are promoting a new vision of healthcare in which people will have their genomes sequenced in supermarkets and stored on mobile phones. Healthy people will be marketed bar-coded functional foods and other health tests,

advice and treatments, which are claimed to be tailored to their genetic risks of future diseases.

Scientific evidence

No existing gene tests for common diseases meet medical screening criteria for use in the general population, because genetic variants that influence disease risk are either very rare or have little predictive value. More predictive tests are unlikely to be developed because the genetic component of diseases is exaggerated by the method of calculating heritability developed by Ronald Fisher in 1918 (Fisher is one of the eugenicists who went to work for the tobacco industry in the 1950s) and because complex interactions will limit the predictive value of computer algorithms that try to combine multiple genetic and environmental risk factors. However, a small number high profile scientists involved in the Human Genome Project - including Francis Collins (now head of the NIH) and George Church (who works for a string of gene testing companies) – continue to make misleading claims about the medical benefits of sequencing everybody's genome.

This does not mean all genetic testing is useless: there are many rare genetic disorders and there are also rare inherited forms of common diseases such as breast and colon cancer, high cholesterol levels (familial hypercholesterolaemia), cardiomyopathies (heart muscle disease) and sudden cardiac death. However, these tests for rare mutations are only suitable for 'cascade screening' (testing within families known to be at risk) and account for only a small proportion of cases of these diseases. They are not relevant to most cases of common diseases such as heart disease and cancer in the general population and they often raise ethical difficulties because the preventative action that can be taken may be unpleasant or harmful. Tests of genetic changes that occur in cancer cells are also likely to be useful – but these can only be done on cancer patients, not on healthy people.

Human Genome timeline

1918	Eugenicist Ronald Fisher publishes a mathematical paper showing how common diseases might be caused by genetic susceptibility to environmental exposures.[1] The paper becomes the basis for calculating the 'heritability' of complex diseases, i.e. the extent to which differences in risk of disease between individuals are caused by genetic differences.
1939-45	Second world war. Eugenic ideas are promoted by Nazi scientists and politicians.
1953	Watson and Crick publish a paper in Nature describing the double-helix structure of DNA.
1954	The tobacco industry sets up the Tobacco Industry Research Council (which later became the Council for Tobacco Research, CTR). Its first director is the eugenicist Clarence Cook Little.
1956	Fisher becomes a consultant to the newly founded Tobacco Manufacturers' Standing Committee.
1957	The British Medical Research Council publishes a report stating that lung cancer is caused by smoking. Fisher counters by publishing a paper in the British Medical Journal promoting the idea that people who are genetically predisposed to smoke are also genetically predisposed to develop lung cancer (later known as the "constitutional hypothesis").[2] This implies that the statistical link between smoking and lung cancer is a coincidence.
1958	Fisher publishes a letter in Nature again promoting the constitutional

	hypothesis.[3] The New York Times reports that Fisher is a consultant statistician to the tobacco manufacturers.[4]
1972	Fred Panzer, Vice President of Public Relations for the Tobacco Institute, advocates more emphasis on the 'constitutional hypothesis', arguing that the public "*must perceive, understand and believe in evidence to sustain their opinions that smoking may not be the causal factor*".[5]
1973	Claims to have developed a genetic test which "*apparently distinguishes cigarette smokers whose genes make them prone to lung cancer from those resistant to developing the malignant tumour*" are made in the New York Times[6,7] by researchers (Shaw and Kellerman) who are seeking funding from the CTR (their funding is approved the day after the article is published)[8,9].
1974	Tobacco industry lawyer Erwin Jacob argues in an internal document that "*newly developed research knowledge and techniques - especially in genetics - provide the possibility of much more extensive and promising exploration of the constitutional hypothesis than has heretofore been even conceivable*".[10] This sparks industry investment in the genetics of nicotine addiction (called 'smoking behaviour' by the industry) as well as follow-up to Shaw and Kellerman's work.[11] In a scientific paper, geneticist Richard Lewontin criticises calculations of 'heritability' for common, complex diseases and behaviours.[12] Other scientists publish similar concerns, demonstrating that Fisher's 1918 paper depends on questionable assumptions.[13]
1977	Jeffrey Idle (at St Mary's Hospital) co-authors a paper on role of the CYP2D6 gene in differences between individuals' metabolism of the drug debrisoquine[14].
1978	The International Life Sciences Institute (ILSI) is founded by Coca-Cola and other food manufacturers to defend food industry interests.[15,16] Artemis P. Simopoulos becomes chair of the NIH nutrition advisory committee, which overseas all nutrition-related research, until 1986.
1979	Simopoulos writes a paper arguing that "*Universal dietary goals for the general public cannot be formulated or implemented. More appropriate would be guidelines to serve as preventive measures for specific groups, based on genetic endowment, age, sex, and condition*".[17]
1982	Henry Rothschild (University of Louisiana), who has been funded by the CTR since 1997, tells the Waxman hearings that genetics may determine who gets lung cancer.[18] On the advice of tobacco-industry lawyers[19], he is awarded a new grant to study genetic factors in lung cancer in Louisiana families,[20] receiving US$160,700 in research funding in total[21,22,23,24]. In September, the US Department of Health and Human Services, ILSI and the National Kidney Foundation jointly sponsor a symposium on nutrition and blood pressure control. Simopoulos is pleased that it shifts the focus away from dietary salt.[25] The NIH begins genetic research on the Pima Indians of Arizona, searching for genes linked with obesity and diabetes.[26] Researchers repeatedly claim that the high incidence of obesity and diabetes in this population must result from their genes being poorly adapted to modern diets (the 'thrifty gene' hypothesis). However, like other populations at high risk, they are marginalised, dependent on unhealthy food aid and many are unemployed.
1984	On 14th January, ILSI adopts new Articles of Incorporation which name Artemis Simopoulos of the NIH as a trustee.[27] Harold E. Varmus, then at the University of California, San Francisco receives $153,099 from the CTR for research on cancer genes, between 1st July 1984 and 30th June 1986.[28,29] Jeffrey Idle joins the Lung Cancer Task Force at the US National Cancer Institute (NCI).[30]
1985	Simopoulos co-authors an NIH report arguing that it is important to be able to identify children who are at special risk of becoming hypertensive as well as

	those who are most likely to become obese or hypertensive or both, by searching for genetic markers.[31] She is forced to resign from the executive committee of the food industry research body ILSI following exposure of her conflict-of-interest by the Center for Science in the Public Interest, but remains on its governing board.[32] She remains chair of the NIH nutrition advisory committee until 1986.
1986	Idle joins the CTR's Scientific Advisory Board (SAB) and tells them that he has found a gene for susceptibility to lung cancer (the CYP2D6 gene) and is collaborating with the US National Institutes of Health (NIH) on further research.[33,34] In the UK, Sydney Brenner (Director of the Medical Research Council Laboratory of Molecular Biology in Cambridge and a member of the Council of the MRC) is told that any human genome mapping must take place within the MRC's existing budget.
1987	NIH researchers (and another member of CTR's SAB, Dr Alfred Knudson) endorse Idle's results in the press and suggest that genetic testing would allow smoking cessation to be targeted at a minority of smokers.[35] This is regarded as favourable publicity by the tobacco industry and Idle makes a presentation to the CTR Board (which includes representatives of six tobacco companies, two legal firms and the CTR's PR company).[36,37] The CTR approve a $47k grant to Professor Henry Lynch to collaborate with Idle[38], as part of Lynch's existing CTR-funded project (Lynch is also a member of the CTR's SAB and believes that his discovery of the rare inherited form of colon cancer known as Lynch Syndrome will be extended to more common cancers[39]). [40,41,42]
1988	In January, CTR and British American Tobacco (BAT) public relations advisors – Alan Campbell-Johnson acting for BAT in the UK and Leonard Zahn acting for the CTR - become involved in helping Idle establish a 'Laboratory of Cancer Pharmacogenetics' in the UK.[43] In February, the Chair of BAT's Scientific Research Group (SRG) informs BAT's Chairman (Patrick Sheehy) that Idle "*is Professor elect at a greatly extended and revamped department of Pharmacology at Newcastle University (where BAT also has connections) and I anticipate that through the Scientific Research Group we shall be supporting his work there*".[44] On 18th March, Idle sends a conference abstract by NIH researchers supporting his findings to the CTR "*in confidence*" and seeks funds to attend a forthcoming conference: "*Caporaso tells me that since his abstract was written they have reworked their data using criteria calculated from our data and their relative risk has shot up. Clearly I cannot miss the show!*"[45,46] Sydney Brenner (Director of the MRC's Laboratory of Molecular Biology in Cambridge) and BAT meet on 30th March, regarding Idle's proposal to establish a laboratory. Brenner supports the proposal and advocates gene screening for smokers. The memo notes that he "*seemed quite willing to meet with BAT again on a specific subject*". In April, Brenner sets up the Human Genome Organisation (HuGO) to lobby politicians for funding for the Human Genome Project (HGP).[47] Following Brenner's endorsement, Idle's BAT project is given immediate approval (bypassing BAT's usual approvals process).[48] On 18th to 20th April, BAT's Scientific Research Group holds a meeting beginning with a dinner at which its PR advisor Alan Campbell-Johnson gives a presentation: 'Press coverage of fundamental work in molecular biology and other New Knowledge'.[49] A BAT consultant writes a paper explaining that the industry's aim in funding projects like Idle's is to identify a "genetically susceptible" minority of smokers so that smoking cessation efforts could be targeted at them and "*the rest of the population can be allowed to puff away contentedly and*

	without serious risk"[50]*.* The Pharmacogenetics Unit in the University of Newcastle Medical School, is "*greatly expanded and revamped*" to create a Chair for Idle and the university receives a five year research agreement from BAT on Idle's move there in September 1988.[51] Idle is a guest in the BAT tent at Wimbledon in June[52] and has lunch with Sheehy on 25th July.[53] In October, Sheehy meets Prime Minister Margaret Thatcher at the launch of the First Night Club[54] (there is no record of their conversation). According to the Wellcome Trust, it was Brenner who gained the personal support of Thatcher for the HGP, after he and Sir Walter Bodmer (a former student of Ronald Fisher) initially had difficulty persuading influential bodies in the UK to 'think big' about the genome.[55] The first independent study is published that fails to confirm Idle's supposed lung cancer susceptibility gene.[56] The CTR congratulates the latest Nobel prizewinners to have received CTR-funding (Louis Ignarro and Ferid Murad) and lists the previous winners they have funded (Baruj Benacerra, Stanley Cohen and Harold Varmus).[57] The US NIH and DOE (Department of Energy) begin to fund human genome mapping.[58] In December, a review of Idle's research proposal by BAT consultant Alvan Feinstein severely criticises his grasp of statistics.[59]
1989	After gaining Thatcher's support, Brenner is awarded an extra £11 million over three years for human genome mapping at the MRC, agreed in February 1989 and paid from the start of the 1989/90 financial year.[60] On 16th May, the New York Times publishes an article predicting that genetic tests for vulnerability to cancer will be available in 3 to 5 years and quoting NCI researchers saying that genetic tests could help focus anti-smoking efforts.[61] The internal response in the CTR is ecstatic, describing the article as "VINDICATION".[62] In July, Idle and NCI researchers publish study of the role of the same gene in susceptibility to lung cancer in workers exposed to occupational carcinogens: the article advocates genetic screening and targeting of susceptible workers.[63] Idle becomes Chairman of the World Health Organisation (WHO) Committee 'Genetic predisposition to toxic effects of chemicals'. In October, the Wall Street Journal cites NCI researchers advocating genetic testing for lung cancer susceptibility[64]. The Nobel Prize in medicine is awarded jointly to J. Michael Bishop and Harold E. Varmus. Tobacco and food company Philip Morris decides to fund a major programme of biomedical research, after interviewing experts including James Watson (then head of the HGP) and James Wyngaarden (the Deputy Science Advisor Designate to the President of the United States and former head of the NIH).[65] In December, Nancy Wexler, president of the Hereditary Disease Foundation and chair of the ethics group of the HGP from 1989 to 1995 tells New York Times magazine: "*As geneticists learn more about diabetes or hypertension or cancer, at some point they will cross an important line. Instead of saying, as they do now, "Lung cancer runs I your family and you should be careful," physicians will be able to ask their patients, "Would you like to be able to take a blood test to see if you are going to get lung cancer?*".[66] Wexler – who has Huntington's Disease in her family and sees tests where interventions exist, such as quitting smoking, as unproblematic[67] – goes on to play a leading role in shaping the ethical question as being 'do you want to know?' rather than 'can you believe what you're being told?'.
1990	In January, a further paper by independent scientists fails to replicate Idle's supposed lung cancer susceptibility gene.[68] In May, the NIH and DOE present a joint 5 year plan for the Human Genome

	Project (HGP) to Congress. In August, the Journal of the National Cancer Institute (JNCI) publishes two articles on genetic susceptibility to lung cancer – one by NCI researchers, which replicates Idle's findings,[69] and one by Sellers *et al*.[70], on which Rothschild is a co-author and CTR funding is acknowledged. BAT describes the NCI researchers as "*close to*" Idle's group[71]. The papers gain extensive press coverage.[72,73,74] Brenner has another secret meeting with BAT on 19th November: the venue is informed "*there should be no need to mention BATCo when greeting Dr. Brenner*".[75] No minutes of the meeting appear to be available. Questions prepared by BAT include: "*Does he believe that widespread screening for particular 'genetic predispositions' to develop particular diseases will eventually take place?*".[76] After the meeting, Brenner's department at Cambridge receives a small donation from BAT of £400.[77]
1991	The first five year plan for the Human Genome Initiative is adopted by the US NIH and DOE.[78] The journal *Pharmacogenetics* is founded with Idle as Editor-in-Chief from 1991 to October 1998.[79,80] Fourteen of 25 tobacco-funded papers published by the Newcastle Pharmacogenetics Unit are published in this journal. A review of lung cancer genetics published by Idle in *Pharmacogenetics*[81] is later described by independent scientists as "*factually misleading and gives an incorrect impression of …the current conclusions which can be drawn from the literature*"[82]. Two further papers published elsewhere by independent scientists fail to replicate Idle's findings.[83,84]
1992	In 1992, 50% of the project funding for "*this and related research*" at the Newcastle University Pharmacogenetics Unit is from the tobacco industry,[85] which spent US$1.5 million on research projects there from 1989 to 1996.[86] The unit also received substantive funding from the North of England Cancer Research Campaign, the UK Medical Research Council (MRC) and the pharmaceutical and chemical company Bayer. Charities that jointly funded the research included: the Wellcome Trust; the North of England Cancer Research Campaign and the North of England Childrens' Cancer Research Campaign; the American Cancer Society; the Norwegian Cancer Society; and Stop Cancer (California). Another paper by independent scientists fails to replicate Idle's supposed lung cancer susceptibility gene.[87] James Watson resigns as head of the HGP and Francis Collins takes his place. In an Op-Ed in the New York Times, Harold Varmus argues that fundamental research on genetics is more important than focusing research on cures for specific diseases.[88] Part-funded by the NIH, researchers from the Universities of Utah, Boston and the National Institute of Health and Medical Research in Paris, publish a paper claiming that genetic variations in the AGT gene predispose people to hypertension, based on the analysis of DNA samples collected in Salt Lake City and Paris.[89] They apply for patents on these genes.[90]
1993	Harold E. Varmus is appointed to head the US National Institutes of Health (NIH), where he remains until 1999. Calling for Europe to allow gene patenting, SmithKline Beecham's head of research and development, George Poste, famously states that "*Genes are the currency of the future*".[91] Professor John Bell founds the Wellcome Trust Centre for Human Genetics at Oxford University.
1994	Varmus again emphasises the need to focus on cancer as a "genetic disease".[92]

	The CTR's President James Glenn boasts in evidence to the House of Representatives that the CTR is now one of the largest private funders of medical research in the USA and has awarded nearly $225 million to approximately 1,000 researchers, sponsoring "*pioneering work in identifying familial cancers, the role of genetic factors in cancer formation, and the identification of oncogenes* [cancer genes]". [93] The New York Times reports Glenn's evidence including reference to Varmus' CTR funding.[94] Philip Morris flies Sydney Brenner to New York to discuss plans to set up a new Molecular Sciences Institute. [95] Kari Stefansson (who relocated to Harvard Medical School on 1st November 1993[96]) flies to Iceland to collect DNA samples for a study of the genetics of multiple sclerosis: the beginning of a process which later leads to the establishment of the pioneering gene testing company DeCode Genetics.[97] Stefansson receives $243,134 in research funding from the CTR for research on a potential biological treatment for brain cancer (glioma) from July 1992 to June 1995.[98] Jeff Friedman of Rockerfeller University files a patent on the ob gene, associated with obesity in mice and the production of a hormone called leptin.[99] The discovery gains enormous media coverage. Amgen pays $20 million upfront for the rights, but rare human mutations causing leptin deficiency are later discovered in only a handful of families. A study in the Lancet later reveals that from 1988-1994 only one UK medical school did not accept tobacco funding.[100]
1995	NIH researchers are surprised that a large twin study finds no inherited component to lung cancer[101]: a genetic test which predicts which smokers will get lung cancer therefore cannot exist. Researchers also discover that Idle's supposed lung cancer gene is not expressed in the lung, so it was never likely to have played a role in lung cancer.[102] Varmus' NIH budget statement continues the focus on DNA sequencing and genetics.[103] Idle co-authors a paper in *Pharmacogenetics* which advocates genetic screening of whole populations, with data stored on individual patient SMART cards, and expert computer systems on every doctor's desk, to aid drug prescribing.[104] The UK Foresight Report on health and life sciences includes *"genetics in risk evaluation and management*" for common multi-factorial diseases, such as heart disease, as a key area for greater investment.[105] The Wellcome Trust, then the largest shareholder in the pharmaceutical company Wellcome PLC, supports a merger with Glaxo PLC by backing a hostile bid from Sir Richard Sykes without consulting the company's board.[106] Sykes becomes Chairman and Chief Executive of Glaxo Wellcome.
1996	The journal Science exposes that Brenner is about to receive $15 million a year for 15 years from tobacco and food company Philip Morris to set up a new research institute at La Jolla in the USA[107]: the plans are dropped after the article is published.[108] Apparently unaware of the history of tobacco industry funding in this area, PR firm Burson-Marstellar sends a memo to Philip Morris, which puts the marketing case for the tobacco industry to undertake this type of research: "*A simple test might eventually be devised to tell a smoker whether or not he is at risk. This would put the burden of any consequence from smoking on the individual, and would clear the way for the non-susceptible population to smoke with a clear conscience*"[109]. British Nuclear Fuels (BNFL) funds the 'North Cumbria Community Genetics Project' near its Sellafield plant in Cumbria, which collects DNA samples from newborn babies over a five year period from 1996.[110,111] The project includes

	research on cancer and genetic susceptibility to radiation.[112] The National Radiological Protection Board later concludes that genetic screening is not likely to be useful to reduce the incidence of radiation-induced cancers.[113] Kari Stefansson becomes President of the new company DeCode Genetics.
1997	New Labour Government elected in Britain with backing from the 'biotech barons' (Sir Christopher Evans, Baron Drayson, Sir Ronald Cohen and Lord Sainsbury). Professor John Bell co-founds the biotech company Oxagen as a 'spin-out' company from the Wellcome Trust Centre for Human Genetics in Oxford. By 2002 Oxagen had filed for over 30 patents on disease-related genes.[114] Myriad Genetics in Salt Lake City is given a license for the exclusive use of the patents on the AGT gene (linked to hypertension by researchers in 1992).
1998	Myriad launches its AGT genetic test claiming that it will "*assist physicians both in identifying which hypertensive patients are at a significantly increased risk of developing cardiovascular disease, and identifying which patients are likely to respond to low salt diet therapy and antihypertensive drug therapy*"[115]. However follow-up research to the original 1992 paper shows that the effect of the AGT gene on hypertension is of borderline statistical significance[116]. NIH researchers find a different group of Pima Indians who live in Mexico, not in Arizona. Subsequent research suggests they are not obese because they expend significantly more energy in physical activity and have healthier diets.[117,118,119,120] The Native American Diabetes Project is set up in the USA to try to help people change their diets and exercise, although genetic research on the Pima Indians continues. A number of studies later find that a belief in genetic explanations for obesity and diabetes is counter-productive to improving health in Native American populations. [121,122,123] A Directive allowing gene patenting is finally adopted in Europe, following lobbying by SmithKlineBeecham. The Directive is supported by the Wellcome Trust (which opposes the patenting of raw sequence data from the HGP but not of genes whose function has been discovered[124]). A controversial Bill on the establishment of a Health Sector Database, to be owned and operated by DeCode, is introduced in Iceland in March. Health data in Iceland is later defined as "*information on the health of individuals, including genetic information*".[125] Oxford Professor John Bell publishes a paper in the British Medical Journal, which claims that "*Genetic information is likely to transform the practice of clinical medicine*" within the next decade and "*Genetic variation will be another form of "risk factor" and will permit early treatment and directed screening*". [126] Chancellor Gordon Brown announces "*the biggest ever Government-led public/private partnership for science*" with the Wellcome Trust. [127,128] The Wellcome Trust (which is cited as a co-funder with BAT, the CRG and others on two of Idle's papers[129,130]) adopts a 'Declaration of Good Practice' stating "*the Governors would expect that individuals applying for or holding research funds from the tobacco industry will not seek support from the Trust*".[131] The Wellcome Trust increases its investment to allow its Sanger Institute to decode one-third (rather than one-sixth) of the human genome.[132] Along with the UK Biotechnology and Biosciences Research Council (BBSRC) it is one of the largest funders of human genomics in the world, after the US NIH.[133] A localised system of electronic healthcare records (EHRs), based in GP practices, is proposed by the UK Department of Health, at an estimated cost of £1 billion.[134]
1999	The Council for Tobacco Research (CTR) closes down. Apparently unaware that claims regarding genetic susceptibility to lung cancer are spurious, on 8th May, the Director of the HGP in the US, Francis Collins,

	makes a major speech in which he describes a hypothetical future in which, by 2010, a healthy 23-year-old college graduate gives a cheek-swab of DNA to his doctor and receives a battery of genetic tests, to assess his genetic risk of colon, lung and prostate cancer, heart disease and Alzheimer's disease, leading to a regime of new prophylactic drugs, annual colonoscopy and the motivation to quit smoking.[135] George Poste (later Sir George) of SmithKline Beecham begins lobbying for a UK population-wide national database of electronic medical records linked to DNA, to be set up as a public private partnership in the NHS, arguing that "*the NHS is probably the largest single source of medical information and well-characterized biological samples in Europe*" [136] and that the plan requires the government "*to stand firm in the face of unsubstantiated claims of risk and scaremongering by anti-technology lobbies, and above all, to recognise that the dramatic pace of change renders many traditional approaches to technology transfer and policy review obsolete*".[137] Poste proposes the idea to the House of Lords Science and Technology Committee when they visit SmithKline Beecham in May and provides written evidence to the Committee in November.[138,139] The DTI's Genome Valley report, developed with input from the biotech, food and pharmaceutical industries, supports the argument that NHS data should be made available to industry to research genetic predispositions to diseases.[140]
2000	BAT informs the House of Commons Health Committee that it still funds research on genetic predisposition to disease[141]. On 13th July, a major new twin study is published which again fails to identify a significant inherited component to lung cancer.[142] Myriad Genetics is awarded a fourth patent on the AGT gene.[143] However, its test fails in the marketplace because cardiologists do not find it medically useful.[144] Glaxo Wellcome and SmithKline Beecham merge to become GlaxoSmithKline (GSK). The Chair of GSK, Sir Richard Sykes, writes a book about the future of medicine and the NHS, in which he argues that by 2020 most treatment in developed countries will be 'pre-symptomatic'.[145] Sykes claims that the UK population spends too little on medicines and that the NHS needs to be reformed to "*deliver innovation"* and *"allow patients ready access to the medicines they want outside NHS funding*", stating that "*The individualisation of patients by genetic profiling will add to their demand for greater control over their care*…". A massive expansion in the market for drugs to healthy people is expected by GSK as a result of genetic testing.[146] DeCode Genetics' Initial Public Offering (IPO) on Nasdaq. On 26th June, 2000, Tony Blair and President Bill Clinton announce the completed draft of the human genome, together with Dr. Francis Collins, Director of the US National Human Genome Research Institute, and Dr. Craig Venter, President and Chief Scientific Officer of Celera Genomics Corporation.[147] A packed press conference is held at the Wellcome Trust. An article in the New England Journal of Medicine criticises the claims that genome sequencing will revolutionise medicine.[148] Evidence from Glaxo Wellcome[149] and SmithKline Beecham[150] to the House of Lords Science and Technology Committee advocates using electronic medical records to create a genetic database in the NHS. In oral evidence to the Committee[151], Professor Sir John Pattison, Director of Research and Development for the NHS and Head of Genetics at the Department of Health, admits: "…*The strategy, of course, is not to go to a national genetic database as a first step, the strategy is to join the MRC and the Wellcome Trust in assembling a large cohort of approximately half a million people…There is an element of this which is going to be, as it were, worked out with a large research study*". Pattison was later made Senior Responsible Office (SRO) for the NHS National Programme for IT (2002-2004)

2001	The scientific publication of the draft human genome sequence[152,153] estimates that humans have only 30,000 to 40,000 genes, only about twice as many as in a worm or fly, and far fewer than the 100,000 originally predicted. More scientists question the claims that genetic tests will be predictive of common diseases[154,155] and others argue that: "*The technology is impressive, but it is the underlying biology that will determine who succeeds or fails*".[156] Other researchers conclude that environmental factors play an overwhelming role in influencing the prevalence of diabetes and hypertension in different populations.[157] The House of Lords' Science and Technology Committee's Genetic Databases report endorses Poste's proposal to build a genetic database and calls for electronic medical records to be centralised into a vast database (the 'Spine').[158] The Committee supports the establishment of the UK Biobank genetic research project (jointly funded by the Wellcome Trust and MRC) as a pilot project for a genetic database of the whole population, despite widespread criticism of the project by medical researchers.[159] Researchers subsequently demonstrate that UK Biobank does not have the statistical power to quantify the gene-environment interactions that it has supposedly been set up to quantify.[160] Health Secretary Alan Milburn announces that the Government will be publishing a Green Paper on genetics in the NHS and that, in time, genetic tests will be developed to assess an individual's risk of cancer, heart disease and diabetes.[161] Section 60 of the Health and Social Care Act 2001 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.[162]
2002	On 18th February, Tony Blair approves the new NHS National Programme for IT, including the central database of electronic medical records known as the 'Spine' at a sofa meeting in Downing Street.[163,164,165,166] On 23rd May, Blair makes a major speech on science to the Royal Society, in which he claims that doctors will routinely sequence people's genomes in the future to predict and prevent diseases years in advance of any symptoms.[167] He states: "*We have a unique resource in this regard in the national health service. There are crucial issues of privacy of genetic information that we need to deal with. But our national, public system will enable us to gather the comprehensive data necessary to predict the likelihood of various diseases - and then make choices to help prevent them*". A review of statistical studies of links between genes and common diseases finds that out of 600 positive associations published, only six have been consistently replicated.[168] Sydney Brenner wins the Nobel prize for medicine, jointly with Robert Horvitz and John Sulston (Head of the Wellcome Trust Sanger Centre).[169]
2003	In June 2003, the Government's White Paper on genetics in the NHS states that the use of genetic knowledge will receive a major boost through the new NHS Information Strategy and that information systems will need to cope with new demands around recording, storing and retrieving genetic information.[170] It recognises that current genetic tests have "*low predictive power*" but "*Over the next decade, however, it should be possible to identify more genetic factors that increase the likelihood of people developing a given disease. There will then be the option to test people for predisposition to that disease, or a higher-than-normal risk. Preventive and monitoring services could then be tailored to an individual's needs.* *Following on from this, the way external factors and genes interact to cause disease or protect us from disease will be better understood. This information will allow people with certain genetic profiles to avoid foods, chemicals or environmental factors, such as smoking, which are particularly risky for them*".

	The White Paper also states: "*It may become possible to test for genes or combinations of genes that predispose to cancer in a less clear-cut way, for example by increasing susceptibility to harmful environmental stimuli such as cigarette smoke*". It includes a controversial proposal to collect and screen DNA from every baby at birth, so that "*it could then be used throughout their lifetime to tailor prevention and treatment regimes to their needs as further knowledge becomes available about how our genes affect our risk of disease and our response to medicines*". Scientists continue to question this approach.[171] In September, press reports based on a new scientific paper[172,173] claim that a genetic test will be developed within three to four years to "*show which smokers face lung cancer death*".[174,175,176,177,178] The Times claims "*Tests that can give an accurate indication of an individual's risk of getting a life-threatening disease such as cancer are likely to transform medicine over the next 30 years*"[179] and asks smokers whether they would want to take the test[180]. The study's corresponding author and press spokesman, Professor Zvi Livneh, has a history of tobacco funding (receiving $519,069 in funding from the CTR from July 1985 to June 1992[181,182,183,184,185,186,187]).[188] A statistical analysis of studies of the gene, published five years later, finds that individuals carrying the genetic variant do not in fact have significantly increased risk of lung cancer.[189] A study in the Lancet finds that only nine links between genes and common diseases have been replicated without significant bias in the findings.[190] In November, Iceland's Health Sector Database is ruled unconstitutional.[191] However, DeCode Genetics continues to operate using the subset of data it has collected with consent.
2004	The Healthcare Industries Task Force endorses Sykes' vision for a partially-privatised NHS, in which healthy people are treated on the basis of their supposed risk of common diseases,[192] stating: "*the early health approach will allow individuals to understand their own genetic propensity to key treatable diseases, so that they can receive regular selective screening…allowing rapid intervention through surgery, drugs or lifestyle improvement*". However, in the scientific literature, calculations show that the potential to reduce the incidence of common diseases by targeting interventions at a 'genetically susceptible' minority is likely to be limited.[193,194]
2005	The MRC funds a consultation on whether babies blood spots taken at birth for medical tests in the NHS should be stored beyond the five years needed to help improve the screening programme and used for other types of research, including genetic research.[195] The outcome of the consultation is never published. The Human Genetics Commission (HGC) rejects the UK Government's proposal to sequence the genome of every baby at birth but recommends that it is revisited in 2010.[196]
2006	The International Journal of Epidemiology publishes a series of articles which criticise the concept of individual genetic risk prediction; the validity of the genetic association studies being used to identify links between genes and diseases; and the use of twin studies to claim that common conditions are highly heritable.[197,198,199] Other researchers question whether searching for common inherited genetic variants that increase susceptibility to cancer is worth the resources being spent[200], and whether any of the existing genetic associations with (non-familial) breast cancer are real.[201] In the UK, Section 251 of the NHS Act 2006 allows for the Secretary of State (through his advisor, the National Information Governance Board) to give permission for specific disclosures of confidential information in the public interest where it is not practicable to gain explicit consent from patients.[202] The National Audit Office (NAO) reveals that the Treasury never assessed the

	claimed benefits of the National Programme for IT in the NHS, the costs of which have escalated to £12.4 billion (to 2014).[203] Biotech venture capitalist Sir David Cooksey's Review of UK Health Research[204] identifies a need "*to ensure that research is fully embedded in and integral to the NHS IT programme, and prioritised on a par with other service uses for the system*" and recommends the establishment of a new Office for Strategic Coordination of Health Research (OSCHR).
2007	Professor Sir John Bell becomes Chair of the Office for Strategic Coordination of Health Research (OSCHR) and it sets up an E-health records research board. The first genome-wide association study published by the Wellcome Trust Case Control Consortium (WTCC) identifies some new genes linked with common diseases, but the researchers also highlight the "*limited potential of the* [genetic] *variants thus far identified (singly or in combination) to provide clinically useful prediction of disease*".[205] A paper published in the journal Health Policy concludes: "*Based on current evidence, an era of healthcare consisting of gene technology built on widespread predictive testing is not desirable from a health economic viewpoint*".[206] The UK Government sets up its Ministerial Medical Technology Strategy Group (MMTSG).[207] The meetings are co-chaired by the US company GE Healthcare, a subsidiary of General Electric, and the Minister of State for Public Health, Dawn Primarolo. The MRC finds that the majority of members of the public feel that consent should always be sought to use their personal information in research, based on a survey[208] and qualitative research.[209] The Government's Science Horizons project, part-funded by GE Healthcare, finds that people have major concerns about regulation of personal genetic information and protection of personal data on computer and DNA databases.[210] A poll by the Guardian newspaper reveals that 70% of GPs do not think that the NHS's IT programme is a good use of NHS resources, and the majority have major concerns about protecting confidentiality.[211] The Times reports a poll showing that only a fifth of doctors believe that a national electronic system for storing patients' records will be secure[212], following the loss of a reported 168,000 patient records by nine NHS Trusts.[213] DeCode Genetics and US company 23andMe[214] launch online direct-to-consumer genetic testing services, which claim to predict genetic susceptibility to multiple common diseases. The gene testing company 23andMe is funded by Google and is jointly run by Google-founder Sergei Brin's wife.[215] In Europe, the EU-funded European Technology Platform 'Food for Life' Strategic Research Agenda[216] - developed by academic scientists and representatives from Nestlé, Kraft, Unilever, Bayer Crop Science, Cargill, Danone, Danisco and the Dutch food ingredients company, DSM - claims that implementation will ensure "*tailor-made, personal nutrition (nutraceuticals, functional food, food ingredients and supplements) that will provide better, healthier food that will form part of a diet with improved health attributes*". The Director of Nestlé research centre visits the Mexican National Institute of Genomic Medicine (INMEGEN), which is researching the genetics of obesity and type 2 diabetes. The company is funding a new Nestlé Chair in Nutrigenomics (nutritional genomics) and two fellowships.[217]
2008	Prime Minister Gordon Brown announces the third stage of the Government's reform of the NHS,[218] stating: "*With new tests to identify women who are at heightened risk of breast cancer, new drugs aimed at preventing allergies, and the discovery of new genes that are key to the progression of conditions like Alzheimer's - to give just three examples - we are at the dawn of a whole new era:*

	• *with growing understanding of individual risk factors;* • *the possibility of anticipating the development of future illness;* • *and perhaps even that of pre-empting such illness with specific advance interventions*." The idea of 'early health' is described in a paper from the industry side of the MMTSG: it involves screening people's genomes combined with "*tailored prevention programmes*", with industry by-passing medical professionals.[219] The paper states that: "*… through Connecting for Health (CfH), the UK is already in an enviable position to take advantage of the opportunities it offers. In the future, the ability to mine the data taken from this environment will bring about a true revolution in the practice of medicine, opening new industrial as well as healthcare horizons*". The final report of the Data-Sharing Review led by the Wellcome Trust's Director Mark Walport and Information Commissioner Richard Thomas recommends that a new fast-track procedure should be created in primary legislation to allow the Secretary of State to override any existing legal barrier to data-sharing without consent.[220,221] A review of commercially available genetic tests finds that fewer than half of the 56 genes included in the tests have significant statistical associations with disease risk.[222] Experts warn that screening healthy people can do more harm than good.[223,224] Google invests in a second DNA testing company (Navigenics).[225] Professor John Bell tells the House of Lords Science and Technology Committee that Google has been in discussion with the Department of Health about creating a vast database of genetic information in the NHS.[226] In its response to a consultation by NHS Connecting for Health, 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 argues 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).[227] The consultation does not mention that data-sharing for research is intended to include genetic and genomic information.[228] Nor does it say who the 'researchers' seeking access to this data are – although the group overseeing the programme includes GE Healthcare, as well as five other industry representatives.[229] A General Practice Extraction Service (GPES) is set up with a view to mining data from NHS electronic medical records from 2011.[230] In the US, President Bush signs the Newborn Screening Saves Lives Act which allows DNA collected from newborn babies during screening programmes to be used for genetic research without consent.[231] 23andMe begins a research project on Parkinson's Disease, jointly with the Fox Foundation, to which Google makes a charitable donation, and which pays 23andMe to outsource the DNA tests.[232,233] Twin studies suggest there is a minimal inherited component to Parkinsons Disease, although some rare inherited forms exist.[234] The company later begins recruiting participants for other 'research' projects.[235] Burrill & Co, a specialist venture capital company for biotech firms, describes a vision for US healthcare reform in which people have their genomes sequenced in Walmart stores, smart cards include electronic health records and DNA, and there is a near-doubling of the pharmaceuticals market by 2020, including the creation of big new markets in 'wellness' (the 'prediction and prevention' of disease).[236] The Sunday Times reveals that gene tests from different companies give conflicting results about the risks of common diseases.[237]

	Nature reports that genes that explain most of the expected 'heritability' of common diseases have not been found despite extensive studies.[238]
2009	The UK Government introduces the data-sharing legislation proposed in the Thomas-Walport report in clause 152 of the Coroners and Justice Bill. The clause would allow ministers to routinely share medical and genetic data collected in the NHS – and any other personal data - with private companies and with the police or foreign governments without consent.[239] Public opposition forces the Government to abandon the proposals.[240,241,242] The Chief Executive of the US gene sequencing company Illumina advocates sequencing every baby's genome, using the blood spots collected at birth in the NHS, and claims that the benefits will outweigh the harms.[243] The aim would be to identify raised risks of developing an array of conditions, including heart disease and many cancers, so that those at high risk could then be screened more regularly, or given drugs or dietary advice to reduce their risk. Science minister Lord Drayson begins lobbying for an extra £1 billion in the budget to speed up genomic research using NHS data (the funding is later refused by Chancellor Alistair Darling).[244] 23andMe and Google lobby the Conservative party – via Cameron's advisor Steve Hilton who is married to the European head of communications for Google, Rachel Whetstone – to hand NHS electronic medical records to Google Health to run.[245,246] However, Cameron later distances himself from the idea.[247] President Obama appoints the former head of the HGP Francis Collins as Director of the US National Institutes of Health (NIH)[248] and senior Google executives become advisors to the Obama administration.[249] Francis Collins tells the American Association for the Advancement of Science, "*Whether you like it or not, a complete sequencing of newborns is not far away*" and claims that 'personalized medicine' will reduce healthcare costs.[250] However, the use of babies' blood spots for research without consent in the US begins to spark controversy[251] and 5 million blood spots stored without consent are ordered to be destroyed in Texas.[252] A PriceWaterhouseCoopers defines personalized medicine as "*products and services that leverage the science of genomics and proteomics (directly or indirectly) and capitalize on the trends toward wellness and consumerism to enable tailored approaches to prevention and care*".[253] It predicts a $450 billion market by 2015, involving companies such as Nestlé, Danone, Unilever, General Mills, Kellogg, PepsiCo, Coca-Cola, Yakult, Procter & Gamble, General Electric, Google and 23andMe. Companies begin to develop smartphone applications to store people's genomes, so that they can scan supermarket barcodes and be recommended 'personalised' products.[254] The House of Lords Science and Technology Committee publishes a report on 'Genomic Medicine' which claims that it will be several years before prediction of common diseases will lead to the realistic possibility of disease prevention, but that this will have a dramatic impact in the future.[255] An assessment of genes linked to common diseases finds that no common genetic variants exist – either singly or in combination - that have sufficient predictive value to meet medical screening criteria for the general population.[256] DeCode Genetics declares bankruptcy but continues to operate its direct-to-consumer gene testing service.[257] Many Icelanders had already lost their savings as a result of investing in the company, after its shares plummeted from an initial reported 'grey market' price of US$65 before flotation.[258] Robert Young of Auckland University in New Zealand announces the launch of his lung cancer susceptibility test, based on multiple genes.[259] The test is criticised as "*bad science*" by geneticists.[260] Young signed a contract with BAT for research on the genetics of smoking emphysema in 2000[261] but, following an article in the New York Times[262], he informs GeneWatch that the contract was cancelled and no funding was received. In the UK, the Respiragene test is

	marketed by Lab21, whose Chair is the New Labour 'biotech baron' Sir Christopher Evans.[263]
2010	In the UK, an Academy of Medical Sciences (AMS) working group – chaired by biotech venture capitalist Sir David Cooksey and including Professor Sir John Bell – argues that allowing commercial companies to use electronic medical records for 'research' is essential, "*regardless of whether a centralised or localised system of NHS patient records is eventually established*".[264] Controversies about the storage and use of babies' blood spots without consent continue in the US[265], Ireland,[266] and Canada.[267] 23andMe reveals it has sold only 30,000 gene tests over two years and been through two rounds of redundancies, despite being featured on the front page of Time magazine and the Oprah Winfrey show.[268] In his popular science book 'The Language of Life', Francis Collins continues to promote the idea that everyone should have their DNA sequenced and integrated with predictive models that make suggestions about diet, lifestyle, and treatments to optimise their health. The result for his fictional character Hope is a healthy and productive life beyond age 100: without 'personalised medicine' Hope dies of a heart attack aged 50.[269] The book argues that electronic medical records should be used to collect data that can be used to develop predictive models for disease: its cover carries an endorsement from President Obama. Google and Microsoft expect to gain a significant boost for their electronic medical record systems (Google Health and HealthVault) as a result of healthcare reform in the US.[270] Collins claims to have taken action to lose weight after DNA tests from 23andMe, Navigenics and DeCode supposedly showed he was at high genetic risk of type 2 diabetes.[271] However, Newsweek describes Collins as a "*high-profile partisan*"[272], for ignoring a series of scientific studies showing poor predictive value and no medical benefit for tests of multiple genes associated with breast cancer[273], heart disease[274], type 2 diabetes[275], and Alzheimers' Disease[276]. A debate at the American Society of Hypertension highlights that two major genome-wide association studies have failed to explain more than a very small proportion of variation in blood pressure: one researcher argues that they have been a waste of money, whilst the other argues that more research will still help identify disease mechanisms, even if the tests have no predictive value.[277,278,279] An article in the Lancet, written by consultants to 23andMe and a number of other companies – including George Church, who has so many conflicts-of-interest they require two pages in a separate appendix - claims that whole-genome sequencing can yield useful and clinically relevant information for patients.[280] However, the claim is based on unvalidated risk predictions in a single patient and is inconsistent with the findings of studies in large numbers of patients (cited above): nor does it provide any evidence of benefit to health. The paper also ignores evidence that genetic testing probably does not improve health outcomes in patients taking the blood-thinning drug warfarin[281] and that the genetics of sudden cardiac arrest is complex – dependent on identifying rare mutations in family members, rather than screening in the general population - and interventions to prevent it are limited and can do more harm than good.[282] On advice from Francis Collins, Obama appoints Harold E. Varmus (former head of the NIH) to head the National Cancer Institute (NCI).[283] In an article in Nature, Francis Collins states that much of the 'missing heritability' of common, complex diseases "*will probably turn up as the technology advances*".[284] Some geneticists – including Sir Walter Bodmer (Fisher's former pupil and supporter of Brenner's attempt to secure UK funding for the HGP) - argue that rare genetic variants are likely to explain much of the

	'missing heritability' of common diseases and that this might lead to more predictive gene tests in the future.[285,286] However, others disagree, and a variety of other explanations have been put forward, including that complexity and non-genetic factors are important and that the heritability of common diseases could be overestimated because Fisher's original 1918 equations are incorrect.[287,288] These factors are likely to mean that the predictive value and medical usefulness of genetic health predictions is fundamentally limited by the complexity of biology and role of the environment in common diseases.[289, 290] The Labour Government fast-tracks the uploading of medical data from NHS patients to the Spine, beginning in London, as concerns about the risks to medical confidentiality increase.[291,292] In May, the new UK Coalition Government is elected. An independent response to the Lords' report on Genomic Medicine finds that it overestimated the importance of genomics for the prediction and prevention of common complex diseases (such as cancer, cardiovascular disease, asthma and diabetes), although it is expected that there will be instances where tests could be used in future to predict and monitor individual drug responses. Conversely, the immediate potential to improve diagnosis and care for individuals and families affected by single gene disorders and inherited subsets of complex disease was not adequately emphasised, despite ample evidence of demonstrable health benefits.[293,294] Sir Richard Sykes resigns as head of the NHS in London, citing a serious difference of opinion with the new Health Secretary, Andrew Lansley.[295] In the UK, hospitals continue to store millions of babies' blood spots which could be sequenced without consent once this becomes affordable.[296] The FDA announces plans to regulate genetic tests.[297] 23andMe is criticised for a mix-up involving 96 samples, as is UC Berkeley (and later, Stanford[298]) for asking students to submit DNA samples to testing by 23andMe.[299] Children's Hospital Boston plans a genetic study of families and children in which it may feed back research results even though they are unlikely to be valid.[300] Privacy campaigners highlight concerns that the Coalition Government appears to be backtracking on both parties' pre-election pledges to scrap the Spine.[301] A report from University College London finds that the medical benefits of the scheme are limited and that millions of people have had their records uploaded without knowing it.[302,303] The GP Extraction Service (GPES) continues preparing to access medical information held in the NHS without consent from 2011.[304]

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