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Science and Technology Committee

# Genomics and genome editing in the NHS

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## Science and Technology Committee

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# Summary

Genomics has the potential to transform medical care across the world and in the NHS as well as dramatically improve patient outcomes in the UK and globally. The UK is considered to be a world leader in the development of Genomics. The 100,000 Genomes Project is a world-leading project that has placed the UK at the cutting edge of global advances in genetic medicine. We applaud the Government policies and on-the-ground initiatives that have led us to the internationally enviable position that UK genomics finds itself in today. Genomics has already led to advances in diagnosis and new treatments especially in certain cancers and rare diseases. The UK is uniquely positioned to benefit from greater understanding of genomics because of the unique strength of our national health service and thus the ability to maximise the collective benefits of very large quantities of reliable and detailed patient data. Nevertheless, much more needs to be done to achieve the full potential that genomics promises. The Government must continue, and increase, its investment in digital infrastructure and ensure that the NHS workforce is prepared for the new challenges associated with collecting, analysing, and acting upon genomic data. It is also essential that the public, who understandably have little knowledge of genomics and the treatments that arise from it, are informed of the opportunities it presents. Genomics is founded on the analysis of large volumes of health data. It is essential, therefore, that the public understands the value of their contribution to improving healthcare, and that the systems managing genomic data command the public's trust.

The Committee welcomes the Life Sciences Sector Deal agreed by the Government which set out a range of measures to support genomics in the UK, including whole genome sequencing of the UK Biobank and an extension of the cancer branch of the 100,000 Genomes Project.

Genomic medicine involves mapping a person's DNA and, through comparison with many other people's DNA and medical records, searching for elements related to disease. It has great potential to improve patient care, particularly for diagnosing rare diseases and for more personalised targeting of medicines and treatments. In July 2017, the Chief Medical Officer published a report, 'Generation Genome', which discussed the scope for embedding it in the NHS. Our inquiry examined the opportunities and challenges involved in that endeavour, including the lessons learnt from the '100,000 Genomes Project'—the first large-scale whole genome sequencing exercise in the world.

The Project is an ambitious initiative that has put the UK at the forefront of genomic medicine worldwide. With the Project aiming to have completed sequencing of 100,000 genomes by the end of this year, it also represents a valuable source of evidence for determining the technology's clinical efficacy and cost-effectiveness when applied at scale. The Government should conduct a detailed evaluation of the Project to inform the introduction of whole genome sequencing into routine NHS care planned as part of the forthcoming Genomic Medicine Service.

Research and evidence-gathering will also need to be continuing processes. NHS England should embed processes for evaluating the impact of whole genome sequencing as it configures the Genomics Medicine Service, in line with recommendations from the Chief Medical Officer's report. Where more evidence is needed to demonstrate the

benefit of whole genome sequencing over existing diagnostics for particular conditions, the existing diagnostics should be maintained alongside genome sequencing unless the genomic diagnostic has proved more accurate for that condition.

Significant digital infrastructure is needed to support routine genomic medicine, and it is welcome that some centres and hospitals already have solutions in place. However, the wider programme to improve NHS infrastructure is running to a later timeframe than the planned Genomic Medicine Service. The Government has expressed its commitment to funding the digital infrastructure required specifically for genomics but the relevant budgets now need to be confirmed. The digital infrastructure in place should be one consideration involved in decisions on providing whole genome sequencing in place of conventional alternative diagnostic tests, to avoid attempting to roll out a Genomic Medicine Service at a speed that cannot be delivered.

There appear also to be some gaps in the training needed for the Genomic Medicine Service. The Genomics Education Programme is playing an important role in raising awareness and expertise, however this was initially a 4 year programme. It is now to be continued, but with a substantially lower level of funding than previously. Genomics will need to be embedded in all relevant training courses and medical revalidation processes. Health Education England should complete detailed genomics workforce planning and modelling as soon as possible and funding for the necessary training should be provided.

Data sharing will be essential for genomic medicine and members of the public will need to be assured that data privacy rules are respected. Public support will be vital. A high proportion of patients involved in the 100,000 Genomes Project consented to sharing their genomic data, but its 'broad consent' model is unlikely to be feasible for routine genomic medicine in the NHS without extensive and continuing public engagement to increase understanding and acceptance. We recognise the Government's determination to implement the General Data Protection Regulation but it should significantly increase its efforts to raise awareness. The Government should consult on, confirm, and publicise, the consent framework it intends to use for the Genomic Medicine Service as soon as possible.

It is important that patients do not refuse to give their consent to receive predictive genomic test results out of concern for how these might be used by insurance providers. As genomic sequencing becomes more common, there may be pressure on the current controls put on insurers' ability to ask for test results by the Concordat and Moratorium agreed between the Government and the Association of British Insurers. The Government should seek to renew the Concordat as soon as possible, and in the longer-term set up systems to monitor any reluctance among patients to undertake genomic testing due to insurance concerns, assess the experiences of countries that ban insurers' use of predictive genetic test results, and be ready to consider putting the Concordat on a statutory footing if the current voluntary system begins to limit the uptake of predictive testing.

Genomics England should seek to maximise the commercial value of its datasets and continue to provide industrial and academic access to these data to facilitate the growth of the UK genomics industry and the development of new treatments, while ensuring

consent and data safety safeguards. Genomics England should explore technological and commercial mechanisms to enable better integration of the genomics data they hold with other NHS data and data owned by private companies. While patient benefit should be the focus of the Genomic Medicine Service, income generated from NHS data can be reinvested in the NHS and further benefit patients in the long term.

We also briefly examined genome editing—a rapidly developing technology that is already a powerful tool for research, and which has significant promise for therapeutic use. Different applications of the technology entail different ethical considerations, some of which are the subject of particular debate. The UK currently has a strong regulatory environment in this area, striking a balance between enabling important research and providing public confidence that ethical and other considerations are given appropriate oversight. The Government should require UK Research and Innovation to closely monitor the development of genome editing for potential obstacles to innovation in this area. If it becomes appropriate to review or amend the current regulations in light of technological developments, the process that accompanied legislative changes to allow mitochondrial donation should serve as a good model to follow.

# Glossary of terms/abbreviations used in report

## General terms

**Bioinformatics:** the science of analysing large quantities of genetic and other biological data

**Clinical pathway:** the full process of steps taken in treating a patient, including initial assessment, referral, consenting, testing, receiving a diagnostic result**,** and the clinical consequences

**Exome:** the 1% of DNA that provides instructions to the body on what proteins to produce

**Germline cells:** sperm or egg cells, in which any changes in DNA will be passed on to future generations

**Genome:** the entire DNA sequence, found in almost every cell in the human body

**Genome editing:** techniques for precisely editing, deleting or inserting genetic material at specific points in genome sequences

**Mitochondrial donation:** a technique that allows women whose mitochondria (structures found in the fluid inside cells) carry serious inherited disease to give birth to children free from mitochondrial disease, by transferring 'packets' of the mother's nuclear DNA to a donor cell containing healthy mitochondria; this technique was legalised by Parliament in 2015

**Panel testing:** panel testing involves sequencing multiple genes simultaneously, varying from a few genes known to relate to a particular condition through to all known genes with disease-related function

**Predictive test results:** genetic test results revealing a predisposition to developing a condition in the future, for which symptoms or any other signs have not yet appeared; because whole genome sequencing tests the entire genome, it can uncover predictive results alongside results concerning the suspected condition that prompted the sequencing

**Pseudonymisation:** a process in which personally identifiable information in a digital record is replaced with a unique code, in order to minimise the risk of identification while still providing a route for the record to be linked back to the individual (for example to return medically-relevant information to them)

**Rare disease:** the Department of Health and Social Care defines a disease as rare if it is a life-threatening or chronically debilitating condition that affects fewer than 6 people in 10,000 and requires special, combined efforts to enable it to be diagnosed and treated effectively; there are over 6,000 rare diseases, which together affect 1 in 17 people in the UK at some point in their lives

**Revalidation:** in order to practise medicine in the UK, doctors require a licence to practise—this must be renewed (usually every five years), and the process of demonstrating continued fitness to practise is called revalidation

**Sequencing:** the process of determining the letters of DNA in a genome, and the order in which they appear

**Somatic cells:** all cells other than those involved in reproduction; changes to DNA in somatic cells will not be passed on to future generations

**Variant:** a difference in a patient's genome sequence compared to the reference 'standard' human genome; variants can be benign, related to increased risk of disease, or of unknown significance

**Viral vectors:** viral vectors are products required to carry out common techniques for genome editing

## Abbreviations

**ABI:** Association of British Insurers

**ABPI:** Association of the British Pharmaceutical Industry

**CMO:** Chief Medical Officer for England and Chief Medical Advisor to the Government

**DNA:** Deoxyribonucleic acid

**HARP:** Health Advanced Research Programme, as proposed in the Life Sciences Industrial Strategy

**MHRA:** Medicines and Healthcare products Regulatory Agency

**NHS:** National Health Service

**NICE:** National Institute for Health and Care Excellence

**RNA:** Ribonucleic acid

# 1 Introduction

1. In July 2017, Professor Dame Sally Davies, the Chief Medical Officer (CMO) for England and Chief Medical Advisor to the Government, published her annual report, entitled 'Generation Genome'.[1] She focused on the opportunities and challenges associated with embedding genomics in everyday NHS care. Genomic medicine involves mapping a person's DNA and, through comparison with many other people's DNA and medical records, searching for elements related to disease. As the CMO highlighted, genomic medicine has the potential to deliver a range of health benefits to patients. These include: providing diagnoses where this has not been possible using clinical symptoms or other techniques; determining which treatments will be most effective, or which will provoke adverse reactions, for a specific patient; informing personalised disease prevention strategies; improving newborn and prenatal screening; and facilitating drug discovery.[2]

2. The CMO's report reflected the aim of the 100,000 Genomes Project, launched in 2012, to "accelerate the uptake of genomic medicine in the NHS".[3] At its 2016 board meeting, NHS England stated that:

> Since its inception the expectation has been that by the end of the [100,000 Genomes Project] NHS England, working in partnership with Genomics England, will commission whole genome sequencing and embed genomic medicine into routine care pathways where it is clinically and cost effective to do so, in line with [the] NHS constitution […] to continue to operate at the limit of science.[4]

3. With the 100,000 Genomes Project aiming to complete the sequencing of 100,000 genomes by the end of this year, NHS England intends to establish a Genomic Medicine Service, offering genetic tests ranging from analysis of single genes to whole genome sequencing as part of routine NHS care.[5] Major components of that Service will include:

- 13 Genomic Medicine Centres, already established as part of the 100,000 Genomes Project, responsible for clinical care, obtaining patient consent and providing clinical data and blood or tumour samples;
- a network of Genomic Laboratory Hubs, each intended to deliver a standard list of genomic tests;
- a central data repository connected to wider NHS digital infrastructure; and
- an annually refreshed National Test Directory, setting out what genomic tests are available and when they are applicable.[6]

1 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
2 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
3 'The 100,000 Genomes Project Protocol', Genomics England (2017)
4 NHS England Board Paper, 30 March 2017
5 NHS England Board Paper, 30 March 2017
6 'Genomics in the NHS', presentation by Prof Sue Hill at the 'Implementing a National Genomic Medicine Service for the NHS: building on the legacy of the 100,000 Genomes Project' joint event by the All-Party Parliamentary Health Group and the All-Party Parliamentary Group for Personalised Medicine, 7th November 2017

The CMO told us that NHS England intends to have the Genomic Medicine Service "operational" in the second quarter of 2018 and have it "mainstreaming" in the second quarter of 2019.[7]

## Our inquiry

4. Our predecessor Science and Technology Committee launched an inquiry into 'genomics and genome editing' in November 2016, but was unable to complete its inquiry due to the 2017 General Election. The earlier inquiry received 62 written submissions[8] and took oral evidence from 19 witnesses, and the Committee published an interim report in April 2017 that flagged issues for further scrutiny.[9] With the publication of the CMO's report in July 2017, and the approaching conclusion of the 100,000 Genomes Project, we decided to continue and complete the earlier work, with a focus on the challenges in embedding genomic medicine in the NHS. During the course of our inquiry, we received 37 further written submissions and took oral evidence from 11 witnesses, including from the NHS, academia, the pharmaceutical industry, the CMO and the Parliamentary Under-Secretary of State for Health, Lord O'Shaughnessy. We have endeavoured to use the large volume of evidence from our predecessor Committee's inquiry. We also visited Genomics England (see Annex).

5. In Chapter 2, we examine the progress of the 100,000 Genomes Project and assess the opportunity presented by whole genome sequencing. Chapter 3 discusses logistical challenges involved in the transition to the NHS Genomic Medicine Service. Chapter 4 looks at access to genomic data, including issues around patient consent, consequences for insurance and NHS engagement with industry. Chapter 5 briefly reviews the related—but distinct—technology of genome editing.

7 Q161

8 Science and Technology Committee, Sixteenth Report of Session 2016–17, 'Genomics and genome-editing: future lines of inquiry', HC 854 (references to this inquiry's written evidence are labelled with a 'GEN' prefix)

9 Science and Technology Committee, Sixteenth Report of Session 2016–17, 'Genomics and genome-editing: future lines of inquiry', HC 854

# 2 Whole genome sequencing

## The 100,000 Genomes Project

6. The launch of the 100,000 Genomes Project was announced by then Prime Minister, David Cameron, in 2012, with the objective of sequencing 100,000 genomes from NHS patients by the end of 2017.[10] A new body, Genomics England, was established in July 2013 by the then Department of Health as a wholly owned limited company to deliver the 100,000 Genomes Project in England. The initiative had five main aims:

- to benefit patients by providing clinical diagnosis and, in time, new or more effective treatments;
- to provide new scientific insights and discovery;
- to accelerate the uptake of genomic medicine in the NHS;
- to stimulate and enhance UK industry and investment; and
- to increase public knowledge and support for genomic medicine.[11]

7. As of February 2018, just over 50,000 whole genomes had been sequenced as part of the Project.[12] Following advice from Genomics England, the Department of Health and NHS England, the Government agreed to extend the sequencing element of the programme to the end of 2018.[13] Accounting for this delay in completing the 100,000 sequences by 2017, Genomics England explained that the project is "working at the edge of known science".[14] Giving evidence to our predecessor Committee in February 2017, Professor Mark Caulfield, of Genomics England, described challenges in preserving cancer samples and building streamlined systems for handling genomic and related data as the two main obstacles that had delayed the project.[15] He indicated that these challenges had at that stage been largely overcome and that Genomics England "anticipate finishing the 100,000 Genomes Project by the end of 2018".[16]

8. Despite the delays, the Life Sciences Industrial Strategy highlighted the 100,000 Genomes Project as one of two examples of large healthcare infrastructure projects that have put the UK in globally leading positions, highlighting that Genomics England "has already set the global standard for healthcare genomic data in rare disease and now, increasingly, in cancer".[17] Professor Sir John Bell, the author of the Life Sciences Industrial Strategy, told us that the UK is now "multiple years ahead of the rest of the world in handling whole genome data".[18] Industry groups reported similarly positive feedback,[19] while other witnesses praised the ambition and progress of the programme, though also highlighting some of the remaining challenges. The Wellcome Sanger Institute told us

10 'Genomics England and the 100,000 Genomes Project', Genomics England
11 'The 100,000 Genomes Project Protocol', Genomics England (2017)
12 Genomics England, 'The 100,000 Genomes Project by numbers', accessed 1 March 2018
13 Genomics England (GNH0018)
14 Genomics England (GNH0018)
15 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Qq16–20
16 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q16
17 'Life Sciences Industrial Strategy—A report to the Government from the life sciences sector' (2017)
18 Q17
19 Association for the British Pharmaceutical Industry (GEN0040) and the BioIndustry Association (GNH0017)

that the project was a "ground-breaking, world-leading genomics initiative", but added that "although an excellent programme, there are areas where recurring concerns have been raised".[20] University Hospitals of Leicester told our predecessor Committee that the project was a "bold and ambitious project that promises exciting benefits for the country, for communities and individuals", but which also "gives rise to several significant educational, social, cultural and economic challenges that require careful research and analysis".[21] Dr Hilary Burton, of the PHG Foundation, told us:

> The way all the genomic medicine centres have been set up, so that they all have the facility to recruit patients, get the necessary clinical information together and submit them for sequencing, with the processes for doing the sequencing and interpretation and feeding back diagnostic information, has been a fantastic leap forward and will set the way for how we eventually use it. Our point is that there is still a long way to go and we still have to put substantial resources into making it happen across the whole country for all the specialties where it is relevant.[22]

9. Professor Sir John Bell told us that setting up the 100,000 Genomes Project as a separate entity from the NHS was key to its development:

> Had we done the 100,000 Genomes Project in the NHS from its pilot phase it would have failed. The only way this works is if you take it out and set it up as an independent company wholly owned by the Department of Health. It was free to operate, employ people and do stuff in a way that the NHS structure would not allow. Once you know it works, you drop it back into the healthcare system.[23]

University Hospitals of Leicester, on the other hand, told our predecessor Committee that the project had missed opportunities to collaborate with existing projects, in particular the Clinical Research Network. They believed that this had led to duplication of "staffing and IT infrastructures, education, advertising, study design, communication and managerial governance arrangements",[24] and to competition between the projects:

> There were missed opportunities for joint working (with no cross-subsidisation of funding) when patients were eligible for Clinical Research Network and Genomics studies […] The demands on clinical genetics departments to lead and deliver the 100,000 Genomes Project, especially those resulting from complex and challenging inclusion criteria, has reduced time to concentrate on CRN study delivery and recruitment. This is compounded by genomics projects often competing for the same patient groups.[25]

Subsequently, the Life Sciences Industrial Strategy has recommended the creation of a Health Advanced Research Programme (HARP), and described Genomics England as one of two "excellent examples for future large-scale HARP projects".[26]

20 Wellcome Trust Sanger Institute (GNH0003)
21 University Hospitals of Leicester (GEN0014)
22 Q101
23 Q15
24 University Hospitals of Leicester (GEN0014)
25 University Hospitals of Leicester (GEN0014)
26 'Life Sciences Industrial Strategy – A report to the Government from the life sciences sector' (2017)

10. Our predecessor Committee highlighted, as an issue for further inquiry, "whether patients are being invited into the 100,000 Genomes Project due to perceived long-term research and commercial benefits, at the expense of more immediate benefits to their health".[27] Genomics England explained that this was not the case.[28] Professor William Newman, of the British Society for Genetic Medicine, assured us that:

> In the 100,000 Genomes Project, one of the eligibility criteria is that patients should have already had their routine clinical care, routine assessment and tests, such that they are not being disadvantaged in any way. The application of whole genome sequencing should be something additional to try to find the answer for their condition.[29]

Professor Sue Hill, of NHS England, confirmed that "with cancer, currently any patient being entered into the 100,000 Genomes Project is having their standard diagnostic testing done, and that includes any genetic-based tests and other tests that help direct their therapies".[30]

11. Concerns had also been raised in our predecessor Committee's inquiry about a perceived lack of planned evaluation for the 100,000 Genomes Project.[31] Dr Hilary Burton, of the PHG Foundation, had hoped that evaluation processes would have been built into the 100,000 Genomes Project to prospectively collect information on the overall results and clinical impact of genomic testing across the whole Project,[32] but told us that her "understanding is that that has not happened".[33] The CMO rejected Dr Burton's concerns, telling us that Dr Burton "is clearly not close enough to the project".[34] Nonetheless, concerns about a lack of evaluation of the Project persist. Dr Edward Blair, of the Oxford NHS Genomic Medicine Centre, told us that "there has been no significant review of outcomes since only small numbers of completely analysed and clinically validated genomes have been provided".[35] Dr Burton told us that "some of the more routine learning about how [whole genome sequencing] would be implemented in normal patient pathways has not been available, but we have to get on with it now".[36] The PHG Foundation emphasised that "to ensure that the legacy of the 100,000 Genomes Project is maximised, we strongly recommend a formal evaluation of its different work programmes from inception to 2017–18. Results will be critical for informing the design and implementation of future NHS healthcare services".[37] The Association for Clinical Genomic Science made a similar plea.[38]

12. **The 100,000 Genomes Project is an ambitious project that has helped put the UK in a world-leading position on whole genome sequencing and genomic medicine. *As the 100,000 Genomes Project approaches the completion of its sequencing target, the Government should formally evaluate it to inform the wider introduction of whole***

27 Science and Technology Committee, Sixteenth Report of Session 2016–17, 'Genomics and genome-editing: future lines of inquiry', HC 854
28 Genomics England (GNH0018)
29 Q58
30 Q60
31 PHG Foundation (GEN0025)
32 Q111
33 Q113
34 Q156
35 Dr Edward Blair (GNH0031)
36 Q116
37 PHG Foundation (GNH0015)
38 Association for Clinical Genomic Science (GNH0036)

***genome sequencing in the NHS (which we explore further below). The 100,000 Genomes Project could be a model for future 'Health Advanced Research Programme' projects, as suggested in the Life Sciences Industrial Strategy. If so, HARP projects should have processes and resources put in place from the start to allow their subsequent evaluation, and should explicitly take account of how existing NHS initiatives and resources will be complemented or absorbed.***

## Whole genome sequencing

13. The CMO's report focused on whole genome sequencing, describing it as "the pinnacle of a pyramid of molecular diagnostics".[39] Other genetic diagnostics, including 'single gene' diagnostics and 'panel' and 'exome' sequencing,[40] are already used by genetics laboratories. In 2016, NHS England stated that it intended to "commission whole genome sequencing and embed genomic medicine into routine care pathways where it is clinically and cost effective to do so".[41] We examine below those clinical-effectiveness and cost-effectiveness issues in turn.

### *Clinical effectiveness*

14. The optimism in the medical community at the potential for whole genome sequencing is clear. The Wellcome Sanger Institute believed that "genomics has the potential to dramatically improve patient care by improving specificity of diagnosis and helping stratify management and treatment".[42] The CMO told us that over the course of the 100,000 Genomes Project:

> It has become clear that whole genomes are extraordinarily important […] we now know that, even if you want the exome, you are much better getting it from a whole genome, because it picks up inversions and quite complicated things and gives you a better-quality exome.[43]

15. Professor Sian Ellard, of the South West NHS Genomic Medicine Centre, told us how whole genome sequencing can benefit the diagnosis of rare diseases:

> In the past we could provide testing only for patients who had the most common rare diseases, because you had to set up a test for each specific condition and it was only feasible to do those tests where there was sufficient volume. This technology means that potentially we can diagnose any rare disease for which the genetic basis is known. That is really exciting. We have seen a huge increase in the number of patients for whom we can provide a diagnosis.[44]

39 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)

40 Different genetic diagnostics differ in which parts of the genome are sequenced. Single gene tests look for mutations in specific genes known to relate to the disease a patient is suspected of having; gene panels sequence multiple genes simultaneously, varying from a few genes known to relate to a particular condition through to all known genes with disease-related function; exome sequencing reads the entire exome—the 1% of DNA that provides instructions to the body on what proteins to produce.

41 NHS England Board Paper, 30th March 2017

42 Wellcome Trust Sanger Institute (GNH0003), see also Q101, for example

43 Q155

44 Q101

She added that whole genome data can be revisited as research discovers new genetic causes of very rare disorders.[45] Lord O'Shaughnessy, Parliamentary Under-Secretary of State for Health, told us that it was such versatility, and the opportunity to replace a range of tests with whole genome sequencing, that had been "convincing to Government".[46]

16. The optimal balance between whole genome sequencing and alternative genomic tests was not, however, always clear. The Scottish Genomes Partnership told us that, in comparison to targeted sequencing panels, whole genome sequencing: takes longer to return results to the patient; generates more data, increasing storage costs; has stricter demands on patient samples; and provides reduced sensitivity to specific genetic targets.[47] In regards to rare diseases, they thought that choices between whole genome sequencing and alternative diagnostic tests were "complex", but anticipated "the eventual mainstream delivery of whole genome testing within NHS Scotland".[48] In contrast, for cancer, they told us that "increasing numbers of scientists and oncologists […] are reaching the conclusion that targeted sequencing panels are a better choice [than whole genome sequencing] for the foreseeable future, for both the patient and the NHS".[49] Several other witnesses expressed a similar point of view.[50]

17. Patients with rare diseases may have spent years seeking a diagnosis. For cancer patients, however, Professor Sir Mike Stratton of the Wellcome Sanger Institute highlighted that whole genome data analysis is needed "within a couple of weeks in order to make the appropriate decisions with respect to choice of therapies".[51] Genomics England told us that "at this early stage of genomic medicine, it may take many months for results to come back", although "in future, this is likely to get quicker".[52] Genomics England are currently running a fast track cancer analysis pilot aiming to return cancer reports within four weeks;[53] Professor Sue Hill told us that "in those small numbers of samples, that is being done in around 20 days", and that "in some instances that is better than standard care at the moment".[54]

### *Cost effectiveness*

18. Genomics England told us that sequencing costs around £600 per genome, which is "affordable for a healthcare test".[55] The CMO's report noted that there are also costs associated with bioinformatics analysis, clinical interpretation and reporting, and that these costs were not falling as quickly as sequencing costs.[56] In return for these costs, Professor Sue Hill, of NHS England, believed that whole genome sequencing could shorten the "diagnostic odyssey" that people with rare and inherited diseases can go through, which can last "12 years or longer", and during which "some will have been in and out

45 Q110
46 Q163
47 Scottish Genomes Partnership (GNH0005)
48 Scottish Genomes Partnership (GNH0005)
49 Scottish Genomes Partnership (GNH0005)
50 For example, the Wellcome Trust, the Association of Medical Research Charities and Cancer Research UK (GEN0038), the Association for Clinical Genomic Science (GNH0036) and Roche Products Limited (GNH0038)
51 Oral evidence taken on 8 March 2017, HC (2016–17) 854, Q181
52 Genomics England (GNH0018)
53 Department of Health (GNH0004)
54 Q60
55 Genomics England (GNH0018)
56 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)

of the healthcare system, utilising healthcare resources".[57] She calculated that "we spend, often, more [on a series of tests] than doing whole genome sequencing", providing the potential for it to save costs compared with current diagnostics.[58]

19. Professor Hill emphasised that "pharmacogenomic[59] profiling associated with [whole genome sequencing] could drive the use of appropriate medicines, rather than a one-size-fits-all medicine approach",[60] which could save costs and reduce the risk of adverse reactions to treatment. A 2016 NHS England report on personalised medicine concluded that "key pharmaceutical interventions are effective in only 30–60% of patients due to differences in the way an individual responds to and metabolises medicines", and that "1 in 15 hospital admissions in the UK are linked to adverse drug reactions".[61] Professor Sir John Bell highlighted how medicines developed for increasingly targeted (and hence smaller) patient populations reflect a more general trend away from 'blockbuster' medicines, with uncertain consequences for affordability.[62]

20. Whether there are net savings or costs from whole genome sequencing is, however, uncertain. Dr Magdalini Papadaki, of the Association of the British Pharmaceutical Industry, explained that:

> All these transformative therapies, whether they are curative or it is early prevention so a disease or cancer does not manifest itself, have long-term healthcare burdens or uncertainties, because you now have groups of people who survive and then can get diseases later on, or in ageing. All those cost offsets from previous deaths, as tragic or controversial as it might sound, will now not exist. We do not know exactly how this cost-benefit balance will play out and what it will mean in the future.[63]

Dr Edward Blair, of the Oxford NHS Genomic Medicine Centre, also described the unknown economic impact of 'additional findings'.[64] An additional, or secondary, finding is one that is unrelated to the condition that led to the whole genome sequencing being conducted. He said that such findings could lead to additional healthcare activity such as clinical testing of patients and their relatives or prophylactic treatment of at-risk individuals, and saw the return of additional findings as a form of targeted 'genetic screening', which he believed should be formally assessed by the UK National Screening Committee before introduction.[65]

57 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q5
58 Q53
59 Pharmacogenomics entails using a patient's specific genetic mutations to inform the choice of drug treatment, identifying which treatments will be most effective and which might provoke adverse reactions.
60 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q5
61 'Improving Outcomes through Personalised Medicine', NHS England (2016)
62 Q40
63 Q40
64 Dr Edward Blair (GNH0031)
65 Dr Edward Blair (GNH0031)

21. The CMO's report acknowledged that personalising medicines and looking for additional findings pose "economic risks", but argued that:

> These are issues for the health system to tackle eventually under any scenario, and the progressive awareness of patients of their own risks with support from appropriate health professionals could be key to managing these issues.[66]

Discussing the cost-effectiveness of whole genome sequencing compared to current genetic diagnostics, her report stated:

> It is possible that because whole genome sequencing can be industrialised as a single common process it will become more cost-effective to draw panels or exomes from a whole genome sequence factory than invest in many bespoke diagnostics for particular conditions.[67]

The Association for Clinical Genomic Science, on the other hand, told us that the affordability of whole genome sequencing could be undermined if competition were weakened:

> There is concern in the community that a monopoly may be created by the transitioning of a substantial proportion of testing to centralised whole genome sequencing that will not encourage competition between commercial providers in the genomic industry and that costs will remain too high to create greater access within the NHS.[68]

The CMO's report also flags the potential for developments in genomic medicine to benefit the economy.[69] We explore the opportunity for NHS England to capture the value of its genomic data in Chapter 4.

### *Evaluation*

22. Professor Sue Hill told us that NHS England would base its assessment of the clinical- and cost-effectiveness of whole genome sequencing on systematic and ongoing reviews of the available evidence.[70] Professor Patrick Chinnery, of the University of Cambridge, believed that there was already strong evidence to support the replacement of some existing diagnostics with whole genome sequencing; that "the diagnostic yield from whole genome sequencing is superior to anything else that preceded it".[71] While he thought whole genome sequencing will have "a more immediate impact" for rare cancers, he was less certain for common cancers, and did not expect whole genome sequencing to become routine NHS care in these cases for five to ten years.[72]

66 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
67 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
68 Association for Clinical Genomic Science (GNH0036)
69 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
70 Q65
71 Q158
72 Q160

23. The CMO's report cautioned that:

> For whole genome sequencing to become part of the regular commissioned service it will have to demonstrate superior efficacy (and efficiency) to alternative sequencing regimes. While there are strong indications that all these conditions will be met as the technology develops, more progress will be required in the 100,000 Genomes Project to help provide the evidence.[73]

Most existing studies, the report noted, "tended to be of fairly low quality", or used "very small patient samples, which is in total contrast to the data which the 100,000 Genomes Project will provide".[74] The CMO acknowledged that evaluation of the cost-effectiveness of whole genome sequencing "is in its infancy".[75]

24. At this stage, there has been no overarching evaluation of the 100,000 Genomes Project. Genomics England has publicised the details of cases in which individuals have benefited from whole genome sequencing and their involvement in the 100,000 Genomes Project.[76] Additionally, Professor Mark Caulfield, of Genomics England, told us that "in rare diseases, 20% to 25% of the participants in the pilot are now receiving potentially actionable diagnoses in the health system today".[77] Professor Sue Hill told us that in cancer, "we are seeing a greater number of potentially actionable changes—up to the level of 65% in some patients—emerging from whole genome sequencing".[78]

25. The PHG Foundation, however, was sceptical about the evidence to date on the impact of whole genome sequencing on clinical outcomes. They believed that Genomics England's evaluations do "not tell us what effect the [whole genome sequencing] test result had on clinical decision making and clinical outcomes for groups of patients with particular clinical presentations arising through routine practice".[79] In addition to recommending evaluation of groups of patients, rather than individuals, they urged that an evaluation span the entire 'clinical pathway', "from assessment, referral, acceptance, consenting, testing, receiving a result (diagnostic outcome) and ultimately to the patient level clinical consequences".[80]

26. Despite the apparent importance of the 100,000 Genomes Project as a source of evidence on the clinical and cost-effectiveness of whole genome sequencing, Professor Sue Hill could not say whether there were plans for a formal evaluation of the 100,000 Genomes Project.[81] She instead outlined a variety of other sources of evidence that NHS England has used to assess the results of whole genome sequencing.[82] In the meantime, the charity Genetic Alliance UK was concerned at the lack of publicly available information regarding the introduction of the Genomic Medicine Service.[83]

73 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
74 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
75 Q156
76 For example, see Genomics England, 'Participants from NHS Genomic Medicine Centres have shared their stories with us', accessed 2 February 2018
77 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q57
78 Q60
79 PHG Foundation (GNH0035)
80 PHG Foundation (GNH0035)
81 Q55
82 Q55
83 Genetic Alliance UK (GNH0022)

27. **There is great potential for whole genome sequencing to improve patient care, particularly for diagnosing rare diseases and for more personalised targeting of medicines and treatments. However, there is not yet sufficient unambiguous evidence gathered to demonstrate its benefit for routine care, in particular for common cancers. As the first large-scale whole genome sequencing exercise in the world, the 100,000 Genomes Project must be an important source of evidence to determine the technology's clinical efficacy and cost-effectiveness across the whole 'clinical pathway', and at the level of patient populations, rather than individual patients. Such evaluation does not appear to have been conducted, or at least has not been made public.** ***In advance of the launch of the Genomic Medicine Service, NHS England should undertake and publish a detailed evaluation of the 100,000 Genomes Project, to inform an assessment of the anticipated clinical- and cost-effectiveness of routine whole genome sequencing in the NHS.***

28. Research and evidence-gathering needs to be a continuing process. The CMO's report recommended that NHS England "embeds implementation research (including cost effectiveness) at all stages of service redevelopment and laboratory reconfiguration".[84] The PHG Foundation concurred, highlighting that "implementation research is a vital element to ensure that resources are used effectively, and especially to underpin the substitution of new technologies for existing redundant technologies".[85] Professor Sue Hill told us:

> There will be an evaluation function within NHS England that will be based and built upon [the UK Genetic Testing Network]. It will include the expert standing committee recommended by the CMO in her report, and this will review evidence on an ongoing basis across all the tests that will be introduced into the NHS for both rare disease and cancer […] We will be working really closely together with the National Institute for Health and Care Excellence (NICE) to ensure that we have a seamless process that helps direct the commissioning system on the basis of the finance that is going to be available and the affordability. We will look at it through the lens of the five year forward view, and on quality, improving access, and then its affordability.[86]

29. NICE has already included genetic diagnostics in its clinical guidelines and in its Technology Appraisals and Highly Specialised Technologies programmes,[87] although these have not yet covered whole genome sequencing.[88] The 2016 independent Accelerated Access Review noted that NICE's Technology Appraisals mostly focus on pharmaceuticals rather than diagnostics, and that positive guidance outside of the Technology Appraisal programme does not carry with it a funding requirement.[89] It recommended that NICE "rebalance its work towards products which, accompanied by appropriate changes in clinical pathways, can improve system efficiency whilst delivering equivalent or better patient outcomes".

84 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
85 PHG Foundation (GNH0015)
86 Q81
87 National Institute for Health and Care Excellence (GNH0013)
88 Q78
89 'Accelerated Access Review: Final Report' (2016)

30. Professor Sir John Bell told us that genomic sequencing is difficult for NICE to evaluate:

> This is hard for NICE because it is not a domain that it really understands and knows about, but it has been quite responsive in helping to think through how to get the value proposition for genomics to work.[90]

Dr Mark Kroese of NICE told us, however, that the CMO's ambition to mainstream genomics in the NHS "fits really well with the NICE work programmes".[91] He reported that NICE had not had experience of the whole genome sequencing yet, but he did not see "any challenges to our abilities to evaluate genomic tests in the diagnostic assessment programme".[92]

31. As whole genome sequencing becomes approved for certain conditions, there will be financial pressure to remove alternative diagnostic tests from the 'directory'. As Professor Bell put it:

> To adopt innovation successfully you have to do two things. You have to invest in it to get it in the system, and then you have to work hard to extract the things you do not need to do any more to get the savings from the innovation ultimately to produce more efficient systems.[93]

Professor Lyn Chitty, of the North Thames NHS Genomic Medicine Centre, commented elsewhere, however, that existing diagnostic tests will need to continue alongside whole genome sequencing in the short term, to allow for comparison and validation of whole genome sequencing.[94]

32. **The 100,000 Genomes Project will not be able to provide all of the evidence required to assess the effectiveness of whole genome sequencing for all conditions. Research and evidence-gathering will need to be continuing processes.** ***We endorse the CMO's recommendation for NHS England to embed implementation research at all stages of redevelopment and laboratory reconfiguration for the Genomics Medicine Service. Where more evidence is needed to approve whole genome sequencing for particular conditions, current diagnostics should be maintained alongside whole genome sequencing, as was done in the 100,000 Genomes Project, unless the genomic diagnostic has proved more accurate for that condition.***

90 Q34
91 Q78
92 Q80
93 Q30
94 'Implementing a National Genomic Medicine Service for the NHS: building on the legacy of the 100,000 Genomes Project', joint event by the All-Party Parliamentary Health Group and the All-Party Parliamentary Group for Personalised Medicine, 7 November 2017

# 3 Establishing an NHS Genomic Medicine Service

33. In this chapter, we examine the readiness of NHS England for its planned Genomic Medicine Service; in particular the infrastructure and training required.

## Infrastructure

34. NHS England plans to develop a network of seven Genomic Laboratory Hubs to deliver the genomic tests that appear in the Genomic Medicine Service's National Test Directory. There were differing views, however, about the optimal number of such sites. Dame Sally Davies, the CMO, told us that consolidating the "cottage industry" of existing genomic laboratories into "factories" will provide "higher quality, faster throughput and turn-round, and cheaper prices".[95] She thought that the Service would ideally have "two or three" sites.[96] The Association for Clinical Genomic Science supported NHS England's planned move to seven hubs:

> The range and complexity of tests in addition to whole genome sequencing is such that a smaller number of "factories" is unlikely to work […] Although the description of UK genomics services as being like a "cottage industry" has been construed as a negative comment, local services can be flexible and responsive to local need and driven by results not the rigidity of a central automated process.[97]

They supported Professor Sue Hill's proposed model in which, "these new hubs will be built around the extant [Regional Genetics Laboratory] network, with the aim of increasing quality, improving access and reducing waste through efficiency".[98] The Royal College of Pathologists suggested that the Genomics Laboratory Hubs should be co-ordinated with NHS Improvement's plans to establish a consolidated network of 29 pathology hubs, emphasising the expertise required to prepare tumour samples for genome sequencing.[99] The College took issue with the CMO's vision of "a minimal number of DNA/RNA testing laboratories which are separate from other pathology services".[100]

35. Professor Sir John Bell told us that the digital, rather than the physical, infrastructure for the 100,000 Genomes Project had been the most difficult element to set up.[101] Professor William Newman, of the British Society for Genetic Medicine, also believed that setting up the informatics infrastructure for the Genomic Medicine Service would be the most challenging aspect.[102] Professor Sian Ellard, of the South West NHS Genomic Medicine Centre, highlighted the "huge amount of work to do" on the digital front before the Genomic Medicine Service is introduced:[103]

95 Q162
96 Q173
97 Association for Clinical Genomic Science (GNH0036)
98 Association for Clinical Genomic Science (GNH0036)
99 The Royal College of Pathologists (GNH0024)
100 The Royal College of Pathologists (GNH0024)
101 Q25
102 Q95
103 Q103

> Each of the genetics laboratories in England already has an IT system, and what we will need to do is link those systems to central databases and to hospitals' pathology laboratories, and then have a way of delivering the results back to the clinicians through electronic patient records, while also having systems in place where those are not yet embedded across the country.[104]

One person's whole genome sequence comprises 3.2 billion 'letters' of DNA and takes 200GB of data to store, roughly equivalent to the capacity of an average laptop.[105] Professor Sir Mike Stratton, of the Wellcome Sanger Institute, indicated to our predecessor Committee that analysing existing numbers of genome sequences already requires "the sort of IT that is available for the Large Hadron Collider", which he said "gives you a sense of the challenges that there will be".[106] He calculated that "the rate at which we are generating DNA sequence, and could generate it from patients' tumours, is much in advance of the rate of improvement through Moore's law".[107]

36. Genomics England currently stores participants' sample and clinical data in a dedicated data centre. Professor Sue Hill explained that "because we have learned about storing huge amounts of data", the NHS Genomic Medicine Service will also store data in "one new data warehouse for the NHS that is not in individual laboratories around the country but in one place".[108] This data centre will be "built by Genomics England and based upon the existing storage for the 100,000 Genomes Project".[109]

37. Professor Hill told us that the NHS Genomic Medicine Service would need to be able to link and process more than just genomic data:

> Routine genomic medicine requires collection and combination of information from [patient] clinical records about a patient's medical history, their presenting condition and symptoms as well as a phenotypic characterisation, and for this to be considered and analysed alongside genomic test information.[110]

This will require connectivity and interoperability between computer systems across the NHS, not just genomics departments. NHS England told us that this information transfer and processing "already happens as a routine in NHS clinical genetic services, although this may not always be digitally captured and recorded, with paper records still existing".[111] Professor Ellard, of the South West NHS Genomic Medicine Centre, described how current systems have genetic laboratories "chasing up small details about how names are spelt, for example, which wastes a huge amount of effort and time":[112]

> When a referral to request a genetic test arrives at a laboratory, currently we have a request form that ideally is completed electronically in advance and

104 Q103
105 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
106 Oral evidence taken on 8 March 2017, HC (2016–17) 854, Q183
107 Oral evidence taken on 8 March 2017, HC (2016–17) 854, Q184
108 Q82
109 NHS England (GNH0029)
110 NHS England (GNH0029)
111 NHS England (GNH0029)
112 Q134

> emailed to us. I had hoped that our existing system would be set up so that we could automatically bring through those data, but I do not think any of the laboratories in the UK has that today.[113]

38. Dr Hilary Burton, of the PHG Foundation, explained that the interpretation of genomic results can be an iterative process, which the current digital infrastructure does not facilitate:

> A variant may be found and a question may go back to the clinician about whether such and such a clinical factor is visible in the patient, which sometimes requires the clinician to go back and look at the records […] To do that, they end up having to go through piles of records, piles of paper, to see whether that other clinical symptom or clinical finding is available. They do not have access to the sort of digital clinical records that would make it comparatively easy to add that extra bit of important information for the interpretation. There is still a lot to be developed in the digital infrastructure to make those things happen.[114]

### *Budgets for implementation*

39. Professor Hill told us that "the plan is to provide all the genomic laboratory hubs, and then the NHS providers with whom they will work, with an informatics solution that enables everything to be ordered and all the data to be captured through the same system and to the same standards":[115]

> The costs of this work fall into two distinct areas; the work needed to build the nationally provided solution and the work needed within the wider NHS to enable all local systems to fully interface with the national solution and to enable capture and uploading of all genomic data in every NHS organisation. The costs for the national solution are in the region of £6–9m in addition to the current run budget of Genomics England […] The costs for the wider NHS development are not yet fully determined as this is linked and integral to the whole of the digital maturity development of the NHS.[116]

The Minister, Lord O'Shaughnessy, told us in November 2017 that the requirement for an additional £6–9m "depends on what is put in place".[117] Funds were not allocated in the 2017 Budget,[118] he informed us, but:

> Clearly, we are all committed to making this happen, so we will fund it from one route or another. Whether it is Paperless 2020 or whatever programme, we will make sure that funding is in place to put it in.[119]

113 Q134
114 Q134
115 Q83
116 NHS England (GNH0029)
117 Q200
118 Q200
119 Q200

40. With regards to the funding for wider digital infrastructure needed to transfer data between separate parts of the NHS, Professor Hill told us:

> There is not a budget for drawing the elements from the other clinical specialties. As to pushing the information from a laboratory hub out, there will be a mechanism to do it, but there still needs to be more budget to support how that would get out to every single provider, because it does not work like that at the moment.[120]

The Minister told us that "plans for growing our genomics capacity" were included in the Government's Industrial Strategy, and that "there is much more impetus and investment going into this as a whole".[121] The Life Sciences Sector Deal agreed by the Government does set out a range of measures to support genomics in the UK, including whole genome sequencing of the UK Biobank and an extension of the cancer branch of the 100,000 Genomes Project.[122] The sector deal also includes commitments to support the development of the UK's health data infrastructure. However, it is not clear whether additional funding has been made available specifically to deliver the infrastructure required for the Genomic Medicine Service.

41. Despite the budgetary uncertainty, Professor Hill told us that she expected the system for sharing genomic data to be in place by this Autumn:

> There will be an operational system in place by October 2018. That is what we are planning. As we are going through live procurement processes, the intention is that between April and October those systems would be tested.[123]

She made the point that although, at the moment, "genetic tests get ordered every day",[124] the genomic infrastructure being developed will be "more extensive and complex" than the system previously developed for the 100,000 Genomes Project.[125] Professor Ellard told us that "things are moving forward",[126] but that it would be unrealistic to expect all of the planned infrastructure to be in place for the launch of the Genomic Medicine Service.[127]

42. Progress on that front will depend on the broader digital information development of NHS organisations through the 'Paperless 2020' programme.[128] The 2016 independent Wachter review of information technology in the NHS determined that "some trusts are currently too financially strapped, and/or lacking the staff, the training, and the culture to digitise effectively" and that "the target of 'paperless by 2020' should be discarded as unrealistic".[129] It recommended pushing back the target for digital maturity across all NHS trusts to 2023—five years later than the planned start of the Genomic Medicine

120 Q91
121 Q200
122 'Industrial Strategy: Life Sciences Sector Deal', HM Government (2017)
123 Q83
124 Q90
125 NHS England (GNH0029)
126 Q134
127 Q105
128 NHS England (GNH0029)
129 'Making IT Work: Harnessing the Power of Health Information Technology to Improve Care in England' (2016)

Service.[130] The Minister acknowledged that the infrastructure currently available for genetic testing varies across NHS England.[131] Professor William Newman, of the British Society for Genetic Medicine, explained:

> There are some centres and hospitals around the country that have solutions in place, but that is not uniform, and there is still a lot of work that needs to be done to provide that infrastructure.[132]

43. **Genomic medicine requires the collection and comparison of a wide range of data, and the digital infrastructure for whole genome sequence data cannot be developed in a silo separate from other data sources. Although whole genome sequencing and other genetic tests are already being delivered by Genomics England and NHS England respectively, it is clear that significant infrastructure remains to be put in place in order to enable an efficient Genomic Medicine Service. Unfortunately, the wider improvement of NHS data systems is running to a later timeframe than that needed for a Genomic Medicine Service that will begin operations later this year. Elements of the required infrastructure do not yet have clearly-allocated budgets.**

44. ***Given the intention to have the Genomic Medicine Service in operation later this year, the budgets for the required digital infrastructure should be agreed and confirmed now. Decisions on when to provide whole genome sequencing in place of conventional alternative diagnostic tests should take into account the digital infrastructure available to support it, to avoid attempting to roll out a Genomic Medicine Service at a speed that cannot be delivered.***

## Training

45. Genomic medicine will require new skills. The CMO's report describes how genomic medicine is expanding the clinical team to include "diagnostic staff in laboratories and imaging; computer scientists; statisticians; (bio)informaticians; and data scientists who assemble, process and assess the data to advise on diagnosis and treatment".[133] The British Society for Genetic Medicine noted that existing genetic medicine specialists, including consultants in genomic medicine, diagnostic scientists, and genetic counsellors (experts in managing appropriate communication to patients and relatives of the long-term predictions inherent in genomic medicine), will be required.[134] As Alison Hall, of the PHG Foundation, told our predecessor Committee, the wider workforce will also have to know enough about genomics "to identify the patients who will benefit most from having testing and to understand the results that are returned to them".[135] Dr Helen Firth, of the Wellcome Sanger Institute, explained how difficult the interpretation of genome sequences can be, and how the "ability to sequence genomes is running very fast ahead of our ability to interpret the data".[136] Professor William Newman emphasised the importance, and challenge, of getting the interpretation of genome data right, to avoid, for example, unnecessary preventative surgery.[137]

130 'Making IT Work: Harnessing the Power of Health Information Technology to Improve Care in England' (2016)
131 Q195
132 Q95
133 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
134 British Society for Genetic Medicine (GNH0009) and (GEN0062)
135 Oral evidence taken on 8 March 2017, HC (2016–17) 854, Q133
136 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q69
137 Q69

46. Health Education England established the Genomics Education Programme in March 2014, with £20m of funding from the Department of Health for four years.[138] The programme provides additional training and courses, and was described by Health Education England as the "NHS's method of ensuring its staff have the knowledge, skills and experience to ensure that the health service remains a world leader in genomic and precision medicine".[139]

47. There remain, nevertheless, concerns about a lack of genomic expertise across several medical specialties. Dr Hilary Burton told us of concerns expressed to the Joint Committee of the Royal Colleges on Genomic Medicine:

> We have 17 clinical champions. These are people in various specialties who are expert in genetics. All of them are concerned that there is not enough expertise within their specialty, at a general level.[140]

The British Society for Genetic Medicine noted that there are unfilled posts in genomic diagnostic laboratories and across genomic services due to a lack of individuals with the necessary training and skills.[141] The Royal College of Pathologists highlighted that not all NHS pathology laboratories have the trained personnel needed to process tissue for DNA testing, noting that it takes over 10 years to train a pathologist.[142] The Association for Clinical Genomic Science similarly believed that there is "a serious risk of under-capacity in the workforce to deliver the full benefits [of] clinical genomics reorganisation".[143]

48. The Association of Genetic Nurses and Counsellors were "extremely concerned that there will not be enough genetic counsellors trained in the UK through the current training routes to meet the growing demands and developments in genomic medicine".[144] The standard training route for genetic counsellors in England had 15 enrolled in 2016–17 and was due to have just 10 for 2017–18.[145] The Association found in 2017 that 16 out of 23 existing UK regional genomics centres would need more genetic counsellors in future, and 17 centres currently had difficulties filling such posts.[146]

49. In response to these concerns, Health Education England told us:

> We recognise that there is more work to be done by [the Genomics Education Programme] across the professions […] We recognise that the medical specialities and general practice are areas that required focused work by Health Education England over the next two years.[147]

In the meantime, they highlighted that through the long-established Regional Genetics Centres there is "already a cadre of well-trained scientists, bioinformaticians and technical staff, clinical geneticists and genetic counsellors who are the backbone of the workforce

138 Health Education England (GNH0007)
139 Health Education England (GNH0007)
140 Q117
141 British Society for Genetic Medicine (GNH0009)
142 The Royal College of Pathologists (GNH0024)
143 Association for Clinical Genomic Science (GNH0036)
144 Association of Genetic Nurses and Counsellors (GEN0027)
145 Association of Genetic Nurses and Counsellors (GEN0027)
146 Association of Genetic Nurses and Counsellors (GNH0027)
147 Health Education England (GNH0037)

requirement for the new Genomic Medicine Service". They believed that, in combination with the Genomics Education Programme, these will be sufficient to introduce an operational Genomic Medicine Service as planned:

> Through the work of NHS England, Genomics England and Health Education England in the implementation of, and the support given to, the 11 Genomic Medicine centres, this workforce has been responsive to the requirements of whole genome sequencing, its interpretation and clinical utility, and practise has changed accordingly as new knowledge has emerged […] Educationally, we feel the workforce is in a position to be operational from end [of Quarter 2] 2018. The Genomics Education Programme will be working with the NHS England Genomics Unit and others toward mainstreaming of Genomic Medicine by 2019. This will be challenging and the Genomics Education Programme will need to ensure that its work programme is co-ordinated with the work of the NHS England Genomics Implementation Unit and other key stakeholders.[148]

Professor Ellard, of the South West NHS Genomic Medicine Centre, similarly told us that although the NHS is already delivering whole exome sequencing, which makes it "well-placed to manage the transition" to whole genome sequencing, "we need more trainee posts and more training for the existing workforce".[149]

50. Health Education England assured us that as the new Genomic Medicine Service takes shape, it will "undertake detailed workforce planning and modelling to inform future training numbers across the professions".[150] Asked what assessment they had made of the roles that would require genomics training, the level of training those roles would require and the proportion of people in those roles who had received such training, Health Education England told us in February 2018 only that a training needs analysis had been undertaken by each of the Genomic Medicine Centres, and that "this is currently undergoing detailed analysis but the common theme emerging is the complexity of determining the training needs when many of the workforce aren't yet sure what and how much genomics they need to know".[151] In the meantime, Dr Hilary Burton explained that the Genomics Education Programme was helping to raise awareness, but not yet providing sufficient training for consultant-level clinical decisions.[152] She was concerned that for the majority of specialty curricula, genomics was not being embedded quickly enough:

> Outside specialties such as oncology and haematology, which are quite genomically oriented, I do not think there is a single specialty where [genomics] is properly embedded in the curriculum.[153]

51. A 2013 review of NHS training curricula found that genomics had been embedded in some specialty courses, but not all.[154] Health Education England will now undertake a new review "to identify the current omissions".[155] They told us that genomics had already

148 Health Education England (GNH0037)
149 Q117
150 Health Education England (GNH0037)
151 Health Education England (GNH0037)
152 Q117
153 Q117
154 Health Education England (GNH0037)
155 Health Education England (GNH0037)

been integrated into all of the scientific curricula, and that there was ongoing work with the Royal College of Physicians and the Royal College of General Practitioners to review the current genetic training provision and ensure that it was at the right level.[156]

52. Professor Patrick Chinnery, of the University of Cambridge, believed that the challenge would lay in training the existing workforce, rather than the new staff coming into the NHS. He advocated including competency in genomic medicine in revalidation requirements.[157] Health Education England similarly hoped that:

> As genomic medicine practice becomes incorporated into the job plans of greater numbers of medical consultants, competence in this area will become part of annual appraisal, and therefore assessed during revalidation.[158]

53. Lord O'Shaughnessy, Parliamentary Under-Secretary of State for Health, told us that the Genomics Education Programme would receive £1m a year to continue beyond March 2018, compared to the £20m it was awarded for the period 2014–2018.[159] The Association of Genetic Nurses and Counsellors expressed concern at reports of "reducing budgets for continuing professional development for health professionals, including genetic counsellors".[160] The Minister told us that the decrease in the Programme's annual funding was due to the 'up-front' training required at the beginning of the initiative, and the CMO explained that preparing coursework and online modules also had to be paid for up front.[161] Health Education England told us that "the programme costs for 2018–19 and 2019–20 have yet to be agreed and are under discussion with the Department of Health and Social Care".[162]

54. **There are widespread concerns about insufficient training and a lack of qualified NHS England staff ahead of the introduction of the Genomic Medicine Service later this year. Health Education England has still to undertake detailed workforce planning and modelling, and there is uncertainty within the existing workforce about the extent of genomics knowledge they will need. The Genomics Education Programme is playing an important role in raising awareness and expertise, however this was initially a 4 year programme. It is now to be continued, but with a substantially lower level of funding than previously. Genomics will need to be embedded in training curricula and revalidation criteria to ensure sufficient genomics understanding by all staff involved in clinical decisions.**

55. ***With the Genomic Medicine Service due to be operational later this year, Health Education England should complete detailed workforce planning and modelling as soon as possible. They should also work with the Royal Colleges of Medicine and other stakeholders to embed genomics into relevant curricula and revalidation requirements as a priority. The Government must support them in this work, and ensure the necessary funding is available.***

156 Health Education England (GNH0037)
157 Qq185–187
158 Health Education England (GNH0037)
159 Q179
160 Association of Genetic Nurses and Counsellors (AGNC) in the UK and Republic of Ireland (GEN0037)
161 Q179
162 Health Education England (GNH0037)

### *Multi-Disciplinary Teams*

56. Asked about the readiness of the wider NHS workforce for the Genomic Medicine Service, the CMO told us that the entire workforce "will never be trained and ready to do [genomic medicine] themselves, in the sense of understanding all the genes",[163] but that this was not required if clinicians have sufficient support to be able to request the appropriate test and follow up on their results.[164] She wanted to see a national network of multi-disciplinary teams established "to review and advise on complex and ultra-rare syndromes".[165] Such teams would include researchers, bioinformaticians and clinicians with expertise in genomics, as well as those treating the patient.[166] The CMO explained that our understanding of the significance of different genomic features will continue to develop over the next five years or longer, and that "patients [will] need researchers to interpret them, because everyday clinicians will not be up to scratch".[167]

57. The British Society for Genetic Medicine pointed to multi-disciplinary teams of genetic medicine specialists already supporting clinical teams in the interpretation of genomic tests.[168] However, a coalition of Cambridge-based institutions delivering genomic healthcare believed that some multi-disciplinary teams do not have sufficient commissioned support to be sustainable, but had instead been developed "using research resources and goodwill".[169] Fiona Murphy, of the Scottish Genomes Partnership, told us that multi-disciplinary teams for cancer patients had successfully evolved out of research teams, and that this could work well for genomics:

> Sometimes, there can be a bit of a lag moving from a research-oriented team meeting to it being part of clinical practice, but I do not see any block towards that as these things become more organised. Generally, it tends to involve some small seed funding to have a co-ordinator who holds things together and has the infrastructure to bring people together.[170]

Professor Sian Ellard explained that the need for multi-disciplinary teams would have to be "factored into the costing of the whole process".[171]

58. **Multi-disciplinary teams will be critical to providing an effective genomic medicine service to patients and to keep abreast of a fast-evolving science.** ***We agree with the CMO's recommendation to establish a national network of multi-disciplinary teams. The Government should set out what funding and support it will provide to enable multi-disciplinary teams to develop from being research-oriented to supporting clinical practice, and factor their costs into the commissioning of the Genomic Medicine Service.***

163 Q176
164 Q162
165 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
166 Q181
167 Q177
168 British Society for Genetic Medicine (GNH0009)
169 University of Cambridge and Cancer Research UK Cambridge Centre (GEN0063)
170 Q125
171 Q125

# 4 Access to genomic data

59. The introduction of whole genome sequencing into routine NHS care will lead to growing volumes of genomic data being linked to medical data, raising issues around consent and access. Here we focus on access to patient data for clinicians and researchers, pharmaceutical companies and insurance companies.

## Consent and the NHS 'Social Contract'

60. The NHS Constitution states a patient's right to request that their confidential information is not used beyond their own care and treatment.[172] The Government promised in its response to the National Data Guardian's 2016 Review of Data Security, Consent and Opt-Outs[173] to "give people the choice to opt out of sharing their data beyond their direct care, which will be applied across the health and social care system".[174] However, since its 2016 review, the National Data Guardian has published an initial review of data sharing for genomics in the NHS, which concluded that genomic medicine is blurring the distinction between a patient's direct care and secondary uses of their data:

> Interpreting the significance of a genetic variant can require access to information about other people, to assess, for instance, how often the variant is linked with disease or not. This may well involve access to data from other patients under the care of different health professionals, potentially living in different parts of the country or even the world.[175]

### *Consent in the 100,000 Genomes Project*

61. The 100,000 Genomes Project uses a 'broad consent' model, under which enrolled participants agree that their past and future health records can be accessed by 'approved individuals' at any point, and used to study many different medical conditions, not just ones that affect them. Genomics England explained that this broad model "permits the Project to use participant data for an unspecifiable range of future research, subject to appropriate oversight, in recognition that for example, some future tests have not been developed yet".[176]

62. Our predecessor Committee identified a potential issue about the "suitability of the 'broad consent' model being employed by the 100,000 Genomes Project, and whether the consent materials and patient recruitment techniques fully inform participants of the potential commercial uses of their data".[177] The National Data Guardian told our predecessor Committee that she "welcomes the significant amount of work that has gone into developing Genomics England's consent model and the care that has been taken to ensure that participants are enabled to make informed decisions about the implications of their agreeing to genomic sequencing".[178] In contrast, EthicsAndGenetics, a campaign

172 'The NHS Constitution', NHS (2015)
173 'Review of Data Security, Consent and Opt-Outs', National Data Guardian for Health and Care (2016)
174 'Your Data: Better Security, Better Choice, Better Care', Department of Health (2017)
175 'Developing a consensus on data sharing to support NHS clinical genetics and genomics services', National Data Guardian for Health and Care (2017)
176 Genomics England (GNH0018)
177 Science and Technology Committee, Sixteenth Report of Session 2016–17, 'Genomics and genome-editing: future lines of inquiry', HC 854
178 National Data Guardian for Health and Care (GEN0026)

group, told our predecessor Committee that it believed that participants in the 100,000 Genomes Project had been misled over the degree of anonymisation of their data,[179] although this was not highlighted as a material issue for concern during our own inquiry.

63. The pseudonymisation process used in the 100,000 Genomes Project involves replacing most identifiable information with a unique identifying code for each participant.[180] Professor Mark Caulfield, of Genomics England, explained in February 2017 that "we remove the direct identifiers, which makes it very difficult for anyone to identify [participants]. There is no name, address or postcode. There is an age and a year of birth, but nothing more precise than that".[181] He said that pseudonymisation is used instead of complete anonymisation so that relevant research findings can be fed back to the appropriate participant:

> When you anonymise the data, the technical effect of that is to disconnect the data from the original person. What that means is that I cannot add other data, because I no longer know the true identity of that person. It would not be safe in a healthcare setting to do that. […] if we could not connect [research findings] back, I could not return diagnoses from the research environment to the identifiable person.[182]

The Data Protection Bill would make it an offence "for a person knowingly or recklessly to re-identify information that is de-identified personal data without the consent of the controller responsible for de-identifying the personal data".[183]

64. The current consent form for the 100,000 Genomes Project informs patients that their "data, and information from [their] samples, will only be used by researchers in a form that protects [their] identity".[184] It also makes clear that research organisations accessing their data "may include commercial (for-profit) companies".[185] Professor Caulfield told our predecessor Committee that "patients have said that they are fully informed. We have a participant panel, made up of people who are enrolled in the project. They are incredibly supportive of the material".[186] Professor Michael Parker, Chair of the Genomics England Ethics Advisory Committee, told our predecessor Committee:

> The approach to consent and the consent materials that are used in the Project were subject to scrutiny by […] an independent Health Research Authority ethics committee. The materials were developed with patients and groups through consultation. They have been evaluated since and the participants have been happy with those, but those materials are very explicit and highlight the fact that these potential risks exist.[187]

179 Written evidence to our predecessor Committee stated that "The Government initially claimed that 'genomic data files from the 100,000 Genome Project to which academics, researchers and industry members will have access will be anonymous'. Freedom of Information requests revealed, however, that the Government's claims were misleading [...] It transpired that all data used in the Genome Project is in fact pseudonymised: as such, public understanding of the level of access that is afforded to private sector actors in the 100,000 Genome Project was distorted." (EthicsAndGenetics (GEN0010))

180 'The 100,000 Genomes Project Protocol', Genomics England (2017)

181 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q53

182 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q53

183 Data Protection Bill [Lords], Schedule 171 [Bill 153 (2017–19)]

184 Genomics England, 'Participant Information Sheets and Consent Forms', accessed 2 February 2018

185 Genomics England, 'Participant Information Sheets and Consent Forms', accessed 2 February 2018

186 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q53

187 Oral evidence taken on 8 March 2017, HC (2016–17) 854, Q110

### *Consent in the Genomics Medicine Service*

65. Following up a recommendation from the CMO's annual report, NHS England and Genomics England have convened a Patient Consent in Mainstreaming Genomic Medicine Working Group to develop a consent model for the NHS Genomic Medicine Service.[188] The PHG Foundation, which is represented on this group, told us that they would examine in particular "the implications of seeking a form of hybrid consent for both clinical care and research".[189] Fiona Murphy told us although such an approach had not been an obstacle to recruiting people into the 100,000 Genomes Project, "it might not be practical on a day-to-day basis to use the broad consent model".[190] Dr Burton similarly believed that the broad consent model "may be too complex [for routine genomic sequencing in the NHS]; it is rather unwieldy for day-to-day use".[191]

66. Dr Helen Firth, of the Wellcome Sanger Institute, highlighted to our predecessor Committee how important data sharing was for patient safety:

> Many variants are just not interpretable without seeing them in the context of variants of other patients with a similar disorder, and in the context of the variation that you see in the normal population. If you try to do it without either of those things, it is only a small number of very well-known variants that you could reliably provide safe advice on.[192]

Other genetics professionals saw data sharing as "necessary and urgent for there to be confidence that the best and safest care is provided to patients".[193]

67. The Minister, Lord O'Shaughnessy, saw data sharing in genomic medicine broadening the meaning of 'direct care':

> The point is that genomics, in effect, breaks down the barrier between research and direct care, because your data can go into research, produce results that mean they know some treatment will work and some will not, and then flow straight back to you without having to go all the way round. That changes what we mean by direct care, because research becomes an integrated part of direct care.[194]

The CMO noted, however, that data used for research is currently treated very differently to data used for direct care in the NHS:

> There is a sharp divide in the NHS between data for direct clinical care and data for secondary uses of commissioning, regulation and research. There are major differences in their legal and Information Governance frameworks, funding arrangements, ethics, consent requirements and patient and public expectations.[195]

188 Genomics England (GNH0018)
189 PHG Foundation (GNH0015)
190 Qq149–150
191 Q141
192 Oral evidence taken on 8 February 2017, HC (2016–17) 854, Q105
193 'Developing a consensus on data sharing to support NHS clinical genetics and genomics services', National Data Guardian for Health and Care (2017)
194 Q214
195 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)

68. The CMO's report raised a potential challenge posed by 'genetic exceptionalism'—the notion that genetic data is more sensitive than other types of medical data. She argued, however, that this does not stand up to scrutiny (in line with the Government's independent Information Governance Review).[196] Dr Hilary Burton and Fiona Murphy, as well as Genetic Alliance UK, similarly believed that genomic data should not be viewed as any more sensitive than other personal or medical data.[197] The CMO nevertheless cited the importance of routine large-scale data sharing as a reason "to rethink—or at the very least reinforce—elements of the current 'social contract' as set out in the NHS Constitution, to take account of the advances in genomic medicine".[198] She outlined three main differences between genomic medicine and traditional healthcare that could challenge the existing contract: greater integration of, and complementarity between, healthcare and medical research; an increasing need to collect, store and share information at scale; and less certainty in how data will be used and what outcomes it will provide, due to evolving clinical practice.[199]

69. The Minister did not think, however, that the Constitution needed to be changed:

> I do not think we need to change the Constitution, but we need to explain to people the nature of the way medicine is going […] it needs to be interpreted very carefully, and explained as such.[200]

The CMO agreed that "that is one way of doing it, as long as we end up at the right place".[201] It was not, she said, "something where a Minister can say, 'Change it.' It needs public debate and discussion".[202] Indeed, one of the recommendations from her report was for Genomics England and NHS England to "engage in an extensive public dialogue on the shared social contract between patient, public, clinicians and academics in relation to genomic medicine".[203]

70. In response to the CMO's recommendation, Genomics England has proposed a "Public Dialogue programme that aims to build trust in future approaches and ensure that any potential barriers can be identified, understood and addressed". This will build on the 'Genomics Conversation' programme that ran in 2016.[204] The Minister also highlighted work being done by medical research charities "to test people's worries and concerns, and how to meet them and reassure them".[205]

71. Professor Chinnery, of the University of Cambridge, and Fiona Murphy, of the Scottish Genomes Partnership, noted that obtaining consent from those participating in the 100,000 Genomes Project had not been problematic.[206] However, such observations relate to cohorts of patients with specific diseases and who received substantial guidance

196 'Information: To share or not to share? The Information Governance Review' (2013)
197 Q142; Genetic Alliance UK (GNH0022)
198 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017); The report refers to this 'social contract' as a "common set of principles and values that bind together patients, the public and [NHS] staff in order to ensure that [the NHS] can be effective and equitable", as laid out in the NHS Constitution, with each party having rights and responsibilities.
199 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
200 Qq214–215
201 Q216
202 Q213
203 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
204 Genomics England (GNH0018)
205 Q209
206 Q207; Q128

through the consent process, which our witnesses agreed would be too demanding for routine genomic sequencing. Dr Burton thought that awareness among the general public of the "absolute critical need for data sharing" was insufficient.[207] A recent survey of the general public conducted by the Wellcome Sanger Institute found that 82% had either never heard of the term 'genomics' or had little understanding of it.[208]

72. In 2016, Genomics England's 'Genomics Conversation' programme found that access to individual data was the most "compelling and consistent issue" for the public, and that although most people "are happy for their data to be shared appropriately and used for wider social benefit", there was still unease about non-NHS access to health data and data security.[209] The CMO found that there is still a problem with public understanding and support for genomic data sharing:

> People were totally surprised when I said it is not in a patient's interests not to agree to put their data into the research database because they will get an out-of-date result, if one at all. That sort of concept is very difficult for a lot of people, but we have had a lot of support from patient charities and from many people. It is going to be a long haul.[210]

73. Data sharing for genomic medicine provides similar opportunities and challenges as the recent 'care.data' initiative, which was postponed and ultimately cancelled in 2016 following the National Data Guardian's review and poor public awareness campaigns.[211] The Minister told us that the "shadow" of the care.data experience "hangs over" the NHS genomics project, "but in a way that is not unhealthy".[212] He cited data security and patient involvement as the two areas that had undone previous attempts at data sharing, but thought now that "we have a much deeper understanding of the need to communicate to patients".[213] Patients, he told us, will be able to opt out of sharing their genomic data. It is unclear, however, what level of care patients who opt out of sharing their genomic data would receive.

74. **The importance of data sharing for genomic medicine presents a challenge to the concept of restricting the usage of patients' data to their direct personal care. Whether or not the NHS Constitution is changed to reflect the increasingly blurred distinction between genomics research and clinical care, public support will be vital to the delivery of an NHS Genomic Medicine Service. It is encouraging that a high proportion of patients involved in the 100,000 Genomes Project consented to sharing their genomic data, but the 'broad consent' process used in the Project is unlikely to be feasible for routine genomic medicine in the NHS without an extensive and continuing public debate to raise public understanding and acceptance.**

75. ***We recognise the Government's determination to implement the General Data Protection Regulation but it should now significantly increase its efforts to raise public awareness of genomic medicine, and the data-sharing needed to enable it, ahead of***

207 Q143
208 Middleton A. Socialising the genome: making genomics resonate. F1000Research 2018, 7:149 (doi: 10.7490/f1000research.1115249.1)
209 'The Genomics Conversation – An Overview', Genomics England (2016)
210 Q209
211 'Review of Data Security, Consent and Opt-Outs', National Data Guardian for Health and Care (2016); HC Deb, 6 July 2016, col 24WS
212 Q207
213 Q209

***the introduction of the planned Genomic Medicine Service. The Government should confirm and publicise the consent framework to be used for the Genomic Medicine Service as soon as possible, to give time for NHS staff and patients to be aware of data sharing implications before routine genomic medicine is rolled out. Following a public consultation, the Government should provide clear information regarding what data will be collected, who will be able to access that information and for what purposes, and an explanation of the benefits and risks involved in sharing genomic data.***

## Insurance

76. A public survey by the British Science Foundation found that although most people would be content for university researchers or NHS workers to access their genomic data (72% and 67% respectively), and opinion was mixed on access for pharmaceutical companies (36% content, 36% not content), 95% said they would not be content for it to be shared with insurance companies.[214] With the NHS providing mostly free and comprehensive healthcare to all, according to clinical need and not ability to pay,[215] the impact of 'predictive' genetic test results[216] on access to medical insurance in the UK will be smaller than in countries with predominantly private health insurance. Nevertheless, predictive genetic test results could in principle affect access to other insurance policies such as life assurance, income protection or private health insurance. It is important that patients are not deterred from undertaking genomic diagnostics as a result of fears relating to any consequences for insurance.

77. Insurance contracts typically follow the principle that both parties to the contract should have equal access to all relevant information. Insurers worry that information asymmetry—where consumers know more about their genetic disposition to future health problems than insurers—could lead to 'adverse selection' problems, with those consumers most at risk disproportionately applying for life insurance policies. As the Association of British Insurers (ABI) put it, "on a large scale, [adverse selection] could potentially affect the viability of some insurance products, given that insurers price products by assessing and pooling the risk of their policyholders".[217]

78. The Government has agreed a Concordat and Moratorium on Genetics and Insurance with the ABI.[218] Under the Concordat, insurers accept that genetic test results are relevant only to life, critical illness and income protection insurance. Customers will not be required to disclose the results of predictive genetic tests for policies covering up to £500,000 of life insurance, or £300,000 for critical illness insurance, or paying annual benefits of up to £30,000 under income protection insurance. Above such limits, insurers may seek information about results from specific tests approved by the Government—so far only for Huntington's disease where the life insurance is over £500,000.

79. Although insurers can ask for predictive test results only in specific circumstances, consumers must disclose any additional screening or preventative treatment they receive as a result of genomic sequencing. Genomics England guidance highlights that such

214 'The Genomics Conversation - An Overview', Genomics England (2016)
215 'The NHS Constitution', NHS (2015)
216 A predictive genetic test is one taken prior to the appearance of any symptoms, signs or abnormal non-genetic tests results which indicate that the condition in question is present.
217 Association of British Insurers (GNH0039)
218 'Concordat and Moratorium on Genetics and Insurance', HM Government and Association of British Insurers (2014)

additional screening or treatments "may alert the insurer to closely examine your personal medical and family history in order to be able to fully assess your application".[219] However, it also states that:

> Any additional screening or preventative treatment that you undergo which is known to reduce the risk of a particular condition will be taken into account by the insurer in assessing your application and setting your premiums, which could result in a better outcome for you.[220]

Fewer than 5% of insurance customers are currently estimated to be affected by disclosure requirements,[221] and the insurance industry has reported no more than one complaint on this issue per year.[222]

80. The Concordat and Moratorium agreement was last renewed in 2014, and applies until November 2019. It was due to be reviewed in 2016 but this was delayed as a result of the CMO's report and is currently being discussed by the Government and the ABI.[223] The introduction of the NHS Genomic Medicine Service could significantly increase the number of people receiving predictive genomic test results, and potentially affect insurers' willingness to renew the Concordat and Moratorium agreement in the future. The current agreement states that:

> Insurers are only prepared to bear the risks and costs of this non-disclosure [of predictive genetic test results], which are spread across the broad pool of policyholders, whilst the number of policies affected by non-disclosure of predictive genetic tests appears to be low.[224]

The ABI noted that genetic testing had already become more widespread since the original Concordat and Moratorium in 2001, without concerns of adverse selection materialising. For the moment, they did not have any plans to seek approval for the use of predictive genetic tests beyond Huntington's disease.[225] The ABI highlighted, however, that "the increased prevalence and availability of genetic testing could theoretically over time lead to a situation where there is a significant information asymmetry between insurers and customers".[226]

81. The ABI supported the flexibility afforded by the voluntary approach of the Concordat and Moratorium, because it allows "all sides to adapt and review the agreement as and when necessary".[227] They argued that inflexible financial limits had already caused problems in jurisdictions that have adopted legislative approaches, noting that Switzerland is currently

219 Genomics England, 'Insurance', accessed 7 February 2018
220 Genomics England, 'Insurance', accessed 7 February 2018
221 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
222 Association of British Insurers (GNH0039)
223 Q218
224 'Concordat and Moratorium on Genetics and Insurance', HM Government and Association of British Insurers (2014)
225 Association of British Insurers (GNH0039)
226 Association of British Insurers (GNH0039)
227 Association of British Insurers (GNH0039)

reviewing its legislation.[228] A 2016 review of regulatory approaches in insurance markets found legal restrictions or bans on insurers' use of predictive genetic data for life insurance in several European countries as well as the USA.[229] In 2017, Canada made it illegal for insurance companies or employers to request genetic testing or ask for the results.[230] The CMO's report concluded that "the UK's voluntary and soft-law regulation of the use of genetic data by insurers has proved to be flexible and responsive to changes in the genomic technologies", and supported a continued "flexible semi-voluntary" regulatory structure.[231] She also argued that legislative approaches "would raise questions about the use of other, non-genetic, information that is predictive of ill health".[232]

82. **A large proportion of the public express unwillingness to disclose their genomic data to insurance companies. It is important that this concern is recognised, and that measures are in place to avoid large numbers of patients refusing their consent to receive additional findings from whole genome sequencing as a result of such concern. A voluntary Concordat and Moratorium, agreed between the Government and the Association of British Insurers, currently restricts insurers' ability to ask for predictive genetic test results. As whole genome sequencing is rolled out across NHS England, the terms of the Concordat and Moratorium may come under pressure.**

83. ***We recommend that the Government seeks to renew the Concordat and Moratorium as soon as possible. The current review should take into account the introduction of whole genome sequencing as part of the NHS Genomic Medicine Service, the likely increase in predictive genetic test results this will cause, and the potential for more conditions to be predictable as genomic medicine progresses. The Government should set up systems to monitor any reluctance among patients to undertake genomic testing due to insurance concerns, assess the experiences of countries that ban insurers' use of predictive genetic test results (addressing in particular the ABI's concerns regarding the potential for adverse selection problems), and be ready to consider putting the Concordat and Moratorium on a statutory footing if the current voluntary system begins to limit the uptake of predictive testing.***

## The genomics industry

84. A 2015 report on the UK genomics industry, commissioned by the Government's Office for Life Sciences, estimated that the global genomics industry was then worth over £8bn and forecasted this to grow rapidly.[233] Its value would come mostly from delivering diagnostics and targeted therapies, or in informing drug development. The CMO's report described the complexity of ascribing health conditions to particular genetic causes, and how this requires "the sequencing of very large numbers of human genomes and the

228 The Swiss Parliament's Science, Education and Culture Committee recommended lifting existing restrictions on using genetic test results for insurance purposes, whereas the Federal Council proposed maintaining the current financial limits (comparable to the terms of the UK Concordat): 'La loi fédérale sur l'analyse génétique humaine (LAGH) est prête pour l'examen au Conseil national', Commission de la science, de l'éducation et de la culture, Press notice, 2 February 2018; 'Message concernant la loi fédérale sur l'analyse génétique humaine', Swiss Federal Council, 5 July 2017

229 'Seeing the future? How genetic testing will impact life insurance', Swiss Re (2016); The list included Austria, Belgium, Denmark, France, Germany, the Netherlands, Norway, Poland, Portugal, Switzerland and some states in the USA.

230 'An Act to prohibit and prevent genetic discrimination', Bill S-201, Parliament of Canada (2017)

231 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)

232 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)

233 'Genomics in the UK: An industry study for the Office of Life Sciences', Deloitte (2015)

correlation of those with data on each individual's clinical conditions".[234] The NHS, as "the single biggest integrated healthcare system in the world",[235] would make that possible. Genomics England noted that the 100,000 Genomes Project is unique in its "ability to link [genomic] sequence data to longitudinal patient records from across primary, secondary and tertiary care for the whole of the diverse population of a country",[236] and that "significant value is concentrated in our dataset—the data accessed through sequencing—and the ability to study this alongside other health data".[237] Sir John similarly highlighted that the NHS has "remarkable longitudinal records of patients, from birth to death".[238] The UK, he told us, is "multiple years ahead of the rest of the world in handling whole genome data".[239] He saw two distinguishing features of the UK's competitiveness in life sciences:

> One is the NHS and the other is access to large amounts of data in the NHS around whole patient care. Those two things are unique. Almost no one else can do it at scale, and that will, without a shadow of a doubt, drive an AI revolution that will change healthcare globally.[240]

85. Professor Bell's Life Sciences Industrial Strategy argues that "in projects where data is the key infrastructure, the UK needs to ensure that some of the benefits are returned to the healthcare system, including access to technology".[241] In our inquiry into 'Algorithms in decision-making', Hetan Shah, of the Royal Statistical Society, urged public sector bodies to be more confident in realising the value of their data, underlining that "the public sector have the magic dataset, on which they have a monopoly".[242] Professor Bell believed that access to genomic and related data would benefit UK companies trying to capture a share of the growing market in genome data interpretation.[243] Genomics England emphasised that partnerships between the NHS and industry were needed in order for new medicines and diagnostics to be developed off the back of genomic data:

> Without the involvement of industry, the NHS and Genomics England would not be able to get the new medicines, treatments and diagnostics for patients that should come from this project. Medicines and diagnostics are always developed outside the NHS and government by the private sector.[244]

Dr Magdalini Papadaki, of the Association of the British Pharmaceutical Industry, emphasised that "clinically relevant patient data and patient outcome data are not wholly owned by the NHS; some are owned by the companies that run the clinical trials".[245]

86. Genomics England had indeed collaborated with industry and provided access to "a selection of anonymised whole genome sequences" through the GENE Consortium,[246] which consisted of 13 industrial partners each paying £25,000 or £250,000 to participate,

234 'Generation Genome', Annual Report of the Chief Medical Officer 2016 (2017)
235 Genomics England (GNH0018)
236 'A Framework for Industry Engagement: Genomics Enterprises Prospectus', Genomics England (2015)
237 Genomics England (GNH0018)
238 Q24
239 Q17
240 Q26
241 'Life Sciences Industrial Strategy—A report to the Government from the life sciences sector' (2017); see also Q26
242 Oral evidence taken on 14 November 2017, HC (2017–19) 351, Q15
243 Qq46–47
244 Genomics England, 'FAQs about how we are working with industry', accessed 1 December 2017
245 Q29
246 Genomics England, 'FAQs about how we are working with industry', accessed 1 December 2017

depending on their size.[247] There were mixed opinions, however, on how well the GENE Consortium had worked. The Association of the British Pharmaceutical Industry welcomed "the effort that Genomics England has provided in maximising value of the data so far collected, while maintaining strict safeguards on patient privacy and data protection through the development of 'safe haven' infrastructure".[248] The Wellcome Sanger Institute, on the other hand, was concerned about "a lack of clarity around data sharing rules and the tools available to those who may be interested in accessing Genomics England's data".[249] AstraZeneca complained that the 'embassy system', in which data can be accessed but not downloaded or copied from the central database, "brings challenges when integrating with other data sources outside the [Genomics England] platform".[250]

87. The GENE Consortium has recently been replaced by the Discovery Forum. Like its predecessor, it does "not sell participants' genomes or their medical data",[251] but provides a secure data centre for use by academic and industrial researchers.[252] The Minister explained that companies will pay to access data, and that they will only be able to extract their analysis from the database, not the data itself.[253] He told us that NHS England would initially look to recoup the operating costs of the data storage system, but he believed that in the longer term, it should look to capture the commercial value of its data, subject to restrictions for protecting patients.[254]

88. The Minister highlighted businesses that had been spun out of teaching hospitals as one way for the NHS to capture some of the commercial value from precision medicine.[255] Professor Bell's Life Sciences Industrial Strategy argued that genomics should play a part of the Government's Industrial Strategy:

> The ambition for genomics in the [Industrial] Strategy must be to maintain the UK's globally leading position and to invest alongside industry to ensure that these genomic datasets are used to improve the discovery and targeting of therapies and to ensure that patients obtain more precise and useful diagnostic information in a range of disorders.[256]

The Life Sciences Industrial Strategy recommended the establishment of "a new regulatory Health Technology Assessment and commercial framework […] to capture for the UK the value in algorithms generated using NHS data", and the creation of "a forum for early engagement between industry, NHS and arm's-length bodies (e.g. NICE, MHRA) to agree commercial access agreements".[257]

89. In response, the Government's Life Sciences Sector Deal stated that "organisations including GSK and AstraZeneca will work in partnership with the Government to

247 'A Framework for Industry Engagement: Genomics Enterprises Prospectus', Genomics England (2015)
248 Association of the British Pharmaceutical Industry (GEN0040)
249 Wellcome Trust Sanger Institute (GEN0024)
250 AstraZeneca (GEN0056)
251 Genomics England, 'FAQs about how we are working with industry', accessed 1 December 2017
252 Department of Health (GEN0059)
253 Q221
254 Qq222–225
255 Q225
256 'Life Sciences Industrial Strategy—A report to the Government from the life sciences sector' (2017)
257 'Life Sciences Industrial Strategy—A report to the Government from the life sciences sector' (2017)

contribute to the whole genome sequencing of the UK Biobank".[258] Genomics England explained that it is working to add data collected by the NHS and through the UK Biobank and other projects to its dataset, and that it would provide "a single portal through which companies and collaborators can gain access to anonymised whole genome sequence and associated clinical and phenotype data; and deliver access that ensures strict compliance with the consents appropriate to each data source".[259]

90. **The data collected by the 100,000 Genomes Project, the Genomic Medicine Service and the wider NHS will constitute the best data resource for genomic medicine in the world. The NHS could benefit greatly from the realisation of the commercial value of the data that are being generated.**

91. ***The Government must be ambitious in aiming to capture the full commercial value of the genomic and associated datasets it holds, rather than merely aiming to cover its costs. Genomics England should seek to maximise the commercial value of its datasets and continue to provide industrial and academic access to these data to facilitate the growth of the UK genomics industry and the development of new treatments, while ensuring consent and data safety safeguards. Genomics England should explore technological and commercial mechanisms to enable better integration of genomics data held inside their portal with other NHS data and data owned by private companies. While patient benefit should be the focus of the Genomic Medicine Service, income generated from NHS data can be reinvested in the NHS and further benefit patients in the long-term.***

258 'Industrial Strategy: Life Sciences Sector Deal', HM Government (2017); The UK Biobank is a health resource following the health and well-being of 500,000 participants and providing their anonymised health information to academic and industrial researchers in the UK and overseas.

259 Genomics England (GNH0018)

# 5 Genome editing

92. Genomic sequencing provides information that can help us understand patients' diseases and determine the treatments that might be most effective for them. Genome editing might be one of the 'personalised' treatments opened up by sequencing. Technological advances are providing an increasing capability to precisely edit, delete or insert genetic material at specific points in genomic sequences.[260] However, as a treatment still in its infancy, genome editing raises different technological and ethical issues to genomics.

93. Research Councils UK outlined to our predecessor Committee the relationship between genomics and genome editing, and the potential applications of each:

> Genomics allows us to pinpoint genes important to animal, plant and human health, farming and species' diversity in the wider environment, and to understand how genes are inherited and how they change across generations. Genome editing allows scientists to precisely modify genes to study their role in biology and disease, to synthesise useful gene products, modify cells for therapeutic purposes, and improve crops or farmed animals.[261]

The Wellcome Sanger Institute explained that:

> Although genomics and genome editing have scientific and technological overlap they represent two distinct areas of research and technology and each have their own distinct regulatory and ethical challenges that do not easily lend themselves to consideration as one entity.[262]

## Supporting the development of genome editing

94. Dr Magdalini Papadaki, of the Association of the British Pharmaceutical Industry (ABPI), told us that genome editing is one form of a "very promising" group of therapies known as cell and gene therapies.[263] She explained that genome editing for therapeutic use is still at an early stage of development:

> We are just starting to see the first clinical successes of cell and gene therapies. We have only eight cell and gene therapies approved in the whole of Europe […] Gene editing is already in clinical trials as a subset of gene therapies, but it came out of the academic pipeline a maximum of one and a half to two years ago. Although we are starting to see some clinical trials, just think of it as the next wave of gene therapy, so it is a bit more distant.[264]

The ABPI told our predecessor Committee that:

> The UK is a world leader in the research and development of [advanced therapy medicinal products], but as other countries continue to invest

260 'Genome Editing', POSTnote 541, Parliamentary Office of Science and Technology (2016)
261 Research Councils UK (GEN0046)
262 Wellcome Trust Sanger Institute (GNH0003)
263 Q23
264 Q23

> heavily in this industry it is important that the UK continues to build on this base to secure its position as a global hub for researching, developing, manufacturing and adopting advanced treatments.[265]

Professor Bell warned that "the UK does not want to miss out on [genome editing]. In a way, we missed out on antibodies; let's not miss out on this, because we think it is going to be quite big".[266]

95. One of the UK's ten Catapult Centres focuses on 'cell and gene therapies', and has been supporting the industry since 2012.[267] Its budget from Innovate UK in 2016–17 was £14m.[268] Professor Waseem Qasim, of the Institute of Child Health, told our predecessor Committee, however, that:

> The UK has set up various programmes to develop cell and gene therapy—the Catapult and so on—but the amount of spend is nowhere near as high as other countries are putting in.[269]

Professor Qasim also highlighted that the development of genome editing was being constrained by the NHS's capacity to deliver new therapies, including limited "bed space, specialist nursing staff [and] laboratory processing capacity",[270] as well as insufficient infrastructure for manufacturing necessary biological products:

> One of the critical things we deal with is that we have to make disabled viruses—we call them vectors—to deliver some of the reagents. The capacity to do that is saturated in the UK; there is a waiting list to try to get into the laboratories to manufacture those types of goods. That needs addressing; it is a bottleneck.[271]

96. Since Professor Qasim gave evidence to our predecessor Committee, the Life Sciences Sector Deal has announced that the Industrial Strategy Challenge Fund will support advanced therapies, including genome editing.[272] Professor Bell told us that measures have been taken to support viral vector manufacturing, but that more still needs to be done:

> One thing that came out of the tranche of money that appeared with the launch of the [Life Sciences Industrial Strategy] is that we are going to create a manufacturing facility for early phase and mid-phase viral vectors, which I think will be really welcome. Will it satiate the need? It will not for sure; there will still be a substantial demand, and I think we need to think about how we can encourage companies in that space to place their manufacturing capabilities here as well.[273]

265 The Association of the British Pharmaceutical Industry (GEN0040)
266 Q23
267 'Cell and Gene Therapy Catapult: Annual Review 2017' (2017)
268 'Cell and Gene Therapy Catapult: Annual Review 2017' (2017)
269 Oral evidence taken on 29 March 2017, HC (2016–17) 854, Q201
270 Oral evidence taken on 29 March 2017, HC (2016–17) 854, Q215
271 Oral evidence taken on 29 March 2017, HC (2016–17) 854, Q215
272 'Industrial Strategy: Life Sciences Sector Deal', HM Government (2017)
273 Q49

Dr Papadaki told us that the ABPI welcomed Innovate UK's open competition to build viral vector manufacturing infrastructure, but warned that "incentives, other than just Innovate UK funding for these companies to expand, are also an important approach to it".[274]

97. Dr Papadaki believed that genome editing was one of a number of new technologies that were challenging the traditional approach to research and development:

> We need to have a greater level of co-ordination between the different stakeholders—NHS, NICE and MHRA—new collaborative schemes and almost a new pathway for decision-making where all those players share the same evidence or are part of a continuous decision process. This was the basic premise [that the Accelerated Access Review][275] put into the picture.[276]

Professor Bell told us that the NHS had in essence applied the approach of the Accelerated Access Review to genome sequencing, and that he wanted that approach to also be applied for gene and cell therapies and for genome editing:

> These are transformational therapies. We do not want to wait four or five years before they get adopted; we want to make sure they are adopted quickly and efficiently.[277]

## Regulation

98. Technological progress will depend, however, on the further evolution of the regulatory regime for genome editing, and the ethical debate that will underpin that. There are different ethical factors involved in the different types of therapeutic applications of genome editing:

- specific therapies involving genome-edited immune cells, for which human trials are already established;
- 'somatic cell' editing, involving modification of adult cells in the affected tissue; and
- 'germline' editing of sperm or egg cells, in which "changes will be passed on to future generations".[278]

The Wellcome Trust, the Association of Medical Research Charities and Cancer Research UK believed that "the differences between somatic and germline research, and the differences between research and clinical applications, need to be carefully distinguished in ethical discourse about the benefits and risks of genome editing technologies".[279]

99. The Wellcome Sanger Institute highlighted areas with fewer potential ethical issues:

> Genome editing is an immensely powerful research tool, and not all uses of genome editing are ethically contentious or require any additional

274 Q49
275 'Accelerated Access Review: Final Report' (2016)
276 Q32
277 Q31
278 The Royal Society of Biology (GEN0042)
279 Wellcome Trust, Association of Medical Research Charities and Cancer Research UK (GEN0038)

> regulation. The use of genome editing to create cell-lines that better mimic human disease or allow high-throughput screening of drugs against cancer causing mutations are examples where genome editing is providing highly impactful research but has no direct consequences for human health or reproduction.[280]

Similarly, for somatic genome editing, provided efficacy and safety can be established, there seems to be a near-consensus that it poses fewer ethical issues. The Nuffield Council on Bioethics reviewed the ethics of genome editing in 2016, and concluded that although "there is always some risk attached to the introduction of a new therapeutic product […] it is unlikely that, for the most part, therapies based on genome editing will raise distinctive issues for the handling of safety and efficacy considerations".[281] The Christian Medical Fellowship agreed:

> If gene editing tools are used with the aim of addressing a genetic disorder and saving the lives of an existing mature embryo, foetus or post-natal individual, without any intention to change the germline, it is a positive therapeutic development that does not raise many new significant ethical problems, other than safety.[282]

The Nuffield Council on Bioethics told our predecessor Committee that "given concerns over the uncertainty of outcomes, a relevant consideration will be whether alterations to the genome in patients' tissues can be neutralised or reversed".[283]

100. In contrast, there is significant debate around the ethics of editing germ cells or human embryo cells. The Nuffield Council on Bioethics told our predecessor Committee that "of all the potential applications of genome editing that have been discussed, the genetic alteration of human embryos in vitro has consistently generated the most controversy".[284] The evidence we have received has described a variety of important ethical considerations,[285] and our predecessor Committee examined many of these,[286] including:

- whether or not genome editing of embryos constitutes medical treatment, given that the 'patient' does not yet exist;
- the need for genome editing given alternative treatments, screening tools and options such as adoption;
- the unknown consequences on future generations;
- the inability to obtain consent from future generations; and
- the potential for genome editing to facilitate eugenics or 'designer babies', and what a market for genetic enhancement would mean for equality.

280 Wellcome Trust Sanger Institute (GEN0024)
281 'Genome Editing: An ethical review', Nuffield Council on Bioethics (2016)
282 Christian Medical Fellowship (GEN0003)
283 Nuffield Council on Bioethics (GEN0051)
284 Nuffield Council on Bioethics (GEN0051)
285 For example, see the Academy of Medical Sciences (GEN0013), Genetic Alliance UK (GEN0050), the Christian Medical Fellowship (GEN0003), the Center for Genetics and Society (GNH0020) and Human Genetics Alert (GNH0021)
286 Oral evidence taken on 29 March 2017, HC (2016–17) 854

101. UK research organisations published a joint statement on genome editing in 2015, acknowledging that genome editing of human germ cells or embryos "raises important ethical and regulatory questions, which need to be anticipated and explored in a timely and inclusive manner as the basic research proceeds, and prior to any decisions about clinical application".[287] Nevertheless, they argued that "genome editing technologies may hold significant potential for clinical application in the future". The Academy of Medical Sciences told our predecessor Committee that "in some cases, the ability to edit the genome of a germ cell or embryo may be the only means by which parents are able to have a biologically related child unaffected by a hereditary disease".[288] Genetic Alliance UK, representing patients affected by genetic conditions, wanted to see potential applications of genome-editing as a reproductive treatment examined further.[289] The 2015 joint statement by UK research organisations concluded that:

> Research using genome editing tools holds the potential to significantly progress our understanding of many key processes in biology, health and disease and for this reason we believe that responsibly conducted research of this type, which is scientifically and ethically rigorous and in line with current legal and regulatory frameworks, should be allowed to proceed.[290]

The US National Academies concluded in 2017 that:

> Heritable genome-editing trials must be approached with caution, but caution does not mean they must be prohibited. If the technical challenges were overcome and potential benefits were reasonable in light of the risks, clinical trials could be initiated.[291]

Professor Chris Whitty, the then Interim Government Chief Scientific Adviser, told us that genome editing is an "area where science cannot stray beyond what the public, as represented by Parliament, are comfortable with".[292]

102. A range of regulators currently oversee different aspects of genome editing in research and clinical application, including the Human Tissue Authority, the Medicines and Healthcare products Regulatory Agency and the Human Fertilisation and Embryology Authority. Therapies involving somatic genome editing are regulated similarly to other gene therapies, and clinical trials of such therapies have already started.[293] The implantation of a genetically altered embryo into a woman is currently prohibited under the Human Fertilisation and Embryology Act 2008, other than under certain conditions to prevent the transmission of serious mitochondrial disease.[294] Research involving human embryos, up to 14 days old, is permitted subject to the conditions of the Act.

287 'Genome editing in human cells—initial joint statement', The Academy of Medical Sciences, The Association of Medical Research Charities, the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the Wellcome Trust (2015)
288 The Academy of Medical Sciences (GEN0013)
289 Genetic Alliance UK (GEN0050)
290 'Genome editing in human cells—initial joint statement', The Academy of Medical Sciences, The Association of Medical Research Charities, the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the Wellcome Trust (2015)
291 'Human Genome Editing: Science, Ethics, and Governance', The National Academies of Sciences, Engineering and Medicine (2017)
292 Oral evidence taken on 17 October 2017, HC (2017–19) 437, Q60
293 'Genome Editing', POSTnote 541, Parliamentary Office of Science and Technology (2016)
294 Human Fertilisation and Embryology Act 2008

103. Many stakeholders supportive of continued research into genome editing told our predecessor Committee that the existing regulations in this area are adequate for the moment. The Wellcome Trust, the Association of Medical Research Charities and Cancer Research UK believed that "the UK currently strikes a good balance with the regulation of genomic and genome editing technologies".[295] The Association of the British Pharmaceutical Industry thought that "the UK is a leading location for robust and proportionate regulatory thinking".[296] The Academy of Medical Sciences stated:

> We support the continued use of genome-editing in pre-clinical biomedical research, provided that the work is scientifically and ethically rigorous, and is in line with the relevant regulatory and legal frameworks […] The Academy recognises that the [Human Fertilisation and Embryology Act] provides a robust and sufficiently flexible architecture to govern the ethically sound use of embryos in such a way, and believes that these regulations are also adequate.[297]

104. The Department of Health and Social Care told us that "the Government has no plans to amend the [Human Fertilisation and Embryology] Act to permit germline modifications".[298] The CMO did not want a review of the 14-day rule,[299] because "there is an ethical debate that will take another five to ten years, but there are risks in opening up that Act, because it is not about mitochondria and gene editing; it is about a lot of women's health".[300]

105. Mitochondrial donation is a technique that allows women whose mitochondria (structures found in the fluid inside cells) carry serious inherited disease to give birth to children free from mitochondrial disease, by transferring 'packets' of the mother's nuclear DNA to a donor cell containing healthy mitochondria.[301] Since mitochondria contain small sequences of DNA, children born following mitochondrial donation inherit DNA from the donor as well as from their mother and father. In 2015, the UK Parliament became the first in the world to make such treatments lawful.[302] The British Medical Association told our predecessor Committee that:

> Should a time arise in the future such that it would be appropriate to consider a specific reproductive application of genome editing, we believe the process of parliamentary and public engagement which preceded the mitochondrial donation regulations would be a good model for policy-makers in the UK to follow.[303]

The process that accompanied the legislative change to allow mitochondrial donation was also raised by others as a good example to follow if germline editing were to be permitted.[304]

295 The Wellcome Trust, Association of Medical Research Charities and Cancer Research UK (GEN0038)
296 Association of the British Pharmaceutical Industry (GEN0040)
297 The Academy of Medical Sciences (GEN0013)
298 Department of Health (GNH0004)
299 Q231
300 Q232
301 'Preventing Mitochondrial Disease', POSTnote 431 (2014)
302 Human Fertilisation and Embryology Authority (GEN0021)
303 British Medical Association (GEN0012)
304 For example, the Wellcome Trust, the Association of Medical Research Charities and Cancer Research UK (GEN0038)

106. **Genome editing is a rapidly developing technology that is already a powerful tool for research, and which has significant promise for therapeutic use. Different applications of the technology entail different ethical considerations, with 'germline' editing being the subject of particular debate. The UK currently has a strong regulatory environment in this area, striking a balance between enabling important research and providing public confidence that ethical and other considerations are given appropriate oversight.**

107. ***We recommend that the Government specifically require UK Research and Innovation to closely monitor the development of genome editing for potential obstacles to innovation in this area. If it becomes appropriate to review or amend the current regulations in light of technological developments, the Government should use a similar process as the one that accompanied legislative changes to allow mitochondrial donation.***

# Conclusions and recommendations

## Whole genome sequencing

1. The 100,000 Genomes Project is an ambitious project that has helped put the UK in a world-leading position on whole genome sequencing and genomic medicine. *As the 100,000 Genomes Project approaches the completion of its sequencing target, the Government should formally evaluate it to inform the wider introduction of whole genome sequencing in the NHS (which we explore further below). The 100,000 Genomes Project could be a model for future 'Health Advanced Research Programme' projects, as suggested in the Life Sciences Industrial Strategy. If so, HARP projects should have processes and resources put in place from the start to allow their subsequent evaluation, and should explicitly take account of how existing NHS initiatives and resources will be complemented or absorbed.* (Paragraph 12)

2. There is great potential for whole genome sequencing to improve patient care, particularly for diagnosing rare diseases and for more personalised targeting of medicines and treatments. However, there is not yet sufficient unambiguous evidence gathered to demonstrate its benefit for routine care, in particular for common cancers. As the first large-scale whole genome sequencing exercise in the world, the 100,000 Genomes Project must be an important source of evidence to determine the technology's clinical efficacy and cost-effectiveness across the whole 'clinical pathway', and at the level of patient populations, rather than individual patients. Such evaluation does not appear to have been conducted, or at least has not been made public. *In advance of the launch of the Genomic Medicine Service, NHS England should undertake and publish a detailed evaluation of the 100,000 Genomes Project, to inform an assessment of the anticipated clinical- and cost-effectiveness of routine whole genome sequencing in the NHS.* (Paragraph 27)

3. The 100,000 Genomes Project will not be able to provide all of the evidence required to assess the effectiveness of whole genome sequencing for all conditions. Research and evidence-gathering will need to be continuing processes. *We endorse the CMO's recommendation for NHS England to embed implementation research at all stages of redevelopment and laboratory reconfiguration for the Genomics Medicine Service. Where more evidence is needed to approve whole genome sequencing for particular conditions, current diagnostics should be maintained alongside whole genome sequencing, as was done in the 100,000 Genomes Project, unless the genomic diagnostic has proved more accurate for that condition.* (Paragraph 32)

## Establishing an NHS Genomic Medicine Service

4. Genomic medicine requires the collection and comparison of a wide range of data, and the digital infrastructure for whole genome sequence data cannot be developed in a silo separate from other data sources. Although whole genome sequencing and other genetic tests are already being delivered by Genomics England and NHS England respectively, it is clear that significant infrastructure remains to be put in place in order to enable an efficient Genomic Medicine Service. Unfortunately, the wider improvement of NHS data systems is running to a later timeframe than that

needed for a Genomic Medicine Service that will begin operations later this year. Elements of the required infrastructure do not yet have clearly-allocated budgets. (Paragraph 43)

5. *Given the intention to have the Genomic Medicine Service in operation later this year, the budgets for the required digital infrastructure should be agreed and confirmed now. Decisions on when to provide whole genome sequencing in place of conventional alternative diagnostic tests should take into account the digital infrastructure available to support it, to avoid attempting to roll out a Genomic Medicine Service at a speed that cannot be delivered.* (Paragraph 44)

6. There are widespread concerns about insufficient training and a lack of qualified NHS England staff ahead of the introduction of the Genomic Medicine Service later this year. Health Education England has still to undertake detailed workforce planning and modelling, and there is uncertainty within the existing workforce about the extent of genomics knowledge they will need. The Genomics Education Programme is playing an important role in raising awareness and expertise, however this was initially a 4 year programme. It is now to be continued, but with a substantially lower level of funding than previously. Genomics will need to be embedded in training curricula and revalidation criteria to ensure sufficient genomics understanding by all staff involved in clinical decisions. (Paragraph 54)

7. *With the Genomic Medicine Service due to be operational later this year, Health Education England should complete detailed workforce planning and modelling as soon as possible. They should also work with the Royal Colleges of Medicine and other stakeholders to embed genomics into relevant curricula and revalidation requirements as a priority. The Government must support them in this work, and ensure the necessary funding is available.* (Paragraph 55)

8. Multi-disciplinary teams will be critical to providing an effective genomic medicine service to patients and to keep abreast of a fast-evolving science. *We agree with the CMO's recommendation to establish a national network of multi-disciplinary teams. The Government should set out what funding and support it will provide to enable multi-disciplinary teams to develop from being research-oriented to supporting clinical practice, and factor their costs into the commissioning of the Genomic Medicine Service.* (Paragraph 58)

## Access to genomic data

9. The importance of data sharing for genomic medicine presents a challenge to the concept of restricting the usage of patients' data to their direct personal care. Whether or not the NHS Constitution is changed to reflect the increasingly blurred distinction between genomics research and clinical care, public support will be vital to the delivery of an NHS Genomic Medicine Service. It is encouraging that a high proportion of patients involved in the 100,000 Genomes Project consented to sharing their genomic data, but the 'broad consent' process used in the Project is unlikely to be feasible for routine genomic medicine in the NHS without an extensive and continuing public debate to raise public understanding and acceptance. (Paragraph 74)

10. *We recognise the Government's determination to implement the General Data Protection Regulation but it should now significantly increase its efforts to raise public awareness of genomic medicine, and the data-sharing needed to enable it, ahead of the introduction of the planned Genomic Medicine Service. The Government should confirm and publicise the consent framework to be used for the Genomic Medicine Service as soon as possible, to give time for NHS staff and patients to be aware of data sharing implications before routine genomic medicine is rolled out. Following a public consultation, the Government should provide clear information regarding what data will be collected, who will be able to access that information and for what purposes, and an explanation of the benefits and risks involved in sharing genomic data.* (Paragraph 75)

11. A large proportion of the public express unwillingness to disclose their genomic data to insurance companies. It is important that this concern is recognised, and that measures are in place to avoid large numbers of patients refusing their consent to receive additional findings from whole genome sequencing as a result of such concern. A voluntary Concordat and Moratorium, agreed between the Government and the Association of British Insurers, currently restricts insurers' ability to ask for predictive genetic test results. As whole genome sequencing is rolled out across NHS England, the terms of the Concordat and Moratorium may come under pressure. (Paragraph 82)

12. *We recommend that the Government seeks to renew the Concordat and Moratorium as soon as possible. The current review should take into account the introduction of whole genome sequencing as part of the NHS Genomic Medicine Service, the likely increase in predictive genetic test results this will cause, and the potential for more conditions to be predictable as genomic medicine progresses. The Government should set up systems to monitor any reluctance among patients to undertake genomic testing due to insurance concerns, assess the experiences of countries that ban insurers' use of predictive genetic test results (addressing in particular the ABI's concerns regarding the potential for adverse selection problems), and be ready to consider putting the Concordat and Moratorium on a statutory footing if the current voluntary system begins to limit the uptake of predictive testing.* (Paragraph 83)

13. The data collected by the 100,000 Genomes Project, the Genomic Medicine Service and the wider NHS will constitute the best data resource for genomic medicine in the world. The NHS could benefit greatly from the realisation of the commercial value of the data that are being generated. (Paragraph 90)

14. *The Government must be ambitious in aiming to capture the full commercial value of the genomic and associated datasets it holds, rather than merely aiming to cover its costs. Genomics England should seek to maximise the commercial value of its datasets and continue to provide industrial and academic access to these data to facilitate the growth of the UK genomics industry and the development of new treatments, while ensuring consent and data safety safeguards. Genomics England should explore technological and commercial mechanisms to enable better integration of genomics data held inside their portal with other NHS data and data owned by private companies. While patient benefit should be the focus of the Genomic Medicine Service, income generated from NHS data can be reinvested in the NHS and further benefit patients in the long-term.* (Paragraph 91)

## Genome editing

15. Genome editing is a rapidly developing technology that is already a powerful tool for research, and which has significant promise for therapeutic use. Different applications of the technology entail different ethical considerations, with 'germline' editing being the subject of particular debate. The UK currently has a strong regulatory environment in this area, striking a balance between enabling important research and providing public confidence that ethical and other considerations are given appropriate oversight. (Paragraph 106)

16. *We recommend that the Government specifically require UK Research and Innovation to closely monitor the development of genome editing for potential obstacles to innovation in this area. If it becomes appropriate to review or amend the current regulations in light of technological developments, the Government should use a similar process as the one that accompanied legislative changes to allow mitochondrial donation.* (Paragraph 107)

# Annex: Visit to Genomics England

Three Members of the Committee visited Genomics England in London on 24 January 2018: Vicky Ford MP, Darren Jones MP and Norman Lamb MP (Chair).

The visit included discussion of issues involved in the Committee's inquiry into genomics and genome sequencing in the NHS, as well as a demonstration of the bioinformatics portal clinicians can use to analyse whole genome sequencing results.

Key points from the discussion included:

- The number of genomes sequenced is growing at a beyond-linear rate, and Genomics England are confident of reaching 100,000 sequenced genomes by the revised target of the end of 2018.
- The Genomic Medicine Service is expected to conduct 750,000 tests per year, a small proportion of which will be whole genome sequencing. This proportion is anticipated to rise to around 100,000 whole genome sequences per year by 2021.
- Individual patient stories demonstrate the ability of whole genome sequencing to provide diagnoses and inform treatment. Health economic analysis of the 'diagnostic odysseys' that individual patients with rare diseases can currently endure also shows the potential for whole genome sequencing to save costs.
- Challenges for delivering routine whole genome sequencing in the NHS remain. In order to establish a national Genomic Medicine Service, with equity of access across England, digital interoperability and common genomic testing protocols will have to be developed and adopted. Policy commitments have been made to provide the requisite funding to establish the Genomic Medicine Service, but not all budgets have formally been agreed.
- Genomics England have an obligation to gain commercial value from the genome data they collect, subject to patient safeguards. Although other companies offer genome sequence and associated data, the scale of Genomics England's data set makes it unique. Genomics England are intent on maintaining control over the data they collect, and are in the early stages of developing suitable business models for external access to their data.

# Formal Minutes

## Tuesday 17 April 2018

Members present:

Norman Lamb, in the Chair

| | |
|---|---|
| Vicky Ford | Stephen Metcalfe |
| Bill Grant | Carol Monaghan |
| Darren Jones | Martin Whitfield |

Draft Report (*Genomics and genome editing in the NHS*), proposed by the Chair, brought up and read.

*Ordered*, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 107 read and agreed to.

Annex, Glossary and Summary agreed to.

*Resolved*, That the Report be the Third Report of the Committee to the House.

*Ordered*, That the Chair make the Report to the House.

*Ordered*, That embargoed copies of the Report be made available, in accordance with the provisions of Standing Order No. 134.

[Adjourned till Tuesday 24 April at 9.00 am

# Witnesses

The following witnesses gave evidence. Transcripts can be viewed on the inquiry publications page of the Committee's website.

| Wednesday 1 November 2017 | *Question number* |
|---|---|
| **Dr Magdalini Papadaki**, Head of Product and Process Innovation, Association of the British Pharmaceutical Industry; and **Professor Sir John Bell**, Regius Professor of Medicine, University of Oxford | Q1–51 |
| **Dr Mark Kroese**, Chair, Diagnostics Advisory Committee, National Institute for Health and Care Excellence; **Professor Sue Hill**, Chief Scientific Officer for England, NHS England; and **Professor William Newman**, Vice Chair, British Society for Genetic Medicine | Q52–96 |

| Tuesday 28 November 2017 | |
|---|---|
| **Dr Hilary Burton**, Consultant in Public Health, PHG Foundation; **Professor Sian Ellard**, Clinical Programme Director, South West NHS Genomic Medicine Centre; and **Fiona Murphy**, Director, National Services Division, NHS National Services Scotland, and Member of the Scottish Genomes Partnership | Q97–154 |
| **Lord O'Shaughnessy**, Parliamentary Under-Secretary of State, Department of Health; **Professor Dame Sally Davies**, Chief Medical Officer for England; and **Professor Patrick Chinnery**, Professor of Neurology, Cambridge University | Q155–234 |

# Published written evidence

The following written evidence was received and can be viewed on the inquiry publications page of the Committee's website.

GNH numbers are generated by the evidence processing system and so may not be complete.

1 Academy of Medical Sciences (GNH0010)
2 Association for Clinical Genomic Science (GNH0036)
3 Association of British Insurers (GNH0039)
4 Association of Genetic Nurses and Counsellors (GNH0027)
5 BioIndustry Association (GNH0017)
6 British Society for Genetic Medicine (GNH0009)
7 Cancer Genetics Group (GNH0001)
8 Center for Genetics and Society (GNH0020)
9 Clinical Genetics Society (GNH0016)
10 David FitzPatrick, Mary Porteous, Austin Diamond and Andrew Jackson, MRC Human Genetics Unit (GNH0008)
11 defenddigitalme (GNH0028)
12 Department of Health (GNH0004) and (GNH0033)
13 Dr Edward Blair (GNH0031)
14 Dr Felicity Boardman (GNH0002)
15 Fight for Sight (GNH0034)
16 Genetic Alliance UK (GNH0022)
17 Genomic Health (GNH0019)
18 Genomics England (GNH0018)
19 HCA Healthcare UK (GNH0006)
20 Health Education England (GNH0007) and (GNH0037)
21 Human Genetics Alert (GNH0021)
22 medConfidential (GNH0026)
23 Medical Research Council (GNH0023)
24 NHS England (GNH0029)
25 NICE (GNH0013)
26 PHG Foundation (GNH0015) and (GNH0035)
27 Pleasantine Mill and Jane Lucas, MRC Human Genetics Unit (GNH0012)
28 Professor Dame Sally Davies (GNH0032)
29 Progress Educational Trust (GNH0014)
30 Roche Products Limited (GNH0038)
31 Scottish Genomes Partnership (GNH0005)
32 The Royal College of Pathologists (GNH0024)
33 Wellcome Trust Sanger Institute (GNH0003)
34 Welsh Government (GNH0025)

# List of Reports from the Committee during the current Parliament

All publications from the Committee are available on the publications page of the Committee's website.

## Session 2017–19

| | | |
|---|---|---|
| First Report | Pre-appointment hearing: chair of UK Research & Innovation and executive chair of the Medical Research Council | HC 747 |
| Second Report | Brexit, science and innovation | HC 705 |
| First Special Report | Science communication and engagement: Government Response to the Committee's Eleventh Report of Session 2016–17 | HC 319 |
| Second Special Report | Managing intellectual property and technology transfer: Government Response to the Committee's Tenth Report of Session 2016–17 | HC 318 |
| Third Special Report | Industrial Strategy: science and STEM skills: Government Response to the Committee's Thirteenth Report of Session 2016–17 | HC 335 |
| Fourth Special Report | Science in emergencies: chemical, biological, radiological or nuclear incidents: Government Response to the Committee's Twelfth Report of Session 2016–17 | HC 561 |