Day 1

Personalised medicine and you

Queensland Genomics Health Alliance

- **Katrina Cutler, Communication and Engagement Manager**

Katrina Cutler: My name is Katrina Cutler and I'm the Communication and Engagement Manager at Queensland Genomics Health Alliance. On that survey, don't worry if you didn't know what it meant, that's what we're here for today, hopefully. If everyone's finished up that survey, I'm going to get you to do something for me. I want to ask you to rank yourself on your knowledge of the health system as a consumer. So, of the Queensland Health system. I've got some signs on the three walls. Over here, we've got little to no knowledge... I can't even see that far, but that's where I'll get you to move if you think you've got little to no knowledge of Queensland's health system. Just bear with me. Over here, I will get you to move to the back wall if you feel like you've got some small of Queensland's health system and over here if you think you've got a fair bit of knowledge. Just to help that make more sense, over here it might be you've used it, but not sure how it fits together. Over the back there, it might be that you've used it, you know the difference between primary and acute care. You kind of know which levels of government fund what kinds of services and how it slots together. Over there, I want you to move there if you're confident to give your friends and family advice on negotiating their way through the health care system. So, can I get you all to stand up and move to your spot. If you feel like you're in between some of them, just stand in between where you think you are. If you're from interstate, let's just broaden it to be the health system in your State. Table of presenters, you're not excluded from this exercise. Don't be shy, we know you're actually mostly experts in this space. Does anyone need me to repeat the instructions? Excellent. Over here, you're an expert health consumer. You'd be confident to give your family and friends advice on how to negotiate their way through the health system. Move to the wall, sorry. I know I'm being a pain.

At the back you've got some knowledge of the health system. You know what the difference is between primary and acute care. You know which levels of government fund which services and over here, you've got basically little to no knowledge. You've used it, not sure how it fits together. That's not true! You don't have to worry about that side of the room being lonely, there is a method to the madness. Excuse me, there's a table here that isn't taking part. I know everybody's names in this audience, so look out. Nobody is safe... not really. Great, we've got a shot of you all. That's kind of what we expected that most people in this room are pretty familiar with the health system, feel pretty confident to give family and friends advice on how to work their way through it. Now, I want you to rank yourselves on your knowledge of genomics, personalised medicine or precision medicine. Over here on the little to no knowledge section, I'll just get you to not move until I've finished otherwise people won't here. You've never heard of genomics, personalised or precision medicine before today and there is no shame in that.

When I applied for the job at Queensland Genomics Health Alliance 18 months ago I had to Google it. Over there in the middle if you have an area of what they might mean and over here, if you've got experience of genomic medicine and/or you consider yourself pretty aware of it and you could give family and friends advice on how to get hold of it. So does that make sense? You can now move. Excellent. When you've found your spot, can you just pair up with a couple of other people and have a quick chat about what you know about genomics or personalised or precision medicine. What is it that you know? Okay, so I'm just going to ask some people to share what they've just talked about. Over here in the little to no knowledge- and this isn't public shaming at all, like I said that was me about 18 months ago- can you talk about what you've just talked about, what's come up for you in that conversation?

Audience member: I know nothing, that's why I've come here. Absolutely nothing about any of it.

Katrina: Sorry, I didn't hear that.

Audience member: No information.

Audience member: I don't know anything, that's why I'm here.

Katrina: Sorry, I missed that again.

Audience member: I don't know anything.

Katrina: Okay, got it. Excellent. Is that everybody in that group generally. Hand up, everyone. Excellent, excellent. What about this group here. Not quite little to no, a little bit. Anyone there want to share. Are you standing there, but sitting here. Got you, I'll get to you. Let's go here, at the back. Can I get you to say your name and where you're from.

Audience member: So my name is Katherine, I'm from the Wide Bay community group.

Audience member: My name is Georgina I'm from Anglicare southern Queensland, hi. What we thought we knew was that it's something you can use to identify pre-existing conditions. It's used for preventative health care. My conception of it is it's mostly private companies that offer these services, but Rachel indicated there is people within Queensland Health who do it and I know I got some testing done when I was pregnant for genetic conditions.

Katrina: Excellent, all right. I think you've underrated your knowledge, FYI. Do you do that a lot in life? Anyone else from this group? Okay, cool. Up the back, who wants to share what they talked about just now?

Audience member: One thing in particular, early diagnosis of something that you've inherited would save Queensland Health a lot of dollars.

Katrina: Excellent. In the middle here there was somebody who was sharing from that group, but this lady with her finger up. Sorry, Natasha, we're

giving you the run-around.

Audience member: Hello, I'm Belinda and I'm from out Laidley Gatton way. My knowledge is that I was sent by a doctor to have genetic testing and I came back with an MTFR gene that's mutilated and yeah, that's about it.

Audience member: Wonky.

Katrina: Thank you, that's great. Anyone else from this section? Miranda's got a mic, excellent.

Audience member: I've got a reasonable list. I had a husband who was tested for a particular variety of chemotherapy based on the genetic test that targeted the treatment he'd get. I have two other friends, there's also obviously the BRACS gene for breast cancer, which I've had some connection with through friends. Also, a stenosis diagnosis which was diagnosed when two members of the same family got tested and discovered that's where it came from. Obviously, the connection with pregnancy and Huntington's disease, which goes back a bit of a way, but one of the early forerunners. I think that's all.

Katrina: You sound pretty expert, too. Anyone else in this group? Excellent. Charmain, is that you?

Audience member: I was going to give it to Gary, because Gary's better at talking than me.

Katrina: He'll get his turn. Can everyone hear the people on the mics? Great.

Gary Hondow: Hi, I'm Gary from Wide Bay and we've had the experience of genetic testing. We exhausted all of Queensland Health's other testing and genomics testing is what found our diagnosis and started our new journey.

Katrina: Excellent, thank you, and we'll hear more from Gary later. What about here, our experts? Come on, excellent. Cathy.

Audience member: Hi, I'm Cathy and I'm here with two hats. I'm here as a consumer. I support or I facilitate a support group on the Gold Coast for people with myalgic and chronic fatigue syndrome and Griffith University have discovered a genetic variant biomarker which is great news for the community who have no services and the other hat I have is that I work on one of the QGHA projects in a professional capacity.

Katrina: Perhaps a genetic counsellor in that group.

Audience member: Hi, I'm Jenny I'm a genetic counsellor at Genetic Health Queensland. I'm sitting on the table outside if anyone has any questions.

Katrina: Basically, she's about as expert as you get in this space in Queensland. Thank you for humouring me with that. You can all move back to your seats. The point of that- actually, I'll wait until you've sat down. Thanks, everyone. So the point of that exercise is really to show us all that in this room of really highly engaged and highly engaged health consumers, probably the most engaged and educated health consumers in the State. Really, there's a lot of people who don't know much about genomics, personalised or precision medicine and it is a pathway that is honestly truly set to transform the health system and Queensland Genomics Health Alliance one of the things we're trying to do is uplift public knowledge around genomics and so we thought this was a good place to start. Just so we're all on the same page, the genome is the complete set of genetic information that's located in each cell of every living thing and genomics is the science that aims to understand the genome. Personalised medicine or precision medicine uses your genome to tailor health care to you specifically based on your unique genetic make-up. This is happening in health care right now and it's set to grow at an accelerated rate, integrating genomics into health care can improve disease diagnosis and inform better treatment options for patients. So today we're aiming to educate you in what's happening in the world of genomics, through the following speakers. Okay, first up we've got Aideen... I'm going to get a better angle

here. Aideen will give us a genomics 101, what's happening in the health care system. Next up I'll tell you a bit about Queensland Genomics Health Alliance and then we've got Nic, who is a co-lead on our ethics legal and social implications and she'll talk through some of the challenges we're dealing with in introducing this new technology. After that, we'll hear from Gary who we heard a quick word from before, who's on our consumer group and then David Bunker the executive director of Queensland Genomics Health Alliance will come back and talk about why community engagement is integral to the implementation of genomics into health care and finally Erin Evans the chair of our community group talk through what we're doing as a community group. There'll be an opportunity for questions after everyone's presentation and now, I would like to invite Aideen is to stage. She is a genetic counsellor and researcher from QUT and a member of the QGHA community group and I'm first going to ask Aideen to share an anecdote of her first memory of the health system as a health consumer. (APPLAUSE)

Aideen: Thanks so much, Kat and thank you to everybody for the opportunity to talk to you today. So I've been a long-term health consumer. So I was a chronic and severe asthmatic as a child. So from the age of 4 onwards, so I have a lot of memories. In fact, there were some years of my childhood where I spent more time in hospital than I spent at home and I don't remember liking needles much and I don't remember liking the percussion much, but I didn't mind the oxygen tent and I liked the ambulance trips to limerick, the paediatric hospital they sent me to. I felt special being in the ambulance and liked and doctors and nurses that looked after me. It became a home away from home in a funny way. Today I'd like to, as Kat said give you a hitchhiker's guide as it were, a review and talk about how it might be integrating. It used to be something people thought about for rare diseases, but now we're going to see genetic testing creeping into every day health care and I'm going to talk to you a little bit about what that might look like. I'm going to start with a review of what traditional genetic testing looks like, what advances have been taking place in genetic testing over the last number of years. The pros and cons of these genetic tests, the clinical implications and how they might translate into personalised or precision medicine. So a quick refresher for those of you who haven't done biology since high school. You'll remember that in the centre of every cell of our body we have our chromosomes. Their job is to

carry our genes and the genes are made up of a string of DNA that's made up of A, C, G and T and the order those letters are in, in your gene affects what protein that gene makes. That's your genetic code. So traditionally when you think about genetic tests people think of a picture like this. These are your chromosomes, take a picture, cut them out, line them up and arrange them and this is what we call a carrier type and it allows you to see whether you've got extra bits of genetic material or any rearrangements. When we think about traditional genetic testing of five years ago, we think about looking at the genetic code or the genetic sequence of one gene at a time. And when I said earlier that the job of a gene is to code for a protein that's not technically accurate. Your gene is made up of different regions called exons. So when they used to look at the sequence of their gene, what they did was they looked at... what did I do? Between the Irish accent and the text, we're going to see great fun. When they look at the sequence of a gene, what they did is looked at the sequence of an exon, so that worked fine if your gene had two exons, but it was very time consuming and expensive if you had 92exons in that gene and similarly, in some conditions it can be caused by multiple genes and what doctors had to do was they had to say let's start with gene a first and the gene would come back negative, didn't find any mutilation and they'd go to gene B and gene C and that was called sequential testing and could take years was it was very expensive. So now there's been a few breakthroughs in terms of genetic testing and the first one that took place quite a few years ago at this point is what we call array genotyping. All an array is you take a bunch of genetic baiting like you're going fishing for something in particular. You take a genetic sequence of the normal sequence where there is no mutilation. In this instance, that's in blue and then you take a genetic sequence of the one with the mutilation in it, and that's in green. You stick them both to a little piece of glass, chop up the person's DNA and see which one it sticks to. That works well for conditions where the same mutilation keeps occurring over and again, conditions like cystic fibrosis, et cetera. The other big breakthrough is what we call massively parallel sequencing. Now you know I told you before that we look at the genetic code or sequence of one exon and one gene at a time before. Now what we can do is look at the genetic sequence of multiple regions throughout the genome in parallel. So tens to thousands at the same time. And the big application of this initially was what we called panels. So you can imagine we take all of the genes that we know causes a particular condition

like, say, intellectual disability or deafness. You put all of those genes on one panel and then you look for mutilations in any of those genes. The other one is what we call whole exom e sequencing where you look at the genetic sequence of all of the exons of all 21,000 genes at the same time. And finally, you hear of whole genome sequencing where you look at the exons, the introns and the areas in between the genes at the same time and that produces 100 times the quantity of data as whole exon sequencing does. Okay, so what are the implications of it? It's faster, a lot more affordable than it used to be. The costs have come down and you also get a higher diagnostic rate. For instance, if you took a child, an infant in a nursery with a suspected genetic condition and went the original route of traditional diagnostic workup, around 11-12 per cent would be diagnosed through that way. However if you do whole exon sequencing at the start, about 56 per cent of those condition will be diagnosed through that way and what's more is that even though whole exon sequencing costs money it's a cost benefit savings to the health system and the earlier you use it, the better the savings. So clinical impact wise, there are some challenges. So things to think about. The first is what we call variants of uncertain significance. Variants of uncertain significance are not new in health care. So that basically means if you sequence my gene and we sequence your gene and find a variant in me that we don't see in you, is that a variant that's going to cause me to have a disease, or is that just part of what makes Aideen, Aideen. Sometimes it can be challenging if you look for that variant in lots of people with a disease and don't see it and looks for that variant in lots of people who don't have the disease and don't see it, you have a hard time saying is this the variant that will cause them to have the disease or is that a variant? Unexpected findings are say I had pancreatic cancer and genetic sequencing and I was found to have a mutilation in BRCA1 or 2. I've got no personal history of breast or ovarian cancer. I am aware that Aunty Mary had breast cancer, but I didn't think that was related to my pancreatic cancer, that would be an unexpected finding for me. An incidental finding is something that's totally unrelated to the condition that you presented with, that's found through the analysis of your whole exon sequencing data et cetera. This can either be accidental, so we're analysing your sequencing data related to your rare congenital condition and we find that you're at increased risk for a certain cancer or a carrier for cystic fibrosis, it just happens to come up in the analysis process. Or there's an increasing body of movement of genetics at the moment that says while

we're doing whole exon sequencing for one condition is it not a good idea to screen for actionable genes where you could increase the morbidity or the mortality of those conditions by knowing that information ahead of time. There are a lot of pros and cons to doing that, but I wanted to make you aware and I think Nic will follow up on some of these in her talk. When you can imagine if you've got an unexpected or an incidental finding there is the potential for that to result in some degree of life insurance discrimination or workplace discrimination, as well and again, this is something that Nic will talk to. So you can easily imagine if we're consenting somebody for one gene and one test that's an awful lot more straightforward than consenting them for whole exon sequencing where you've got to cover variants of uncertain significance, incidental and unexpected findings et cetera. That requires time and a degree of expertise or training to do that. Similarly giving people results back takes more time, as well. We're getting better at it all the time and more comfortable with doing it, but it just takes more training for medical personnel. So, personalised medicine, how is this going to translate for you and your loved ones in the foreseeable future? The first area is cancer sequencing. I should pause at this stage and say that when people think of genetics, they automatically think about what they inherited from their mum and their dad, what was there from the egg and the sperm from once they were born. What they don't realise is throughout our lives our cells continue to copy and divide as we grow up and get older and in that process, new mutilations happen. Most of the time they're not in an important place and they don't have any significance. However, occasionally there'll be a mutilation in a place that affects how that cell grows and develops and all of the cells that are made from that cell will contain the same mutilation. If you get additional mutilations in that group of cells they have the potential to go on to develop into cancer. So all cancer is genetic, but cancer is very rarely inherited. Does that make sense? So if you look at the genetic sequence of your cancer, you have the potential to identify mutilations that will tell you a little bit more about the diagnosis, about the prognosis that mutilation is associated with a better survival or a better outcome than this mutilation. And it could also point you in the direction of treatments. People who have that mutilation respond better to that treatment. They're not going to respond to that treatment at all, so don't make them sick by giving it to them in the first place. So how is it done? All you do is extract DNA from the cancer from the tumour and you can either do it the

old-fashioned way where you look at five genes or seven genes that are known to be important in that particular cancer. Like somebody said earlier on about KRAS, that's well-known in cancer. You sequence that and look for those mutilations. Increasingly what we're doing is doing whole exon sequencing and looking for any genes known to be important in cancer. The other big area is pharmacogenomic. So pharmacogenomic apart from being, I like to say a good scrabble word- I'm such a nerd- is basically all it means is the extent to which your genes affect how you're going to respond to a medication. That's all it means. And people are particularly interested in pharmacogenomic, because we want to reduce what we call adverse drug reactions, improved safety. Adverse drug reactions account for 2-3 per cent of all hospitalisations in Australia every year and they can have severe or even fatal outcomes, particularly in vulnerable populations. And genetic factors are estimated to account for about a quarter of all ADRs. So you can imagine if we knew that ahead of time that we'd be able to reduce those risks significantly. People are also interested in efficacy, whether a person is likely to respond to a drug, or not respond to a drug. Obviously that's particularly beneficial in cancer, but applies to other areas as well and also even this person will respond to that drug, but they'll need twice the dose as the person next door to them in order to get a therapeutic benefit. Similarly, will they be resistant to that drug, as well? You can do something called pharmacogenomic on that microray technology that I talked about, the piece of glass for an affordable amount per person. In conclusion, genetic testing is transitioning from rare disorders to more common disorders, and for example cancer genomics and pharmacogenomic or cancer genomic sequencing is already here for a lot of cancers. Not so applicable for other cancers, but for most it's there and pharmacogenomic you're going to hear much more about in the next coming years. Interpreting and managing all the data that comes out of these tests can be challenging, but again we're getting better at it all the time and the clinical implications of testing means that we need additional time and training for consenting and result disclosure. And that's it. So thank you so much.