Annual Public Lecture 2020

Professor Dame Sue Hill

Genomics and Healthcare - New opportunities

Transcript
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University of Bristol

>> Hello, I'm Rachel, director of the Elizabeth Blackwell Institute for Health Research. And I'd really like to welcome you to the 2020 Annual Public Lecture we hold every year to celebrate the legacy of Elizabeth Blackwell. By way of housekeeping, you can ask questions using the Q&A function in Zoom. We're recording this session but your cameras are turned off and microphones are turned off as well. You can access subtitles today if you'd like to by clicking the CC button on Zoom. That's on the Zoom taskbar. So it's my great pleasure to introduce the 2020 Elizabeth Blackwell Institute lecturer. She's Professor Dame Sue Hill. She's the Chief Scientific Officer for NHS England in the NHS under associated bodies. She's also the Senior Responsible Officer for genomics in NHS England. She leads developments in the area and established the genomics medicine centers and led the NHS contribution not 100,000 genomes projects. Sue is a respiratory scientist by background and she has an international represent her ground breaking reso I know we're all really looking forward to this lecture today. And it's goings to cover a lot of really important and incredibly timely ground. Remember that you're very welcome to ask questions throughout the lecture you can use the Q&A function to do so. I know Sue is looking forward to answering these questions and will do so live after her talk today. Sow thank you for joining us. I'm really pleased to pass the microphone over to you now.
PROFESSOR DAME SUE HILL: Thank you very much, Rachel. Good afternoon, everyone. I'm delighted to be giving this 2020 Elizabeth Blackwell Institute lecture on genomics and healthcare and new opportunities. Elizabeth Blackwell was a truly remarkable woman and am I next slide outlines the contribution she made in terms offing a trailblazer. She was originally from Bristol, emigrated to the U.S. with her family and went on to become the first woman to receive an MD from an American medical school. And she led various healthcare developments both in New York and then further in New York state around Buffalo and Syracuse.
Later when she came back to England she became the first woman to be placed on the general medical council's medical register. And over her lime she pioneered promoting education for women in medicine.
And women in healthcare in general. She set up the national health society and used the motto "prevention is better than cure" a motto all of us in healthcare live by.
I'm now going to move into my talk and start with the context and the context really comes back to those principles that were outlined in Dr. Black well-'s pioneering starts that she took in healthcare back in the late 1800s. There were a number of challenges to healthcare systems wherever we

are in the world in terms of delivering affordable healthcare, having an aging population, providing equity of access, delivering high quality care. And meeting the individuals needs and future direction for healthcare systems is one that's much more focused on improvements to population health and more of preventive approach. Dr. Blackwell's spirit. And increasingly personalization of treatments and approaches so that we can ensure an individual's getting the best possible outcome I can go to my next slide.

Genomics encompass the spectrum of testing and World Health Organization defines the study of hereditary and genomics as study of genes and DNA and functions and related techniques and a gene that we look at through DNA analysis a region of DNA that encodes the function and I'm going to be telling you about what we've been doing to sequence all the genes but all the genomes so all of those 30,000 genes but also the information that's contained in between. There's also important elements lug RNA which sets out implementation strategy in the body and how that gets translated into the process happening. And then something we call circulating products that actually tell us the end stage of a particular process.

If I go to my next slide, genomics has a real potential for healthcare both in terms of delivering protocol-based medicine both in terms of enabling us to move from protocol-based medicine to data-driven healthcare, from volume based healthcare into value based healthcare and into a one size fits all to better tailored and targeted intervention.

And this gives us the opportunity to deliver a better outcome for patients in terms of prognosis, better diagnosis, to fewer adverse events to optimized treatment selection to improve access to those treatments to better disease monitor and ensure that individuals can effectively participate in clinical trials and NHS genomics encompass the whole full WHO definition from single gene to whole genome sequencing. All the genes and everything in between and from DNA to end products. I'm not going to talk about all of those today because we're some way from introducing those into the healthcare system but that's our intention. My next slide sets out fairly recently the UK government published the UK strategy and set out an many place for the government to create the most advanced genomic healthcare system in the world but underpinned by the latest scientific advances to deliver better outcomes at a lower cost. Part of this is how we harness the power of health data. A number of different elements, one is diagnosis and personalized medicine. The second again in the spirit of Dr. Elizabeth Blackwell is a focus on prevention. And the third is on research. And recognising that to underpin we need to develop our workforce engage in dialogue, support industrial growth in the U.K. to make sure we've got cutting edge diagnostics, and to maintain the trust that I'm going to come back to.

>> Any next slide sets out that genomics is over 70 different initiatives in the countries across the world with over $4 billion actually invested in these activities. And standards to enable responsible genomic data sharing across the world to improve outcomes for patients. The second that I'm very actively involved in sitting on the Executive committee and leading several work streams is the global genomic medicine collaborative which is to foster global collaboration to drive genomic medicine into healthcare systems.

my next slide is starting me on a journey to do tell me how have driven healthcare systems. The Genome Project was initiated by the then Prime Minister caved Cameron as a legacy project after the London Olympics actually wanted to ensure the U.K. remained world leading in terms of its use of DNA and DNA analysis.

But cutting edge healthcare treatment. It set up a project and to sequence, to hold genome sequence so those 30,000-i odd genes plus bits in between of 100,000 people with rare disease -- rare and inherited disease and with cancer.

And this was divided into terms of how this was delivered into several different components two of which are on this slide. Firstly, NHS organized 13NHS genomic centers centered on the patient element. On right-hand side genomic was set up as part of the project infrastructure and owned by the Secretary of State. Set up the ability for that sequencing to take place in a sequencing center and for samples to be put into a bio repository but through informatic and data architecture set up the ability to be able to provide data for researchers and to academics and industry partners through the concept of a reading library rather than a learning library. You can see that there were over 122,000 genomes that are -- were samples that were collected and received at the U.K. bio center most of those were collected were in rare disease but 36,000 in cancer. This represents around 18,000 people because people with cancer gave both a blood sample as well as a sample of their tumor. There are now over 107,000 genomes in the research environment. Because individuals consented at the beginning to provide longitudinal health data there's primary clinical data now on nearly 90,000 participants. This remains world leading Despite all of that investment I talked about earlier in other countries across the globe.

My next slide really set out that what was unique about this -- the way this project was constituted is the role of participants that enabled participants to be put at the heart of the project. What I'm delighted to say is that one of the local Bristol residents has been chairing the panel for at last few years, she's a civil servant by background, has a son with a rare disease and that's Jillian hastings who has done a remarkable job. What this has enabled is for that patient, that participant input to be put into everything. Whether it's in that discovery forum with industry looking at the data that's been collected but in a deidentified way, whether it's in researchers accessing this or whether it's thinking about the ethical concerns. They've really, really shaped the project and continued to shape the project and outcomes to this day. Next slide outlines project focused on rare disease and cancer these were the areas with the most unmet need. There were 6,000 rare diseases that have been identified. Only a quarter of those have a molecular basis for their disease. In this project, 1200 disorders were studied. And by increasing the way in which individuals with rare disease were characterized using something called HPO terms, if we got more of those, we got a much better outcome in general in rare disease over standard of care patients received about 25% of patients received a diagnosis which increased to 40-50% some disorders. In this project it showed sometimes this brought to the end a diagnostic odyssey of years in many patients costing an inordinate amount of money in the healthcare system.

So the clear message of this is whole genomic sequencing does deliver better outcomes if you

characterize patients carefully, it increases diagnostic. On cancer side on previous slide, that's it. If you could broaden that out for me, the cancer there were 24 cancer types included. And changes, genomic changes were found in 13 search potentially actionable genes across all the solid tumors that were studied and that was 5,700.

And so 50% of those have a known actionable or potentially actionable -- which is information we didn't know before but cancer is a result of disordered genomics. But this was ground breaking in terms of how we think about using genomics and cancer going forward.

My next slide sets out that of course it's the outcomes that matter here Jessica age 4 took part in the project. She'd been having really difficult to control seizures for many, many years. Lots of different investigations. But a genetic variation was found in a gene that makes a protein that transports a particular type of sugar into the brain.

When these patients who have this Glut1 deficiency have a very low carbohydrate diet, a keto genic diet. Can actually help reduce the number of seizures and this is what happened to Jessica but on the right hand side this tells you what really matters as well. Which is when our laboratories don't really know whether the genomic variant that's been observed is really clinically relevant, the genomics England clinical interpretation partnerships working with the academics and industry, you can see that data on this slide -- have actually returned 141 diagnoses to our NHS laboratories since January 2020 and this is contributing to patient care. These were unknown at that time. Genomic variants sha have been found that could be actually important. Many of these are important and are enabling people to move into new forms of treatment or further investigations.

So it's that bit of aligning, clinical care with research endeavors that's really important as we come and look forward to the future. My next slide really outlines there's still more to do do complete the project. A real question about how often we should realise whole genome extensions, what the potential implications are. There's a need for focus on how we use whole genome sequencing to improve care beyond the primary question that was being asked about the patients. For example, whether they are potentially going to get adverse reactions to drugs that they might take or pharmacogenomics or whether we can find anything else in their genome that might mean that they have an inherited disposition to certain diseases like cancer or high circulating facts in their blood called clusteremia. What we need to do is understand the impact on NHS services and make sure when we roll this out there is an equitable approach across the country. Where have we taken this then? My next slide sets me into the next section of my talk which is creating the future NHS service.

The long-term plan for the NHS in England has set it out for the next 10 years. Committed to sequencing 500 genomes by 2023. But all children with cancer to be offered whole genome sequencing to extend our access to molecular diagnostics in cancer and increase testing, that's inherited condition I just referred to called familial hypers cluster emia are associated with cardiac death particularly in under 50-year-olds and in terms of research, to really continue to press to link and correlate genomic and clinical data together to make sure we get the best possible outcomes.

In October 2018, if we go to my next slide, what we did is launch the genomic medicine service and this brought together all the developments in genomic in NHS since it ban back in the 1960s and laboratories for example from genomic services.
Right through to the learnings from the 100,000 genomes project and we set out that we would launch and introduce a genomic service that provided consistent and equitable care knowing there would be variability across the country, that's variability in terms of access but also in terms of quality. We wanted a national approach to patient consent and patient and public involvement against a strong ethical framework, working to common national standards and that includes common for example contracts notice way we can monitor data so we know what the access is equitable. To institute a consolidated national genomic network made up of 7 laboratory hubs with partnerships across local providers and geeing fizz between 5 and 10 million building on the NHS genomic medicine center model. And integrating with clinical specialties across the care continuum.
A single mandated national test directory for the NHS that's linked to the payment system. All technologists from single gene to whole genome sequencing and inclusive of cancer and a single knowledge base to continue to ensure that we support research and discovery but we improve outcomes for patients.
And a single coordinated unit in NHS England. My next slide outlines ha this look likes visually. There's genomic laboratory hubs that national genomic tests directory informs patients and involvement in this creation of their services. A link to clinical genetic services and broader clinical teams. But at the bottom a national whole genome sequencing provision that's actually delivered through a partnership in genomic England and where patients provide their informed choice/consent. That data will go into a U.K. genomic knowledge base and deidentified format in the same way I outlined earlier.
And then what we're about to announce this provide multidisciplinary clinical leadership to embed genomic medicine across end-to-end patient pathways aligned to those genomic laboratory hubs. This is a eastbound world leading infrastructure. Nowhere else in the world has done this. And many other places have -- it's very difficult to even contemplate to do this.
My next slide sets out that within the southwest there are really a strong partnerships there were two genomic centers as part of 100,000 genomes project. This just shows the west of England. Genomic medicine center across the Bristol and Bath and surrounding areas.
There's now a southwest NHS genomic laboratory hub based at Bristol genetics laboratory. But servicing the whole of the southwest right through to the Isles. As I'll be scoring at the end of this afternoon there will hopefully be a southwest NHS genomic medicine service alliance. You can see there the partners who are going to be part of that.
But there's an important link here with the university and academic providers across the patch.
My next slide says that in terms of this testing that will be undertaken, this will -- the genomic medicine service and test directory has a deliberate focus on the whole continuum. Whether it cease disease focused informing treatment decisions, whether it's population based, or whether

it's predictive.
And that means it will cover from targeted testing to panels to exome sequencing to genome. So at the bottom end of this targeted treatment this will include cascade treatment for those inherited diseases that makes it more predictive and preventative but at the other end we will be introducing to the service 21 rare diseases that will move into whole genome sequencing for the very first time as well as a small number of cancers in addition to childhood cancers. My next slide -- next three slides will set out services that are being delivered in the southwest by three remarkable women in the spirit of Dr. Blackwell's legacy.
The first is national sequencing service for young individuals in intensive care.
And that may have a likely mono genetic cause for disease. We commission the service from world ex ter hospital in October 2 '09 -- 2019. There's 520 of those to date. And there's diagnosis that's been returned in 37% of the patients. And at least 10 cases where a genetic dice sis has changed and this just tells the story of Ellie Rose here who was ill until 18 months old when sequencing through this service revealed she had a condition her diagram was paralyzed she's now receiving treatment and is progressing well at home.
We've extended this service to include children with a severe COVID-19 phenotype. There's been a small number of referrals to date. But in some patients the potential for the change in a variant to be a cause of their disease is opening up potential treatment options.
Our second remarkable woman and remarkable service that's being delivered is the southwest service delivered by hypercholesterolaemia. Maggie and her team have been a real pioneer for introducing hypercholesterolaemia. Disease. They've driven the way genomic variants should be classified and driven this finding and done much of the testing for the rest of the country.
So really important development because this is estimated to have a prevalence of 1 in 250 in the U.K. And links to as I said earlier, increased risk of acute cardiac events.
My third remarkable woman who is recent import into Bristol and the southwest laboratory hubs is Rachel Butler who came in together with other colleagues and revolutionized the way services are going to be delivered across the southwest.
With a much more comprehensive offer not just for all the tumors whether they're solid tumors or malignancy tumors but also different ways in which we can analyse for example lung cancers for colorectal cancer and this will start to bring the testing across the peninsula and southwest all into Bristol for this remarkable service.
Whilst I move into my next slide, this says that part of what we're doing as we move forward is establishing a shared platform for diagnosis and research just like we've done before in the 100,000 genomes project but this time focused on the NHS genomic medicine service and setting up research collaborative of all the genomic medicine service alliances, genomic laboratory hubs the enable us to coordinate research and drive improvements in diagnostics and treatments and discovery and in evaluation. And all genomic data will be deposited into that library we're creating so that it can be used for continually sort of reevaluating our interpretation genomics to make sure that we get the best possible outcomes for patients. Of course, this is based on our patients

actually providing their consent at the very beginning. But also in developing eye shared informatics and data platform that will sit across the NHS genomic medicine service in conjunction with genomics England to let this happen. My next slide sets out this interface with clinical improvements with research side on the right being genomic England. Left-hand side being the NHS England and what we'll be doing together is making the loop work as an efficient, robust, and scalable system to help patients, to help healthcare teams and to help our system. And it's particularly important at this interface, that intersection on research and healthcares that we can ensure we enhance diagnostic interpretation.

I'm going to move now into the next part of my talk. Before I do that, into just saying I wanted to mention also one individual from the southwest from Bristol and that's Andrew Munkford a hematologist who led achievements in hematology both in terms of driving forward research into people with blood disorders in the 100,000 genomes project but also how this can be driven in terms of clinical translation into the service. So that's infinity loop actually being in action and in action already.

So the next part of my talk goes into how we can use genomics to personalize medicine.

And to personalize treatment.

This is a vision that we all know Dr. Blackwell had. Diagnosis, treatment selection, and monitoring with currents. Important part is bring together clinical data that will help us move into personalizing treatments. My next slide outlines that just a few weeks ago we introduced and announced a pilot that will potentially revolutionize the way we can attack more than 50 cancers and you can see on the right hand there the quote from Matt Hancock. This is a project that will be delivered in conjunction with Braille that will start to look at simple blood test using targeted genomic sequencing and a range of cancers both in those that may have no symptoms and therefore, we may pick it up much earlier before people even have symptoms but also in people that have symptoms but where no known cause can be found and where they're particularly difficult to diagnosis.

So this will start to bring into the NHS that bit that Dr. Blackwell said at the very beginning about prevention is better than cure.

My next slide sets out that we have lots to do in terms of how we introduce a standardised approach in terms of those end-to-end pathways to improve outcomes. Whether it's in breast cancer to identified genetic drivers and then the likely toxicity of any primary treatment or future treatment options. How we use genomics in colorectal cancer where we know it's happening on the cluster analysis of the genomic variants. It leads into a surgeon or person looking after a patient with colorectal cancer into different types of approaches including organ preservation. In the NHS onset diabetes that Sean and the team in Exeter have led that many cases misdiagnosed and some not being found and also pharmacogenomics where we know that pharmacogenetics (lost audio) when they think about what this might mean this is disassociated with adverse web reactions and understanding that and doing more work on that will be critical as we move forward.

So a lot of work to do to ensure that we can standardize our end-to-end pathway I'll talk about in a

minute.
My next slide actually outlines what this means in reality and to really do this, we have to bring all this data together and use this to ensure that there's the correct delivery of the personalised treatment according to national guidance. So it's not an easy matter but it's something. But, if we get the slides and we're committed to this and are improving outcomes for personalised medicine strategy in NHS England this will ensure that patients get the right treatment with a lower amount of adverse reactions. My next slide, just really sets this out saying this will end the one size fits all era of medicine from traditional approach and broad diagnosis where everybody receives the same medicine typically it's only 30-60% effective to more personalised approach where it's tailored to match an individual's makeup and response. More effective, fewer side effects, better value for money for the 17 million pounds that we spend on drugs in the NHS every year. My next slide just outlines and if I could have this on a wider screen, how when get it right, it is very individualised but it can have a tremendous impact. This was 11-year-old child with a brain cancer who had whole genome sequencing. The patient relapsed shortly after having the genome sequencing. There was an urgent review which revealed a novel particularly graft fusion. And that fusion wouldn't have been detected by conventional testing.
The clinician applied for a particular type of therapy following discussions with experts in brain tumors in Germany. And then after conventional therapy, the family was given that opportunity to access that personalised targeted treatment. with a better outcome. And that's just one example of how personalised it can actually get when you have this extra level of detail from genomic characterisation and cancer. My next slide just outlines as we move towards the future there are novel concepts for how we start to personalize cancer medicinally using lots of computer modeling in realtime alongside standardised approach to clinical trials. That means clinical trials can be much more reactive. If I can move then towards the end of my talk, and on to my next slide, just saying provision for personalised medicine is that genomic med is in accessed pathways and linked to optimisation, we use data sets from clinical purposes to ensure equitable access and we incorporate pharmacogenetics. If I can move on, key challenges to embedding genomics in mainstream care remain in terms of how we develop our workforce and the genomics education programme in health education England has been critical in understanding how we use core genomic concepts how we conceptuallise those in a post registration text and how we embed those in clinical practice and you can see this terms of the resources that are shown along the bottom here, the data that's been generated from all the access to those resources. My next slide sets out that you really want to build me a learning community in terms of clinical genomics, we have to continue with education training that's at the core of the change in knowledge and embedding this is just data taken from showing pre2016 before the Australian genomics project and post 2018 where they've done a lot of education and training. And my next slide really sets out that we have to retain and build public trust though and in the study that was done it recognizes that we had to focus on three elements linked to reciprocity, altruism and solidarity. And that within this approach some of them are red lines like the use of not selling data and not

genetic engineering. But this is a critical part of ensuring that we remain true to ourselves. Go to our next slide. We have to work within an ethical framework and the debates are gathering in terms of whether we should sequence at birth and indeed the study at Boston is already starting do that at baby Sed and looking at how this might replace screening and also how it may diagnose rare disease earlier and therefore, prevent the number of under 5-year-olds dying early.

My next slide sets out that here in the southwest there's been tremendous educational partnerships that is both looked at how staff can be up skilled, how clinical and professional staff can be focused in terms of training. How genome can be socialised and how developments can be introduced in conjunction with cancer charities for example. And, of course, at the University of Bristol and University of Exeter have both developed a raft of different programmes to support the multi professional team. My next slide.

I just want to spend just a couple minutes and then I'll be at the ends of my talk -- about genomic and responding to a public health crisis so genomic and SARS COVID 2. There have been 1.57 million indications so far and over 57,000 deaths across the world. If we go my next slide, COG-UK consortium was made this year to demonstrate where genomic sequencing of this virus can be a benefit to public health and in doing that established the evidence and infrastructure to move into a routine service within the test and trace programme for interactions.

Next slide sets out this is a partnership that's funded by the body across the bottom. Welcome sign has been critically involved as well as full public health agencies but what the graph on the right shows is that the U.K. have sequenced more than 50% of SARS2 genomes than the rest of the world. They've done over 50% of the genomes sequenced across the world.

My next slide shows that what the focus has been on transmission and outbreak investigation, mutation of analysis and tracking, central genomics surveillance such as genomic. If I can go to my next slide. I've got two slides I'm going to cover very quickly. First of all, just to give you very breaking data, some of the mutations under surveillance are to a particular approach on the SARS could 2. What we know is when the virus first emerged, this wasn't present, this particular mutation. Called the D6146g but it's now almost ubiquitous in all strains. This replacement is associated with higher viral loads and younger patient age. This increasing frequently is consistent with a selective advantage by the virus.

And there's information on the right-hand side of this slide to show that the increased transmissibility of some of these things that we're actually seeing may have originated in Europe.

My next slide shows data from Scotland with an analysis of genomes to the quarter more of around positive examples showed there were independent introductions of the virus into Scotland. Following the first lock down most of those changes in the genotype are that we're circulating in the population between distinguished and few persisted over the summer but seconds wave was caused by new changes in the genotype introduced predominantly for countries outside of the U.K. and most likely associated with holidays. My next slide just says there's a key project starting to look at the virus as well in a COG-UK database but in the host as part of genomic -- and mildly

effective patients and comparing those outcomes with Genomics England and U.K. biome data sets. This next slide just shows that paper that was recently published that there were seven genome wide specific loci detected that were associated in that host with poorer outcomes and some of those for example are associated with the way in which certain types of blood cells called monocytes migrate into the lung. This will start to give us information about identifying the genetic reason for why some people develop mild disease and some develop more severe disease. If I could go to the next slide there are a number in terms of and ability for patient and public healthcare professional most importantly industry academia and many opportunities not just in the diseases I've spoken about and in other diseases that we'll see over the next few years.
And to conclude, I'd like to finish with a quote from Elizabeth Blackwell herself. It's not easy to be a pioneer but oh, is it fascinating. And I can definitely subscribe to that quote. And say this really is fascinating but it's also life changing for many people. Thank you so very much.

>> Thank you so much, Sue, that was Absolutely fascinating. You covered a lot of ground and given us a really clear sense of recent innovation. I'm sure Dr. Blackwell who have been right at the heart of this work had she been here today. So in the spirit of thanks, at this point, if we were on stage in Bristol, what we'd like to do is present you with a piece of Bristol new glass with a piece of engraving on it. That's partly because this lecture is supported with a very generous donation from the center of Dr. Elizabeth Blackwell. So we sented you a piece of glass in advance so we very much hope -- there it is, fantastic. We very much hope you will enjoy having that blue glass in your home or in your office to remind you of today.
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PROFESSOR DAME SUE HILL: I most definitely will. Having been brought up in the southwest it obviously means a lot to me as well.
>> Fantastic. Sue, we have questions flowing in thick and fast, so just a reminder to our audience, if you've got a question you'd like to ask, pop it into the Q&A box on Zoom. We probably won't have time in the next 10 minutes to cover all of them but we'll do our utmost to get through them. What I'll do is read them out as they're written so Sue can have them as if you were in the audience today. First of all, people are saying a warm thank you. Thank you very much, Sue. First question I have here and I'm going to read it directly so I get the wording right to be true to the audience is how do we move genomic medicine from those who are ill to healthy carriers. And in doing so, can we identify those at risk and so initiative preventive measures?
>> That's rather a quite broad question.
I mean, we are addressing this as I spoke about in my lecture. One was when people are having genomic investigations like whole genome sequences for other conditions that we could find out if they've got an inherited disposition for some cancers. But I think where we need to go towards is more -- and I hate to use the word "Screening" but more targeted testing of certain populations to really understand whether they have an increased risk of carrying certain genes for example for cancer or for familial hypercholesterolaemia. We are starting to work nationally on a familiar hyper

cholesterolaemia programme that will start to see more extensive screaming in the community to try to find these cases and that's essentially where we will have to go. That's also why there's an interest in newborn screening and whether having a genome on someone's record may well be something that would mean that we can move into a different type of preventive healthcare approach. But there's lots of public debate that needs to happen in that area.
>> Fantastic. Thank you. So next question is probably quite a nice follow-on from that. And it asks: Whole genome sequencing represents a lot of benefits but no technology is perfect.
What are the plans to address the shortcomings of whole genome sequencing when it's rolled out across England and there's an example given. For example when looking at disease caused by large or repetitive genetic rearrangements. What are the plans relating to new technology that could pick up the slack?
PROFESSOR DAME SUE HILL: One of the things I didn't say and meant to say as part of lecture what we're talking about at the moment is using a particular short ray technology but how I feel we should move in terms of our service is a bit like we've done with imaging which is have multi modality DNA analysis that might see us analyzing whether it's a tumor or patient with rare disease whole genome sequencing with both long ray, short ray technologies but bringing a raft of different genomic testing to make sure that we can try to find the cause of that person's disease if there's evidence that suggests that it might have a genetic makeup. And indeed there's very good evidence from North America sharing why we need to move to this multi modality approach. We will also have to think about where we use whole axiom sequencing as well in this. But part of the challenge is at the moment though the price has come down dramatically, we need to get it closer to the patient and reduce the cost even further and also reduce the turnaround time even further.

>> Thank you. So then the next question complexities the other one and asks about other data and the request he reads what other types of data other than genomic data do you think we'll need to move toward data-driven healthcare and the question says they're thinking of outcomes, coding diagnostic and Simpson data for example how will need data need to impact?
PROFESSOR DAME SUE HILL: All of that needs to come together. Indeed in terms of the database that Genomics England will be continuing to curate and annotate, if a patient provides their consent, then consent to the longitudinal health data to be pulled.
Now that data may not be in enough detail to actually properly characterise an episode and that's why it's really important at the point that genomic testing is done that it's done in a very, very characterized way but that we actually have the ability to pull in data from all the different diagnostic service and to start to capture outcomes data that means we can understand whether there has been an impact on individual patient. Within that service we'll be starting to collect outcome data as well as understanding where people have indeed got access to testing. And we will be linking to across the country what are called regional medicines optimisations committees to make sure everyone with a given mutation if there is a targeted treatment available, that we know that they've been considered for that targeted treatment or that they've been considered for

entry into a clinical trial.

>> Great. So there's a questions about research studies. Particularly the GRAIL study. And the question is that the questioner has read a lot of criticism about the ethics of the GRAIL study. Do you have any comment about this?
PROFESSOR DAME SUE HILL: I think that's the reason we want to do the pilot actually is because there are conflicting results. There are lots of results have been presented at different places across the world. But, if we look at -- in a pilot in both essentially naive people so people with -- who aren't symptomatic, or people who are on the 2-week cancer wait then we can start to get an understanding about where this particular test may be utilized in the healthcare system. And it's a pilot for a very good reason.
Which is probably what your questioner was getting at.

>> Okay. So then that moves us to think about treatment. There's a really interesting question from the audience about personalisation of treatments. And to be specific, the question asks how will personalised tablets work when in hospitals tablets and pills are delivered in rounds at fixed times rather than at times that they might need to be delivered such as before and after food? So a question about treatment.
PROFESSOR DAME SUE HILL: Yeah. So I mean the most important thing to start with is that we'll focus on drugs where there are known adverse drug reactions if they carry a genomic variant and on the slide I put up on cancer services in the southwest, I mentioned what was mentioned on there was the testing for something called DPYED, which is a genomic variant associated with a fluoride pyrimidines, a particular type of cancer therapy that sometimes there can be fatal adverse toxicity events. That is being rolled out. But in terms of personalisation or in terms of the dosing, I think we've really got to understand what this actually means in terms of dosing pre and post food, in terms of when people take it within a day. But because we've got pharmacists now heavily involved in the genomic medicine service and it truly is multi professional, then we will ensure pharmacists will be a key conduit to making sure that the individual does get that targeted treatment. We know from chemotherapy treatment though and for many other treatments that need to be givens at a particular time this can be done in the health service. It just needs to be done in a systematic way.
>> Fantastic. Thank you, Sue. I think we've got time for maybe two more questions. So there's another one here that says thank you for a fantastic presentation. And then asks about nice guidance and the question asks are there any plans to incorporate pharmaco genetic decision support in stratification as part of routine mass guidance.
>> We're working with NICE to work that into the guidance to understand how it would work. And particular I didn't talk about it today but we have earlier this year NICE introduced a lice or licensed two drugs for -- or provided guidance for two drugs for M track gene fusions. And what we have started to do, that actually puts us in a very different position with NICE about the genomic testing

that needed to be done. And how that would fitted into the guidance and how it would be treated in terms of the economic analysis. So we've got the start of how pharmaco genomics could be introduced into NICE guidance and that's what we'll be doing as we move forward.
And on my vision for personalised medicine the bottom actually part of that just said broader interaction with other system partners like NICE and like NHRA.

>> Thank you, Sue. So a very final one which takes us kind of back into big picture territory again. It's about cost. And question asks whether individual treatments will increase the cost of drugs.
>> So individualised treatments with all the new treatments that are introduced there's a cost analysis done. What we know though already that by personalizing treatments, some treatments can be stopped and indeed in some of the diabetic examples that Exeter and Andrew can provide will tell you sometimes people have been on insulin injections but when they've had genomic analysis done they can be changed to relatively low costs. So there will be different types of approach. There may be higher cost approaches. And that's a good example of where we need to do more extensive genomics to understand when that drug in B. cell lymphoma where it won't work but this will be about balancing what could be access to more expensive treatments to access to treatments that are lower cost that have a better outcome.
>> Fantastic. Thank you so much. And thank you to the audience for all those fantastic questions that you sent in. I'm sorry we didn't have time to answer all of them. I know Sue says she's happy for you to contact her if you have a question we were unable to answer today. Thank you.
So it just remains for us to wrap up to thank everybody for coming today. I know there's several hundred of you out there. Thank you for joining.
Thank you so much, Professor Dame Sue Hill for giving the 2020 annual lecture. I learned a lot. I'm sure everybody else has as well. Anybody would like to revisit the lecture it will be recorded and it will be available online at the Elizabeth Blackwell Institute Web site. Sue, Thank you.

>> Thank you. And it's been an absolute privilege and pleasure to give this lecture. In honour of a truly inspirational woman.
Thank you so much.
>> Thank you, Sue.