Centre for Personalised Medicine podcast

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Navigating a genetic diagnosis

SPEAKERS

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Rachel Horton
Welcome to the Centre for Personalised Medicine podcast, where we explore the promises and pitfalls of personalised medicine, and ask questions about the ethical and societal challenges it creates. I'm Rachel Horton, and I'm here with Gabby Samuel, and in today's episode, we're thinking about what it might be like to navigate a genetic diagnosis, and share it with family members.

To help us think about this, we're really lucky to be joined by Julie from the CanGene CanVar Patient Reference Panel. Julie first found out that she had Lynch syndrome, a genetic predisposition to some cancers, after being diagnosed with cancer at a young age.

Thank you so much for joining us, Julie. Please could we start by asking a little bit about your story, and how your diagnosis of Lynch syndrome came about?

Julie Young
In 2018, I was diagnosed with rectal cancer. And this was four years after my father's diagnosis of the same cancer. I'd always had a feeling inside that something like this would happen to me. And so in all honesty, I was not surprised when my diagnosis was made. I'd had the same symptoms as my father, and my father's treatment had been successful, which was reassuring to me. I knew from some investigation into family history that other family members had also suffered from a similar diagnosis, and had similar treatment. And so this raised alarm bells for me.

However, there'd always been a family divide and so it was a difficult path to navigate, as my father himself wasn't aware of his family's history of illness. It also became apparent that my father and another relative were the same age at diagnosis, which was 64 years of age. In normal circumstances, this would not have raised a flag. But as they were both unaware of each other's illnesses, and both of an age that was classed as normal for this illness, nothing was seen as an issue.

This, of course, became very different on my diagnosis as I was 44. Having seen my father's treatment was successful, I requested the same consultant. And I had some trust in him, which was good. I knew he had an interest in family history. And I followed the same treatment path as my dad. I was referred to clinical genetics for testing. And this confirmed my Lynch diagnosis of *MSH6*.

Rachel Horton
Would you mind telling us a little bit about Lynch syndrome?

Julie Young
Yeah, on diagnosis, I hadn't heard of Lynch syndrome. And I wasn't alone, very few of the GPs had either, which wasn't exactly reassuring. However, I am very fortunate as my GP surgery is very proactive in this respect.

Lynch syndrome was previously referred to as HNPCC, or hereditary nonpolyposis colorectal cancer, and is a mistake in your genetic code, or DNA. It's a mismatch repair gene, which means that where normally, cells the body sees as being rogue or bad cells, are targeted by our body and destroyed, in the case of Lynch syndrome, this doesn't happen. And so cells mutate, and they hide, and eventually cause cancer. This puts people with Lynch syndrome at a higher risk of cancer than the normal population, not just colorectal cancer, but also endometrial, ovarian, prostate, urethral, kidney, stomach and some others.

Gabrielle Samuel
What is the diagnosis of Lynch syndrome meant for you?

Julie Young
For me, my diagnosis was not a surprise. And in fact, I felt empowered. But I'd seen other members suffer, like family members, and looking at the family tree it suddenly became increasingly obvious how many cases of cancer there had actually been. So here was something that I could actually do to potentially help others.

Above all, I could maybe prevent my family, my sons, my grandchildren, from having their own cancer journey? So that was a good thing. You have the chance of having regular bowel screening and preventative surgery, if you wish, and although this can be unpleasant, it can save lives. I was also relieved that this was not something I could have avoided, because I'd always taken care of my body, I'd never smoked and never drunk. I tried to keep a good weight to exercise ratio.

Gabrielle Samuel
Oh, thank you for explaining that all to us. It's so interesting. I was wondering if we could just come back to the bit where you were talking about your family, and to ask how's it been sharing your diagnosis with others in your family, and whether that was an easy decision?

Julie Young
Do you know, whether it's right or wrong, I was actually quite excited to let people know. I really wanted them to have the knowledge that I didn't. And to have the opportunity to spread greater awareness and hopefully save them their own cancer journey. So it was an easy decision for me to make, that one.

Gabrielle Samuel
And I mean, you talk about the easy decision, but then… would you mind, if you're okay to talk about it, how you went about letting your family know?

Julie Young
The first thing I did was visit my parents, to show them the letter that I'd had from genetics. And I felt by doing this, it was a good thing. My dad had always felt that his cancer was a result of smoking. But this proved that wasn't necessarily the case. However, I was met with a less than enthusiastic response. I think in a way, my dad, he felt guilty. But in actual fact, I believe that guilt was unfounded. Because being genetic, who knows how far the trail went back?

I left letters for my parents to pass on to my siblings. And I knew they would be proactive in booking in a test which was good. As it turned out one sibling was negative but one sibling was positive. Other family members are yet to be tested, unfortunately. For me, that's hard, because it worries me that they could now be having screening, which they're not. However, they're both adults, which means I can only advise them and not enforce anything upon them. And one family member who tested positive, took it quite badly and struggled for a while. Although they're now being screened and have come to terms with it, to some extent.

There are also family members that we had lost contact with. And so I had to do my own digging, to track them down to let them know. I felt that it was my responsibility to ensure that they were aware. And then the decision about whether or not to be tested was up to them. And so I visited their house. I wasn't able to see these members of the family, but I did explain the situation to a relative who was living with them, and left letters from the genetics department to be passed on to them. However, I've unfortunately no idea if they actually got the letters and eventually got tested. But at least I know I tried my best. And sadly, I've since discovered that they have both passed away. And so that's something I will never find out.

Gabrielle Samuel
Wow, it sounds like such an awe-inspiring kind of life journey that you've been through. I was wondering, I mean, I had a few questions coming out of that, but I was wondering if you could just- just because the audience who might not have been through these processes might not understand what those letters are, that kind of come from the genetic departments? If you could just say a little bit more about what those letters are and where they come from?

Julie Young
Yes, of course. When you visit the genetic counsellor, from my perspective, I was visiting from having a cancer diagnosis. So they had a sample of my tumour. They took a sample of my blood, obviously analysed the results and came up with the result that was *MSH6*. From there, they explained, when you go in to see a genetic counsellor, exactly what a DNA mismatch repair gene is. They actually show you some really interesting information on DNA, diagrams, and they explain everything really thoroughly, including, you know, positive steps you can take, such as the surgery and the screening that you can have, and then, they kind of help you to go around navigating *who* you might want to pass that information to. And, you know, the way that that might, information might be taken by other members of the family- some people are positive, some people are negative in the same family, and the

negative people can take it really badly as well, because they have this guilt factor. That, you know, they maybe should have had it, when somebody else *did* have it?

So, they give you letters to take to your relatives, or you can post them if you don't, sort of want to go and see them, with a prepaid envelope. And that relative would fill in, on the letter, their details, whether they want to go in and be tested, or whether they just want to kind of leave it, because not everybody wants to know. That's another, like, sort of side to the story. So yeah, it's a really helpful situation, the problem is actually getting everybody to be proactive, and making those steps. And obviously, the more people that do take those steps, the better it will be, we'll have more information and more data and better outcomes for everybody, hopefully.

Gabrielle Samuel
Thank you for explaining that. I think it makes it a lot clearer to understand the process. But when you're talking about it, it sounds like you felt like this really strong sense of responsibility that you need to kind of pass this information on to people in your family who might be affected? And even that's the case when you're perhaps not in contact with them for a long time. So could you just talk a little bit more about that responsibility that you feel?

Julie Young
Yeah, of course, I did feel responsible to tell people, but at the same time, I feel that that was the right thing to do? I think it would have been a lot more formal and scarier, if people had found out randomly from a clinician or a hospital letter. I feel at the correct time when the clinician took over, they were better able to explain the condition than I would have been, and answer any important questions, and talk about all the things I was unsure of. So that worked for me. And it's more plausible, obviously, if it comes from, you know, the medical profession rather than somebody in the family.

Rachel Horton
It sounds like this, this kind of diagnosis has been important information for you – has it felt similar for your relatives, do you think?

Julie Young
I've found the information to be *so* valuable. And if I can, in turn use this to help even a small amount of people, then that's all worth it. Might sound selfish, but it makes me feel good to be able to help people. I think relatives at the time were a little bit stunned, and in some way didn't want to accept it, because they felt a responsibility for it all. But in essence, this wasn't the case. This path has helped to spread awareness.

Gabrielle Samuel
Have the people that you've let know *always* kind of had that eventual seeing the positive? The positivity of the information?

Julie Young
Sadly, not always. Some had tests straightaway, some didn't as they were scared of the procedures such as colonoscopies and the gastroscopy, which is… not lovely, but used to detect early signs of cancer or precancerous lesions. And maybe it was the thoughts of

preventative surgery, or the possibility of passing it on to their family? And especially as young adults, when they don't feel ready to face it all. It does worry me because I tend to think, you know, they might not have it. And they could be sitting worrying all this time for nothing.

Gabrielle Samuel
It must be quite a difficult situation, right, where you pass on information, but people might not be taking it forward in the way that perhaps you'd want – you would, or you'd want them to.

Julie Young
I think it's maybe a lot simpler to navigate when you come in from the angle of having had a cancer diagnosis, rather than being younger, and possibly having what they perceive as a cloud hanging over them. I imagine myself in this position, and I think I would have been terrified, to be honest. But hindsight's a wonderful thing. It's hard to break the stigma of what might be, rather than what might *not* be. People find it, like, so much easier, to think that they're definitely going to have a positive diagnosis, rather than the relief they would have if they *didn't* have it.

Gabrielle Samuel
So given that, what sort of things do you think would make it easier for people, like, newly diagnosed with Lynch syndrome? Do you have any, kind of, I suppose advice, or useful tips?

Julie Young
Yeah, when I was diagnosed, and that was only three or four years ago, and the knowledge base of the GPs, hospital doctors and consultants, and even the public was a lot less. I was often faced with "Oh, Lynch syndrome, what's that?" My colorectal surgeon was fantastic. But at the time, she said that she was only aware of two families in our trust that had it. And unfortunately, she's now retired. Obviously, the data that's coming out now means that there are probably a lot more people that have it, then we realised.

However, even in this short space of time, I can see a greater awareness around. So now when I go for a colonoscopy, and I say I have Lynch, there's a feeling that they actually know what I'm talking about, which is very reassuring. I was given no information at the time on the use of aspirin, or the test for helicobacter. And in fact, the best source of information at that time was the Facebook group, and Lynch Syndrome UK. But not everybody's social media savvy. I do think at the time if I'd maybe been signposted to a support group, or links to information online, maybe even a web chat for people that want support, or confidential advice and support, it would have been really beneficial. But the awareness has come a really long way in a short space of time, so fingers crossed. It was through Lynch Syndrome UK site that I saw an advert for CanGene CanVar, the project, and immediately felt a pull, sort of to raise more awareness to help others. So that was my next move.

Rachel Horton
Please could you tell us a little bit about the CanGene CanVar project, and the work that you're doing with it?

Julie Young
Joining the CanGene CanVar programme has been so enlightening for me. I'm eternally grateful to the people involved with this project, both the professionals and the patient reference panel. The CanGene CanVar project is incredible. It's funded by Cancer Research UK as a five-year programme, and we're currently in the fourth year. It aims to gather data on cancer susceptibility genes such as *BRCA1* and *2*, Lynch, and many more. Think that list will go on for a long, long time. And then this will lead to better screening and cancer prevention, but also improved treatments in the case of disease. They're also working on information resources for patients, and educational tools for medical professionals.

So yeah, the project is split up into six work packages. And the work package that I'm helping with is work package 4, which aims to produce patient resources. I have the pleasure of being on the patient reference panel, which is a group of patients who are involved in every aspect to make sure what is being produced is patient-friendly. They're a fantastic bunch of people, both the patients and the professionals involved. You really feel like your opinion matters. Even when you think it's the silliest detail it's listened to. We have a lot of meetings on Zoom and meetings in person, which aim to update everybody involved on the ongoing progress and any issues that arise.

It was through the patient reference panel that I had the opportunity of an ethics placement with CanGene's ethics work package – 6 – at the Ethox Centre in Oxford, to see what the ethics team do, and how they are involved. I got to meet some fantastic people, such as Professor Mike Parker, and Professor Anneke Lucassen and the lovely Dr Kate Sahan. And I also got to spend some time sitting in on the winter school exchange programme which was absolutely fascinating. I was so unaware of the work that work package 6 were involved in, and yet they're the building blocks. They focus on the research and the data involved. And if it's not correct, things would fall apart very quickly, and the information and data is constantly evolving at such a very fast pace. I totally admire the work they do. And I'm so fortunate to have visited and seen this first-hand.

Gabrielle Samuel
That's so lovely to hear, isn't it, that you've had such a wonderful experience?

Julie Young
It was fantastic. It really was.

Rachel Horton
Thank you so much for talking to us about it and what it has involved. Can I just finish with a question that we ask everyone on this podcast – if you had to pick one message for people to take away from this podcast, what would it be?

Julie Young
Definitely *don't* be afraid of what *might* be, nothing's for certain in life. And it could just as easily be what might *not* be. And also, the more awareness we raise, and the more data we gather, the greater the prevention of disease, but in the instance where there *is* illness, there will also be better treatments. So it's win-win for people. And if you can only encourage them, that will be, you know, a good job done.

Rachel Horton
Thank you so much, Julie, for joining us and for sharing your experiences. It's so kind of you. And thank you for listening to this episode of the Centre for Personalised Medicine podcast. If you'd like to find out more about personalised medicine and its promises and challenges, please visit the Centre for Personalised Medicine website at cpm.well.ox.ac.uk.