

Science and Technology Committee

Oral evidence: [Genomics and genome editing in the NHS](#), HC 349

Wednesday 1 November 2017

Ordered by the House of Commons to be published on 1 November 2017.

[Watch the meeting](#)

Members present: Norman Lamb (Chair); Vicky Ford; Bill Grant; Adam Holloway; Darren Jones; Clive Lewis; Stephen Metcalfe; Neil O'Brien; Graham Stringer; Martin Whitfield.

Questions 1 - 96

Witnesses

I: 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.

II: 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.

Written evidence from witnesses:

- [Association of the British Pharmaceutical Industry](#)
- [National Institute for Health and Care Excellence](#)
- [NHS England](#)
- [British Society for Genetic Medicine](#)

Examination of witnesses

Witnesses: Dr Papadaki and Professor Sir John Bell.

Q1 Chair: Welcome to both of you. Thank you very much indeed for your time. We have a number of questions to ask you. My questions to start with are addressed to you, Sir John. The Industrial Strategy Green Paper highlighted your work on a life sciences “sector deal” as one of the ones identified, and your report was published in August. Did you ask the Government for the opportunity to pursue a sector deal, or did they come to you to put that proposition to you?

Sir John Bell: They put the proposition to me, although as we developed the report it was always part of the discussion that there would be a sequencing. I would try to lay out a strategy that was one that was worked up by industry but in collaboration with government to create a holistic strategy that we all felt we could deliver, and in the subsequent weeks or months we would put together the first wave of the sector deal. That turned out to be quite complicated because there is a whole set of deals all rolling in and the interesting question is: do you stop and do it now or wait a bit? Those are the conversations that are going on at the moment.

Q2 Chair: But in the run-up to the Green Paper they came to you to ask whether you would be willing to lead on this.

Sir John Bell: They did.

Q3 Chair: On the same day you published your reports there was the announcement of additional funding of £160 million over a four-year period.

Sir John Bell: That is right.

Q4 Chair: Was this a co-ordinated announcement? They knew what you were proposing and broadly agreed to it, and a negotiation about money took place.

Sir John Bell: Yes. I was less involved in the detail of the money than in the principle. I tried to make this a report that everybody bought into, so it required quite a lot of conversation with the NHS. There is no point in plonking down an industrial strategy that does not work for the NHS. It needed to work for BEIS and the industry. There had been quite a lot of to-ing and fro-ing so they knew what was coming. Manufacturing was a rather important piece of that, and that £160 million was focused largely on state-of-the-art manufacturing capabilities for the UK, which is a space where we had emphasised the need to catch up, because we had fallen badly behind in life sciences manufacturing for a variety of complicated reasons, but we see that as a very important part of the strategy going forward.

Q5 Chair: Are there still areas that need to be sorted out and agreed with government as we seek to implement the plan, as it were?



Sir John Bell: Yes.

Q6 **Chair:** If so, what are those areas?

Sir John Bell: We are in the process of negotiating some of the HARP projects listed in the report. This is the health advanced research programme. These are the large infrastructure or rather bold experimental-type structures. We have an interesting conversation going on with UKRI at the moment as to what it and industry might contribute to make those a reality. In all the cases we are looking at, we have very significant industry investment of at least 50%, in some cases 60% or 70%, with Government playing a less than majority role, not a minor role, in terms of funding. Those are going through the system at the moment. They have not been finally approved, but we are having good conversations about them.

There is a longer-term issue about things that will be fundamentally harder to achieve. If you are an American company wanting to build a European manufacturing base for your pharmaceuticals or a new RNA therapy, of which CRISPR would be a good example, and the Czech Republic says, "We'll give you £20 million," Ireland says, "We'll give you £78 million," and, when you come here where the science base is unquestionably the best, you say, "We really want to be in the science base," but the UK says, "If you want any money we're not giving it to you," there is an issue. It is not an easy one to solve, because working out how you distribute money like that and where it comes from in significantly challenging financial times is hard, but we need to work our way through that to try to land this.

To remind you—I am sure you have read the report—this is the most productive sector in the UK economy, and that is the most productive bit of that sector. Manufacturing of pharmaceuticals generates enormous value to the economy, so if we can grab it we should do so. I am not saying we should write a lot of cheques, but we need to think about how we incentivise people to invest inwardly and build that capability in the UK.

Q7 **Chair:** Your report argues that we should be aiming for the upper quartile of OECD funding of R and D spend and we are not there at the moment. It has been put to me by many that we need to have incremental increases. We cannot later on in the period during which the Government are aiming to hit that target suddenly chuck in a load of money because it will not be well spent. Are you hoping for an incremental increase in the budget this year?

Sir John Bell: To be clear, the Government and Treasury have been very generous to the science base in the UK. We have an uplift of more than £2 billion coming into the science base between now and 2021. I think we will have quite a hard time spending that really well, and a big load of new cash on top is probably not the right solution; but looking forward from 2021 we need to continue to grow our science base. Taking a bit of



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time over that is right, but we should not wait until the ninth year out of 10 and then say, "Now we are going to load you up with a ton of money," because that is not a very effective way of getting money out systematically.

The second important point about the R and D figures is that they relate to both private and public sector spend. One of our problems is that our industrial base in the UK is not as knowledge and R and D-based as it should be. Again, life sciences are by far the dominant player in the R and D space. The trouble is that heavy manufacturing is not very R and D oriented; there is basically no R and D in mineral extraction. We need to think quite hard about what the mix is and encourage the growth of knowledge-based industries that will put a lot of effort into the R and D activity. You will be familiar with the paper from the Treasury on funding innovative companies that is out for consultation. We welcome that very strongly because, if we can find a new mechanism for private capital to be deployed in knowledge-based industries, we will generate a very big growth in R and D without the Treasury having to produce all the money. The private sector has a responsibility and role in this space, and we need to expect it to help.

Q8 **Chair:** I take all of that, but to go from where we are, which is approaching 1.8%, is quite an ambition. I think 2.4% is the average, and the aim is to get there by 2025.

Sir John Bell: Yes.

Q9 **Chair:** We will be at 1.8% in 2021. It is going some to get from 1.8% to 2.4% in a four-year period, is it not?

Sir John Bell: You are absolutely right, because I have done this thought experiment myself and thought, "My goodness, how are we going to get there?" Heavy reliance on Government spend makes that near-on impossible. If you expect the public sector to carry most of the weight in that growth period, it will not happen. One of the interesting things to emerge from the Treasury consultation on innovative firms is the fact that more than £3 trillion of capital in the pension industry is sitting in the City, but we still operate by the "prudent man" rule America operated in the early 1970s, which makes it almost impossible to invest even a tiny amount, say 1% or 2%.

Q10 **Chair:** You are saying the US has moved on from that.

Sir John Bell: The US moved on in 1974, and a great burst of venture capital came in the second half of that year; it almost happened like that.

Q11 **Chair:** With no adverse consequences.

Sir John Bell: I do not think the US pension industry is any worse off than ours, frankly. When you look at the mix of investments that we currently almost insist our pension industry invests in—gilts and long-term bonds—it is no wonder our pensions are all under water. There are



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risks associated with this, because you cannot just pour vast amounts of that money into the risk-based highly innovative sector, but, if you do the thought experiment, if most of that money goes into the tech centre, broadly defined as IT, green energy, life sciences and the like, it will all be spent on R and D. You get your numbers quite quickly if you want to get to 2.5%. The real question is making sure there is not a big accident on the way, because if you have a lot of pension money and managers who do not know how to manage it, who lose all of it, then we are never going back. It needs to be handled with a bit of caution, but if in the period 2021 to 2025 we can get some of those things in place quite a lot of the R and D growth will come hopefully by the deployment of capital from the private sector.

Q12 **Chair:** That is very interesting. Dr Papadaki, welcome. My question to you is: does the ABPI fully sign up to Sir John's report? Are there any areas you would like to have been given a different priority?

Dr Papadaki: Our members believe that the life sciences industrial strategy is a very strong blueprint and robust document that can put the UK in a very strong position to reap the benefits from health advances and the scientific innovation that has been happening for at least the past two decades.

We believe and expect the Government to show a level of ambition through a sector deal that can fully meet the recommendations of the life sciences industrial strategy and cover the entire value chain. Referring to a specific point in your introduction, this is not only a living document; it has to be applied in full, looking end to end from basic discovery all the way to the absorption of innovation in the health service but also skills and making provision for a long-term talent pool here in the UK.

Q13 **Chair:** Essentially, you endorse it.

Dr Papadaki: Yes.

Q14 **Neil O'Brien:** Sir John, genomics runs all the way through your recent report. Can I ask you to summarise in a nutshell which of your recommendations are the most important? In particular, of the different things you are recommending which do you think will be the most difficult to bring off successfully, and how do you suggest we do that?

Sir John Bell: During the course of writing the report we did a thought experiment: what will healthcare look like 20 years from now? If you want to build industries, you should build them for the future. Although you invest now, you are really looking at a 10 or 20-year timeframe before they get really exciting. If you look at antibodies, the early work on it was done by Genentech in 1999. You know what it has done; it now dominates the whole sector, so the ability to get into some of these domains early is important.

When we did that thought experiment a few things floated very rapidly to the surface. One of them was the ability to use genetics to predict



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disease much more effectively but also to identify patients who would or would not respond to drugs, to stratify patient populations and make the treatment of cancer much more precise and efficient than it is now, because it is on the verge of breaking the healthcare system and we need a way to do that. We could see enormous numbers of opportunities to do that.

There are several things that will look after themselves. One is that the technology will drive down the price of doing genomics very dramatically. Some of you will have seen the dramatic falls in the cost of DNA sequencing that led to the creation of the Genomics England and the 100,000 Genomes programme. All of that was driven by the price coefficient in the formula, so in a way that looks after itself.

What does not look after itself is the handling of data. There is a very big data analytics problem here, because we are talking about more than terabytes of data that will have to be carefully stored but also analysed to be able to extract the optimal outcomes for patients in the system.

If you had asked me this question three years ago when you and I were having other conversations, I would have said the biggest problem is to get it embedded in the national health service because it does not do innovation well and these sorts of things cause all kinds of trouble, but I think we have got over that hump and it has embraced genomics in a way no other healthcare system in the world has done. I think it needs credit for that because this is not easy. It is new technology; nobody quite knows how to use it. There was quite a big pilot study in which it was heavily involved, but our success in genetics at the coalface has been in very large part driven by collaboration with the NHS, which has been very helpful. There are big challenges on data management, but the other bits seem to be working pretty well.

Q15 Clive Lewis: You have just mentioned that the NHS has done very well. Are there any specifics in terms of how the NHS is structured that has put it in a position to benefit from and go on the front foot of genomics, because I see that some insurance-based systems may not be able to cope in the same way that the NHS has? Can you talk us through that?

Sir John Bell: As always, there are strengths and weaknesses. Let me talk first about the strengths. It is a single payer healthcare system with a unified structure. It used to have 23 genomics labs doing small tests all over the country, which was very cost-ineffective. If there is the ability to consolidate around a single platform of genomic sequencing provided at a very low price to inform decisions being taken and driven by lots of people around the system, only in a healthcare system like the NHS can you get to the point where you see that work and you can pull a lever and say, "Hey guys, we're not doing this any more. We're going to step down the 23 small sites and create a set of larger sites. We're going to have a hub that does most of the sequencing and save a ton of money."



NHS gets badly beaten up for being unable to do those productivity gains. I think this is an example where it is on track to generate productivity gains, but, to be clear, 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. I think there is a very important message there about how we do other service transformation activities in the NHS, which is one of the great challenges for the next five years.

Q16 Stephen Metcalfe: Our inquiry is into genomics and gene editing. I want to take us back a step. First, how closely related are those two issues? Does one feed into the other? Secondly, what are the challenges and benefits of the two different technologies? Can we do different things with them?

Sir John Bell: You have it exactly right. You need an understanding of the genome and how the bits of it relate to individual diseases before you can start snipping bits and replacing them; otherwise, you get into really big trouble. All of the knowledge base will be driven by an understanding of the genome.

Some of those genetic variants are present inside the genes that produce proteins and they will be the first place the gene editors go for, but there is also quite a lot of very important information that sits outside the genes in regulatory sequences and the like. There is an enormous opportunity to modify the risk of disease by changing those regulatory elements that will allow you to alter the risks of things like cardiovascular disease, some forms of cancer and neurological disease, because those are the key genetic determinants of those disorders. You need to sequence the whole genome.

The thing that the UK does better than anyone else in the world is sequencing whole genomes. That is what we do. You will go to lots of places and they will say, "Why don't you just sequence the exomes?" Our view is that exomes are pretty interesting, but there is a ton of information outside the exomes, and for gene editing that is what is of most interest. Indeed, I saw a Boston-based gene-editing company two weeks ago that is looking at doing things in the UK. What it is very attracted to is our genomics programme, which will give it all that data. That is why it would like to relocate some activity in this country.

Q17 Chair: Are we alone in that or are other countries looking at the whole genome?

Sir John Bell: We have a big head start. There are other countries going pretty hard at this. Iceland has had a programme in whole genomes for quite a while, but it is a small country of 250,000 people, so it will be hard to compete. I do not know how many years ahead we are, but we



are multiple years ahead of the rest of the world in handling whole genome data.

Q18 Stephen Metcalfe: Once you have that whole genome data, are there things you can do with it other than use it to feed the gene editing?

Sir John Bell: All the prediction of disease and understanding of disease pathogenesis comes from a close interrogation of the genome. I will give you some interesting data in cancer. It turns out that cancer can be caused by environmental factors—smoking and the like—but it emerges that those factors produce cancer by altering the genome, so it is actually a genetic disease. Once it gets going, the variation it incurs because of the instability you get in the genome produces lots of mutations around cancer genomes.

So, what you want to do is sample the cancer and sequence it to find out what the landscape for genetic variation looks like. No one has done that at whole genome level. Genomics England were the first people to do it. When you look at the first 1,000 genomes that have come out of that bit of the programme, 60% of people have actionable mutations in their whole genomes. By “actionable mutations,” I mean there is something in the genome that tells the doctor there is something that can be done to help the patient. That is six out of 10. If you are a person with cancer—and this is a really interesting question—why would you not want your genome sequenced? That is where we are trying to get to.

Some of it is about whether they have a bad disease or a less bad one. Do they need chemotherapy? Do they need targeted therapies? Are they going to get metastases and, if so, where? Those are the kinds of things we imagine we will learn from the genomes in malignant disease, so it is a game changer.

Q19 Stephen Metcalfe: We like talking about game changers. How far away is this game changer?

Sir John Bell: We now have several thousand genomes in GeL from cancer samples. These are really noisy because there are lots of mutations. We can extract quite a lot of information, although we know we are leaving lots of other information behind, so there will be an evolution in the amount of data we get out. Genomes are now being used in some centres to look after patients. We do that in Oxford. We will regularly sequence the genome of a patient, and, on the basis of that, the doctor will make certain decisions.

I can tell you an interesting story about a patient we saw not long ago. She had endometrial cancer. The pathologist looked at it. She was a relatively young woman with three children. Everybody said, “This is really bad. Things are going very badly. You will need radiotherapy and chemotherapy and be sick for a year, and even then we don’t think we’ll save you.” We sequenced the genome and said, “No, no, no. This is a completely benign disease. You can go home and spend time with your



kids. It's fine. You don't need chemotherapy or radiotherapy. Forget all that." She is fine. It would be nice if we were doing that across the whole of the NHS, which we are not, but the ambition has to be to make that available to everybody.

Q20 **Stephen Metcalfe:** And that is by sequencing the whole genome.

Sir John Bell: Yes. We would not have got the data without the whole genome. It turned out she had a mutation in a very interesting protein. It was a POLE mutation, which is a polymerase that replicates DNA. She had an error in the polymerase that produced lots of interesting products. It is a complicated story, but it was a classic one that had good patient benefit.

Q21 **Stephen Metcalfe:** Briefly, how long did it take to do that sequence?

Sir John Bell: Routinely, we do them in a couple of weeks, in the timeframe necessary to make decisions about patients.

Q22 **Stephen Metcalfe:** That is a tangible example of sequencing the whole genome, but in terms of genome editing how far are we from therapies?

Sir John Bell: Maybe I should get Magda to talk a little about that.

Chair: Please come in if you have a contribution you would like to make.

Sir John Bell: I talk too much; that is my problem.

Dr Papadaki: To make sure it is clear what genome editing is not, when we talk about genomics we mean the ability to sequence an individual's whole genome and we also include the technologies we use to do that, which is genomics; it is a bundle thing. Using that information to tailor medicine or discover medicines specifically for a patient, or assess their risk of getting a disease or not, is what we call simply genomic medicine or precision medicine and high-end precision medicines.

Genome editing is something very specific. You will be interested to know that generally these are molecular mechanisms that exist in other organisms as well. John mentioned cancer and bacteria. We use it to create very precise scissors to cut and paste the genome the way we want it so we can get rid of faulty genes and put in the right ones. Industry and clinicians believe that this can generate the therapies of the future. You have probably heard that cell and gene therapies are the next wave of transformative therapies. We believe genome editing will exceed even the promise of those by increasing their accuracy.

Genome editing is not just a therapeutic; it can also be used as a tool. We can use it to create new types of cell lines for animals that more closely resemble the disease, so they can help us tailor drug discovery as well. Genome editing is a much broader church in the things it can be used for.

Q23 **Stephen Metcalfe:** But in terms of delivering those genome-editing



therapies you spoke about, how far away are we from seeing them regularly deployed across the country—or the world even?

Dr Papadaki: Taking a step back, genome editing is going to be a part of what we call cell and gene therapies, or advanced therapy medicinal products. You might have heard of them as ATMPs. 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, and even fewer reimbursed. Although they are very promising, their uniqueness is that they promise even to cure disease and certainly have a longer-term management of disease than traditional small molecules. Gene editing is already in clinical trials as a subset of gene therapies, but it came out of the banks and 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.

Sir John Bell: As to the big challenges in all these forms of gene therapy—Magda is right in saying they form a group of normal therapies—to be clear, the UK does not want to miss out on it. 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. This particular CRISPR Cas9 methodology, which is the fashionable term for gene editing, has the ability to clip out and replace literally single base pairs or clusters of base pairs. There are things you need to know before you start to deploy that at scale. We saw a few interesting experiments in human cells and probably in humans in places like China very early on. That sort of stuff does not go on in the US or Western Europe, rather helpfully.

The things you need to know before you start to deploy are: what is the real specificity of these tools? Very often, specificity is crucial. If you get to the bit you want to excise but you also have a 1% noise where you clip something else out that you do not want to clip out of the genome, that is a bit of a disaster. People have been working through specificity. I have to say that, originally, I was a bit sceptical, but I am encouraged that they will be highly specific.

If you administer them systemically, you also run the risk of changing not just blood cells in the periphery but germ cells in your gonads, which produces a heritable change in the genome. There has been a view that, in principle, it would probably not be a good idea because of long-term evolutionary issues to start fiddling around with germ cells. I have been reassured that that appears to be very low risk, but I have not seen the data. I think the regulators will be pretty interested in that before they push the button to let it roll out. We have to go through a couple of steps before we are ready for prime time with CRISPR, but companies exist and interesting things will be done in the next few years.

Q24 **Vicky Ford:** I have a bunch of questions about the NHS in this area. You have both called for the NHS to engage more actively with the life sciences industry. How do you think the current partnerships among the NHS, Genomics England, academia and industry are working, and what



actions would you prioritise? I am going to ask Magda to go first.

Dr Papadaki: Genomics England and the 100,000 Genomes project is a very successful example of early engagement. Industry already has about 13 partnerships working with genomic medicine centres to create a seamless route to precision medicines they are discovering all the way to the NHS. They are building early on that relationship and working with them to understand how to adopt them.

On John's earlier point about the management and analysis of the magnitude of data produced, we have also seen that the early engagement with industry has started to inform the thinking of the NHS about the appropriate and safe storage of data and data sharing between external partners and between companies and the NHS; appropriate clinical reporting; and patient enrolment. All these external networks need to be in place to start embedding genomic information in the NHS.

It is a very productive dialogue so far. Despite the fact Genomics England and the 100,000 Genomes project strongly position the NHS as a very important national resource, we see persisting challenges, especially around the commissioning of diagnostic and screening tests. This also hinders further down the adoption and use of patient-tailored medicines. First, you need to screen the population; you need to use the diagnostics so you can narrow down and identify the patient groups who will benefit from the drugs. If you are not using the diagnostics and applying them, you cannot use the medicine further down.

There were very clear recommendations in the life sciences industrial strategy through the HARP project for the NHS to start rethinking and restructuring the networks it has in place. We welcomed the recent action by the NHS to start recommissioning its national genomic laboratory hubs and linking them with its national testing services, as well as the national genomics services, to create a network that can ultimately secure equitable access by all the patients across the UK to the latest technologies and tests, but also ensure that they have good quality analysis and, further down, contribute economies of scale and reduce cost because there is no variation, and also secure reproducibility and replicability of the analyticals of genomes and standardisations. What are the risk thresholds we see with a specific test for individuals to get cancer? Tackling that variability across centres and establishing a standardised practice across the NHS will be very valuable.

Sir John Bell: I agree with that entirely. In the genomics area, the NHS is a bit of a model for other people to follow. You can write that down because I will not say that very often, but in this space it has been terrific.

Vicky Ford: The NHS is terrific.

Sir John Bell: Exactly, and it is a wonderful combination. You have the ability to do things at scale. Fifty-five million is a lot of people. You now



have increasingly remarkable longitudinal records of patients from birth to death. They are largely digitised and are hugely powerful if you are trying to analyse genomes against clinical outcomes. It has increasingly adopted the model set up originally by GeL quite aggressively. I think that in the end it will have adopted this in cancer as well as in rare disease. It is a model of how the NHS can transform its services by adopting innovation. It is often criticised, rightly, for being slow to adopt innovation, but in this case it was quite fast. I think there are lessons to be learned about how we can make that happen again and again.

- Q25 **Vicky Ford:** I want to drill down on access to the data. You have described this discovery forum as a reading library. You can access the data but cannot share it with or download it to other third parties. Some of the people who wrote to us suggested it was still not clear enough how industry was accessing that data. Is it clear enough? Is it working well? Are the restrictions balanced?

Sir John Bell: In the first instance, the database for holding it was the hardest bit of the project. To be honest, we did not think it was going to be the hardest bit but it has turned out to be. The reason is that ultimately you want complete data security because this is people's data, but you also want people to get in and work on it because it is valuable only if you are comparing one genome to the next with other stuff.

At the moment there are a number of both academic and industrial partners doing research on the data. There is not very much of that going on at the moment. The 100,000 Genomes project set itself out to service the clinical need first, which is the right thing to do. That was the first objective. The second objective was to create a resource for the discovery enterprise that will help us deliver better medicines in the future. We are just getting to that now, but it is being used in that way. Those who have used it report that they have had success in trying to get at the data they want without removing any of it. To be clear, all these patients have consented that their data can be available in this way.

- Q26 **Vicky Ford:** Should the NHS charge for access to that data?

Sir John Bell: This is a really interesting question. These companies are paying for access to the data. This has even more relevance when you get into artificial intelligence in the NHS. As my report says, if you identify the distinguishing features of the UK going forward and its competitiveness in life sciences, they are twofold. 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.

If companies are using anonymised NHS data to make algorithms and sell them to other healthcare systems, what does the NHS get out of it? I have argued in the report—it has been picked up by some of the newspapers—that there needs to be an agreement that something has to



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come back to the UK taxpayers and the patients of the NHS because it is indeed their data that is the source of value. There is a misunderstanding, in part generated by Google, that this is all about data analytics and machine learning. It is not. We could both do machine learning if we wanted to, but what we cannot do is get access to very large amounts of high-quality data. All the value in this is in the data.

We need to work out ways to make sure the NHS and UK taxpayer benefit from the fact their data has been used to create new algorithms that get used. I will give you one example that is out there at the moment. A small company has developed an absolutely transformational approach to analysing images of people who have heart disease that greatly enhances the ability to identify people who are going to drop dead and those who are not. That is a pretty helpful thing. It is all based on 10,000 stress ultrasounds done in cardiac patients, consented as well, but the company has decided that it would like to provide that for free to the NHS. It will not charge anybody in the NHS for its use, but it will continue to get the flow of data from the NHS so that it can continue to enhance its abilities to detect disease better and better. It started as being 80% accurate; it is now 96% accurate, and it will go to 100% accuracy. This is a really big step. It would like to make sure that is available to the NHS for free and charge everybody else \$100 a pop. It will be based in the UK, pay tax in the UK and employ people in the UK.

We want to avoid people coming here, extracting knowledge from NHS data, heading back to San Francisco, selling it all from there, paying tax in the US, not here, and employing people in the US, not here. Who created all the value? It was us. I am really keen on this. I think it is important we get the ground rules right; otherwise, we will be taken to the cleaners.

Q27 Chair: Does either of you agree with the Wellcome Trust Sanger Institute, which is concerned about lack of clarity around data-sharing rules? Does this act as an impediment to participation?

Sir John Bell: I am not sure it acts as an impediment. I think the risks are the ones alluded to. People would be quick to come and take data, do algorithms and scamper for the exit. We have to be clear about who gets access to what data and on what terms. They do not need to be punitive terms; everybody can share in the value here, but unless NHS patients see the primary benefit from this it is an issue.

Q28 Vicky Ford: In its evidence the Wellcome Trust points to commercial products that offer integrated sequencing databases that may appear attractive, but if it is a proprietary system the NHS does not have access to it and that locks in the system. The Wellcome Trust says that we should therefore use generic solutions for sequencing. Is that overly-simplistic?

Sir John Bell: I think that is quite a complicated argument. At the moment we should not be too worried about that because we lead the



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world in our interpretation of the genome, and we are going to do it better than everybody else. The day may arrive where there are other commercial products that we want to access, but that is not for now.

Q29 Vicky Ford: Is there anything else you want to say about algorithms, because in your report you say it is the combination of those and the data that is valuable?

Sir John Bell: It is the combination of both, and that will be hugely valuable because genomics will end up being a set of algorithms and how you interpret them with regard to outcomes.

Dr Papadaki: The business model becomes pertinent only when we have the connected genomic infrastructure of the NHS in place, but to do that it needs to bring together a number of data sources. It is not just about sharing but who owns the data. Currently, 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, so there is sharing or a business model that needs to precede what we are talking about here. How will all these data resources be brought together under the NHS banner? A lot of this, especially around rare diseases, might be shared globally with other jurisdictions. A rare disease clinical trial is jointly happening in the UK and Sweden, so it is a more complex argument.

Q30 Bill Grant: To what extent are NHS budget pressures or commissioning structures constraining the growth of genomics and genome editing in the United Kingdom? Are there budget pressures? I sense that the NHS was doing very well, so maybe it is quite a wicked question.

Sir John Bell: To be clear, the budget pressures on the NHS constrain almost everything, particularly in regard to the adoption of innovative technologies. We are by far the slowest healthcare system in the world to adopt innovation. I made the point that we would never have adopted genome sequencing had we not been part of a Genomics England programme that proved the principle. 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.

Chair: The old ways of doing things.

Sir John Bell: Exactly. We are not very good at that. We are slow to adopt; we do not make the investments to make new innovations successful; and we are really bad at getting stuff we do not need any more out the door.

Q31 Bill Grant: The recent accelerated access review on genomics made a number of recommendations. How applicable are those recommendations to genomics? Do any of them come to the surface as being vital or very important? They all have a degree of importance, but do any come to the surface that are significantly important?



Sir John Bell: The AAR is a good example of where you could apply this very profoundly to genomics. In a sense, the NHS for genome sequencing has done what we would hope the AAR would do. It took a look and helped to develop it, and when it saw it was likely to be successful it pulled it into the system and used its levers to get it implemented in the system. We would like to see it not just for genomics but a lot of other things—for example, for gene and cell therapy and 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.

Q32 **Bill Grant:** Would a single national diagnostics commissioning system improve access to genomic diagnostics? Would a single system be helpful?

Chair: Magda, I think you mentioned the commissioning issue a little earlier. Do you have a view on whether that is the solution?

Dr Papadaki: Absolutely. We totally believe that the nationalisation of both the laboratory services and the quality standards for that, but also commissioning and how the NHS understands and quantifies the cost efficiency in the use of whole genome screening and diagnostics, is the way forward. The discussion that has been taking place over the past two years on how this system will be rolled out, how the laboratories will come together and the regulatory standards to come out of that, is one that we are expecting to move forward.

On your question about AAR, the basic premise of it was that a lot of the innovations we are looking at—genome editing, cell and gene therapies and even the digital space—are putting the traditional system of research and development to the test. To change that, 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 AAR put into the picture. That is why we believe that the correct implementation, perhaps with minor deviations for a therapy area, treatment area or innovation area, will make a big difference for this country and its global offering.

Q33 **Bill Grant:** First, is there a problem or challenge about the way NICE currently deals with genomics? Secondly, for my own understanding, you told us a lovely story—a delightful story—about a young mother who was diagnosed using new technology and she is back home. I am sure we all welcome that. Would the diagnostic abilities of genomics dovetail with existing diagnostic systems, or would they be a parallel system of diagnosis using genomics for particularly special or difficult cases?

Sir John Bell: I think the whole field of molecular diagnostics will bring together genomics alongside other diagnostic tools, which will give you much more precise information.



Q34 **Bill Grant:** It is another tool in the toolkit.

Sir John Bell: Yes. It happens to be quite powerful, but there are other very powerful tools. We must not forget about things like digital pathology and those sorts of things, which also need an opportunity to develop and expand. Digital pathology is a good example where the NHS has not adopted something. It was raised in the Carter report. We have been talking about it forever and have made strong recommendations, and we are now moving forward through the industrial strategy to try to get it implemented, so that is a good example.

Can I talk very briefly about NICE? 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. A lot of this is about the diagnostic odyssey that people take to get diagnosed when they have a genetic disease and no one knows what is wrong with them. If for a relatively small cost you get the answer from a genome, that is really powerful, but it is also about how you fundamentally change the value proposition for healthcare systems. If you say—this is part of my 20-year thought experiment—that one of the key things that will happen 20 years from now is that we will all be diagnosed with our chronic diseases long before they are symptomatic, we will move the whole diagnostic framework way forward.

Q35 **Chair:** There are enormous consequences, including psychological ones.

Sir John Bell: There will be lots of psychological consequences but also benefits. If you ask me about the best way to cure cancer, it is to diagnose it early; it is the best way. You can develop all kinds of fancy drugs, but the truth is that if you diagnose it early you are done. You have your pancreatic cancer for 14 years before it presents and you die six months later. The ability to detect disease early—I mean cardio-metabolic disease, diabetes and probably mental health disorders, cancer and the like—will be hugely powerful, and will change fundamentally the way we run our single payer healthcare system.

Q36 **Chair:** In the case of dementia, which at the moment appears to be resistant to any solution, one can imagine a lot of people being affected pretty badly if they know they are likely to end up with that condition.

Sir John Bell: Part of this is the hope that you will have interventions that will work for people earlier. The experience of therapeutic trials in the pharmaceutical industry so far is that late-stage treatment of dementia patients, when they have very large amounts of fixed amyloid in their brains, simply does not work.

Q37 **Chair:** The route to a solution is early diagnosis.

Sir John Bell: Yes, and the same applies to diabetes and cardiovascular disease. If you do the thought experiment, I think that 20 years from now most people will be being screened for these chronic diseases in



their 30s and 40s. When you find things that are not right, you will probably prioritise them based on their genetics. With early diagnosis, you will be able to intervene because the problems arise from diagnosing late-stage disease when it is harder to treat.

- Q38 Clive Lewis:** Obviously, in the NHS we collectively share the risk of our associated diseases and pathogens. If you have a social insurance system and that risk is individualised, how is that going to work? As this technology advances, clearly with an individualised risk-based healthcare system there will be winners and losers, and for a number of people it will be a form of Russian roulette.

Sir John Bell: This again goes to the strengths of the NHS. The NHS is essentially a social insurance system that is equal for everybody.

- Q39 Chair:** It is the pooling of risk.

Sir John Bell: Yes—the pooling of risk. In my conversations with the insurance industry, which I have from time to time, it has a problem because in that pool will be individuals who will have a higher risk of this but a lower risk of that, and the next guy will have a lower risk of this and a higher risk of that. It becomes pretty complicated. The whole insurance industry is based on pooling risk. There are bad outcomes but you hope to have more good outcomes. One of the good things to happen in this country is that we have had a moratorium on insurance companies using genetic data, and long may that last. I think it will cause all kinds of confusion and trouble where the private sector is providing insurance cover in a wider sense.

- Q40 Martin Whitfield:** This has been fascinating. I am going to ask you to look in a crystal ball to see the future. The sequencing technology is creating more accurate specific medicines, leading to stratified patient care. Would you like to offer some conjecture on the financial consequences as we start creating drugs that apply specifically to only a handful of people at great expense? Are we going to see huge cost savings, or are we going to see a fundamental shift in the economics of medicine, in particular pharmaceuticals? The bulk purchase system of the NHS is not going to work in the future. Feel free to delve into the future.

Dr Papadaki: That is a very interesting question and one that troubles me personally. People think that long-term resources and affordability arises mainly from the pricing issue. Prices at the beginning might be high because companies are looking to offset their R and D investment and the smaller patient pool, as you said, but there is another element to it. 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. As you can understand, it is a much bigger conundrum than just pricing.

Sir John Bell: It drives to the heart of the innovation system in the industry as well. Here is an interesting fact that I learned yesterday. If you go back a decade and take the top 10 selling drugs, they had applicability for 400 million people. If you take the current top 10 drugs, they have applicability for 40 million, so there is a problem. I think we have rightly moved away from the blockbuster model because many of them were not as effective as originally advertised, but we have got to a point where the costs have gone up and the number of patients in the applicable population has fallen quite dramatically. I do not want to pretend there is not an issue; there is one, and how one gets around it I am not sure.

- Q41 **Martin Whitfield:** How resilient do you think we are to that forthcoming problem, or is it going to cause huge economic waves through the pharmaceutical industry and insurance industry, but possibly not the NHS since we have such a wonderful system?

Sir John Bell: One of the reasons the cost of drugs is so high, be they for large or small populations, is that our paradigm for developing them is very clunky and old school. It is all based on a set of criteria laid out in the early 1990s—the so-called ICH GCP criteria—designed to capture data in trials outside healthcare systems. That led to the growth of the CRO industry, but these are enormously expensive exercises because you have to set up a whole system outside a healthcare system.

I think there is now a view that, if you could collaborate with healthcare systems and say, “We have interesting things that could help your patients. Why don’t we work together inside your system to capture data, efficacy and safety, and recruit patients from patient registries and the like,” you could save an enormous amount of money. Last night I spoke to a company that is coming to the UK to do exactly that. It thinks it can take a development programme that costs 1.4 billion and do it for 300 million. If those savings are passed on, as I would expect them to be, to the collaborator, which would be the NHS, I think we do have a sustainable system that is able to acquire those efficiency gains.

Dr Papadaki: That is why the accelerated access review tries to set out this vision as such an important next chapter for the country.

- Q42 **Martin Whitfield:** That re-emphasises the value of the data, the control data and the relationship between not only large companies but small companies that come up with innovative ideas.

Dr Papadaki: Yes.

- Q43 **Clive Lewis:** One of the things that keeps coming up before this Committee is the fact that as legislators we are trying continually to keep up with rapidly advancing changes in science across the board. That is one of the reasons this Committee exists. You have already touched on



bits of it, but perhaps you could give us an overview of some of the challenges to the kind of regulatory framework for genomics and gene editing that will be needed in the coming years.

Sir John Bell: I think you should be pretty proud of the fact that we have a dynamic and effective regulatory system for these things in the UK. The gene-editing company I mentioned earlier in my discussions had come here to get advice from the MHRA. I said, "How did that go?" and I was told it was one of the most informed conversations it had had with any regulator anywhere on the planet. That tells you we have an enormous asset. To be clear, it is important we do not lose that in the presence of Brexit discussions, the EMA and all the rest of it. I do not want to get into that, but that is a huge asset for our industry.

As to the challenges associated with genomic regulation, for example, I think the UK's position has been powerful. It has thought about it very hard. Of course, it is easier to get approval within a single payer system. In the north American system it becomes really difficult because, if you have algorithms that come out of genetic data, you get them approved. If you pour in a lot more data and get a better algorithm, you have to get them approved again. Then you pour in more data. The idea of a learning algorithm does not exist in American regulatory environments, but it does in the UK. We need to be at the front end of that whole regulatory agenda to transform our regulatory system to deal with technologies that we never thought we would have five years ago. I have to commend the MHRA as a stunningly important piece of it.

Chair: We will have to be quite fleet of foot.

Sir John Bell: We will, because this is changing really quickly.

Q44 **Clive Lewis:** My last question is about product-based regulation versus process-based regulation.

Dr Papadaki: Do you mean especially for genome editing?

Clive Lewis: Yes.

Dr Papadaki: In technologies that are so early in their life cycle, we need to leave room for learning. That is why we generally believe it should be product-based regulation where you look at the result of the specific application. That is much better and allows you to learn, and not to nail the technology and guidelines that might not work further down when we know more about it, rather than a process, where you just cancel something or allow it based on the general mechanism.

Q45 **Clive Lewis:** So, it is permissive at the earlier stages and then more regulation at the latter stages.

Dr Papadaki: Yes. Have a flexible learning framework, which MHRA is very good at doing. To make it clear, for genome editing the majority of the therapeutic applications we are looking at are for somatic cells, the



ones that do not go into the germline and do not carry the risk of long-term effects in other generations.

- Q46 **Darren Jones:** We have talked a lot about successes in sequencing but less so in interpretation. I understand from the Deloitte report into the genomic industry in the UK that about 60% of revenue comes from sequencing. What more do we need to be doing to make sure we gain the benefit of interpretation, which I sense is the valuable bit, so that we hold on to that competitive edge in the UK?

Sir John Bell: It is a really important question. We missed our big chance in sequencing when we sold Solexa to Illumina. The biggest dominant sequencing player is Illumina by a mile. It is a great company, but it is located in San Diego and is based on British technology, which is kind of dumb. The second big one is Oxford Nanopore Technologies. Again, we lead the world. I hope we will be able to hang on to that. We will be a powerful player.

The truth is that those technologies are going to be a tiny fraction because we are rapidly heading towards genomes that cost a couple of hundred dollars each. Most of the added value is going to be in the interpretation of the genomes. We have some good small companies in that space that could grow and develop. We also have the intellectual base in the academic community. The EBI at the Sanger Centre and the Wellcome Trust Centre for Human Genetics are terrific places. Without a shadow of a doubt, these are the world's best genome analytical people. We need to try to convert those into applications and then products. That is a major objective. You are absolutely right to highlight it, because that is where ultimately all the value will lie.

- Q47 **Chair:** Do you know what is needed to make that happen?

Sir John Bell: First, we need to be better at making sure they get access to our tremendous resources of data in the genomic space. As the database of Genomics England gets better, we want those small companies to have opportunities to roam around the data and understand and learn what they are going to do. We also hope we will be able to sequence resources like UK Biobank, which will be a terrific asset for small companies trying to develop algorithms and the like.

One of our problems is the very thin base of risk capital for small companies in the life sciences and elsewhere. I think we are always at a disadvantage to American biotech companies because they have very deep risk capital pockets and we do not, so the ability to scale these companies to be big, chunky international players is very limited. That is something we need to think about quite hard.

- Q48 **Darren Jones:** On the point about accessing and using data, I do not know whether you have had a chance to review the Data Protection Bill, which is in the House of Lords at the moment, and the EU General Data Protection Regulation. Do you have any macro-concerns with those pieces



of incoming legislation that might limit our success in this area?

Sir John Bell: That is very timely. I know that you guys have thought about this as well. I tracked the GDPR all the way through the European Parliament. We worked hard; the Wellcome Trust was great. It was going to be much worse than it is now, but it is not good. Whether we are in or out of Europe, we probably have to stick to it, but interpretation of the law will be very important, and the Information Commissioner's Office needs to take a pragmatic view. I am totally with the idea of protecting people's data and making sure it does not get out there, but the level of sanctions and requirements for repeated consent will be very limiting in our ability to use healthcare data to patient benefit. That is my biggest concern.

Dr Papadaki: I absolutely agree. The only thing I would add is that perhaps in the Brexit negotiations there might be some flexibility in the Department of Health to think what a more risk-proportionate approach to the application of that to a genomic medicine system in the UK might look like, but we do not know whether there is any wiggle room and what the flexibility is.

Q49 **Darren Jones:** Interestingly, we get the chance to debate the GDPR in this Parliament; we are calling for the opportunity to do that, so perhaps that will come up.

Moving from sequencing to interpretation and the gene-editing point, I understand that when you are trying to install genetic material into cells you need to use viral vectors, but they are in short supply. How do we solve that shortage, and is there something more we should be doing in the UK to have that part of the future market?

Sir John Bell: One thing that came out of the tranche of money that appeared with the launch of the report 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. It is not as if we have not done anything; we have done stuff, but there is much more to do.

Dr Papadaki: There is an open competition, which we welcome, from Innovate UK to build this infrastructure. We have a robust base of SMEs that are currently over-subscribed to produce vectors, so incentives other than just Innovate UK funding for these companies to expand are also an important approach to it.

Q50 **Darren Jones:** I think I already know what the answer will be to my last question because you have touched upon it. A lot of the innovative companies in this space tend to be start-ups, scale-ups and pre-commercial businesses, but my understanding is that a lot of them are being purchased by international companies. My sense is that you are going to say that is a problem for us in the UK and we should try to keep



that proprietary work here. Is that right?

Sir John Bell: Yes. We were great promoters of the patient capital review done by Damon Buffini. There is a real will for people to keep companies here if they can be properly capitalised. I think there are two points: one is to increase the flow of risk capital that can be deployed—hence my comments about pension funds—and the other is to make the public markets in the UK work for the life sciences, which they do not. That is why people go to Nasdaq and get bought. If you ask me to do two things, it would be those two. I do not know whether Magda wants to add anything.

Dr Papadaki: For us, it is not necessarily okay, but if the companies can still stay here and create jobs, or the outcomes can be used to progress further innovation, it is not necessarily a loss, but certainly incentives and access to capital have to be ameliorated in the UK.

Q51 **Vicky Ford:** When Professor Chris Whitty came before this Committee he said that genome editing was, in his words, “an area where science cannot stray beyond what the public ... are comfortable with,” and therefore ethical acceptance by the public. How is industry dealing with the ethical issues? Are there lessons we can learn from, for example, the public and GM crop arguments? What more do we need to be doing to make sure we have the right legislative framework but also public acceptance? It is a simple question.

Dr Papadaki: It is a simple question. It is very similar to the GMO issues. We should not be afraid of public debate; we should welcome it and be part of it. The Nuffield Council on Bioethics is doing a very good, vital job. We are contributing to that and want to continue to do so, but from a technology perspective it is very important to segregate what is happening in areas where there is not much of an ethical debate or risk. What people are worried about is germline modification and the Pandora’s box that this might open in terms of eugenics, designer babies and so on, but in terms of therapeutic applications, other than the off-target effects and making sure the technology is safe, the ethical implications are not that critical. Nevertheless, as we learned from the GMO space, it is very important to open that debate proactively and inform people as well as engage them.

Sir John Bell: Part of it is that genome editing is a bit of a scary term for the guy in the street, and I think that is a problem. I entirely agree with Magda. If you can deal with the issue of specificity and germline modification, which I think can be done because it is possible to scrutinise that quite carefully at single cell level—these days you can sequence at single cell level—this is like any other therapy. It has the possibility of doing enormous good for sick people, and that is where it is different from GMOs. I am a fan of GMOs, but the truth is that you are not fixing anybody who is going to die, whereas with this stuff you will have a profound effect on some pretty ill people.



Chair: On that positive note we ought to end. You have given such good and full answers that it has played havoc with our timing. Thank you so much. It has been a fascinating session, and we appreciate your time.

Examination of witnesses

Witnesses: Dr Mark Kroese, Professor Sue Hill and Professor William Newman.

Q52 **Chair:** Welcome to you all and thank you for your time in being here. I am sorry it is a late start with this session. I fear that we might have a vote at 4 pm, which might interrupt proceedings, but we will return as quickly as we can. By way of guidance, because we are tight on time, do not feel you all have to answer every question that any of us asks. To start, can I ask you what you see as the main opportunities and challenges of genomics and what do you make of the chief medical officer's report on this?

Professor Newman: We are very positive about the chief medical officer's report. We think it is wonderful to have genomics centre stage of the delivery of medicine looking forward to the next 10 or 20 years. There is always the slight sense—just as music did not start with The Beatles or football with Sky Sports—that there has been genetic medicine and genetic services established for a long time in the UK. I represent 1,800 professionals within the NHS—doctors, counsellors and scientists—who have been working very hard in this space over a long period of time. We are hopefully going to see an evolution, rather than completely thinking that we have to start from scratch, and building on a lot of the good work that is already in place. We are going to see a transition from the exciting increase in diagnosis that we are able to make with the new technologies, and link to the 100,000 Genomes project and other such initiatives, to a phase where we are going to be spending more of our time focused on treatment and using some of the new technologies that are developing, of which you will be aware.

Q53 **Chair:** Perhaps one of the others of you could answer this supplementary. How sure can we be about the proposed benefits of widespread genomic sequencing? Dr Jean Abraham, who is an academic honorary consultant in medical oncology at Cambridge, said that she felt the jury was out on whether or not whole genome sequencing merits widespread clinical implementation. That is quite a challenge. Who wants to respond to that?

Professor Hill: I will pick that up. To answer the first question as to the CMO's report, it has been helpful to the system to have what she set out in each of the elements of that report and what we need to do to capitalise on the benefits. We know the benefits will be significant for patients. This is not all about whole genome sequencing; it is about the whole gamut of genomic technologies, from DNA-based technologies through to other technologies, that enable us to understand what a genetic change—a change in a gene—might mean in an individual patient and how it might give us different technologies to monitor that



expression and development of disease over time, or, particularly important for the NHS, to understand the interaction with drugs and what might be an effective drug for an individual or what might, for example, cause adverse effects.

We certainly see that there are significant benefits. This would underpin a personalised medicine approach that enables us to think about prevention and to give a more precise diagnosis than we have done before based on objective, underlying genetic cause to personalise treatments—we have not always had the tools in the NHS to do that—and then to engage patients in the decision-making process in what it is they want to use and, for example, share their data with.

Within the NHS, we are planning only to introduce whole genome sequencing where there is evidence that there will be benefit in an increased yield of diagnoses for patients. It would give us a better-quality outcome, therefore, and it is more affordable than the current processes.

If we look at the technologies that are being utilised in the NHS, they tend to be utilised in a more serious way. One test is done, then another one added and another one added. That means we spend, often, more than doing whole genome sequencing. Part of it is about understanding that whole genome sequencing may not give us all the answers, but even if we look at what we can utilise at this moment in time it has given us more actionability.

Our plan in NHS England is to introduce from October 2018 for the very first time a genomic test directory that will set out right at the very top, from whole genome sequencing through to single genes, in what condition it is best to apply that technology, on the basis of both the objective clinical and operational assessments. It will not be all about whole genome sequencing. It will be about what is appropriate at this time.

Q54 Chair: Has there been a formal evaluation of the 100,000 Genomes project, and, if so, what conclusion was reached in it?

Professor Hill: The 100,000 Genomes project is still ongoing. It is not due to complete until towards the end of 2018.

Q55 Chair: Does that mean a formal evaluation follows at the end of that?

Professor Hill: I cannot comment today on the plans that Genomics England has, but, as to what we are doing in NHS England, NHS England has supported the establishment of 13 genomic medicine centres. It has supported the NHS to contribute to the project right from identifying eligible patients through to eventually validating the outcome and then using that in treatment pathways for individuals. We have constantly taken evidence, whether it is from clinical transformation in the NHS or the evidence from the conditions where we have whole genome sequencing outcomes and we know we are getting diagnostic yields, or from other studies, on which to base NHS England decisions.



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Q56 **Chair:** Are you saying that the application into the NHS should all be very strongly evidence based as we have progressed forward?

Professor Hill: Very strongly.

Q57 **Chair:** But you are saying it is not necessarily as important to do a formal evaluation of the 100,000 Genomes project. Is that right?

Professor Hill: I am saying that the evidence review is an ongoing process. With the use of these technologies, it is important that it is recognised that this has to be done almost in real-time as the data is generated with enough patient cohorts to make sense of that and then to make an informed decision over whether it is better than what we are doing now, when patients are at the centre of all our decision making.

Chair: Thank you. Do either of the others want to add anything to that or are you happy? Okay.

Q58 **Bill Grant:** The previous Committee's inquiry into genomics raised potential concerns that involvement in the 100,000 Genomes project could impact a patient's health, and it is suggested that is because of the time genomic analysis takes. Is there any truth in that risk or concern?

Professor Newman: 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.

Q59 **Bill Grant:** This is an additional diagnostic facility that runs in parallel to existing diagnosis.

Professor Newman: Yes. What has been established, as the CMO's report has made clear, is that there is quite different practice across the country for a whole range of reasons. Patients are having access to different levels of diagnostic investigation to try to find out the cause for their particular condition. The 100,000 Genomes project, when it was initially set up, had set criteria that raised some concerns that patients would only be eligible if they had had certain investigations. That has now been diminished to ensure that it is all equitable and that every patient who is eligible with a particular condition can have access to this sequence analysis.

Q60 **Bill Grant:** This question revolves around the speed of diagnostics compared with samples coming back for tumours, blood samples and so on. How will all this be speeded up by using the new brand of diagnostic—the genome testing? Is there a significant time difference?

Professor Hill: 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. That is being done as standard. Within the 100,000



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Genomes project, at the moment a small number of NHS genomic medicine centres have been submitting samples that have been fast-tracked through the whole genome sequencer and then back to the referring clinicians. That has been done to help inform decision making.

In those small numbers of samples, that is being done in around 20 days. In some instances that is better than standard care at the moment, but in cancer, from not necessarily across all but in some tumours, currently we are seeing a greater number of potentially actionable changes—up to the level of 65% in some patients—emerging from whole genome sequencing. This means that not only could some patients receive other treatments, but it confers greater eligibility to enter into clinical trials that they would not have entered before. This is providing us with evidence of where we could use whole genome sequencing in certain tumours from an NHS perspective, or where we can do more extensive testing within our genomic laboratory infrastructure, or the new infrastructure that we will be putting in place in the NHS from October 2018.

Professor Newman: It is feasible to hit the 20 days, but that is the best-case scenario at the moment. There have been concerns that—

Q61 **Chair:** Will that come down further?

Professor Newman: It might come down a little further, but the challenge—and there have been a number of samples—is that it has taken much longer than that, so it is about getting the pipeline robust. From taking the sample and going all the way through, it is 20 days, or a number of months or a number of weeks, for every single patient, not just for a select few. It is about getting that process in, which will happen. It is just that it is very challenging to do it.

Q62 **Bill Grant:** I have one final point. It is probably quite a wicked time-based question, but, given a fair wind, when might cancer patients start to benefit significantly from genome sequencing?

Professor Hill: They are already starting to benefit from it now. What it is also—

Q63 **Chair:** What particular cancers are we talking about?

Professor Hill: Our genomic medicine centres are now recruiting across 18 different cancer types. The cancers that we are recruiting most to are breast, ovarian and colorectal, so it could be in any of those areas, but we are also moving now into haematological malignancies where we know that there is likely to be more actionability.

The project has shown us in NHS England the variability of access to molecular testing for cancer patients across the country. That is why, as we start to plan our service in the NHS, we will be doing more extensive testing of cancer tumour samples as we go forward, but not all up to the level of whole genome sequencing until we get further evidence.



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Bill Grant: It is delightful that people are already benefiting; it really is. Thank you.

Chair: Thank you very much, Bill. Vicky, you might as well get started before any vote.

Q64 **Vicky Ford:** You have talked about timing already, but when do you expect NHS England to take over sequencing from Genomics England, and, once we get past the 100,000, what are the scale-up opportunities for more widespread routine sequencing? Would you see any routine sequencing?

Professor Hill: The NHS will cease its commitment of providing samples to the 100,000 Genomes project by September 2018.

Q65 **Vicky Ford:** It is fixed.

Professor Hill: As to "fixed," that is the intention. We know, for example, in rare disease we are on track to finish earlier than September. For cancer, at the moment the trajectory is going out to September and all the plans are in place to meet that. But at the same time, if I may just explain what the plans are, we have already been planning right from the very start of the 100,000 Genomes project to create essentially a new NHS genomic medicines service that builds upon everything we have been doing in genetics and genomics in the NHS since the 1960s. That service will see a new set of genomic laboratory hubs introduced. They will deliver against a new genomic test directory, as I have said. So, from October next year, we will start to see whole genome sequencing being introduced for NHS patients for some conditions. We are on schedule for that.

We see this as mainstreaming all genomic technologies because some patients do not have access to some tests that do not need whole genome sequencing, which Professor Newman has already said. In October, there will be a new genomic laboratory network that will act as a national testing service so that we look at the population of England as a whole. It will deliver a genomic test directory with prescribed tests for cancer and rare disease. It will be underpinned by an informatic solution, which means that all genetic tests will be able to be ordered electronically and they will go through an approval process by the lab so that the right person gets the right test instead of overburdening them.

Vicky Ford: I need to leave; I am sorry. I was waiting for the vote.

Chair: There is no vote. Keep going, Professor Hill. I am sorry about that.

Professor Hill: That is okay. It will enable us in NHS England to understand in real-time, because of the generation of management information that it will enable, exactly what is happening and how we align our commissioning and funding system alongside that. There will be a new funding model introduced. This will also enable the NHS to align the routine clinical care activity with the research and development and



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other industrial endeavours that have been articulated in the life sciences strategy. We will systematically, and on an ongoing basis, review evidence on the basis of whether the technology would give a better outcome for patients and provide value for money for the system. We will constantly evolve what is done at the level of whole genome sequencing, because, as the evidence emerges, we would want patients to benefit from that as soon as possible and we would stop doing other tests.

- Q66 **Chair:** I want to understand this. As I understand it, at the beginning of October this year there had been 36,083 genomes sequenced. The suggestion is that on the current rate of progress it would take until July 2020 before you got to the 100,000. Is that still going to happen, or will we end up doing fewer than the 100,000?

Professor Hill: Obviously those are questions that need to be answered by Genomics England rather than me sitting in NHS England.

- Q67 **Chair:** What is your understanding?

Professor Hill: My understanding is that there is a plan to complete the sequencing within the financial year 2018-19.

- Q68 **Chair:** What about to get to 100,000 or potentially to fall short of that?

Professor Hill: How the number of genomes is calculated is quite complicated and what that means because of what needs to happen in cancer, because they are read at a greater depth to find all the different changes that mean a difference to patients. We would expect in that period, and as the NHS sequencing activity starts to take up the activity, that the remaining sequence activity in the project would be diminishing. There are plans to complete it within that financial year.

Chair: Thank you very much. I am going to move on, in Vicky's absence, to Clive at question 13 next; thank you.

- Q69 **Clive Lewis:** How prepared are NHS staff for some of the quite radical changes that could potentially take place from the genomic and gene-editing revolution? We obviously hear in this place quite often that there are issues with staff retention, recruitment and so on. These are quite specialist posts. Some of those being talked about are counsellors and people who are able to do intermediate work. How prepared are you and what are the main challenges that you see in the coming years? Are they simply budgetary?

Professor Newman: No, absolutely; thank you for raising that, because most of the discussion so far has been focused on the technology. Regarding the technology, we will get there; that will happen.

The key element of anything working well is the people and having those staff. We have, already, wonderful staff in this area in the NHS, both in genomic medicine and clinical genetics but also some very leading people in other areas of mainstream medicine such as cardiology, cancer care



and neurology, who are, let us say, the early adopters of genetics and bringing it into their clinical practice.

There has been a significant focus over the last few years on building relationships between genetic services and other clinical specialties to ensure that the work that can be done in those other clinical specialties at the coalface can be done there. Cardiologists can order genetic tests. Already, paediatricians and obstetricians are ordering lots of genetic tests. Genomic medicine should be providing advice, support and that complex interpretation, because finding a genetic variant is not the same as that person having a particular condition, as we all know. That is the key thing. We know that computer algorithms—better informatics—can help us but can only take us so far. It is that relationship between having the patient in front of you and saying, “Does this gene variant that I have identified using this test really make sense? Can this really be the cause of that person’s problem?”, because if you get that wrong that not only has implications for the patient but for lots of their family members.

We have seen a number of examples—particularly an important paper in the States earlier this year—where there was over-interpretation of genetic information and a large number of women ended up having breast surgery that they did not need because they were thought to be at a high risk of developing breast cancer.

Q70 Clive Lewis: The clinician’s interpretation of this new evidence or new material is critical.

Professor Newman: Yes.

Q71 Clive Lewis: The Genomics Education Programme and its funding runs out in March next year. What does the future hold for that and how are you going to cope with that?

Professor Hill: There have been significant strides made in the Genomics Education Programme and I have also been working with the HEE team on that. For example, as you may know, there have been 61,000 CPD interventions and then people accessing what has been a new masters in genomic medicine. Health Education England is at the moment in a procurement process to re-procure the MSc in genomic medicine, but with a more flexible approach to delivering, for example, access to single modules right up to a full masters programme. The resources will still be available, and Health Education England is now embedding this into business as usual. Some of that will be embedding in undergraduate medicine and their training and education, into postgraduate education and training programmes, as well as actively promoting workforce development for the existing workforce that is in place. This will require an awareness of genomics right up to highly specialised skills if we are going to fully take advantage of the NHS being the first healthcare system in the world to do this systematically.

Q72 Chair: It is quite a step change that is required, is it not, to upskill the



workforce?

Professor Hill: It is. It is a big step up. It will require a variety of different interventions to support that. That is why, for example, from an NHS England perspective, we are starting to work in a network with the medical Royal Colleges, because it will touch on every medical Royal College, but also with specialist societies like the BSGM.

There has been investment through the Genomics Education Programme that will continue in the specialist workforce, so in the specialist bioinformaticians and the specialist scientists that are going to be needed, particularly in cancer genomics, but this will be an ongoing piece of work to ensure that we have the workforce development.

Bill made a really important point, and it was a point that the CMO made in her report, on the importance of multidisciplinary teams in genomics to ensure that the expertise of people like Bill and his colleagues can be brought to bear on other clinical specialties that may be referring patients so that the right decision is being made in terms of how important that particular genomic variant is, the type of treatment intervention that could or could not be based on that, and what further evidence would be required to make that clinical decision.

Q73 **Clive Lewis:** I want to read a quote from the Association of Genetic Nurses and Counsellors—because that sounds like a healthy place to be for the NHS—who have described themselves as “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.” They have also expressed concern at reports that NHS trusts in England and hospitals in the rest of the UK were reducing budgets for continuing professional development for health professionals, including genetic counsellors. Could you talk us through that?

Professor Hill: I will do. The first thing is that, under the Genomics Education Programme, for the very first time we have formalised within the Health Education England education and training system genetic or genomic counselling training. They now undertake a postgraduate three-year training programme with an underpinning masters programme that is commissioned alongside commissioned education and training for nurses, scientists or doctors. That has been a significant change. There is a significant further development to develop a higher specialist training programme for them.

In answering the specific question around the NHS trusts and their uptake of genomic counselling—

Q74 **Chair:** And their reducing budgets.

Professor Hill: We know at the moment that as to the NHS genomic medicine centres—the 13 that have been created—from an NHS England perspective, we are looking at revising the clinical genetics service, and



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genomic counsellors also form part of that; it is a commissioned service. Also, we are looking to re-procure our genomic medicine centres, recognising that genomic counsellors will be an important part of that, with a process to get the right numbers of people in the right places. But I think the conversations that we have had with genomic counsellors, with professionals like Bill, have been that going forward we will need to embed some of those genomic counselling skills in the broader workforce and use our genomic counsellors for very difficult family situations.

Q75 Chair: Is their concern legitimate?

Professor Hill: I think their concern is legitimate, but there has been a formalisation and now there is a process for properly identifying their workforce needs that there was not before. The second is that from an NHS England commissioning of genetic services—and we are re-looking at that—we will be looking at that again.

Q76 Clive Lewis: The concern that has piqued in my mind, knowing the kind of budgetary problems that many trusts have and face, is that in many ways this is dealing with something that is changing and in a way is a little bit ahead in the future, whereas many of the pressing concerns trusts have are on acute issues, mental health issues and so on, here and now. You could quite easily see, when looking at which budgets to put money into and which to take money from, how the genomics side of things could fare quite badly.

Chair: Professor Newman, do you want to answer that?

Professor Newman: Absolutely. That is part of the reflection that we have seen over the last number of years. You see quite variable levels of service across the country, partly reflecting on those sorts of issues. Some trusts have invested very significantly in genomics and in genomic medicine and staff because they see it as a key element of delivering medicine for the future. Other trusts have not been in that position because they have been dealing with those day-to-day acute issues.

The fact is that there have been postgraduate training programmes in genetic counselling for over 30 years in the UK, and we led the way in Europe in introducing them, so there has been very good work there. Their role has changed somewhat and has broadened, and they have become a much more independent, professional organisation, which is a fantastic thing, but the concern about the numbers is absolutely right. I think that a steer is needed to increase those and to recognise the very important role that they play, and not just counsellors but genetic doctors and the lab staff as well—that this is a tripartite approach to delivering the care.

Chair: Thank you very much, Clive. Stephen wants to come in on the back of that, or are you okay?

Q77 Stephen Metcalfe: I am okay, but I could go to question 16, which is where I was going to, because it leads into this about the dissemination



of the most up-to-date research within the NHS.

Professor Sir John Burn suggested that he had seen different members of the same family with the same genetic risk for breast cancer being given different advice from different centres as a result of using out-of-date research. What process is in place to ensure that everyone is using the same current guidance and guidelines?

Professor Newman: I can pick up partly on that. We have recognised, as a professional organisation, that there are differences in practices. We have worked very hard over the last couple of years, bringing all the different regional genetic centres together and other organisations, to ensure that our interpretation of genetic variants is more standardised, working very closely alongside the American society—the American College of Medical Genetics and Genomics—who have realised that an individual who gets a genetic result in one place might get different information. That partly reflects the complexity of it, that it is not always straightforward, but there is better that you can do to try to make sure that that is as consistent as possible.

Another thing we have looked at is that sometimes new information emerges quite quickly that might mean that a genetic change you thought meant one thing means something else. For example, when you thought that that genetic change for a person could lead to a particular condition but new evidence comes out that says it does not, how can you disseminate that quickly? We have been working with the network to try to come up with a system to ensure that there is gradation, a little bit like the MHRA use around drug safety, so that if there is something that is absolutely vital it is disseminated straightaway, and other information that may be interesting and relevant but is not immediately actionable is shared, but in a more routine manner so that people are not bombarded with new information all the time. You highlight the things that are most important.

Professor Hill: Obviously, to ensure that you move away from what is a clinical decision made by $N = 1$ to something that is made by a group of experts in that particular condition, we are planning, through the informatics developments that will underpin our new genomic medicine service, our new genomic laboratory infrastructure. That informatics system is being developed with Genomics England. There will be the ability to hold national multidisciplinary teams so that you start to disseminate that information, particularly when, for example, a genomic variant is identified when that particular clinician who is looking at it, or that team, either do not have the expertise or do not perhaps have the latest evidence.

Clinical genetics is a specialty that has been working on the leading edge of adopting research, but, as we move to more genomic information being generated, we have to ensure we have a system that wraps around this so that we use the best possible expertise not only in this country but potentially overseas if we need to, if the expertise in understanding that



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particular genomic variation might reside elsewhere. It requires the informatics platform to be able to do that and to bring people together, and through the work that we are doing at the moment with Bill's societies and with other societies, we are moving towards standardised reporting and linking to other sources of evidence. That is important in this fast-moving field.

Q78 Chair: Thank you very much. Dr Kroese, thank you for your patience, first of all. I want to ask you one or two questions. How do NICE guidelines and technology appraisals fit in with the CMO's ambition to mainstream genomics in the NHS?

Dr Kroese: It fits really well with the NICE work programmes. Genomics is a major interest for NICE, and we welcomed the CMO's report and its recommendations. I would emphasise first, though, that NICE is already dealing with the benefits of genomics developments—not whole genome sequencing yet, but we have developed clinical guidelines that have included genetic testing and have included diagnostic guidance specifically. The most recent one is with regard to genetic testing for Lynch syndrome in those with colorectal cancer. We also have technology appraisals and highly specialised technologies that evaluate medicines, and the field of companion diagnostics is developing very quickly. Diagnostics and genomics, in particular, is very central to the outputs of NICE.

Q79 Chair: The accelerated access review argued that you should be rebalancing your work, did it not, towards diagnostics? Do you feel that you are doing that?

Dr Kroese: We feel we are, but clearly diagnostics crosses a number of different work programmes, to which I have just made reference. NICE has worked very hard to ensure that there is liaison between those different work programmes to ensure that the appropriate evaluation of the diagnostics is occurring, whether it requires a full health technology assessment, in which case it comes to the programme I chair, which is the diagnostics advisory committee and its diagnostic assessment programme outputs, versus those that go through technology appraisal, or whether they remain in the clinical guidelines. There is important work going on with regard to balancing the appropriate evaluation efforts within NICE to ensure we get the most important outputs.

Q80 Darren Jones: In the previous hearing I think it was Sir John Bell who said that genomics is difficult for NICE and that you do not understand it. You have just said everything is fine. So, do you understand why he might criticise you, because we never got into the detail of that with him?

Dr Kroese: I was not sure, because I was here, and I was very interested to hear that comment. He may be referring more towards his future vision—how the world is going to change very dramatically and genomic information is going to be used fundamentally differently than perhaps diagnostics is currently. That is how I have interpreted it. I



certainly do not see any challenges to our abilities to evaluate genomic tests in the diagnostic assessment programme. I was just looking through the list. We have done at least four or five guidance documents that are genomic-based, genetic testing, and in my assessment or when I participated in the full committee reviews of those there was not any problem.

I should emphasise that we include clinical specialists, clinical geneticists, laboratory experts and molecular scientists as well to help us understand what are the issues when we are evaluating these particular diagnostics. So, I do not think my experience is that it has come up with a fundamental problem. We have been able to manage the evaluation as we would do with other diagnostics as well, but with the appropriate specialist input that we require for all diagnostics, whether it is radiology or another form of biomarker or molecular genetics. Unless Professors Newman or Hill disagree with me, at the moment I do not think the NICE programmes are unable to deal with the current programmes or products that are coming through.

Professor Hill: For the last 17 years—I think it is about 17 years—we have had the UK Genetic Testing Network that has been based on a methodology that was established in the States. The UK Genetic Testing Network has provided the evidence review that has really directed the testing that has been undertaken within the NHS. For example, in the last two years 50 tests have been introduced into the NHS on the basis of their recommendations. Those are based on the evidence that might emerge from academia, from within laboratories that have been utilised in a clinical setting, and then they are reviewed by an expert committee within the UK Genetic Testing Network.

As we move forward, and in line with the recommendation in the CMO's report, in NHS England working together with Genomics England, we have established an expert group that has reviewed all the technologies, because within the NHS, in terms of affordability, we need to look not just at single tests but at the whole testing repertoire and all the technologies, so that, if we keep adding on, then it is very easy to add a further million or two on to the testing strategy.

Q81 **Chair:** Certain diagnostics will drop out, presumably.

Professor Hill: Some will drop out. There will be an evaluation function within NHS England that will be based and built upon UKGTN. 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. Some of those tests that will be in utilisation will then feed into the NICE programme in terms of its relationship to use within an individual clinical condition as that has been provided in a clinical guideline or, for example, through other types of approaches—the health technology appraisals—that direct drug therapy and companion diagnostics.



If we continue to look at single tests, it would cost the NHS a lot more money to provide it, and it would not necessarily be provided at the right quality and with the right outcomes for the patient. It is about working together, and we will be working really closely together with 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. For some of it, it is critical that we replace technologies we really do not need to use any more.

Dr Kroese: Just to follow on from Professor Hill's comments, I would like to emphasise as well that NICE is not complacent in looking at the methodological issues with health technology assessment and sponsors research in anticipation of some of the challenges; at the moment we do not know what they will be.

As we see some of the new products and diagnostics, and, as Professor Hill has outlined, those kinds of new characteristics in that tests move away from the single-test approach, NICE will in early negotiations be able to anticipate where some further work needs to be done with relevant methodological experts in the UK. We have very well-established arrangements with those experts, and we review our manuals, as we call them, quite regularly to make sure that we can carry out the tasks we are being asked to do.

Professor Newman: I absolutely agree. UKGTN has been a real force for good. If we want to introduce a test into clinical practice, we have to provide the evidence; we have to show that we can do it and that it has some benefit. One concern around UKGTN, moving forward—I represent the British Society for Genetic Medicine; it was the UKGTN and that has been subsumed within NHS England—is that it is important that we ensure that those links across the whole country are maintained with Scotland, Wales and Northern Ireland; that we do not end up becoming isolated within England; and that the benefits are shared across the whole nation.

Q82 **Darren Jones:** So you disagree. It will be interesting to see whether he feeds back on that.

My second question is whether we have the kit to do the job properly. It was said in the last session that our biggest challenge is around the storage and processing of data in order to analyse and interpret it. I understand in a previous Committee hearing before I was here that it was said that the NHS IT system was not up to scratch in order to allow this genomic processing for the whole population when we get beyond the 100,000. What are we doing to ensure that we are able to deliver the service we are talking about today?

Professor Hill: As I said a few moments ago, we are developing some of the infrastructure in conjunction with Genomics England, which has been



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developing the 100,000 Genomes project data storage arrangements, whether that is for working with NHS Digital on patient identifiable data that eventually is de-identified and then enters essentially into the reading library with access through a firewall.

In moving forward, because we have learned about storing huge amounts of data, and thinking about the NHS being able to do that and what we require to drive up and enhance clinical interpretation of what will be quite complex genetic information, the plans that are being delivered in conjunction with Genomics England will be to create one new data warehouse for the NHS that is not in individual laboratories around the country but in one place, which can be linked, if patients provide consent, with a research database for access if potential users meet conditions for research and development purposes and for industry.

This data is going to become increasingly complex. We need also to be able to ensure that researchers can access de-identified data when the consent is in place to start to drive the type of questions that will lead us to understanding what might be diagnostic and what might be able to drive a drug discovery. The plan is to create one data warehouse for all the genomic data, with, for example, different elements of that relating to the new genomic hubs, with virtually instantaneous access for the genomic laboratories, for the clinicians within there if they have the level of permission, and to do that piece that I talked about earlier—to enhance the clinical interpretation of the outcome. This is going to be really important for the NHS and for the broader benefits.

Q83 **Darren Jones:** That sounds very sensible. One of my first jobs was as a clinical coder in GP practice taking the old Lloyd George notes and turning them into the codes for the quality and outcomes framework. That was 16 years ago, and yet even now, with this big NHS project on going paperless with digital records, my wife still has to carry her pregnancy blue book with her everywhere because GP surgeries and trusts cannot communicate with each other.

Chair: There are faxes going round the NHS every day.

Darren Jones: There are faxes going around the NHS. If we have been trying to deal with paper records for more than a generation and still have not done it, when are we going to be ready to do this huge amount of data sharing around genomics?

Professor Hill: 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. It requires a set of data standards. We require that interoperability and functionality you talk about, but 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, so it gets away with some of



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the difficulties that you are talking about in coding, whether that is in primary care or in the NHS. We can only move forward if we have those types of developments to enable what we need to do with this data so that we get the best outcome for the patient.

Q84 Chair: Are you satisfied we are making a sufficient investment in the digitalisation process, or do you not think that there needs to be a step change in the level of investment to ready the whole system for this technology?

Professor Hill: To ensure that the NHS can interface with all these platforms, there will need to be further investment at the level of individual hospital trusts, for example.

Q85 Chair: Exactly. That is critical to make this actually work.

Professor Hill: Yes.

Q86 Chair: Professor Newman?

Professor Newman: Absolutely; there is no doubt. I was in clinic this morning and was writing in paper notes for my patients. If we are going to share this information, what we have been talking about around genetics is broader than genetics. We need to be able to draw in the information from cardiology, from the images, from neurology and from their tests. So, this should not just be seen as an investment in genetics and genomics; it should be seen as a broader healthcare investment because that is the only way that you can maximise the value. Genetics is partly a tool to enable good healthcare. It should not be seen as something completely separate and so it should be integrated to that. We need an overview where you get a sensible investment ensuring—this word again—interoperability, that the systems really can talk to each other, and that you have the permissions in place to share that information not just within England but across borders, because there are certainly issues around that as well.

Chair: It feels like quite a massive challenge from where we are at now to get there. Darren, do you have a final question?

Q87 Darren Jones: To get this project done on the connectivity and the digitalisation of the network, what is your budget, how much of it have you spent, and do you need more to ensure it delivers successfully?

Professor Hill: The budget for the interoperability piece with the NHS would be within the budget that is available for Paperless 2020, which is not within my remit, but obviously we are having conversations about that budget and what might be available through capital investment developments.

Q88 Darren Jones: So there is no specific budget for the genomics project. You are borrowing it from the Paperless 2020 project.



Professor Hill: No. As to the capital investment that might be required to work with the required informatics solution, currently there is not a capital investment programme to support that. As to all the other developments that we are talking about, this is part of the ongoing commitment to Genomics England through to 2021 from the Government. There are two separate elements to this. The capital investment is the piece that we have been talking about and to which Professor Newman has alluded. That is where we do need further investment.

Q89 **Darren Jones:** At the moment you do not have a budget for that.

Professor Hill: We do not have a budget. We have had £20 million in capital investment as part of the 100,000 Genomes project, but as we go forward then we will need more capital investment to make the necessary changes.

Q90 **Darren Jones:** I did not mean to ask a further question, but you talked about how you plan to roll out this project. How can you plan if you do not have a budget?

Professor Hill: There is a budget for the actual informatics structure that will be put in place through the laboratory hubs. There is a budget that Genomics England has, so that is all part of that budget that was agreed between the Department of Health and Genomics England in creating the infrastructure. We are talking about something that is very much about how an individual hospital might interact with a system.

Darren Jones: That is the critical point.

Professor Hill: Yes, but at the moment, within the system, genetic tests get ordered every day, and there will be a mechanism to ensure that this will be in place by 2018. As to further capital investments to make this seamless end to end, there has been no commitment to that.

Q91 **Darren Jones:** The bit to get genetic information to the patient in the hospital has no budget.

Professor Hill: 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.

Q92 **Martin Whitfield:** To continue slightly to explore that theme of money, we heard from the first panel that the potential of genomics is enormous to change the very economies and systems that are used. How much do you anticipate—starting with Dr Kroese—the procedures within NICE are going to have to develop and grow to reflect these changes?

Dr Kroese: It is completely to be expected that processes will need to change, depending on the needs of both the health system and the information required from NICE in supporting and improving health and



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social care. As I was referring to earlier, NICE has never been in a very stable position with regard to its approach in terms of its methodologies. It is always looking to evolve, so in a way it depends on what NICE receives. Particularly, if I can focus on diagnostics, we get diagnostics products and services referred to us, so we are a little bit dependent on what comes in.

Also, importantly, NICE is very keen on, and has developed capabilities with regard to, working with manufacturers through its science advisory unit and its unit for market access to get early intelligence with regard to what products and services are being developed. From that, there is a feedback loop so that, if we know the nature of the products being designed, we can already start thinking about how our evaluation processes are going to cope. Ultimately, the test is when we do the evaluation, and we do learn from it. Sometimes when we do an evaluation or a health technology assessment, we come across certain features where, on reflection, we have to think about how we can do it better next time round because it presented us with particular interpretation problems.

Q93 Martin Whitfield: Do you anticipate any unique problems with regard to genome sequencing—a genome coming down the line towards you? Are you anticipating any problems?

Dr Kroese: At the moment we are not anticipating any, but we are keeping a very close view on that. We have not had the experience of the whole genome sequencing yet, so I think in a way we are waiting in anticipation, but we look forward to it.

Q94 Martin Whitfield: If I broaden that slightly, one thing that has been highlighted—I have to say in the first panel the NHS was spoken of very highly as a source of data, and probably rightly so—is that it is a unique set of individual units that fit together, and you have identified the problem of passing the information back down the line. What anticipation has taken place of the problems that might come down the line given the huge change in the playing field that these diagnostic techniques, as they broaden, may bring with them? Perhaps I am including that simply because my constituency is East Lothian and there is the connection with the Scottish NHS; and I know there are Scottish GM centres there as well. There is that interrelationship between the two, because it seems to be that much of diagnostics is based on big data and how that can apply and improve one specific individual—the bigger the data, the better the service. What do you anticipate are the really big problems coming down the line to you?

Professor Hill: If I could answer the question around working with the other devolved Administrations—the other countries of the UK—we are working with them to make sure there is a seamless service because some countries of the UK access services in England and vice versa, so we need to ensure that that works.



I want to go back on a response I gave earlier on the data, which is that, obviously, everything we are doing in genomics is fitting with the broader Paperless 2020 work programme and all their interoperability and functionality developments. This is most definitely within that and plays a key part.

As to big datasets, which is part of this—we touched on this earlier, as did Professor Newman—as we move forward, we will be moving into a new way of working that might involve working with people outside the borders of the UK in other countries to agree what might be a particular genomic variant and its classification as something that should be considered significant within an individual and therefore treatment.

As we move forward with the data, there will be considerations we need to think about. One is working in that broader context, from a national, a UK and an international perspective. The second is recognising that the amount of data that will be generated from a whole genome sequence will have more information within it than we can possibly interpret today. Part of what we are looking at and considering is the re-analysis. As more evidence emerges on what might be important in a patient, it is building in the ability to re-analyse and to feed that back to individual patients. Then it is about how we start to structure data that enable that process to happen, to make sure that we get all the possible benefits out of the data and that we can link it. The important thing for the health service is how we link this data with drugs and other interventions, because that will enable us to be more objective in our medicine spend. Our next challenge is about re-analysis, the linking of datasets and then the feeding back of that.

Professor Newman: I have maybe a slightly different perspective but probably linked to some degree in that we have been doing this for a long time, both at a society level and in individual genetic centres around the country where the people within those centres and within our society are thinking about what are our main priorities. You cannot do everything all of the time. You have to think about what things are going to make the most difference that you can actually achieve and that are affordable but are also going to make a difference to patients. For the society over the last year, as we mentioned earlier, it has been about focusing on getting that standardisation so that whatever information you get is the same across the country and making sure that we have that in place, that we have updated our approaches to how we consent patients and the confidentiality of their data.

At a local level, we are starting to think about our practice: what is my work as a doctor going to be in 10 years' time? Is it going to be much more focused on diagnosis, or is that going to be seen as something more routine, where we will have other tools that will help us, and that we should be skilling people to focus more on some of the treatment elements or that interpretation element?



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Coming back to an earlier point, workforce planning and education are going to be absolutely key to that. I think there are different levels. There has to be a central overview of the big picture around data analysis and linking up centres, and there have to be more local decisions made around provision of services and ensuring that is done effectively.

Q95 Chair: What is your main anxiety about the delivery of all this—the biggest challenge, as it were?

Professor Newman: It is difficult to predict that. There certainly is a huge challenge, as Professor Bell flagged, around informatics. That is something that has been very hard to deliver on within the NHS. 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. That is a real challenge.

Around rare diseases and the potential within that area, we are going to find new diagnoses for lots of patients, which is wonderful, providing answers for patients who have been searching for those for themselves and their family members for years. Starting to see that increase has been truly wonderful. However, on the flip side of that, you have the concerns around the budgets for some of those treatments, which are incredibly expensive, that may be required downstream of that new information. Working with NICE and other organisations to devise a mechanism to identify ways of ensuring that those treatments, first, are truly effective and, secondly, available to people in an equitable way is going to be absolutely key.

Q96 Bill Grant: I have a brief supplementary. Professor Hill, you mentioned clinical specialties and your input. If my terminology is right, does genomic diagnosis lend itself to certain disciplines or certain specialties in a ranking order? Would it benefit cardiology and neurology on a sliding scale, or is it beneficial across the board?

Professor Hill: At the moment it is beneficial across not all clinical specialties but a significant number. There are some 50 to 60 recognised different clinical specialties, depending how you group them, but at the moment it would apply across around half of those. As we go forward, though, and we understand more about the use, for example, of these more cutting-edge genomic technologies, it is likely that they will start to apply in more common diseases. Our approach has been to be very systematic about the clinical areas in which we currently use genomic testing and to look at the areas where perhaps we have not had more systematic access to those technologies. One is genetic testing associated with familial hypercholesterolemia—those with high levels of circulating fats in the blood that means that people can die early, under the age of 50, from cardiovascular disease. That has been a very ad hoc access. In areas where we have had difficult access, those have been corrected. Over time, as we have more evidence from either this country or other countries in other common disease, we will look at that systematically. In



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many different specialties, though, there will be a genomic application, but it will not be in all.

Chair: Does anyone have anything else, finally? No. Thank you. We have gone on significantly longer than we had expected. We really appreciate your time and you staying on to answer questions. Thank you all very much indeed.