**Reanalysis Webinar transcript**

Hi, I'm Rebecca Middleton, Vice Chair of the Participant Panel at Genomics England, and you're listening to the G word. This week, we're sharing the reanalysis webinar for participants that I co-hosted recently with Jillian Hastings Ward, chair of the Participant Panel at Genomics England. In this webinar, myself, Jillian, Chris Wigley, CEO of Genomics, England, Dr. Suzi Walker, Head of Translational Genomics, and Dr. Ellen Thomas, Clinical Director and Director of Quality, delve deeper into how science and technology are evolving a Genomics England, and what impact participant data is having. Listen to find out more on Genomics England's approach to reanalysis - we hope you enjoy!

Jillian: Hello, and good afternoon, everybody. And thank you very much for joining us today for this Genomics England webinar about reanalysing the data which they hold from the 100,000 Genomes Project participants. I'm delighted to be here and to be talking to you and to be able to bring forward the great news that we have been hearing as a Participant Panel for a while now about what Genomics England are doing with the data that we have all shared with them in the course of the 100,000 Genomes Project. I'm delighted to be welcoming today, the Vice Chair of the Participant Panel, Rebecca Middleton, here to help me ask the questions that you have already sent in and that we will have today. And answering those questions are Chris Wigley, who's the Chief Executive Officer of Genomics England, Dr. Alan Thomas, who is Clinical Director and Director of Quality at Genomics England, and Dr. Susie Walker, who is head of Translational Genomics, but we just call her the gene detective, because he's doing some incredible work there in the background. And we will be hearing a lot more about that in the course of the webinar. And any questions that we don't get to answer today, we will be able to take and answer afterwards. And those questions will be available on the Genomics England website, in due course, along with the recording of this webinar, and a blog, which is going to summarise the key points. If you don't have time to watch a whole hour in retrospect, then we will be able to share the blog with you which will have the headlines in it. So, without further delay, thank you very much again, Chris Wigley for joining us. My first question is for Chris, perhaps you could start by giving us an overview of where Genomics England have come from to get to where you are today, and how you've been working with the NHS, in bringing patients into this and what's happened.

Chris: Thanks, Jillian, very happy to do that. So, I guess we go right back to the beginning, Genomics England was created as a government company to deliver on the 100,000 Genomes Project in partnership with the NHS. And I thought it might be helpful as a first step to just talk through the different phases of that work, and who's doing what along the way. So, if the gods of technology are with me, I'll hopefully share this slide. The first phase of the 100,000 Genomes Project back in kind of 2013-14, when it was just being designed was really in this planning work. The blue boxes on here are things that the NHS are doing, the pink boxes are things that GEL are doing, and the green boxes involve either consultation or activities with patients and participants. So that first phase was really all about the joint planning and design, which was it was kind of co-created with early patient representatives into the recruitment phase of the project where patients who had cancer or undiagnosed rare diseases, had a conversation with the doctor, saw the materials that explained what the programme was about, and chose to join to the project, gave samples and gave consent for how their data was going to be used. Those samples were then sequenced to generate the genomes, we tapped into other clinical datasets as well. And GEL then spent a lot of effort in sequencing and analysing those results and returning the results to the NHS. At that time, the NHS teams were the genomic medicine centres that are 13 of those I think that processed the findings, confirmed them because the confirmation of the findings has to be done by those teams of doctors and clinical scientists, and then returned those primary results back to the participants. Where now you know, that wasn't the end of the story, that was really, to some extent, the beginning of the story. And so those patients who had a positive finding from the first wave of the projects, were to go into treatment pathways in the NHS. And we're now in a sort of ongoing phase of researching those genomes, those datasets, working with clinical interpretation partnerships - who are groups of academics, and also leading working in house, which Suzi and Ellen will talk through in more detail, to keep looking at those genomes, keep bringing the latest science and the latest findings to bear on those. And then just as with the primary findings, passing those research findings through to the NHS to kind of confirm and pass back to patients and participants. That hopefully gives us a sense of, kind of who's doing what and where are we up to.

Jillian: I'll say a few words here about who the results are going to be coming back to when we said we receive results via the doctor for any further onward work - which doctors are going to be hearing about those?

Chris: We passed the research findings to one of seven regional Genomics lab hubs, where the clinical scientists confirm those, they will then pass them back to the relevant consultant who was leading the work and recruited the patient into the programme. Ellen, of course, is one of those. And we'll say more about that, that interface her section of the webinar. I guess the other piece that's important to mention is that, you know, the 100,000 Genomes Project has been a real-world leader and has laid the foundations for a lot of broader activities now, which Genomics England and the NHS are involved in. First and foremost, that's the launch of the world's first nationwide whole genome sequencing, diagnostic service, the NHS Genomic Medicine Service. And as well as that, we've done a lot of work through the pandemic on COVID-19, for example, and other research programmes, the largest of which is programmed to sequence up to 100,000 newborn babies, which will be happening over the next few years. And I think the really important point to make about those, is that the more work that we do, the more there's a sort of positive reinforcement loop, because there's still so much that we don't understand about the genome. And the more data that we have, the better everyone benefits from that. The additional work that we're doing is not sort of separate to the work of 100,000 Genomes Project. It's intimately connected to it, because that helps us to learn more and pass more diagnoses more findings back to the original 100,000 Genomes participants as well. And the final point, I guess, just to make about the slide that I shared is also, you know, Genomics England and the NHS work really closely in partnership, but we each have quite specific roles. And the role of the NHS is to work directly with patients, and our role is to support them. And so today, we'll be talking a lot about the work that Genomics England is doing in support of that. But we should also be clear that we're not the people who actually treat patients, you know, that's the NHS, but the work that we're doing and in support of that is ongoing, as I say,

Jillian: Thank you very much. That's great. Okay, Rebecca has the next question for you.

Rebecca: Chris, in lay terms, could you briefly describe the state of play on the science that really is underpinning all the activities that you guys are engaged with right now?

Chris: Yeah, absolutely. And as a layperson, myself, I always need to put it in simple terms for myself as well. So that's always helpful. So, when we talk about Genomics, we're talking about our whole genome, all of our DNA. And there's a copy of that in every cell of our body. Across that genome, there are 3.2 billion base pairs that we represent with letters, obviously, they're like little molecules, but we represent them with letters. And within those 3.2 billion base pairs of letters, there are 22,000 genes. One of the analogies that I like to this is, if you think about a kind of a piece of string that stretches from London to New York, you've got kind of 22,000 beads along the string, which are the genes that that make proteins that then then do all of the things in our body. And so that's about 2% of the DNA. If we look across all humans, about 99% of our DNA is the same. And so, we're looking at the where one person's genome is different in some specific places from a kind of, quote unquote, normal genome. Of course, we're all different in lots of different ways. There isn't a kind of single perfect genome, but we're looking for where people have little sort of differences or glitches that we can try and investigate to see if that's what's causing whatever symptoms it is that someone's being recruited for. It's worth saying, as we talked about at the beginning of the programme and continue to talk about the science is moving really fast here. The technology is moving really fast, and we continue to learn more about the genome and how it affects our body and our wellness and, and sickness and so on. There is still a lot that we don't understand about that. When we talk about these variants or glitch in our in our DNA, we can classify some of those really, really confidently. We know that if you have this particular glitch that you will have sickle cell anaemia, for example, there are others that we suspect may be associated with a specific condition or symptom. And there are others that we know are doing something, but we still don't know what they're doing, so that they're what we call variants of unknown significance. And there's still lots and lots and lots of variants of unknown significance, that back to the kind of positive feedback loop, but the more that we learn, the more we can actually classify those and become more confident. But the final thing that's worth saying is that some diseases, genetics plays a really big role, where back to something like sickle cell anaemia, which just caused by one change in our DNA. In other diseases, genetics plays some role, it might change our risk factor, or how our body responds to that disease. And in other areas, genetics won't play a role. So well, genetics and genomics are really powerful tools to help us understand what's happening in our body. They don't give us all the answers for all conditions. We’re continuing to work with leading scientists around the world to bring the latest advances into the work that we're doing both with the NHS and on the research side. But it's still not a kind of magic wand that tells us everything about what's happening in someone's body.

Jillian: Thank you for that. And right time to bring in Ellen. She is the NHS clinician among us, as well as being closely involved in the work at Genomics England. Ellen, how have you been using participant data up to now? And how are you going to be using it next?

Ellen: Yes, thank you, Jillian. There are really two sort of broad ways in which the data from 100,000 Genomes Project participants has been used and continues to be used. The first way, which I think is of immediate interest to many participants, and has been and will continue to be, is really looking at those 3 billion DNA letters in the genome that Chris was talking about, and trying to target a very specific question to that data. The specific question is, is there anything that we can see in the genome, which explains the reason why this particular patient developed these particular symptoms? And that is then a question which if we can answer it then obviously unlocks a lot of things which are very helpful in terms of understanding a condition and understanding implications for a family and so on. So that kind of diagnostic question that we target at the data, was very much the question that was the target of the first round of analysis. So as Chris said, we developed an automated bioinformatics pipeline, where we use the genomic data and the clinical data from participants, I put those together and tried to reach something, which was a potential answer to that very specific question. And then the output of that was sent to NHS clinical scientists, who looked at the output of the automated pipeline, and made expert human decisions about which parts of it met the evidence thresholds to be useful now, to look after families in their health care, based on what we know about the genome and about that family today. So that human review of the data by these experts, people in the NHS, is really crucial, and happened for all of the main findings in the in the 100,000 Genomes Project. As Chris said, you know, that's really only the beginning of the story, because we have since carried on looking at the genomes and carried on trying to answer that same question. Because we know that knowledge moves on over time, we will understand more about genomes, and how they relate to our symptoms and our healthcare, we are continuing to target that very specific diagnostic question at the genomes. And when we find new diagnoses, those are returned to the NHS genomic laboratory hubs via what is called the diagnostic discovery pathway. And that is a pathway which the NHS is absolutely with us in running that pathway. And it's mentioned in the NHS England genomic strategy across the NHS. So that's really helpful for continuing to make sure that this pathway functions, and I think, as one of your earlier questions was suggesting, you know, not people, the person who originally suggested that a patient joined, the project might have retired or moved on, but the Genomic Medicine Service is still there, and is still receiving these findings, and is using standard NHS processes for changes in staff over time to continue to receive that information and do the right do the right things with it. So that's really the first way in which we look at genome data.

The second way we look at genome data is in a sort of broader, more zoomed out sense is how can we use that data really, to understand more at a basic and quite sophisticated level, about the way the human genome works, the ways in which the human genome can develop problems and the ways in which those problems can lead to healthcare issues. So that's a much shorter if that's not targeted at answering a specific question for our specific person, that is more of an advancing science altogether. But while doing that advancing science, sometimes something happens, which then means that we do have a new diagnosis for somebody. If we advanced science by findings by a researcher, for example, finding that there isn't enough evidence to prove that a particular gene causes a particular condition, then the people who were studied as part of that research out of that research will get a diagnosis because their diagnosis is now a known gene rather than an unknown gene. We also have the diagnostic discovery pathway available to us. So that as well as doing the specific looking for diagnostic questions, if when we're doing the broader research, we come across diagnostic answers, we have the processes in place to get those back to the NHS, for that all important pinnacle scientists review. That's really the key ways in which we're looking at the data at the moment.

Jillian: Thank you. We've heard a lot that where about a quarter of the rare disease patients or rare disease families who signed up for the 100K originally have got a diagnosis so far. But I think Rebecca has a question which will be on the lips of the other 75% of them, which is when a lot of people come and ask us this, so I'm sure a lot of people will be really interested to hear what you have to say.

Rebecca: Thank you. Yes, I'm one of those many people who didn't get a diagnosis or haven't received a diagnosis so far. What should I do? Should I have another test? If so, what test should I have? What should be my next steps?

Ellen: Yes, thank you, Rebecca. So really, that question is tricky to answer at a sort of level for everybody, because everybody who came into the project came into it with a different type of symptom, a different situation in their family, they've then had different life events, or different choices that they've been making in life and different evolution of the symptoms that they originally came in with. There isn't really a single answer to the question about what other tests people should have. It's definitely the case that if things have changed for you, or your family, or you have any questions about your healthcare, or you know, your specific city or your specific situation, then going back to your NHS team is very much to the right way to go about that. Obviously, that starts with the GP. But also there are a range of experts, including clinical geneticists and other sub specialist experts who are available to GPs to consult if they need to. So that specific question for each individual is going to be very much dependent on their own condition and context. I think it is worth saying that even if you didn't have something found on the first analysis, then the things that Suzi is going to be talking more about in a minute about how we're continuing to target diagnostic questions at the data all the time. So it doesn't mean that something won't come out of that for you. And obviously, it's difficult to predict exactly when that might happen for any one individual. But we are continuing to look and continuing to return those diagnoses. If you did get a negative result, the first-time round, that was very much a nothing has been found. So far. It wasn't nothing has been found and we've stopped looking. Thank you very much.

Rebecca: And we've talked a lot already in this webinar about the rare disease arm of the 100,000 Genomes Project. But what's the news on the cancer side? What can you tell us about how things have gone with that? Because obviously, people who joined who had cancer already had a diagnosis there. But the question was there anything that could be done to further understand their cancers or to find a treatment or trial for them?

Ellen: Yes, absolutely. Cancer genomics is quite different in its context from rare disease genomics. In cancer genomics, what we're really aiming to do is to look at the tumour that's developed, so we're interested in the tumours DNA. And what has happened to the genome in the tumour, which has driven that tumour to grow and then driving it to develop, and the nature of tumours is that they are not static over time. They may change over time, if they if they do, if they come back, for example, or sometimes they're taken out surgically, and then we will very much hope that at that point, they've gone and they won't continue to change because they've been taken out and cured. In terms of how we're using the cancer data, we are very much still looking at it and still drawing lots of research conclusions from it, and learning about how you use tumour genome data to how you analyse it better how you visualise it, how you pull out the useful elements of it. But for the patients, that's quite different because for a patient who had cancer during the course of the timeframe of the 100,000 Genomes Project, any new information that came out now from looking at their tumour genome is very unlikely to be relevant to them because either they don't have their tumour anymore, or they have a different tumour and that now because it won't stay the same. If participants who joined the cancer project do develop a new tumour or their cancer relapses, then, as part of their standard care, they will be talking to their clinicians about if there a different genomic test that we should be doing now on the tumour. Genomics is still very much being used now to help understand tumours that are developing on their own being diagnosed now, but new information that we learned about tumours that happened five years ago, for example, are very unlikely to be of any have any relevance to the ongoing health care for people. When we're thinking about how we return how we focus on returning information from our ongoing research into the NHS, that is very much focused on the rare disease context, because we know that the germline genome, so the genome that we all inherit from our parents and pass on to our children, is relatively static over time. So that's something that we sequenced five years ago, if we find something new in it now, then that is still there and still relevant now. So that's why this conversation has really been very much focused on rare disease.

Jillian: Thanks very much, Rebecca.

Rebecca: Yeah, thanks, Ellen. Another question from my side, I suppose an obvious question that as participants, especially those who haven't had any result, or have a condition where things are changing? Why can't we put participants back through the pipeline? Why can't we look again, at their genome? Because as we've heard from career science is moving at a pace?

Ellen: Yeah, I think that's a really important question. I want to sort of zoom out a little bit in addressing that one. I'm very aware of that, in the past, during the main sort of phase of the of the 100,000 Genomes Project, we said to our participants, that when everyone in the project had finished receiving the first round of results, and the first round of additional findings, we would make sure that all participants benefited from the learning that we had made during from the data that they had contributed to the project. That absolutely 100% has never changed, that that commitment. And we're absolutely committed to continuing to do that. One of the issues here has been that at the time, when we were first saying that, we thought that we knew what the best way of achieving that would be. And we thought that the best way to do that would be to take everybody, every participants genome if they didn't have an answer from the first time around, and put them back into the to the new version of the automated pipeline, and put them back through the whole process. But since then, actually, we have done a lot more learning than we expected to about genomes, and about how to interact with genomes and how to interact with that data. And actually, we don't believe that would be the best way of doing things. So our commitment to wanting to go back to participants, and make sure that everybody benefits from the learning is absolutely intact. And because of that, that we believe that we found a better way of doing it than putting everybody back one by one through the pipeline.

So firstly, I just wanted to apologise to everybody. I think we were overconfident in the way that we explained what we were intending to do. We didn't take account of the amount of learning that we would do through the project. And I think we said that we would take specific technical steps, which now we don't believe are the right technical steps to take based on the learning. I apologise that we did that and were overconfident on our messaging about that one. But as I say, we are completely committed to continuing to look at the data. And the reasons why. Suzi is going to talk a bit more about what we're doing, instead. But the reason why we think broadly that we think that we have a better solution now is that, firstly, that the pipeline is one way of looking at a genome, it's one way of targeting a question at a genome. But it's not the only way to target questions at a genome. And if we take the same approach, again, versus taking a new approach this time, actually, we think that we can find things, and we have already found things, we think we can find more things by using a different approach, rather than by using the same approach again, as well as finding the things that we would take by running the same approach again.

And then the other thing, which I think is really important is that it took us about five years to take every participants genome, run it through the automated pipeline, and then run it through the NHS process, which is crucial to making the data useful. We spent five years doing that, if we kick that off and started again, it would realistically, take us another five years. It is a big undertaking, which would mean that some people will be waiting another five years before they got to the point where their data had been back through the genome. That would mean there would be another queue and everybody would be in the queue. Whereas with the approach we've taken now, where we look at all of the genomes and target questions across all of the genomes together, it means that everybody's at the top of the queue every day. Nobody is waiting five years to start the process of having another look got their data. So that's why we really believe that this is the right approach to take.

And the final thing is just to say that all of the new diagnosis that we find must go via the NHS, because that is where the experts are to say, Yes, this is appropriate to use in healthcare. It's that the NHS is where healthcare experts sit. And everything that's going to be used for our healthcare must, you know, it's, I would want everything for my health care to go by those by those experts. But what we can do by using the current approach is giving the healthcare experts a bit of a helping hand, by adding in more evidence and information and presenting that back to them to help them with that process just to make it a bit a bit more efficient for the NHS, to then process those and return them to patients. We really feel that this is the approach we are taking gets the best balance in terms of sticking to that original commitment to make sure that everybody who joined the project and who donated data to the project is benefiting from that donation that they made.

Rebecca: Thank you very much. Yeah, we were wondering about whether there's an analogy that we can share to help people understand the difference between the original one by one pipeline approach and the new approach that Suzi is developing. I suppose it's equivalent to if you're trying to find in a football stadium, people whose birthday is the third of April, for example, how do you find the people who is that relates to as fast as possible? Do you ask them one by one? Or do you just say to the whole studio audience, put your hand up if that's you? And I think that's the sort of scale of difference that we're talking about here, between the original intended approach, and where you're talking about getting to next. I think this is a good opportunity to bring in Suzi, and who's been patiently waiting to tell us all the science side of things. Thank you very much for joining us today Suzy. And first question we've got for you is, can you tell us what you and the team are doing with participant data to help find these new diagnoses please?

Suzi: Yes, thank you. Slightly to recap, and just to set this up nicely, and what we spoke about before, but everybody has so many millions of genetic variants in their genome. And in the case of families with rare conditions, we're often looking for a really small number of those changes that might be related to somebody's health condition, we're looking for one or two genetic changes. So that's a lot of genetic changes in somebody's genome we have to work through to find the really pertinent changes that we're looking for. And when we first did this, we looked at everybody one by one, and everybody in their families, because that's how we have to look at people when they present and need an exploration of their genome. But now we're in a really fortunate position, as Ellen said, that we have everybody's genomes in the research environment and in the National Genomic Research Library. And that gives us a huge amount of power to look across everybody's genomes together. And then everybody that has really kindly shared their data for research purposes, can help to benefit other families across the country to help everybody collectively find more diagnoses. And this is what we're doing now and as Ellen said, there are research groups working across the country and across the world to help find new diagnoses. And this may be academic groups looking from universities and other institutions. There are also commercial enterprises that are using the data perhaps with the objective of developing new therapies. But they may have specific interests in a specific condition, or they may have a specific type of genetic change that they're interested in. And so what we're doing inside Genomics England, is really working with those groups, but also independently in our own work to make sure that the new learnings and the new science that's coming through is available to all participants that recruited were recruited to the project, and everybody has an opportunity to have a new diagnosis identified. And there are some really key areas where the science has developed, and the technology is developed over the last few years. By looking at everybody's genomes together, we're really able to zoom in on the areas where we think there's a really high probability or high potential finding for one or more families in recruited to the project. And so, as Chris said, there are over 20,000 genes in the genome, and we don't understand yet what all of these genes do. It's a rapidly developing science. And we're gaining more and more knowledge as time goes on. And so it might be that you were recruited to the project at a time where the gene that might underlie that particular condition in your family wasn't well known and wasn't well understood. But we know now through science, which genes have been better described which genes we understand better in 2022, than we did in 2018. And we can look across everybody in the cohort, and say, who has a genetic variant in one of these genes that's been newly understood that might be related to their health condition.

Similarly, we know which areas of the genome are technically very difficult to work with, and we know and perhaps where though the family-by-family type of analysis might have limitations that make things difficult to find in that way. And by knowing the sort of the technical side, as well as the scientific side of how the analysis works, we can look at regions of the genome where it might take somebody to sit and patiently look through potential findings in that region of the genome to make sure we truly understand them properly, because that region of the genome might be tricky to understand. And we really do have this deep understanding of our pipelines, we continue to develop these as part of our work with the NHS. And that really helps us to find areas where we think we've learned something that might mean that we can find something for our family that was analysed previously.

Jillian: How are you going about finding these new diagnoses?

We're using different techniques to those that we used in the first analysis, we are selecting genes and regions of the genome where we think there might be a diagnosis - we're not necessarily using the same sets of genes that we used to look for diagnoses in the first analysis. In the original analysis, nobody's analysis was restricted to a particular set of genes. But we might have used a set of genes to prioritise genetic changes that we think are most relevant to their healthcare, whereas now we're taking a different approach and looking at genes, looking across everybody at genes that we think could be relevant to the health condition for anybody in the project. To follow your analogy Jillian, we’re looking at a gene and saying, ‘does anybody think that this gene might be relevant for them’ but using their genome to answer that question.

Jillian: Can you just talk a little bit about the difference between what the gene panel could tell somebody compared with what you can do now?

Suzi: Yeah, so in the first analysis, we use gene panels to prioritise genetic variants that were found in that family, for genes that are known to be associated with a particular condition that is was known for that family. That's not to say that only those genes were looked at in the analysis, it's just that it was there was a hypothesis that those genes might be the first ones to look at based on what was known about the family. And in many cases what the underlying diagnosis was found in one of the genes that was prioritised using the panels. But in other cases, it can be very difficult to predict which genes should be included on the panels, which are the right panels to use for somebody's condition, if it's a very complicated one. And again, we know that new genes have been described since that time. So now, rather than using this panel-based approach, while we're sort of using the panels in another way, we're asking the panels to show us whose genomes might have a genetic change in one of those genes known to be associated with a condition rather than using a panel to prioritise variants in any one individual genome.

Rebecca: Thanks Suzi can I jump in, I'm an ultra rare patient, how can I be sure that you're not going to miss me or miss my genes, as a rare disease patient?

Suzi: We're not looking at everybody's genome one by one, we're looking at everybody's genomes all of the time. On any one particular day, that there's a possibility that a diagnosis may be found for any one individual in the project. We understand that there are people with ultra rare conditions. And in some cases, it might take a long time before we can find a diagnosis because the genes underlying that condition may not be well understood today in a way that can be used in healthcare. But by using the genomes all together, and looking at everybody in the project together we might be able to accelerate that process by finding that actually, there's somebody else in the project that has a genetic change in their genome that's very similar to a genetic change we can find in your genome perhaps, or somebody else's genome. And we then can see that the symptoms and that the clinical presentation of those individuals is very similar. And then suddenly, we not only helped to find a diagnosis for you but bring the science forward as well at the same time. And in other cases, we might see that ultra rare conditions are actually very similar to a condition that we know very well, but might be slightly different from or a slightly different form of a very well known condition due to the nature of the specific genetic change in your family. And again, by having the ability to look at everybody together, we can start to see these complicated scenarios that we all know are hidden in our genomic data.

Jillian: Thank you. Is there a way for participants to know where they are in the process of all of this? It's really reassuring to hear that you're looking at everybody every day, but is there any way of knowing how long it might be before somebody might get an answer?

Suzi: Because we are doing to do this in a different way to the first time, we looked at everybody’s genomes, and this isn't something that everybody is going to go through the process and come out, go in the beginning and come out the other side - it's an ongoing thing. And so we can't necessarily tell you where you are in the process, other than to tell you that every day everybody's genome is being looked at. And every day there is the potential for a new diagnosis to be found for your family. This work will continue, and we don't necessarily know when a diagnosis might be found for you. But you can feel reassured that your genomes are constantly being explored, and with the aim of trying to find something for your family.

Rebecca: Thank you. And I suppose a question for you Ellen, as participants we are keen to play our role. Is there anything we can do to help this process?

Ellen: Yes. And as Suzi was saying, this research, work looks at all participants all the time.It's not something where you need to say please, can you look at me, or please can you make sure that I'm included, unless you have withdrawn your consent for being an ongoing participant in the programme, you will be included in it. It's not something where you need to nominate yourself. People are sometimes a bit worried that, you know, well, I've got a new diagnosis now compared to where I was when I joined the programme. But we get refreshes of the data that we get. For example, if you go into hospital, then hospital will enter a code to say that you've been in hospital and to say what you were in hospital with. And that data is collected by NHS digital, and is then available again with your name, and your NHS number and everything taken off it in the National Genomic Research Library alongside your genome data. So we do have that refreshed data coming into us, so we are able to look at that at that updated data. We are we are looking at all the genomes, we are looking at updated data about your health. And it doesn't matter whether you know, you don't need your clinician to ask us, you don't need to be still in touch with a doctor, it doesn't make any difference whether you are still being seen once a month in an NHS clinic, or whether you haven't seen a doctor since the day you joined the project, we are still looking at the data and we're still feeding it back. Really there isn't anything that you need to do in order to make sure that you are included in this process - because you are.

Jillian: Thank you, I'm sure that's enormously reassuring to the whole audience. Thank you, Ellen. And coming back to Chris, we've covered a lot of ground in the last 45 minutes. And we're wondering, what sort of summary or review can you pull together for us.

Chris: When I guess the first thing, I would say is thank you, the 100,000 Genomes programme really was ground-breaking in terms of the science, the ability to translate that science into clinical treatment, not just in this country, but in the whole world. And I've been really struck, since the pandemic has kind of eased back a bit travelling to other countries and talking to other programmes, all of them really hold up the 100,000 Genomes Project as this is massively ground-breaking work. And our commitment is to make sure that everyone on the call and everyone who is a participant in the programme gets the most benefit that for them and their families as they can for being a pioneer and coming on that journey with us. And I think on that note, the second thing I would say as the journey continues, you know, it's not over, as Suzi and Ellen have said, no one has been forgotten, you know, everyone's on the bus. And we want to move forward together, the more work that we do, whether it's in COVID, whether it's in newborns, whatever, everyone's in it together, and the more the more people there are, the more everyone benefits.

I do think it's worth just repeating one of the points I made at the beginning around, we may never get to a genetically driven reason for everyone's condition, because not everyone's condition may be driven by genomics. Again, that doesn't mean we've forgotten those people or that they're not on the journey. It's just that of all of the tools available to medical science, this one, this one may not be the one that that shines light on that condition. But the more that we do together, the more we'll know. And the more we learn, the more we can bring those diagnoses back to those patients and those families. And so we want to keep working on that together kind of hand in hand with, you know, patients and participants, as you Jillian and Rebecca, you know, convened the panel group, but also, you know, on behalf of all the participants that we serve, that's what gets us out of bed in the morning is trying to do the best that we can for everyone.

Jillian: Thanks very much. And then I think we're all always really interested to know what's happening next, so this has been a great opportunity to hear more about it. And thank you all again for your contributions today. It's been interesting.

Thank you for tuning in to this episode. If you've enjoyed listening, giving us a five-star review really helps others find out about the podcast. And if you have any suggestions of topics or guests do get in touch with us at podcasts at GenomicsEngland.co.uk. We're also currently looking for new Participant Panel members. So, if you'd like to apply, do get in touch at Participant Panel at GenomicsEngland.co.uk See you on the next episode of the G word!