



HOUSE OF LORDS

Science and Technology Committee

Corrected oral evidence: Innovation in the NHS: personalised medicine and AI

Tuesday 10 March 2026

10.15 am

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Members present: Lord Mair (The Chair); Lord Booth; Lord Drayson; Lord Duncan of Springbank; Baroness Jones of Whitchurch; Lord Patel; Lord Ranger of Northwood; Lord Willis of Knaresborough; Baroness Willis of Summertown; Lord Winston.

Evidence Session No. 1

Heard in Public

Questions 1 - 10

Witnesses

I: Professor Sir Mark Caulfield, Professor of Clinical Pharmacology, Queen Mary University of London.

USE OF THE TRANSCRIPT

1. This is a corrected transcript of evidence taken in public and webcast on www.parliamentlive.tv.

Examination of witness

Professor Sir Mark Caulfield.

Q1 The Chair: Welcome to this Science and Technology Select Committee. We are embarking on a new inquiry, Innovation in the NHS: Personalised Medicine and AI, and we are very pleased to have as our first witness Professor Sir Mark Caulfield, who is the professor of clinical pharmacology at Queen Mary University of London. Sir Mark, by way of an opening statement, please by all means introduce yourself but perhaps you could give our committee an overview in simple terms of what we mean by personalised and genomic medicine, what its potential is, where it stands today in the UK, and what major areas of application this committee should look into. To what extent are we able to use analysis of individual patient genomes to give them personalised care, and what are some of the near-term applications of genomic medicine that are the most promising? Further, what can we do now for patients that we could not do when you started the 100,000 Genomes Project, and what do you think might be possible within the next five to 10 years? There are some challenging questions; over to you.

Professor Sir Mark Caulfield: Thank you very much. It is a real privilege to be here and to share what I know about the 100,000 Genomes Project and other aspects of Genomics England and the status of precision medicine or personalised healthcare in the UK, but also in the global context. I am currently vice-principal for health at Queen Mary and director of the National Institute for Health Research Barts Biomedical Research Centre and, as you have heard, I am a consultant physician and a clinical pharmacologist by training at Barts Health. I am also a non-executive director on two NHS trust boards, Barts Health and Barking, Havering and Redbridge. I am on the council of the Medical Research Council and Research England's clinical medicine panel for the research excellence framework. I also advise many countries across the world, and I am on the board of the Canadian genomics infrastructure company advising Canada on its sites in Montreal, Toronto and Vancouver. I am here because between 5 July 2013, which is the birthday of the NHS, and July 2021 I was seconded from Queen Mary to be chief scientist for Genomics England Ltd, a wholly owned Department of Health company, where I was an executive board director and I led strategy and delivery of the 100,000 Genomes Project, which worked predominantly in England initially, but because we want to include the entire UK I also secured money from the Medical Research Council for Scotland, Northern Ireland and Wales to be part of the project.

As I see it, personalised medicine is more precision medicine because it is an approach to healthcare that tailors prevention or intervention and diagnosis to the genomic, which is about your and my genetic code. Our genomes are 3.3 billion letters that code for our entire life. They may make us the individuals we are but they may also carry susceptibility to disease and that, of course, is what we want to discover, ideally at a time when we can prevent it. In doing precision medicine we integrate

different bits of data and we move away, most importantly, from a one-size-fits-all approach. What we are aiming to do is to deliver the right treatment to the right patient or right group of patients at the right time, and we can use the genome, your and my genetic blueprint, to do that. But I submit to you that we are now moving into an era of what I will call multiomics, which is where we are focused not just on the genome but on other components that make us function as humans. We might be looking at the message that is taken from the DNA and transferred into proteins, we might be looking at metabolic signatures in blood or urine, but we will be taking a holistic approach to that entire cascade that makes us work as organisms and function and survive, but also understanding what part it can play in disease.

To do precision medicine, what do we do? We integrate clinical information, clinical features of the person in front of us alongside their test results, their digital imaging, scans and suchlike and their digital pathology, and we combine that with data from their genome and increasingly nowadays with other omic data, as I mentioned a moment ago. When we started the 100,000 Genomes Project it was focused on the genomes, but we future-proofed it because the collected samples on 35,000 of the participants allow us to test these other omics that I am referring to, and I will share with you some of the data from that. It also integrates the entire genomic make-up. The whole genome is as much as you and I can measure today of your and my genetic code, and that gives us a comprehensive inventory of the variation within our genome. That allows us to detect causes of disease, potential drivers to cancer or maybe things that mean we should avoid certain medicines because they would be harmful to us.

It really matters because it takes us away from population treatment to a small subset of individuals or an individual itself, and I can give you some examples of that from the 100,000 Genomes Project. We do not just use the genome. We also integrate environmental data, so exposures such as cigarette smoking, which is very important for certain cancers, and living conditions, damp or poor quality housing, are also integrated with lifestyle factors such as dietary excess consumption of salt or alcohol. This is a holistic picture of a patient, which allows us to subset and get down to an individual or a group of individuals and therefore give them the right treatment first time, ideally. Would you like me to move to how we did that in the 100,000 Genomes Project?

The Chair: Please do, yes.

Professor Sir Mark Caulfield: To give you the extent to which this can be used for precision healthcare, I will rely on the 100,000 Genomes Project. This project was an Olympic legacy project from London 2012. It is an unusual project. When I started on 5 July 2013 I was given four letters, about three sides of A4. You can find them on the web. One was about rare disease, one was about cancer, one was about infection and the fourth one was about IT infrastructure that you might need. They all said more or less the same thing. They said, "Essentially, nobody has

ever done this. Here are some things you could do. We are not entirely sure how this will turn out. Good luck". So we really did not know how to do this and we were starting more or less from ground zero. There were some people who had done small numbers of whole genomes so, as you would expect, we toured everywhere that we could find that had done whole genomes and tried to get understanding and learnings from that. We spent a week in America evaluating different centres, and it turned out that nobody had a way of end-to-end analysis of a whole genome. They had little bits of software that did bits of it but they could not integrate it. Very few people in the world had done any whole genome sequencing and certainly not at scale.

What did it bring to people? We were set a number of challenges that the Government asked us to address. The first was to bring benefit to NHS patients. The second was to do that within an ethical and transparent framework. The third was to kick-start industry. The fourth was to generate income for the country. We did most of those things in the whole framework of the 100,000 Genomes Project and I can give you some specific examples. If we move to rare disease, there are about 7,000 to 10,000 rare diseases. They affect about one in 17 people in the UK. That is about 3 million people living today with some impact of rare disease. Only 50% usually get a genomic diagnosis and in 2013 the situation for rare disease was very difficult in this country. It was almost a postcode lottery whether you would get the right test for the right person and even more people did not get a diagnosis, often after significant odyssey.

The diagnostic odyssey is the journey that these people go on, many of them children. Let me give you some facts and figures about that. I looked at babies born after 2003 who came into the 100,000 Genomes Project. They spent six years, 68 hospital appointments, to get no diagnosis, and we spent £15,530 on each one of them. The total spend was £87 million to not get a diagnosis, and at the beginning of the 100,000 Genomes Project we could do a whole genome for around £900. Of course, the stimulus of a major government project has accelerated price reduction so today a whole genome costs less than an MRI scan. This is doable and is cost effective in the system.

Let me give you a couple of specific examples to bring this into real focus, because it is much more helpful if we visualise a human. The first child to get a diagnosis had been born and was falling behind her milestones and was clearly not progressing as other children in her peer group. She started to have epileptic seizures, so in the time I am here with you today she probably would have a couple of fits on a good day. This child was becoming increasingly intellectually disabled due to the lack of oxygen to the brain. We analysed her genome and, to explain what happened, we discovered that she had an epileptic encephalopathy, which is where the epilepsy is due to a metabolic cause, some defect in metabolism that means the brain is not getting enough nutrients. In this case she had a mutation in a sugar transporter—very simple. It takes sugar from the bloodstream inside the brain, and she could not do that.

Every time her sugar dropped down, she had a fit. There was a treatment for this, which is a high-fat diet, and because of a starvation mechanism that you and I have, you can make sugar in your brain from fat. She does that now and she is on a high-fat diet. She has improved. She will never regain all the losses that happened, but she will be much better and will have a different life as a result. To give you an idea of the journey that her 3.3 billion letters went on, there were 6 million variations in her genome. We had to sift through them all: 600,000 were rare and 2,228 changed a protein so could be the cause of her disease, but one was different from her mum and dad and that was the clear-cut cause. The other impact this result had on that family was that her mum and dad, who were never going to have other children because of how she was, discovered that this mutation had occurred at conception in her—it was in her only, not in them—so they then went on to attempt to have other children.

I will not pretend to you that everyone gets a treatment. On the contrary, most people do not get a treatment, but I have witnessed the journey that they go on and the pain and pressure that these people put up with. It is often a military operation to go to the hospital; I can remember one child in the programme whose family came from another part of the country to London so that they could attend an appointment the next day at lunchtime. They got up at 5 am to get their child ready, who was severely disabled, in a wheelchair and on a disabled ventilator, and that 5 am start matured into a 1 pm appointment at Great Ormond Street. That is what these people go through, so they are disproportionately elated when we say, "We think we will find the mechanism for this disease". That is what precision medicine can do. They are disproportionately elated because they know that if you do not know what the cause of their disease is, you do not understand the biology of their disease and therefore there is no prospect of a treatment because you do not understand what is happening to them. They know that this is part of the journey. If you were to talk to many of them here today, they would share with you that they do not think this programme will definitively benefit them with treatment. They are doing it so that it can benefit future generations and that people do not have to go through what they did.

The cancer programme was very challenging. In cancer we sequence and read the genome of the tumour and we compare it with the genome that you inherit from your mum and dad, usually from the bloodstream. We take DNA from the white cells and then we take pieces of the tumour and compare the two. By subtracting the two we can see the mutations in the tumour that may be driving the tumour to grow, expand and spread, but also that may choose therapies. That is the real goal here. I will give you an example. A middle-aged lady presented with breast cancer—no family history of breast cancer at all—and we found in her genome that she had a mutation you may have heard of called BRCA. She had a BRCA2 mutation. This meant that she was eligible for a trial in 2015 that she would not have got into if we had not done that molecular test. Her

BRCA2 mutation meant that she could enter the OlympiA trial, which has now reported the benefits of a drug, Olaparib, that is now used in the treatment of breast cancer, so she had that benefit. To emphasise the familial-wide influence of this, her daughter, as a result of discovering her mother had this mutation, decided to be tested herself and she has the BRCA2 mutation too. She was in her 20s. From the age of 30 she has entered intensive breast screening and she has also considered breast reduction surgery. Her brothers and uncles in the same family, the men, could be at increased risk of prostate cancer, so you see how precision medicine does not just move through just the individual but can have broad ramifications. Occasionally, people do not want to know these things, but getting the opportunity to focus screening on those most at risk is what we should be doing in the health system, especially if we are to honour the 10-year plan of sickness to prevention.

I will move to the next sub-question: what can we do for patients that we could not do? All the people who had rare disease in the programme had diagnostic unmet need. They had no diagnosis. That was the one requirement. The other thing we did was to test involving more family members. If you are just the affected individual it can be quite hard to get line of sight on a diagnosis, but if you have mum and dad too you can filter out noise in the genome and you are much more likely to get line of sight on a diagnosis. Another thing we found was that the more you clinically characterise these patients, the more likely you are to get a diagnosis.

The other thing that we learned was we could make diagnoses that were absolutely life changing. I will give you one other example from the more recent newborn programme, which is also a rare disease. A few weeks before Christmas, Genomics England presented one of the early diagnoses from that programme. I was responsible for persuading the Chief Medical Officer to support it and for drawing up the blueprint for it, and it is now live. The family of a child, within four weeks of birth, knew that he had a mutation in the back of his eye. This caused a tumour of the retina—it is called retinoblastoma—and, as a result of that, every six or so weeks he now has screening under anaesthetic. Already they have discovered several tumours in the back of one eye and have given laser therapy. Alternatively, he might have to have chemotherapy and radiotherapy and then lose that eye, and if both eyes are affected he might lose sight in both eyes. If he makes it to his sixth birthday, this mutation dampens down and then he may retain his sight in either one or both eyes. That is the opportunity of this to change the outlook for these patients.

I will give you another example. We had a child who was born and admitted immediately to intensive care, never left intensive care, and sadly at four months he died having had repeated changing neurology. His nervous system was not working properly and he had repeated infections. No tests revealed any cause for that, and his mum and dad asked if they could enrol him in the 100,000 Genomes Project. For future reproductive health, we allowed people to enrol in the 100,000 Genomes

Project their child who had died. In this case, the mother then became rapidly pregnant again and said, "Look, I really don't want to know the diagnosis; don't tell me", and at month eight, just before the birth of the second child, she became really anxious and asked to know. We discovered a change in the DNA that affects how cells in the body take up a vitamin you have all eaten in the last 24 hours, vitamin B12. It is in many foodstuffs, very simple, and there were case reports, not major trials because in rare disease case reports are often as good as it gets. We were able to use those case reports to consider whether, if the second child was affected, we would give high-dose vitamin B12 by injection weekly. Normally in B12 deficiency, we might do it monthly. This would allow the B12 potentially to get inside the cells by other routes. The second child was born and within a week the NHS had tested him and very sadly he was also affected, but he received the weekly B12 and he has had a completely different life. These are the changes it can make.

In cancer I will give you another example. The West Midlands centre enrolls most cancer patients. That is Birmingham and its outreach to about 17 other hospitals where cancer is treated in the West Midlands region. We sequenced 3,200 patients from cancer; 700 were reviewed as a result of the genome by a genomic multidisciplinary team and 25% had different care as a result of that. For some we found changes in their DNA that might make certain medicines that would be used to treat the cancer harmful to them. I am referring to a mutation called DPYD, which can make it harmful to have certain doses of 5-fluorouracil or capecitabine, widely used chemotherapy agents, so we can reduce dose because we know about that. That is now live and routine for all cancer patients in the NHS as a result of the programme; 208 out of 400-plus people entered clinical trials as a result of their genomic make-up, and 90 we found had a hereditary cancer risk. As a result we can screen them for that cancer because we know about their risk.

I can move to what we did there in Covid, but I should probably stop and see whether you want to ask me any questions about what I said—otherwise, I will just talk.

The Chair: Thank you very much. You have given some very instructive, interesting and fascinating examples, so we are very grateful for that. I think we are already beginning to understand much more through your very lucid explanations. We do have more questions.

Q2 **Baroness Jones of Whitchurch:** Congratulations, because clearly the 100,000 Genomes Project has achieved a huge milestone in NHS care. You said you started with a blank sheet of paper, and obviously you have learned a huge amount over that time. When you look back now, in the broader sense what do you think it has achieved? How much has it changed the way that medicine is considered in the UK? What was the overall impact of that piece of work?

Professor Sir Mark Caulfield: Essentially, it has brought genomic medicine to the NHS, and from the project we established a new Genomic

Medicine Service. We were not particularly asked to do this, but one of the reasons this project was a success is because we took a different approach. We involved the NHS, public and participants from the outset. We placed public and participants through all our structures. The public and participants were key decision-makers on who had access to their data. The participants also spontaneously organised themselves into Facebook groups to talk about what was happening when things were slow, and at the start it took us a long time.

A way of viewing the 100,000 is that we built the aircraft as we were flying it. Although that is an uncomfortable thing to do, we learned a lot more because we were doing it quite rapidly and we were also able to change things rapidly. That allowed us to bring to the NHS the platform for a new Genomic Medicine Service. When the project finished—we finished sequencing at 2.40 am on Sunday 2 December 2018, to time and target—we had already started work with Professor Dame Sue Hill from NHS England, who is in charge of the Genomics Implementation Unit, on the blueprint for a new Genomic Medicine Service. My team and I reviewed 300,000 tests that were currently deployed in the NHS and, working with NHS England, we upgraded them to new technologies in 25% of cases, including whole genome sequencing. We are one of the first services in the world to have whole genome sequencing in routine care free at the point of delivery in the NHS in England, and Scotland, Northern Ireland and Wales are following suit. That is the really big benefit.

A second benefit was that we were asked to kick-start a genomic industry, and when we started we wanted to be open, transparent and fair about how we selected our partners for the programme. We did what you might more associate with cakes. We did a bake-off between the sequencing technology providers to find out who was the best and who could do this at scale, so that at the end of it we would leave a pipeline that could deliver this at scale for the NHS but, most importantly, was accredited end to end for clinical care. As a result, Illumina, Inc—which had a technology that was born here in Britain, in Cambridge, by Solexa, which was taken over by Illumina—built a sequencing centre with us, invested £70 million in the United Kingdom and created 100 jobs and a new European headquarters at Granta Park, which is still there today. It still works with Genomics England on this project. We chose it because although there was one other that was very good, the technology it had was not fully developed so we could not be confident that it would be ready to do this at scale and on time. I know for a fact that Illumina invested a lot of money itself and gained a lot from learning about how to do this project.

The other thing that has happened is that we created an ecosystem of researchers. When we started we realised instantly that we did not know enough about this, so we created a global coalition of intellects. At peak about 3,500 people from 33 countries volunteered. We openly advertised in a scientific journal called *Nature* and we said, "You can have free access to the data. You can't take it away. You will have to work in our

environment but you can work on it for free. We will pay for the cost of that, but you have to show us that you will drive up the value of this data for patient care". Basically, we harnessed a whole load of intellects we did not pay and this country did not pay, which is also important.

Another thing we did was to build the world's first trusted research environment. With the footprint of a genome, you have a tablet in front of you and some of you have laptops; your hard drives are about a terabyte. You could probably fit three genomes on your laptop. You would not really be able to analyse them, because you need a high-performance computing facility. We built a data centre because shipping these things around the world and distributing them would have been very difficult. It would also have been very difficult for us to be able to assure the patients that we had full control of the data. The patients said very clearly that they wanted their data to be in the UK. We did that and we built a high-security data centre in Corsham in Wiltshire. That housed the data for many years, and then when the cloud services were in Britain we moved it with patient approval into the Amazon cloud, which is where it is now. The evolution of that has created the concept of a trusted research environment.

I would like you to view that like a reading library, not a lending library. I do not give you the data. You do not take the data away. You come into my place and you analyse the data with all the tools that we provide. If you want to have another special way of analysing the data, you can ask to bring that in through an airlock. We take a look to make sure that it is not something bad that would damage the data centre, and then we move it into the data centre and you can run your analyses. There are 1,500 researchers working on these data today, long after the project finished, but because today we have achieved in total still only slightly north of 40% diagnostic yield, we need that coalition intellect to make sure that everybody who can will get a diagnosis eventually, because that is what they crave. The lasting legacy is really the way of doing this in the system.

We built in an unusual thing for healthcare commissioning that does not exist in many other settings. We built in a dynamic review, so every year the genome test directory is inspected for its contemporary value and accuracy. We ask the question of every test: is it the best test we could have in the world? There is not much else in healthcare commissioning that we do not fix for three or five years, but the genomic test directory is not fixed. Every year it is reviewed and updated, and today the whole genome sequencing is available to NHS patients across five different types of cancer: childhood cancer, blood cancers, ovarian cancer, brain tumours and sarcoma, which is a tumour of the muscle or the bone. I could show you data that shows that the whole genome can define mutations that we know affect cancer. Following the patients longitudinally over life course, we can see how their outcomes are with those mutations and how it changes things for them. We can also potentially see signals of benefit or harm from treatments. This is a giant opportunity, and every person consents to longitudinal life course follow-

up. We ask for all electronic health data and it comes together with the genome. That goes back to my precision medicine definition of integrated multimodal data coming together to provide more precise diagnoses for the individual or a subset of individuals.

This has the potential to keep giving us new things that we can bring into the health system. The consent allows us to work on any disease or any exposure that the patient has; they fully know this and are very happy with it. The participants monitor what we do all the time—what I did when I was there and what they still do now.

Baroness Jones of Whitchurch: To follow up very briefly, that is a very profound impact from the learning from the project and very interesting, but do you think that the Government and the NHS have seized the opportunity sufficiently, taking it forward? It has been a long learning process that you have been through, but are we now capitalising on it?

Professor Sir Mark Caulfield: The thing that we did very differently in the 100,000 Genomes Project is that, although there were at its peak about 100 people in Genomics England, mostly they were analysing the genomes. We worked with NHS England in partnership to get the NHS to do the project by the NHS, for the NHS. At the end of it we had 5,000 people who touched this project at some part of their working week in the NHS, and that had a profound impact on the outcome. It meant, as you may know, that the National Institute for Health Research, NIHR, the Department of Health and Social Care's research arm, has data. If I publish a clinical trial today, it could take me between nine and 16 years to get the National Health Service to adopt the finding. We did all this in five years. Why? Because we marched 5,000 people to the top of a hill, and at the end they did not want to stop so they became the champions of the project. They said to the NHS in England, "We want to continue doing this", and as a result we did. I had a great partner in Sue Hill and we both wanted to do this. We did not want this to stop. We could not do it for the participants. It had to go on. The NHS made money available for the Genomic Medicine Service.

To properly answer your question, this project has had cross-Parliament support. It is a project born out of London 2012 and a Conservative-Liberal Government at the time, but it has survived that. It has survived a Conservative Government and now it is being championed by a Labour Government. Cross-Parliament support, including from Cross-Bench Members in this room, has been profound and important. When I worked there I served three Prime Ministers, three Secretaries of State and nine Health Ministers, all of whom were absolutely committed to this project. That commitment is borne out in the fact that the current Government committed in their life sciences plan, alongside the NHS 10-year plan, £65 million a year for the next 10 years to Genomics England to spread newborn screening across the NHS, to understand whether we can use genomic medicine and precision medicine to assess risk of patients so that we can accelerate sickness to prevention as part of the 10-year plan.

If I summarise the total amount of money that has been spent on this, I estimate it to be £1.3 billion of government support for this, but this country is a world leader in the application of genomic medicine in direct healthcare as a result. In other investments that this Government and other Governments before them have done—UK Biobank, Our Future Health, the NIHR BioResource—we have some of the best cohorts to understand disease in the world. Increasingly, we are addressing the one major gap here that I would like you to focus on in your priorities: diversity in the genomic sciences. We have not had enough diverse cohorts. We are getting there but we are not there, and that is vital because one size does not fit all.

Let me give you an example to further answer that. My colleague Emma Magavern and I discovered in a study called Genes & Health, which is 65,000 from the British Bangladeshi and Pakistani community, that there is a variant that we have known about for some years that is present in about 30% of us in this room. About a third of us will not make the drug called Clopidogrel, which thins blood after a heart attack, work. It will not be activated. In south Indian Asians, this is 57%. What do we do in our heart attack centres? We give out Clopidogrel to everybody who comes in, but not any more because we now know that that is not the right thing to do. In my heart attack centre at Barts, the majority of the 2,000 people who come through are south Indian Asian because of the communities we serve. This is what this can do for us. I believe the Government have shown great commitment to it.

So what do I need you to do? I need you to ensure that the momentum is not lost on the newborn programme. I see this as vital. We need to maintain the annual test directory updates and reviews, and we need to make sure that we have the ecosystem from which to leverage this and the opportunities from the Health Data Research Service, which I think you will ask me about in a moment.

Today, when I go back, I am meeting a delegation from Tokyo who have come to find out how we did this. People are still coming to me five years after I left Genomics England to discover how we did this. In fact, on one occasion we were sitting in Genomics England watching a slide display from Thailand when suddenly I realised that they were using my slides and all they had done was put "Genome Thailand" on the slides. There have been some amusements, but that is a sincere form of flattery.

We have in NHS Genomic Medicine Service the means. There is regional equity of access for 57 million people to genomic testing should they need it, and it will spread across the UK. That means precision medicine is alive in our National Health Service today, and you would not have bet that in 2013. Even in 2018 we were not sure we could do it, but we had to be resolved to do it and we were greatly helped by the extremely strong support of our participants, who were with us in step, shoulder to shoulder, throughout.

The Chair: Thank you very much for that explanation.

Q3 Lord Patel: Thank you so much for coming today. Listening to you is quite inspiring. Of course, the 100,000 Genomes Project has been a huge success and the learning that has come from it, not least the Genomic Medicine Service. The problem now will be that, as you and I and Lord Winston know, implementing every innovation in the NHS is a tough order. How will you do that, including, for instance, the Genomic Medicine Service? You and I both know that a lot of the mutations that occur in people with diseases, with cancers, are not tested for; therefore, they are given drugs that may not be effective or they are given drugs that are probably the wrong drugs for that cancer. What are the lessons learned so far in implementing the Genomic Medicine Service and how do we improve on it? How will we get it universally accepted?

Professor Sir Mark Caulfield: I think the answer to that is severalfold. The first was to win the hearts and minds of the National Health Service so that they became its champions. That is the case, and now they are organised into seven genomic lab hubs and Genomic Medicine Service alliances. To explain the Genomic Medicine Service alliances, they are where the clinicians are. Naren, they are where you, Robert and I would be. Then behind them there are the lab hubs that do the testing, and there is also a central sequencing facility for whole genomes but increasingly that will become distributed. The test directory means that the reimbursement for genomic testing is dependent on using an approved test in the test directory. I would agree with you that this is a dynamic area and it requires vigilance, and that is why I built in this annual review. I felt that we would just fall behind time if we did not do that.

It could be that some people are delayed in getting the right variant at times because the test directory has not been upgraded, but it seems to me that the NHS is moving very quickly to adopt things—faster in many ways than it has moved in other areas. This is probably a trailblazer for how we could accelerate adoption because we are, I am afraid, slow adopters. If we can change that, with agility in adoption and route to market, this will be a great place to come because we will have a Health Data Research Service. We have Genomics England, the 100,000, UK Biobank and Our Future Health. If we can crack that, that is absolutely right. I would agree with you, Naren. I do not want to put words into Robert's mouth, but we would probably both agree that we could do better, but we have a mechanism to do very well and certainly faster than most other countries in the world.

Lord Patel: How can this committee help to accelerate that?

Professor Sir Mark Caulfield: There are several ways you can accelerate things. The learning from this was to get the NHS to do this. Sometimes we create research teams that sit slightly outside the health system and then they come in and do something, and at the end the NHS knows that they have done something and what it is but does not feel part of it. Making the people in the front line feel the benefits of this as you are doing it makes them champions. I have said that several times,

but I do not think we would have got this into the NHS without that support. That is number one, and I think we could do that elsewhere.

If we were looking at the Health Data Research Service, which we might come on to, that is a £600 million investment. That is very similar to Genomics England in that it has been created as an arm's-length entity to deliver a solution for 67 million people's health data. The first thing I would do if I was doing that, and this might be something you would say, is put a lot of effort into building the trust of the public and participants. We have not always got that right. Genomics England was born in the era of care.data, where we lost some confidence from some of our primary care clinicians in what was happening to the data. That caused us some uncertainty and unsettlement about the amount of data we were collecting. We are over that, through that and out the other side, so I would say that we could encourage the Health Data Research Service to learn from Genomics England. Of course, its chair is in common with Genomics England, Baroness Blackwood, whom you know well. We can use this approach to short-circuit the whole process of adoption.

There are five things that I would like you to do. The future is multiomic. It is not just about DNA and the genome. It is about RNA, proteins and other things that we measure, and that data needs to be multimodal. The more data you have, the better, and the more likely you are to get a precision medicine outcome for a patient. The Health Data Research Service needs to learn from the successes and, sadly, from prior mistakes such as care.data.

The Government and their funders must create the ecosystem for AI. They are working on this and it is writ large, as you will have seen, in the life sciences strategy, but we have the datasets at scale. One of the things about AI is that AI in this space is still a work in progress. Artificial intelligence in the genome is being used to analyse genomes, but at the moment it is adding incremental gain. It is not a step change, but we can see the direction of travel here. It is very likely that sooner or later these algorithms will offer a step change in diagnosis. This is the country to adopt them and we must let that ecosystem be built. It is a vital part of that, and you in this room have the power to oversee and be vigilant to make sure that ecosystem persists, not just for one cycle of government but for multiple cycles.

There is a platform for therapeutic innovation here. We have amazing companies. Some of you may know of a company that spun out from Demis Hassabis, who won the Nobel Prize for a folding protein program. He devised a company called Isomorphic, which is using the power of the Google cloud, the entire Google cloud and its compute, to predict drugs that we cannot predict with normal mechanisms. This is the sort of thing we can do in this country because we have aggregated big datasets. Those big datasets at scale allow us to find niche things if AI works. We are not there yet, but we can get there. We can accrue data if we have the patient and public trust of our entire population. There are very few

other people who can do that at scale today, but they will catch up. Of course, AI in China is rushing ahead.

If we could do that, and alongside that you helped to create an agile framework for adoption, I think we should also focus on the risk appetite of our investors. Solexa had to go to the US to be fully realised and developed. Other things have left these shores and gone to other countries because of investors with higher risk appetite. I think you should try to envisage a system where we have a more systematic but higher risk investor group and what mechanisms might be brought to bear to try to encourage that so that more of the inventions that this country makes do not have to go to the United States to be developed and matured as technologies and that the benefit is realised at the point of origin. If we do that and get a pipeline that gives a clear route to market for these companies, they will be here in droves and then the £41 billion of growth in life sciences from £108 billion per annum today is entirely realisable. I do not know about multiple companies at a value of £10 billion. I will leave that to someone else to worry about, but I do think that this framework is within our grasp should we choose to implement it.

Q4 Lord Winston: I have huge admiration for your work. It has been quite transformative and, as you know, I would feel like that. Some of the things I will ask you might sound a bit critical of all this but it is not, of course. Indeed, my own research has benefited from having your background, particularly when it came to, for example, pre-implantation genetic diagnosis. There is also an interesting problem because if we look at the difficulty of transforming some of these diagnoses into the health service we find that it is still horrendously difficult. There is a very good example of many patients who carry a specific mutation which, if they had a biopsy of the embryo, would prevent that embryo being transferred into the uterus and would guarantee, in fact, a totally different outcome to that child. There is no question but that in the long term this would be very cost effective, because the treatment is not terribly cheap but bringing up a child is colossally expensive and it is still very difficult to translate these things into the health service. Can you tackle that issue first?

The other thing is something that has come up repeatedly in the House of Lords. Both Lord Patel and I have been involved with questions in the Chamber, one on prostate cancer, one on breast cancer and one on cancers of the brain, where each time the people asking these questions in the Chamber have very little understanding of the Minister's answer, which is made basically on the risk analysis and the problems of false diagnosis, false positives and false negatives. We are very short on time and I am conscious of asking you too long a question, but could you briefly try to address some of those issues? I will not ask you anything else.

Professor Sir Mark Caulfield: The pre-implantation genetic diagnosis was not within the 100,000 Genomes Project, as you know, because

there were good research projects looking at exactly that outside the 100,000 Genomes Project. We deliberately did not disrupt existing research because we felt that would be very counterproductive. I agree with you that we are sometimes very slow adopters and we tend to look at things from the point of view of the cost of the individual test or the cost of the therapy. For example, in sickle cell there is a potentially curative gene-editing therapy that we have now adopted. It is £1.65 million per treatment. Okay, that is very expensive, but what is the societal total cost of a lifetime spent like this?

In the 100,000 Genomes Project and other projects around the world looking at cost effectiveness, we can show that it is very cost effective to do these things. Barriers to routes to adoption should not pertain or remain. However, I accept that they do, and therefore if you are struggling to get pre-implantation genetic diagnosis done in the way that you believe the research is, I would be talking to Sue about how we could fit that inside if it is not inside the test directory.

Lord Winston: It is the structure of the funding of the health service, the internal market, which makes that so difficult.

Professor Sir Mark Caulfield: Yes. It is the structure, but these are the points you can make to the Government about how we could extend this, given the investment they put into Genomics England. These are the ways in which we could explore future developments of this technology under the programme that has been funded and then lead that through to adoption.

Lord Winston: Just to switch things for a second, can we just address that issue of, for example, the screening and the diagnosis of common diseases such as some of the cancers I mentioned and the lack of understanding of how in many cases that would be much more limited in ways that were not expected?

Professor Sir Mark Caulfield: I agree with that. In the 100,000 Genomes Project we found a much higher rate of hereditary predisposition to cancer and in all cases it had never been tested for, even though there was a family history. Obviously, we now have hereditary cancer testing in the NHS so we can do that. Previously, we have also been very conservative at adopting screening methods. In the case of whole genome sequencing in the NHS, I was talking earlier about perhaps a handful of people affected by a very rare disease where it is very hard to get the absolute evidence for adoption but in the majority of those cases this works. I think this is a situation where perfection is the enemy of extremely good. If what you are saying is that people do not understand risk, I think that we often overcomplicate the answers we give to risk and that some of the things that we are looking at and that you will hear about in your forthcoming deliberations, such as risk scores that can be derived from genetic variation, could come to the fore in places such as cancer where we have no good biomarkers. There, perfection would be the enemy of the very good.

If I can find some more people who are at risk of the awful diseases such as brain cancer, we would want to do that even if the test was not outstanding. To qualify that, we measure a prostate-specific antigen to detect prostate cancer. It is not a good test but we still do it. We need to be careful about not using risk to deny opportunity to individuals. If adjusting your lifestyle a little bit turns out to make very little difference, if it is a little bit and not very much, is it that bad a thing to do? It is very cost effective because it is usually you doing it with your food, stopping smoking or something like that, but in fact you are better off if you stop smoking so I think there is a real opportunity for us to take a different view on screening and I would like that to happen. We sometimes require a level of evidence that means we will never make a decision to do certain screening. There is a risk of false positives—I accept that absolutely—but if it is just a dietary shift or something, is it that harmful? Probably not.

The Chair: Can we move on to your views on the role of AI?

Q5 Lord Ranger of Northwood: Professor Caulfield, thank you for coming today and fundamentally thank you for all your work in this space. I recently had an NHS health check and it felt very unpersonalised, so I am quite keen to see how we move the NHS into personalised medicine. You mentioned the challenge of how the NHS is slow to adopt and adapt. With the influx of AI, part of our motivation for this inquiry is how we can see the impacts of rapid deployment of AI on personalised medicine, including developments such as the deep-learning model AlphaGenome and other AI tools. In your view, how transformative can these AI tools be? In all the areas you mentioned and all the examples, you did not really refer to AI. From 2013 onwards you were probably using some kind of machine learning. Greater compute was coming online and a lot of developments have happened in the last five years or so. What do you think we can use now in practice and how can it help increase the pace of what you are trying to do?

Professor Sir Mark Caulfield: That is a great question. AI is being used in genomics and we did use it when I was at the 100,000 Genomes Project. It was, as you correctly describe, in its infancy. Towards the end of my time, I did two experiments that were AI-based analytics that looked for variants at specific points in the genome. To do this they looked across all the Genomics England dataset, and this is the virtue of scale to find niche. The program looked at various points of the genome and said, "This person here has a very different letter from everybody else. You had better have a look at it". Now, if I had had to do that manually it would have taken me many lifetimes. I have given you an impression. We probably have 5 million or 6 million variants in an individual. You cannot do that with individual scrutiny. The AI packages were able to identify certain areas where we should really focus the human attention to work out whether they were causing disease, and in some cases they did. The gain was not massive; it was incremental but it does add value, and those papers I published on. There was recently one in *Science* called promoter AI, looking at the regulatory region of a gene,

but there are also other programs that look at the junctions in the gene between the coding region and the non-coding region. We have trialled those and they do produce incremental gain.

We also trialled AlphaMissense, a product based off AlphaFold. AlphaFold revolutionised structural biology overnight because previously we had to try to make crystals of every protein and work out how the protein folded. AlphaFold can predict the folding of the protein and has been a major advance. That is the basis for Isomorphic and how it is using AI to work out what drug targets could be on proteins. We looked at AlphaMissense. Again, it was incremental.

We also ran machine learning in my time at the 100,000 Genomes Project to do a number of things. Sometimes people had a secondary deposit of their cancer, which was biopsied and it was realised that that was a secondary deposit but it was not clear where the cancer had come from. The organ of origin was not clear and therefore there was some unsettlement about how to treat the patient. By looking at the mutational architecture of that patient's cancer we could gradually tease out different mutations that were telling us what the likely tissue of origin was, and we did this with machine learning, as you said a moment ago. There was a cancer of unknown primary diagnosis where we had a brain secondary deposit; we looked at that secondary deposit and first we found common mutations that are in many cancers. That was not very helpful. We then found that there were lots of mutations in the cancer. Certain cancers have lots of mutations, such as lung cancer. Finally, we found that the person had a molecular signature that occurs only if you smoke cigarettes, so this was most likely lung cancer. Then other factors added to the diagnosis, so we could tailor the treatment in a precision medicine manner as a result of having done that.

Occasionally, in the health system—Lord Winston and Lord Patel, close your ears—our colleagues are not as good at recording things as they might be. Even though nobody can be treated with cancer in the NHS today without cancer staging, we were submitted data from cancer registries and hospital episodes and primary clinical data from the individual sites that had no cancer staging with it. What did we do? We got the pathology reports that are always in the cancer registry, ran machine learning and staged the cancer for ourselves so that we could back-fill that data asset. Cancer staging is very important to tell you what treatments you will be eligible for. If you are not staged you cannot have cancer treatment. We knew they had to be doing it, but they just were not telling us.

We have created a reading library where we can deploy these things. If you had a good idea for an AI thing and you had a company and wanted to come along, you could come to Genomics England and say, "I have a great idea. I will pay for the compute. You can test my algorithm. I want to run it across all the genomes that you have". Today, if you go into the research environment, not in cancer but in just the genomes that you inherit from your mum and dad, as of 3 March there are 140,000

genomes available for bona fide researchers from the NHS, academia and industry across the world to bring these tools. Although I cannot tell you that AI is brilliant, I can tell you that we built the platform for AI to become brilliant, maybe, if it works well. My colleagues around the world, the 1,500 scientists, have access to those germ line genomes, which are the genomes we inherit from our mum and dad. They have 825 million variants to work on. We will definitely need AI because you cannot possibly sort through those. Of course, my eye is not on the 40% of rare diseases or the 25% of cancer patients who get a change in cancer care. It is about what we can do for the unmet need that remains, which is considerable.

One other final thing—we were not particularly tasked with doing this, but we had approval from the patients to do it—is that we looked across the genomes, 76,000 of them, and found that the most common thing in your and my genome that can cause us harm is a variation that changes how we handle or respond to a medicine. Some 99.5% of us in this room right now have at least one gene variant that if we come across the medicine, it either will not work or will harm us. That will come live as part of the NHS next phase. It is not AI, but a lot of that work was done by algorithms that were forerunners of AI. Some 25.4% of you, including me, have at least four of these. This will be brought live in the NHS, so we will be improving the health check.

Q6 Lord Willis of Knaresborough: Thank you very much indeed, Professor Caulfield, for coming, and my apologies for not having the qualities that some of my colleagues have within this committee. I was in a hospital yesterday and I took the opportunity to talk to the chief executive about coming here today, talking to you and looking at some of these issues. I must confess that she said that she had not a clue what I was talking about and whether that would ever affect her regional hospital in the north of England. In other words, she was saying that this happens with key hospitals—“Whether it will ever get to us, we don’t know”—because of the cost and because of the difficulty of doing so. The third thing she said was that it never seems to affect elderly patients. It is more to do with young patients. AI seems to me to be the most incredibly useful equipment to be able to help move this right across the country, not simply in the key hospitals and research centres. Do you feel that there is a real difficulty with the NHS in accepting removal of it into other parts of the country?

Professor Sir Mark Caulfield: Lord Willis, let us start with your visit to the hospital yesterday. I am unsurprised that people locally are not so engaged in this. The genomic lab hubs operate regionally, but in the 100,000 Genomes Project we reach 98 hospital trusts out of 220. The Genomic Medicine Service does reach all 220; it is just that the lab in the hospital—let us say that it is doing cancer care—will contact the genomic lab hub about the appropriateness. It does not have to worry about the day-to-day detail of this in a general hospital across the country, because distributing this is too much work for people who have to be rigidly focused on what is coming through the front door. I am unsurprised that

they do not see it, but it will be feeding into their care as long as their hospital plugs into the system. The NHS has committed to making this universally available in England, and people from all hospitals can gain access to this technology.

I agree with you that we have to have a facilitatory system for artificial intelligence. I will give you a couple of examples. From my experience so far on the Barts Health board, we had a presentation on AI and what we could do. The problem is that the different approaches to AI are expanding at a vast rate, so we need to have a good way of assessing what might, on the face of it, be well worth deploying and having testing environments. In some ways, that is why data assets such as the Genomics England data asset, Our Future Health and UK Biobank are great because they do not necessarily require front-line NHS care to do the testing. There are some things in the health system where only AI can be used. For example, my colleagues and I at Barts Health have projects that are reporting scans and X-rays using AI and then flagging up certain people who need to be specifically checked. They have also made diagnoses using AI that would have taken much longer to do if we did not have those systems. The enthusiasm in the workforce is there for adoption. It is the weight and the workload that is slowing this down.

We have yet to realise the potential benefits of this technology. For example, in some hospitals, using the electronic health record of an out-patient consult, Copilot, which is available on your computers—you can all use it—is writing the clinic letters for the doctors and the doctors just inspect the final product. They do not have to dictate; they are moving to a new level. Obviously, that requires very great care to check the detail, but there is an increasing view that we should be adopting these technologies.

The NHS faces an enormous weight of people turning up and saying, “I have this great AI thing, can you deploy it in your data centre?” What is happening both with the Health Data Research Service and individual NHS trusts such as mine is that the recognition of the value of this is there and they are therefore aggregating their data from routine healthcare—real-world data collected by clinicians, nurses, allied health professionals and pharmacists across the NHS—and mobilising that in platforms at trust level and at secure data environment levels in regions such as Manchester and here in London, where we are doing that, to create the platform for AI testing. If we go piecemeal to do this trust by trust, it will slow down adoption. We need to use our national assets and the Health Data Research Service to create a testing ground where these algorithms can be brought in and we can test and validate, because in AI you want a test dataset and then you want to validate it before you deploy it in healthcare. That is where the bottleneck is. If I were doing the Health Data Research Service, which I am not, I would encourage it to run for the finish line on creating an environment that could do such testing so that the UK can take advantage of the global AI market and bring the best benefits to healthcare directly.

Q7 **Baroness Willis of Summertown:** I would like to move on to the research infrastructure or data infrastructure priorities. I use the UK Biobank database for my own research, and when I was at Kew we did a lot of work on the plant genome database. So I am aware of the massive infrastructure you need in the background in order to process and analyse this data and even to hold the data. Earlier you gave us an excellent example of how you built up this data infrastructure, but then you moved on to say that you have moved it on to the cloud and that it is managed by Amazon. There are two questions there. What are the challenges going forwards in order to maintain this research infrastructure? Then to just push back slightly on the Amazon cloud infrastructure, is that secure and does everyone really understand the risks that now poses with the data being dispersed all over the world in these data centres rather than being UK based?

Professor Sir Mark Caulfield: When we consulted at the outset with public and participants, they said, "We don't mind where you put your data as long as it's in the UK". We could not use Amazon for years and years because it was not in the UK. Now the data sits in the London cloud in Amazon, but before that we had to build our own data centre in Corsham in Wiltshire. When I left we were already at 80 petabytes of stored data, and it is now much more than that. That is why it is important to have a single data centre.

We found it very valuable to operate as a reading library so that people could come to an ecosystem. Of the 33 countries that volunteered, scientists from low-income countries could not afford Amazon's charges. When the decision was taken in 2021 to migrate to the cloud, it was because of the security levels that were continually refreshed in the cloud, which we were having to maintain ourselves on our own on-premise data centre in Corsham in Wiltshire. That extended to employing a company that tried to break in physically and over the web to the data centre several times a year. We had our own company that attempted to break in and find whether there were any back doors, because as you probably know from your own work, sometimes the people who structure these data centres leave little back doors in them and you have to seal them all up, because otherwise you have a vulnerability and someone will find it.

In terms of the migration, we very carefully evaluated this. It fitted at the time with the Government's cloud-first approach, but we were assured that the security levels in Amazon were better than we could manifest in our own environment. I would always say, and I would say to any of you here, that we have always been very up front with participants to say that we will do our level best to secure their data, but I cannot absolutely guarantee that somebody will not manage to get into it. The participants know this. They are bombarded by scam emails or communications every day, so they know that there is a community of nefarious people who want to break into these data centres. We did have a phase of a lot of cyber attacks from various parts of the world, but they did not get in.

Baroness Willis of Summertown: Going back to the Amazon provision and just looking at gaps in the current provision, one of the things that many people are now aware of is the problem with the Amazon system that the costs are going up and up. How do you manage that aspect of it?

Professor Sir Mark Caulfield: Like UK Biobank, Genomics England negotiated an extremely good deal for early-career researchers and the younger people who might not have the grants to fund this, but you are right. There are some upsides of being charged back. For people who do not know this, the charges from the Amazon cloud are often charged back to a credit card, which might be a university credit card for a particular department or whatever. This provides a transparency in what they are using. Occasionally my younger colleagues do not optimise their code very well for the environment they are using it in, and they can run up significant charges because the code is inefficient at running in the environment. That is hidden on the on-premise inside Genomics England, but we at Genomics England—I am not there now—still pay for the compute for people using it, so it is not billed back to them at the moment. We negotiated a very good deal.

You are right that we will have to all review this, because right now on-premise storage is much cheaper than in the cloud. I acknowledge that. At that time, that looked like the best move, but Genomics England keeps this under review. I am not in touch with where its current thinking is, but you might be interviewing one of them shortly and maybe they will be able to put more flesh on it.

Baroness Willis of Summertown: One quick question related to that is about the Health Data Research Service. Will that service be able to tackle this, the economic issues and even things such as the basics of people not being very good at writing code and therefore using huge amounts of data space or computer space?

Professor Sir Mark Caulfield: We managed it at Genomics England. We did not aggregate 67 million people's data—that is a much bigger task—but some of the principles also apply. I am always available if they want to know what we did. Baroness Blackwood knows what we did, so she will bring that rigour and determination to get this right to that project. For the UK this is a bold move. It requires us to maintain trust and public confidence, but more importantly we have to get it right, because false starts have occurred before with big data projects and they create doubt within the scientific and medical community and the NHS, and they also create doubt among public and patients. We do not have that in Genomics England because we went the extra 1,000 miles to make sure that never emerged.

The other thing we did is that we always told them when we got something wrong. When something did not work, I would go in front of them and say, "We tried this thing and I thought it was a good idea, but it has turned out to be rubbish". Because we were open and transparent, people travelled on the journey. People who are affected by these

diseases know how hard this is, because they think that if it was easy, we would have had a diagnosis by now. They would not have been having to go through this.

Q8 Lord Winston: Can I come back, because it is a health service issue, to the training of doctors and the inclusion of genomic medicine and what we call precision medicine or personal medicine? Is there an issue there, because sometimes personal medicine is somewhat mocked by the idea that it is impersonal, that what we are doing is looking at a computer and training doctors to look at a computer much more than examining the patient? When we started doing medicine, that initial examination of the patient coming into hospital, the detailed examination of every aspect and the detailed history, is something that we no longer do. I sometimes wonder whether we have gone too far in looking at the results of tests generally, and at the computer screen, rather than at the patient's face.

Professor Sir Mark Caulfield: Do you mean, Lord Winston, that we have become too American?

Lord Winston: I found it in America a bit, too, but I think it is true here.

Professor Sir Mark Caulfield: They definitely do it that way around. They look at the tests and then they look at the person. Earlier I suggested to you that the number of clinical features you tell me, the more you tell me about that patient, the more likely I am to get an answer for you. We have to maintain the balance that you are highlighting. We are of a generation where we took a history, we examined the patient, and then we did some tests. Those tests were usually quite modest in number, very tailored, very much around a set of probabilistic characteristics that we thought were going to be the treatable diagnoses for those patients. We did not have the luxury of scanning everybody's head when they turned up in A&E because we did not have the scanners to do it, so we had to rely much more on clinical medicine. I think there is a balance to be struck between clinical assessment of patients, as we would have done it, and the role of tests. I emphasised at the beginning that to bring a precision medicine system live you need multimodal data. I need to clinically characterise you, Lord Winston, I need to do tests on you, I need your imaging, I need your pathology and then I might need your genome or other omics. That integrated multimodal data is what gives me the answer that allows me to give you either personalised or precision healthcare.

You highlight an important point, which is that there probably is not enough training yet on the role of precision medicine in healthcare at undergraduate level. We focus somewhat on traditional factors, but there is a pressure from some of the genomics community to improve the content level in the curriculum, and perhaps to remove some other things that we may need less of, so that we equip our young people for the healthcare informatics era that they are entering and for the genomic medicine era that they will also enter.

Lord Winston: As a brief corollary, do you not feel that that will be one

of the issues about trying to get genomic medicine much more part of medical care in the way that it currently is not?

Professor Sir Mark Caulfield: In my answer to Lord Willis I said that the structure that the NHS has now has been designed to deliver the service to hospitals that may not themselves have to know much about genomic medicine. They may consult with a genomic lab hub, the genomic lab hub may advise them on the appropriate tests, they may send their samples to the genomic lab hub, it will do the test, it will send it back and it will give interpretive information that will be used locally in cancer by the multidisciplinary team in the assessment of what chemotherapy or treatment they give the patient. I am saying that it is not necessary for every part to fully understand the elements that comprise genomic medicine or precision healthcare, but it is necessary that there are sufficient experts who can deliver that for an entire service that covers 57 million people—and Scotland, Northern Ireland and Wales as well, which is very important.

Q9 Lord Drayson: I need to declare my interests before asking my questions. I am a science entrepreneur who has worked in life sciences for a number of years, and I have roles and shareholdings in Locai Labs, Freevolt Technologies, Arcturis Data and Advent International.

Sir Mark, my questions will focus on the commercialisation challenges. I preface that by congratulating you on the undoubted success you have had in transforming care within the NHS. However, as you have said in your evidence, the NHS has invested £1.3 billion of taxpayers' money in this project since 2012, and, over the past 14 years, no return has come to the Treasury from this research programme. If we look at the companies that have been developed or have grown as a result of this investment, you have already mentioned all the cloud storage being done by Amazon, which is a US company. The one spin-out from the Sanger, Congenica, was acquired last year by a French company. The sequencing was done by Solexa, then taken over by Illumina, and is now all done by an American company. The AI comes from another American company: Isomorphic Labs, which is owned by Google. Why is it that the undoubted commercial opportunity that has come out of this investment has led to no return at all back to the Treasury to help fund future care by the NHS?

Professor Sir Mark Caulfield: I am very happy to answer that. Earlier, I mentioned that Illumina invested in Britain as a result of its contract—£70 million—but I accept that that did not necessarily come back to the Exchequer. In terms of the mission that we delivered, the area where we are yet to fully realise the benefits of this is in having a commercial platform that stimulates substantial inward investment. That is just an honest answer, first of all, and getting it out there.

You mentioned Congenica, a Sanger spin-out. For several years, Genomics England supported Congenica in getting itself to an analytic level where it had a strong business proposition. It has done that. Congenica is a success story, but, in effect, we made that platform available and paid it to deliver the service to us; it did diagnose rare

diseases in the early stages. We had more than one company. Another one, the name of which I have forgotten, was also involved at that time, and we paid it. You are absolutely right to highlight the extent of investment required, but the Exchequer will most likely receive the value of this project as benefits in costs saved, as opposed to cash generated now. You are a former Minister—

Lord Drayson: I am sorry to interrupt you, Sir Mark. I absolutely accept the benefits to the Exchequer from the improvements in health outcomes from the NHS. I am focused on a very particular problem that this country has, which this committee has investigated and recently issued a report on: the failure of this country to ensure that the science it invests in, using taxpayer money, leads to growth, investment and economic return to fund this country in future. The model that has been pursued by Genomics England—the 100,000 Genomes Project—and other projects, such as UK Biobank, all follow the same principle, which is that the IP generated is not harvested by an economic body that provides a return back to the UK, unlike what was done in Iceland, what has been done in Estonia and what has been done in Qatar. Was that a mistake?

Professor Sir Mark Caulfield: There is a duality of mission here that creates a small conflict. We were set up to transform patients' lives in the NHS. We were also asked to generate a commercial income. Doing both simultaneously can be hard. I accept that we could have done it differently; with hindsight, we possibly should have. When we attempted to stimulate the market using the platform of the project, there were not, at the outset, many mature companies that were able to take advantage of it. However, we did stimulate an industry. Congenica is a good example that you gave earlier. On whether we did it enough, it is probably the one area that I look back on with some regret because we did not manage to do more.

Lord Drayson: As you have said, this has been a tremendous success story in one dimension, in terms of the health outcomes—I accept that these are the most important thing—but it has failed totally in the other dimension throughout a series of Governments. So this is clearly not a party-political problem; this is a problem that has beset Governments over many years. What would your advice be to this Government on changing their policy relating to such projects, such as Our Future Health, UK Biobank and Genomics England, to stop this happening once and for all?

Professor Sir Mark Caulfield: The benefits of the project are a bit more than one-dimensional; I will push back on that. I agree with your point about commercialisation and commercial opportunity. We have to do better. You had Lord Vallance here recently. I should declare a conflict: I am on the MRC, but I am not that close to this because it is relatively recent. The assignment of moneys to buckets, with an overarching ambition of growth, is designed by UKRI to address this from public funding in future. That is a start base. The message that has been

received in United Kingdom universities is, "If you're not showing us that you're going to generate some growth, we might not fund your research".

Lord Drayson: That is very good to hear, Professor, but Genomics England is an example of a government company.

Professor Sir Mark Caulfield: Exactly.

Lord Drayson: I am looking for your advice relating to government companies. My proposition is that there is a cultural problem in the NHS in that these matters of commercialisation—I speak from some experience—are not taken seriously. It is not seen as a core role of the NHS to generate wealth to pay for the NHS or to contribute to paying for the NHS. Do you think that that is fair?

Professor Sir Mark Caulfield: These are important points, and I accept them to an extent. As I said earlier, one of the things this committee might choose to do is recommend a more agile approach to technology adoption and a route to market, which is a vital part of this process and which we have been slow to do. If it takes nine to 16 years to adopt a piece of clinical research, will companies bring to us their big trials, which could generate income and help the NHS? The ambition that has been enshrined in Lord O'Shaughnessy's report and in the statements you make needs addressing. I agree with you in principle that we need to do more to generate growth and opportunity. However, even my academic colleagues have smelt the coffee. They know that, when UKRI funding comes back online, particularly through the MRC, we will need a different approach. There are some things that the Government cannot do on their own. The community has to step up to the plate and do them. I feel that, although there has been some criticism of the current strategy, in the current worldwide climate, we do not have much of a choice because the growth will not come from anywhere else unless we grow it ourselves. There is no cavalry coming.

Lord Drayson: That is very interesting—indeed, no cavalry is coming. Has the board of Genomics England smelt the coffee?

Professor Sir Mark Caulfield: I have not been on it for five years. I need to be honest: I cannot say what it is thinking today. When I was on it, commercial was a priority. It was difficult at that time to do the things that the commercial companies always wanted with the level of activity that they would require on our side. Therefore, we prioritised, as I hope you will understand, the NHS mission of delivering a transformed genomic medicine service, which we did. However, I agree with you. For me, this is not so much a "lying awake at night" area, although it does trouble me that we did not generate more inward investment that was beneficial.

Lord Drayson: Given that this is NHS money, controlled by NHS England, does the NHS have the expertise to do this? Is it that it does not want to or that it does not know how to?

Professor Sir Mark Caulfield: In some places, it does. For example, at some of the larger NHS trusts that are linked to larger universities, there is very good IP infrastructure and commercialisation of some advanced therapies. Imperial College, where Lord Winston is, has a very good track record of doing that across medtech and other areas. UCL has a very strong track record. We have spun out a number of companies at my university, and we often do that work with the NHS.

When you ask, "Does the NHS have the infrastructure to do it?", if it has a strong university partner, the answer could be yes, if that partnership is strong. Where it may not have that infrastructure is where it is a stand-alone trust with no obvious university partner. There, we need to build an ecosystem; that is why I put it in my five things for you guys to do to make the NHS more agile and ready to adopt technology. If we do that, Lord Drayson, the money will follow the adoption.

To give you an example, at the moment, I am working on a 1 million square feet life sciences estate in Whitechapel where Queen Mary, Bart's Health, the local authority and the community want to build an extensive life sciences estate that invents and has small and medium-sized enterprises next to the hospital to test and deploy in the hospital and in the community. We want to invent, test and deploy. That is the successor version of this. I am saying that we need to do more of that and harness more of it.

We also have to change how we look at this from a regulatory standpoint. We are becoming far better at accelerating new therapies. Previously, we would have looked at things such as the gene therapy for sickle cell, which I mentioned, and said, "Nah, we're not going to do that". Nowadays, we are much better at doing it because we are thinking about total societal cost. The cost of not addressing these diseases is enormous but, because it is buried in various bits of the tax system and the Exchequer's mission, it is not visible to us. You have to calculate it because, suddenly, expensive things look like good value.

Lord Drayson: Thank you, Professor; that is really helpful.

The Chair: Sir Mark, you have been wonderful. I have a final question to ask you. I am conscious that Professor Birney and Dr Goldstone have been waiting patiently.

Professor Sir Mark Caulfield: I am sorry if I have kept them.

Q10 **The Chair:** Not at all. You have been extremely informative, and we really appreciate that. Is there a workforce problem in terms of the ability to attract, recruit and retain clinical academics, clinical geneticists and bioinformatics experts in the structure of the NHS? Everything you have been describing points to the huge importance of the workforce.

Professor Sir Mark Caulfield: What we did with NHS England was generate training programmes to build capacity in advance of this; it has been somewhat successful in plugging some of the gaps. I would say that

there still is a gap in the area of bioinformatics and analytics. We are trying to plug that training gap, together with the NHS. The bioinformatics element requires universities to join the NHS to train people, because they have, through their scientific groups, access to some of the datasets that will allow them to cut their teeth on this type of analysis. It is a non-trivial undertaking, but we have to do it.

There are some gaps, but, in clinical genetics and other areas, the important thing is to go back to Lord Winston's earlier point, which was absolutely correct. You have to mainstream things in medicine, not keep them as the preserve of a few. Let me give you a final example. In the 1980s, I was the first HIV house officer at the Royal London Hospital. We used to have to phone a counsellor to come and speak to a patient for an hour before we did an HIV test. It became very difficult; there was a lot of tension around it and concerns about it. When I registered with a new GP recently, the nurse asked whether I was okay with having an HIV test. I said that that was fine. Things need to be mainstreamed because, if they become the preserve of a few, a false market develops: a small number of people hold on to something when it should in fact be more generalisable.

I am with Lord Winston on training the majority of our clinicians, nurses, allied health professionals and midwives better to face the world of precision medicine and genomic medicine, so that they at least know in their day-to-day practice from whom they need to seek help and can get to the right person. When we do that in medicine, typically, in the NHS, we are at our best, because we cannot possibly know everything in the modern world, but we need to know who to call and when to call them.

That addresses Lord Willis's point about a CEO not knowing much about this. There will be some people in our organisation who do know something about it, but they will not know as much as the genomic lab hubs, if you see what I mean. We are trying to apply the resource at the most effective point to deliver a national service that is equitable and gives regional equity to 57 million people. There probably are some things, as Lord Willis highlighted, that we could do better in distributing that knowledge. The position is that there is an ongoing capacity-building exercise, but there is also something about mainstreaming and upskilling our existing workforce and not relying on something new that we have to invent at great expense when, if we mainstream it, everyone can become engaged.

The Chair: That is a very good point on which to end.

Professor Sir Mark Caulfield: Thank you for having me. It has been a privilege.

The Chair: You have answered many of our questions extremely well and been very informative. We are very grateful. Thank you again.

Professor Sir Mark Caulfield: I thank you all very much for your time. I am happy to come back if you need me to do so.

The Chair: We will suspend the session now while we get organised for the second session.