**Transforming the NHS with whole genome sequencing**

**The G word transcript**

**Rebecca: Hello and welcome to the G Word. My name is Rebecca Middleton and I’m the Vice Chair of The Participant Panel at Genomics England. On today’s episode, I’m joined by Professor Dame Sue Hill, Chief Scientific Officer and Senior Responsible Officer for Genomics in the NHS, and Dr Rich Scott, Interim Chief Executive Officer for Genomics England. Today we’ll be reflecting on the last ten years of genomics, including the impact of embedding whole genome sequencing into the NHS, how it all started with the 100,000 Genomes Project, and how patients have influenced the shape of the Genomic Medicine Service today. If you’ve enjoyed today’s episode, we would love your support. Please like, share and rate us on wherever you listen to your podcasts.**

**Thank you, Sue and Rich, for joining me today as we look back at how genomics has developed in the NHS over the past decade and impacted tens of thousands of lives. It all started with the creation of Genomics England and it’s first groundbreaking initiative, the 100,000 Genomes Project, which sequenced around 85,000 NHS patients affected by rare conditions or cancers and led to groundbreaking insights and discoveries for so many families. I’m one of those rare condition patients and my genome sits in the National Genomics Research Library besides thousands of others. Along with the project, I’ve been on a journey over the past ten years and I’m still hopeful that through time and further scientific discovery, my family and many others will get the answers they need for the future.**

**Today is a chance to reflect back over the progress of the past ten years and to look forward about what’s next for genomics, for genomic science, the genomic service, and for the patients and families it impacts. Sue, welcome. If we can come to you first, and it’s a very big ask coming up, but can you briefly sum up your critical role in genomics over the past ten years and talk us through how you’ve shaped the service in the NHS to date?**

Sue: My role in genomics in the NHS has actually been much longer than ten years, because particularly genetic services have been part of the NHS journey since it was formed in 1948. As Chief Scientific Officer for England, part of my responsibility since I was first in that post in the Department of Health at that time and now subsequently in NHS England, but still with a crosscutting health and social care role, genetics and genomic services actually sit under the remit of the Chief Scientific Officer for England. Shortly after the 100,000 Genomes Project was announced and that the NHS would be a major contributor to the 10,000 Genomes Project, I was asked to lead the NHS contribution to the 100,000 Genomes Project. My role has been both of leading the NHS contribution to the 100,000 Genomes Project, and then as Senior Responsible Officer for Genomics in the NHS in introducing the NHS Genomic Medicine Service to the NHS and its subsequent role in delivery and in supporting research and other initiatives.

**Rebecca: Rich, over to you. Ten years ago I believe your role was very different and you were in clinic, so how has it changed over the past decade as genomics has embedded itself into the NHS?**

Rich: That’s right. As you say, I’m a doctor by background and ten years ago I was consultant in clinical genetics at Great Ormond Street, where I still practice, I still do one clinic a month, but my role is primarily sat there meeting families with a child normally with some symptoms or some problems which people thought might be those of a rare condition and thinking about how we did that testing. At that time I was beginning to think about how we use in Great Ormond Street some of the newer technologies that were coming along. Using, for example, gene panels to help diagnose children who had epilepsy of early onset. Eight years ago, I joined Genomics England, where I could see the work of Genomics England and the partnership with NHS to deliver the 100,000 Genomes Project was something where at national scale we could do something, which at that stage I was just thinking about within one hospital setting. That’s really changed things for me in clinic, but also my role in that has changed. I joined Genomics England originally as the clinical lead for rare disease, so bringing that specialist clinical expertise to give advice on how we establish the rare disease component of the 100,000 Genomes Project.

More recently, in my role as Chief Medical Officer, I’m actually now as interim CEO thinking about how we’ve made that transition from the learning that we’ve gained through the 100,000 Genomes Project to working in partnership with the NHS and Sue and team to play our role in supporting their NHS Genomic Medicine Service. The next phase, if you like, or questions for us to make sure that we are still thinking in a forward looking way about how genomics can do what we believe it can do to be really there in the mainstream for everyone in terms of healthcare.

**Rebecca: And it really has been quite a journey over these past ten years, moving from a research project with 100,000 Genomes Project to a live clinical service and all the challenges that that must bring. Sue, what are you most proud of, what are those challenges that you’ve had to overcome and how do you see genomics medicine service moving forwards so it can help even more families?**

Sue: I think in answering your question, first of all, the Genomic Medicine Service is much broader than the whole genome sequence service that is delivered in partnership with Genomics England, and I’ll come back to that. In terms of what I’m most proud of, I think when we started the 100,000 Genomes Project there was a view that we shouldn’t involve the whole of the NHS in recruitment and in feedback to participants. I pushed really hard to have the whole of the NHS involved, recognising that if we were going to enter into a transformative project particularly for the use of cutting edge technologies by whole genome sequencing and the analytics that went alongside that, if we only started with a small number of centres we wouldn’t get the transformation that was required within a whole health system.

I’m really proud of the NHS contribution because the number of patients that were recruited over the period of time where we didn’t start active recruitment until 2013 and then we completed early in 2019, to deliver this from routine care in the NHS in terms of recruitment and then for feedback I think is something that is unsurpassed by many other research projects, let alone research initiatives in genomics across the world. So while this is a world leading project, it’s also I think a world leading contribution from the NHS from its routine care position.

I was also proud myself to be a participant in the 100,000 Genomes Project within the cancer arm of the project and being able to speak at different public events around the benefits of sharing data through the National Genomics Research Library, in that it’s a benefit that is much broader than you as an individual and has the potential to impact on thousands of people.

The other thing I’m most proud of is introducing the NHS Genomic Medicine Service because we still remain in the NHS world leading. Of course, a key part of that is that we have whole genome sequencing now available within routine care, within the NHS for patients with rare and inherited disease and cancer. Obviously not for all of those patients, but for the group of patients that fit within those broad-brush clinical groupings where there is the most need, but also the ability to deliver a diagnosis compared to what we could do from standard of care testing.

I think it’s those two halves for me with myself being a participant and being part of the NGRL right in the middle. Because, of course, from the NHS Genomic Medicine Service, which is what many other countries are grappling with, as soon as you introduce a whole genome sequencing service within a health system, how do you also continue to support research and continue to populate a research database that can be accessible, access is approved and in a safe data environment, how can you continue to support that?

**Rebecca: Over to you now, Rich, on what you’re most proud of for yourself, but also for Genomics England and being the custodian of people’s data, that people have given their data through the 100,000 Genomes Project and they continue to give their data through the GMS. If you could pick up also on the research side, so the role that Genomics England has played in the development of the Genomics Medicine Service and the genomics within the NHS, but also in the wider ecosystem as well in terms of driving discovery and driving answers for the many families and for many patients out there who are still looking for those answers.**

Rich: I think really there is one word that I come back to quite a lot which is the word together, where the journey that we’ve been on as Genomics England, me playing my role at Genomics England, but all of those involved across the ecosystem, that key partnership that we have with the NHS and with our participants, but also broader than that into the other people involved in delivering a live clinical service now that we support the whole genome element of. Also, collaborators in research, whether that’s in academia or industry, this is a team sport. What I’m proud of most is the impact that we’ve had together and recognising that when this journey started there was a real vision about the potential that genomics could bring in the coming years because of the changes that came. For example, the next generation sequencing technology, but also the changes in ability to hold and analyse data at scale. I think rightly no one would have pretended to know what the journey was.

I think the thing I’m most proud of is that we have navigated that together. In a way, we’ve continued to learn and we’ve learnt from the challenges that we have encountered, whether it’s through delivering the 100,000 Genomes Project or our work since, because there always will be challenges. The reason that we’re so proud of the impact that there has been is because we recognise it’s hard to do. I think that point particularly of linking healthcare and research is absolutely key. That’s something that we’re working with Sue and the teams across the NHS are absolutely committed to and recognising that this is an ongoing learning area. That means learning how we do every element of it, but it also means that marrying clinical care and research is absolutely critical to getting the best outcomes for the system as a whole and for participants/patients individually.

We’ve learnt how to set up a system that works in that way. We’ve worked through the consent models that patients in the NHS receiving routine care are comfortable with. The models of presenting data de-identified for researchers to use for purposes that those participants are comfortable within, as we call it, a trusted research environment, is a model that comes with challenges in terms of the data access for researchers but is one that is really broadly accepted and we can get to work at scale. I think it’s that ongoing learning and that we’ve now I think shaped an approach to genomics across clinical care and research which no one would say is perfect, but we definitely understand that we’ve learnt about a model that we can keep iterating on and, crucially, we’ll keep learning for participants present and future.

So that, as you say, Rebecca, one example of that situation is where families have had a test, whether that’s through 100,000 Genomes Project or more recently through the NHS Genomic Medicine Service, if today’s knowledge can’t find the answer in terms of a rare condition diagnosis, we know that one really important element of that research offer is that researchers will continue to look for answers. If something is found that is relevant, that can be fed back to the clinical laboratories to look at. If there is something that is clinically actionable, that can be reported.

**Rebecca: Thank you, Rich. I suppose, Sue, we’ve had a decade of navigation, a decade of learning and a decade of adapting to really take us from the 100,000 Genomes Project to the NHS Genomics Medicine Service. There have been challenges along the way, no less we’ve had COVID to deal with, a global pandemic. What other challenges have you had to overcome to embed a workable world class service within the NHS, how have you navigated that with your partners such as Genomics England?**

Sue: What’s been really important is actually understanding the challenges. I see the challenges more in the sense of the transformation that we need to drive rather than them actually being challenges. Some of the transformation that was driven through the 100,000 Genomes Project we’ve actually baked into the Genomic Medicine Service. For example, during the 100,000 Genomes Project we understood the importance of clinical leadership; particularly if genomics was going to be embedded across the NHS for patient benefit, then it would involve more clinical specialties than clinical genetics. Through the 100,000 Genomes Project, we really drove leadership and engagement across multiple clinical specialties.

We also drove this whole model that Rich talked about earlier about data sharing for broader benefit, and that benefit has then transferred over into the Genomic Medicine Service. We also recognise that if we were going to hold genome sequence a number of the processes, technical processes that happen within now our genomic laboratory hubs, needed to be standardised with quality and also external quality assurance at the core. That’s right from taking a sample from a patient, extracting DNA, the sequencing methodology, whatever that is, whether it’s whole genome sequencing of the type of testing within the NHS, so large gene panels, whole exome sequencing, or even smaller gene panels and other types of testing, that had to be consolidated and standardised. When results are returned we needed a standardised approach to results and interpretation. Across all of those areas if we’re trying to drive a national approach as we were in the 100,000 Genomes Project and we’re now in the Genomic Medicine Service is having an external quality assurance process that can look externally at each of those components that has been an important learning from the 100,000 Genomes Project into the Genomic Medicine Service.

A key other element of transformation, and I hope you’ll agree with this, Rebecca, was the involvement of members of the public and also participants. So right through the 100,000 Genomes Projects from Genomics England establishing The Participant Panel, through to the involvement of patients and public throughout the national programme for the 100,000 Genomes Project in NHS England, through to the genomic medicine centres that we created at that time, all of that has now been reproduced in the Genomic Medicine Service. So, patient and public involvement is a key part of the delivery mechanism.

Finally, we’ve had to change and continually adapt and develop the underpinning data and digital infrastructure in the NHS. Initially in the 100,000 Genomes Project we standardised the data that was collected for rare disease. We introduced the use of terms called human phenotype ontology system that enabled individual patients and their presenting characteristics to be classified; that’s continued on into the Genomic Medicine Service. But still more work to do in the 100,000 Genomes Project, we have to get multiple informatic systems to talk to one another. As we moved into the Genomic Medicine Service, we’ve both with Genomics England had to develop the analytical pipeline. We’ve had to develop a system that’s enabled whole genome sequencing, for example, to be ordered and then to be returned after sequencing and the semi-automatic analytical pipeline in Genomics England to generate a report that could then be looked at and interpreted in the genomic laboratory hubs and returned to patients.

What’s been a key part of that has also been the establishment of genomic multidisciplinary team meetings that came out of the 100,000 Genomes Project, but now is embedded into the Genomic Medicine Service. Of course, the difference between the 100,000 Genomes Project contribution and now in the genomic medicine service is to ensure there’s equity of access across the country in terms of the testing that is provided. A key part of the way in which the testing is offered is that introduction of the National Genomic Test Directory that sets out the standardised offer that will be funded by NHS England. That’s across where an inherited disease or cancers, as well as common diseases and some other pharmacogenomic applications.

The challenge always is standardisation, equity of access, and the infrastructure and leadership that makes this happen, together with developing a workforce that is genomically enabled so that it can spread out beyond that clinical genetics specialty into those multiple specialties to make sure that it’s embedded. So remain in terms of some of the challenges around making sure that we change clinical pathways where genomics means that we can do things much earlier on in a patient pathway and get a definitive result and intervene. This is particularly important in cancer, but it’s not just cancer, it’s also in rare disease.

Secondly, it’s about how do we develop the whole of the NHS workforce. We have 1.3 million people that are directly employed by the NHS. There are another 600 that actually are associated with the NHS through the contracts that they hold. It’s a huge task that we still have to undertake to make sure that genomics is available to all. There are two other elements, one we have to continue to take the public with us, and I think we’ve learnt from COVID that the public does understand now the importance of molecular tests. But there’s still more to do as we use genomic information more broadly across the NHS and to drive treatment decisions that might mean that a patient thought they were going to get one cancer drug but they’re going to get another because their genomic mutation says treatment B might be better for them than treatment A. We have and will continue to have a number of ethical issues that will arise as we consider whether it’s some of the research initiatives that are undertaken or whether it’s some of the decisions that might be made within the NHS Genomic Medicine Service or for the use of genomics.

That’s just a few, but it pulls it together from what we’ve learnt from the 100,000 into the GMS, what else the GMS is doing, and what some of the challenges are that remain.

**Rebecca: And a great deal has been done. There are a number of key challenges ahead. As you say, it’s been a learning process, it’s been a navigation process, but it’s been driven by the people, by systems, by people, and they have played a critical role and will continue to play a critical role in ensuring the success going forward. I sit as the Vice Chair of Rare Conditions on The Participant Panel. Rich, if I can come to you next, how has the patient voice, how has The Participant Panel but the wider patient voice been heard and how are their view, their needs being reflected in addressing these four big sort of buckets of challenges and how are we learning these lessons going forward thinking of the new projects? For example, the newborn genome project, The Generation Study, could you give us some examples of how that learning is going forward and we’re learning from the past but preparing for the future?**

Rich: I think it comes back to one of the really key words here is transparency and transparency in a number of ways. One of those is about the fact that this is a journey we’re all on together. So, one of the things that was there right from the beginning of the 100,000 Genomes Project before I arrived was putting participants absolutely at the centre of project and the design and then in time that came for us in Genomics England wider in terms of our organisational governance. Establishing The Participant Panel on which you’re a co-chair I think was really important for us early on to make sure that participants whose data it is we hold, it’s no one else’s data, it’s our participants’ data, are there driving and at the centre of the decision-making process, for example, through our Access Review Committee around who accesses the data. Participants sit on various of our governance groups and that’s a template which I think is one that people have seen in various fields as working really well. It’s one that Sue has touched on as being looked at and has provided useful input as to how patient and participant involvement has been set up in the Genomic Medicine Service.

I think recognising that much of this is us all collectively finding the right path forward is how we approach every question that we tackle. Sometimes that’s around really very practical questions. So, for example, Rebecca, you will know we often come to you guys about how we phrase a letter that might go out to participants, because recognising that from the inside of an organisation you see things one way but you might not recognise some of the nuances that are really important. Through to thinking about the really important questions around how we should set up access and safeguards around access that are there and, again, having participants sat on our Access Review Committee is crucial. And on to finding our way in new areas where the Newborn Genomes Programme I think is a really nice example where in many ways it’s quite similar to the 100,000 Genomes Project in that it’s a research study and it’s delivered in partnership with the NHS. It’s asking big questions around whether genomics can be used in a particular setting and if so, how could we use it? I think a really critical part of that and one that’s been, as you know, sat in a number of the different strands and in the overall governance for the programme, Rebecca, having participants guide us, whether those people who like yourself are already part of the national genomic research library or whether they’re people who might join the study themselves, or whether they’re people with a different perspective that is important to include, including that engagement work as well as just with the broader public as part of the study is absolutely crucial.

Before we even started the design of the study we set out with a public dialogue around attitudes to do with genome sequencing in newborns jointly with the National Screening Committee to understand where public views were to allow us to do a bit of a deep dive, not just a superficial vox pop view on what’s your attitude to a one-liner question, but really to work with people on understanding some of the nuances here. There’s a lot of nuance in most of the questions that we’re engaging with, and then through the programme into different elements, whether that’s designing the materials for consent or whether it’s understanding how to practically design the process for contacting families or feeding back findings as part of the study, making that part of the process rather than a separate endeavour I think is really crucial.

One of the words that I often hear people use when talking about challenging questions around how we make advantages in medicine is around explaining what people are doing. I actually think that’s a really interesting word which I don’t like. Most of the time this is about dialogue and it’s about discovering together what we are doing and it’s not people sit in with the best of intentions and with great expert knowledge in a closed room to decide what’s the best approach, which is often an easy way to think about how to design a research study, for example, but this needs to be an active process where there’s genuine dialogue and we learn and find our ways together.

**Rebecca: Some great examples there, Rich, of how powerful the participant and the patient is in the designing future services for even more patient and participants going forward and ensuring how needs and views are reflected. But, Sue, it doesn’t just happen in Genomics England, there are patients and participants across the GMSAs as well, which is fantastic to see and I sit on the panel at the East GMSA as well. How important was that for you to establish that as part of establishing the Genomics Medicine Service? How important was that for you to ensure that the patient and participant view was there locally as well?**

Sue: So, I think we learnt from the 100,000 Genomes Project about the importance of patients and participants being part of the research element of the 100,000 Genomes Project and how that was designed, how the different pathways were put in place. In NHS England the patient is at the centre of everything when we come to our services. In all of our major programmes we have patient representatives, patient for an ongoing discussion with patient groups. This was both building upon what we’d created together with the Genomics England Participant Panel in the 100,000 Genomes Project, but then making sure that it fitted with the new genomic medicine service infrastructure that NHS England commissioned from 2018 onwards. It was making it a key part of that, making sure that coproduction with patients and families and really having a temperature check on an ongoing basis about the experience of patients and families of the genomic medicine service that they were experiencing has been a key component of our infrastructure and how we’ve put the infrastructure together. I always think there is more we can do, there’s more we can do to monitor the experience particularly of services. That having been said, we will continue to drive forward the involvement of patients and families in the future iteration of services, whatever that might look like.

I think if you put patients and families at the centre, that actually helps you determine the type of services that need to be commissioned nationally, the type of concerns that people have of the service and the experience that’s feeding up, but it makes sure that patients and public representatives are part of all the important governance groups. For me, that’s where the conversation needs to happen, it needs to happen both at an individual service level but through all the levels of governance that actually govern a service that is commissioned by the NHS in England for the population that is being served. Even if we haven’t got it totally right, I hope that we’ve got it as a key component of all of the services and set out in commissioning specifications such that it’s a requirement as is having the technology in place to deliver a bunch of genomic tests.

**Rebecca: Thank you, Sue. The Genomic Medicine Service is unique in the way that it provides a clinical outcome that is an answer for a patient, and also includes the option of joining the research library which supports further discovery. What are the benefits of this?**

Sue: The positive benefit of having the National Genomic Research Library has been through the researchers, scientists who’ve been granted access to the data. To date, we’ve had over 1,500 putative diagnostic variants returned to the NHS, so to our NHS genomic laboratory hubs, for further investigation, further discussion with clinical teams. About 80% of those have been returned to clinicians and therefore to patients to, for example, give them a diagnosis or to update the diagnosis that they’ve been given or make treatments available. That is a real positive benefit from that pipeline to individual patients. But also the evidence that’s generated enables us to evolve the genomic test directory. It enables us to add to genes if new genes have been discovered to the test directory, changes in eligibility criteria, so it’s this continuous evolving learning system. From patients providing samples and their consent for their data to be used to the research library, to the feedback loop back into the NHS that influences both individual patient care, but also the type of tasks that get offered in the genomic medicine service overall.

In conjunction with Genomics England we have also been working on an NHS Genomic Medicine Service research collaborative that’s enabled us to look at the projects and initiatives that industry or other researchers would like to undertake, would like to have access to samples or to data, and to consider that on the basis of would this support the overall national endeavour in genomics, would it add to the National Genomic Research Library and create that learning system? Is it something that we need to do nationally rather than just locally in a research project? It’s making the infrastructure available for those research projects over and above the ones that are part of Genomics England spending review initiatives or NHS England’s Genomic Networks of Excellence. But enabling us to work with industry and researchers to support their research endeavours in a way that is contained and make sure that we create and continue to create and add to the National Genomics Research Library and this overall learnings infrastructure.

**Rebecca: And Rich, anything further to add there?**

Rich: I think that creation, that word, that learning infrastructure is the key thing there. I think the process that has taken us here where we’ve worked out how to integrate clinical care and research is so valuable, both for the individual patient and participant and also for the system as a whole, often making the choices that allow us to arrive in the direction actually all point together towards doing the same thing. It’s really constructing things around that central vision and I think that is so important.

**Rebecca: Thank you so much. We’ve had a whistlestop tour of genomics over the past decade which and improved and informed the lives of thousands of patients and families. But to finish, let’s look forward. What is your one hope for the future of genomics within the NHS? Rich, perhaps we could start with you?**

Sue: I think my wish is a relatively simple one, which is that we maintain this momentum that we’ve got and we’ve built together. We’re on a journey and it’s momentum towards genomics being absolutely part of the day-to-day, the mainstream of healthcare so that wherever you are in the country, whoever you are and often potentially without the clinical teams needing to feel they’re doing anything very genomicsy, if you like, genomics is there and bound into the routine care that one has to deliver. I think when we look and we compare ourselves to other countries, because of that link that we’ve made and that partnership between clinical care and research, we are in a really strong position. It’s therefore about maintaining that momentum and getting us to that place where genomics is just a routine part of everyone’s care.

**Rebecca: And Sue, finally over to you, what is your one hope for the future?**

Sue: What I’m looking for when we put the patient at the centre is that we adopt all of the genomic technologies that would really enable us both to diagnose a genomic cause for patients that of presenting symptoms, or to inform their more preventative or inform their treatment such that genomics becomes part of everyone’s pathway of care in the NHS, and that we really maintain the NHS Genomic Medicine Service as the most advanced service within the world and that it continues to work to populate a National Genomic Research Library with Genomics England such that patients can benefit from ongoing analysis and interpretation of their data. That we really become the leader across the world of this learning ecosystem and we give as many patients as possible a diagnosis and that we inform as many patients as possible treatment pathways. I believe we’re in the next wave of genomics following the discovery of DNA in 1953, and now it’s how do we make genomics available to everyone across where an inherited disease, across cancer, across common and acquired disease and in pharmacogenomics.

**Rebecca: Thank you to our guests, Professor Dame Sue Hill and Dr Rich Scott, for joining me today. It’s been great to talk to you and understand the journey so far and what’s ahead for genomic healthcare. Happy 10th birthday, Genomics England, and happy 75th birthday, NHS. Here’s to the next decade of supporting patients and more scientific research and genomic discovery to drive home. If you’d like to hear more like this, please subscribe to the G Word on your favourite podcast app. I’ve been your host, Rebecca Middleton. This podcast was edited by Mark Kendrick at Ventoux Digital and produced by Naimah Callachand. Thank you for listening.**