**The G Word Transcript**

**Genomics England Research Summit 2**

**Chris:** Hi, I'm Chris Wigley, CEO at Genomics England, and you're listening to The G Word podcast. In today's episode, we're sharing another brilliant session from the last Genomics England Research Summit, where I spoke with Professor Dame Sue Hill and Vivienne Parry, about the state of genomics research and the pathway to clinical implementation. What does it take to scale an idea like whole genome sequencing diagnostics across an entire health service? Keep listening to find out more. Enjoy.

**Vivienne:** And with no more ado, I want to come to our first, and possibly our most important partnership of all, that with the NHS. So, I'd like to welcome to the stage Sue Hill, she's Chief Scientific Officer at the NHS, but that really doesn't begin to describe what she's done for genomics, and also Chris Wigley, Chief Executive Officer of Genomics England. Welcome to you both. How lovely to be here in person with you. First of all, for Sue, as part of the NHS Genomic Medicine Service, Genomics England supports the whole genome sequencing for patients with cancer and rare disease. I mean, this is a national clinical service. And I say to you all: a national clinical service, the first in the world. But we're here talking today about genomics, and research. So how do the two come together?

**Sue:** So, thank you very much, Vivienne. And good morning, everyone, both those of you in the room and those of you online. They've come together, I think, Viv, over many different years, but not in a systematic way. And you know, some of the images that you're going to see behind me depict the very start of the NHS in 1948. We've had genomics in the NHS, genetics in the NHS since that time. But what happened was any advancement was not implemented systematically across the NHS. What really was a game changer was really understanding the amount of money we were putting into the service, but that we didn't get equitable access to all of the technologies available that coincided – so there was variability in outcomes, variability in access – with the NHS contribution to the 100,000 Genomes Project, and NHS England contributed to the NHS, part of the 100,000 Genomes Project. So that was the start of an investment, a tripling of the investment in the genomic medicine infrastructure in the NHS that led to the launch of the Genomic Medicine Service in 2018.

But right, what we learned from the 100,000 Genomes Project was the importance of routine care being coupled with research and development. So to really support that innovation pipeline from discovery, through to translational research, through to spread and adoption. And as part of the Genomic Medicine Service, we've made that one of our key principles, is that routine care would be aligned with research and development. We'd work in partnership with Genomics England to introduce a national whole genome sequencing service, and that when individual patients and their families consented their data, and that longitudinal data record could be pulled in to the National Genomic Research Library, curated and annotated by Genomics England.

Vivienne: And that's where you come in, or Genomics England.

**Chris:** Hopefully not me personally, that would mess it up. But this, I guess this comes right to the heart of our partnership with the NHS and our strategy as Genomics England, in trying to bring these two worlds together of healthcare and research. And, so, if we maybe explain a bit how the system works. On the healthcare side, as Sue has outlined, you know, this is a clinical service now where a patient will see a doctor, and for diagnostic or prognostic reasons will think, ‘Ah, okay, we can learn more if we sequenced this person's genome’. We'll get a blood sample, sequence that in the lab in partnership with Illumina, that data will come to Genomics England, we’ll run bioinformatics pipelines, other analytics, and present results back to the NHS lab to interpret, send the results back to the doctor who can then treat the patient. And so that kind of closes the first loop of the healthcare service that generates huge amounts of data, clinical data, genomic data, operational data, and all of that helps us to learn and we can de-identify that data, we can make it available in a research environment for researchers to do their work, and we're going to hear a lot about that over the course of today. But then, critically, the partnership with the NHS allows us to feed those insights back into clinical care. Sue may say a few words about the test directory in a few minutes, but this is a learning and an innovative system where we can update our knowledge and our clinical treatment as the research moves forward. So, the more we do in healthcare, the better the research asset becomes; the more we do in research, the more insights we can bring into healthcare. And so we see this as, you know, a sort of mutually reinforcing system.

**Vivienne:** So, give me the pitch for the researcher who thinks, ‘What do I do with this? Has it got any value for me?’.

Chris: Absolutely. So, on the research side, we now have over 60 petabytes of data. So, over 150,000 genomes, all of the billions of associated clinical data points, we're bringing in high definition, cancer images, and all sorts of other assets there. The basic concept is one of, what we call a trusted research environment, which means that the researchers come to the data. The reason there's a picture of fish on the visuals here is that we use this metaphor of an aquarium, you can come in and admire the fish, you can study the fish, you can't take the fish away with you. It's an aquarium; it's not a fish shop. And we keep all of those data safe in the ways outlined there, the five safes. But researchers can bring their own data, they can bring their own application so that they can do what they need to do in that environment. And, critically, there's then, as we say, this kind of live wire for bringing those insights in to be meaningful for the treatment of patients.

**Vivienne:** So there, Sue, the NHS is both the producer and the consumer of innovation.

**Sue:** It is. And in terms of the pipeline that's been established for whole genome sequencing, the first step in that pipeline is the feeding back of primary findings into the NHS. So when the results are tiered through the bioinformatic pipeline, that first stage is pretty straightforward, although it still needs to be validated to be returned, for clinical care purposes. But the second stage is when variants of unknown significance are generated. And together with all of the raft of data that goes along with each and individual person who's provided their consent for their data to be in that trusted research environment, there's the opportunity for researchers, whether they're clinician researchers, many are in the audience today, whether they're in academic departments, or whether they're in industry, to do more work on those variants of unknown significance and establish whether they should indeed be fed back to an individual patient. And from the 100,000 Genomes Project, there have been nearly 200 variants that have been fed back for clinical action. And that is the key of what we're doing. Of course, what we want to do is make sure that the bioinformatic tools evolve, so that we get primary findings that are comprehensive at the first stage. But I think bringing the two together enables diagnostic discovery, with a trusted mechanism for ensuring those variants of unknown significance can then be fed back.

**Vivienne:** And, of course, you've got the national test directory, which Chris mentioned earlier, which brings together, actually, those discoveries because it's updated every year.

Sue: And, Vivienne, that's a key part of our infrastructure. Our infrastructure that we've invested in is not only seen as a point scientific directors, in our genomic laboratory hubs, research directors in our genomic medicine service alliances, so we can bring that loop together. It's established a research collaborative in conjunction with Genomics England and NIHR. But, importantly, Viv, it’s enabled us to have that mechanism to feed back and you enter, people we're here today, about the causal genes that have been identified, how clinical guidelines have been changed, and how was part of our mandated national test directory, covering from target gene testing up to whole genome sequencing, how those can be added to that test directory in a very rapid way. So, what I say is from discovery, into implementation in the NHS, that can be as quick as one year for us to agreeing that to be part of our mandate.

**Vivienne:** And it used to take perhaps a decade. How many clinicians have we got in the audience here? Hands up.

So these are the committed hardcore, and I'm looking at you online too, hoping there are a lot of clinicians, and perhaps those who are perhaps interested in genomics, but not yet sure how to implement it. So if I am a clinician, thankfully for patients, I thought, what does it mean for me? Particularly if I, you know, I'm still in the genetics era, and I'm probably a bit scared of genomics, frankly.

Sue: Well, hopefully we're bringing them out from underneath that stone, Viv. That’s part of our active, our focus is how we embed it, embed genomic systematically into the NHS, into all clinical specialties. But what this means for individual patients is sometimes it's an end to a diagnostic odyssey that may have gone on for years. The second is it may be a return of a variant that's associated with the presenting symptoms of that individual. But thirdly, it may help drive the access to precision medicines, and other repurpose medicines. It's not all about precision medicines, sometimes it's repurposing existing medicines for use in these cases.

Vivienne: Or realising that a particular medication isn't going to work for you.

**Sue:** Exactly. And that's, that's another part is really understanding our maps with other wrapped around genomic testing, whether adverse drug reactions may occur.

**Vivienne:** So, we know that Health Education England are doing some absolutely sterling work, and shout out to Kate Tatton-Brown if you're listening. Fantastic to help upskill the workforce. But Chris, we are doing an enormous amount at Genomics England to try and make a user centric element to all of this information that's going out.

**Chris:** Absolutely. And for us, the interface, I guess, with the clinical community is really, when we're reporting the results of all of the data analytics and bioinformatics into the seven regional genomics laboratory hubs, which we can see on the graphic there. And we should bear in mind that, typically, when we sequence a patient's genome, often we're doing that with the genomes of each of their parents as well as, a trio so that we can understand what's new in the actual patient themselves. There is a huge amount of information there, there’s the 3.2 billion base pairs of DNA, we're looking at the differences in that DNA against all of the other DNA out there and the reference genomes in other datasets, as Sue says, you know, which of the variants do we know about, which ones are uncertain, and so on. And the work of our teams on the interpretation side, is to try and present all of that information, distil down to what are the most important insights so that a really busy clinical team can understand the headlines of that as quickly as possible, but also have the tools and the opportunities to kind of dig into more details, if there are pieces that they want to go deeper on.

**Vivienne:** So what he's really saying is, don't be frightened, you're not going to get 10 books worth of numbers and letters that you've got no idea about. You're getting the headlines. Sue, we talked at the beginning about the NHS at its outset. I noticed, by the way, there was a politician talking to a patient in a bed, doesn't change, does it? But one of the issues that there is always when rolling out something new is about equity of access, that you see some places, you know, going along really well, but other places still struggling. And levelling up is really important, not only at the moment, but we've know that there have been a lot of disparities in healthcare services. So, how are we going to make sure that genomics is not just the preserve of major hospitals?

**Sue:** So right from the outset, so in 2018, when we launched the NHS Genomic Medicine Service, we had a number of key principles that the service was founded on. One of those was that it would be clinically led. The second is it would drive equitable access, because we knew that had been a problem previously within the service. And the third is patients and their families would be informed and involved individuals in the service right from the outset, and it would be data driven. Equity of access, because we've got a mandated test directory that sets out what every single patient in the NHS, if they're eligible, should receive, irrespective of whether they're in Nuneaton, or whether they're in the centre of London, which is really critical. But the important thing is, how do we measure that? And we've introduced, within the NHS, patient level contract monitoring, which means we can monitor what each patient actually gets in terms of the test, and that includes whole genomes. But also the technology that's been used, the time it takes to get that response and whether we've actually got informed consent for their data to enter the Genomics England trusted research environment. And to date, Vivian, in the whole genome sequencing conditions that we've got eligible for whole genome sequencing, we've got a consent rate of 94%, which means there's only a relatively small number of people not making a choice for their data to enter that trusted research environment.

Our next step, and this is why it's so exciting, I think, to have the first of these conferences, Chris, is to ensure that in that trusted research environment, all the genomic data that's generated in the NHS, actually becomes part of it. So that includes our large cancer gene panels, where we're running panels in the NHS of up to 600 targets, DNA and RNA targets, as well as all the other specialist gene panels that are run for rare disease and, obviously, some of our common diseases. That will make it a really comprehensive database, won't it, Chris? And linked with the other developments in informatics in the NHS, bring to the research environment, or the other data sets that are critical to interpreting the genomic data.

**Vivienne:** And patients can play a key role, I think, in trying to promote and make sure that these services are actually being rolled out. And we've got a very different situation in the UK to in the US. Where, you know, the beauty of the single NHS number that follows us throughout our lives has made inequity less of a problem.

**Chris:** Absolutely. Well, I mean, it can sound like a cliche, but it's so true. Obviously, all of this work both on the research side and on the clinical side, only exists in order to bring benefit to patients, which ultimately is all of us. And, Sue mentioned the 94% number about people sharing their data with the research community, which is fantastic, but is only happening and only possible because of a level of trust that's been built up over time.

**Vivienne:** Now, you've both got a patient story to illustrate what's been achieved. Sue, let's start with you.

**Sue:** So this isn't, actually, a story from the 100,000 Genomes Project.

Vivienne: We’ll let you off with a caution.

**Sue:** But, thank you, it’s from our non-invasive prenatal testing service that's just identified genes associated with the development of retinoblastoma. And that was identified very, very quickly. There are about 50 babies a year born with retinoblastoma that can either lead to blindness or to them losing their life. And so, we're rapidly rolling out that that testing, but what we do know is, and Claire Shovlin is going to be presenting today some data about respiratory patients actually, from the 100,000 Genomes Project, which means causal genes have been found, for example in your pneumothorax, but also in Hereditary haemorrhagic telangiectasia (HHT).

**Vivienne:** This is a respiratory physiologist speaking.

Sue: And what the research, the Genomics England clinical interpretation partnership around respiratory disease found was causal genes in both of those conditions. It's led to changes in guidelines and we've rapidly added gene targets onto the test directory.

**Vivienne:** Fantastic. One from you, Chris.

**Chris:** Two very quick ones, if I may. One is more of a quick conceptual one, which is – it's really always super inspiring to see the research community who we have with us today, feeding back diagnoses into the healthcare system that can help those individual patients. We think we'll do over 1,000 of those this year. Hugely inspiring. And just to end on a sort of human moment. Soon, I had an email from a colleague who's on the frontline of delivering the whole genome sequencing service in the NHS, a mum had come in with a sick kid, not from a privileged background, had six kids. And she had, like many parents, got super smart about this condition, had said, ‘Look, I know that whole genome sequencing is going to give the best insights for my kid, how much do I have to raise? Who do I give the money to? My husband is going to run a marathon, we're going to we're going to do a fundraiser. And the doctor said, ‘No, no, this is this is now available for free on the NHS’. And I think that's just such an incredible human moment. And the more of those kinds of human moments that we can create together, the more successful these kinds of partnerships will be and, ultimately, that's where all the research goes to, it’s those human moments.

**Vivienne:** Fantastic. Thank you both so much.

**Chris:** Thanks so much for tuning in to this episode. If you've enjoyed listening, please do give us a five star review. This really helps others to find out about the podcast. And if you have any suggestions of topics or guests, do get in touch with us at podcast@genomicsengland.co.uk. That's [podcast@genomicsengland.co.uk](mailto:podcast@genomicsengland.co.uk). Join in the national conversation on genomics, and we'll see you on the next episode of The G Word.