**Hope for those with “no primary findings”**

**The G Word Transcript**

**Lisa: Hello, welcome to the G Word.**

[Music]

**Lisa: I think in the back of my mind, subconsciously, I had hoped that when we eventually got a diagnosis, it would – I don’t know, bells and whistles, balloons going off, fireworks, etc. And then the experience of a letter thumping on the doormat, and I recognised the postmark quite quickly, and it was at that moment I suddenly thought, “Oh gosh, I haven’t buried all these feelings of hope.” Because I opened that letter with quite trembly hands, and then this diagnosis or lack of diagnosis, you know, nothing had been found, and it was a bit… I don’t know if it’s been described as like a nail in the coffin experience, because I really hadn’t realised I was still clinging to this hope all that time, and then again it was, you know, another, “No, nothing’s there.**

[Music]

**Lisa: My name is Lisa Beaton and I’m a member of the participant panel at Genomics England. On today’s episode, I’m joined by Dr Celine Lewis, the principal research fellow in Genomics at UCL, Great Ormond Street Institute of Child Health, Jana Gurasashvili, a genetic counsellor, and Louise Fish, the CEO of Genetic Alliance. Today we’ll be discussing the impact on parents with children with rare conditions, who received a no primary findings result after diagnostic whole genome sequencing. If you enjoy today’s episode, we’d love your support. Please like, share and rate us on wherever you listen to your podcasts.**

**Can I ask all of us here present to introduce themselves, please?**

Celine: Hi everyone, I’m Celine, I’m a behavioural scientist in genomics at UCL Institute of Child Health, and I currently hold an NAHR advanced fellowship to look at the implementation of WGS, or whole genome sequencing, in the NHS.

Jana: I’m Jana Gurasashvili and I’m a genetic counsellor at Northwest Thames Regional Genetic Service, and prior to that I was at Great Ormond Street, involved with consenting families to the 100,000 Genomes Project, and I also have an ongoing interest in the lived experience of patients and parents of genetic counselling and rare disease.

Louise: Hi, I’m Louise Fish, I’m the chief executive of Genetic Alliance UK, and we are an alliance of around 230 charities and support groups that work with patients and families who have particular rare conditions. We also run a really longstanding project called SWAN UK, and SWAN stands for syndromes without a name. And the SWAN UK project supports families with children that have been through genetic testing but have not found a result following that genetic testing. So, it’s clear they have a genetic condition, but science hasn’t quite advanced far enough yet to tell us what that means and what that will mean for their child, and what that will mean for their family over the coming years.

**Lisa: And I personally can attest to the wonderful support that SWAN UK can offer because, as the parent of a still undiagnosed child, I have been involved myself with SWAN UK since my daughter was around the age of three to four years old. It’s brilliant being a part of my big SWAN UK family. We first realised that there were some – I suppose something wrong with our daughter when she was around two weeks of age, but it wasn’t something I could specifically put my finger on. I couldn’t at that point have taken her to a doctor and said, “I don’t know what’s wrong but there’s something wrong.” I just knew in my heart of hearts, probably because I have three elder children, that there were issues, and things weren’t developing as they should. She cried a lot, she screamed a lot, she never seemed to be comfortable in any position when you held her, when she was asleep, when she was upright. It didn’t seem to matter what you did, she was just a rigid, stuck child, for want of a better word. And all my mum senses were screaming, but it completely sounded ridiculous to take her to a doctor saying, “She feels wrong.”**

**And I think that’s quite a SWAN UK experience, from chatting to other families with similar situations. The parents just know that there’s something not right, but it can be very isolating not to be able to identify kind of where that starts and what it is. In our case, it wasn’t until our daughter was nine weeks old that things became much more obvious, that there were developmental concerns physically and medically, and at that point we went from my sort of mutterings that there was something wrong but I wasn’t sure what it was, to a sudden hospital admission with quite a shocking turn of events. From something that had started out quite normally, as a routine visit to the baby clinic, to suddenly being seen by a troop of different paediatricians, and doctors coming in and out constantly, asking different questions, and sending us off all over the building for different tests and x-rays and imaging. And being given a partial diagnosis that our daughter had a condition called arthrogryposis, but it was clear that there was much more going on than that, and we would need referring to many more different fields. And that day really our diagnostic odyssey, for want of a better word, began.**

**So actually, in terms of that diagnostic odyssey, many parents of children with rare undiagnosed conditions experience this, and when we agree to have genetic testing, we feel that we are going to get these answers straight away, and that every appointment that you go along to is going to be the one that brings you the answers. But certainly in our experience kind of 15 years on, that’s not been the story at all. Celine, can I ask you to explain what the words no primary findings actually mean when a parent receives that regarding their child?**

Celine: So, there’s a range of different possible outcomes from a genomic test. So, the results might provide a diagnosis to that patient and family, or other situations, there might be a variant of uncertain significance, so we don’t necessarily know if the gene that we found, a genetic variant is the likely cause of the condition, or we might find no particular gene at all that we think is linked to the child’s phenotype or clinical condition. So, that’s what we mean really when we’re sort of saying no primary finding.

**Lisa: Louise, would you be kind enough to explain what you think the impact of no primary findings means to families like my own, parents who don’t have a genetic likelihood cause, just a gene thrown up to diagnose their child?**

Louise: Yeah, I think it’s a huge challenge for families, and you’ll obviously know that from your own experience. People go to have genetic testing hoping it will give them some answers, first and foremost, just to kind of understand, you know, what condition their child has and what the likely impact that’s going to be on their child and on the child’s life, and on the family’s wider life. And I think one of the things that we really ask genetic counsellors and geneticists to do is help people understand before the genetic testing takes place that there may be nothing found from it, so that that kind of expectation is built in. Because people hope that they will get a diagnosis that will give them answers about what the impact of the condition will be on their lives. In a best-case scenario, access to a particular treatment that might be a huge help for their child, but at the very least, access to a range of services and support for their child. So, that kind of diagnosis is often seen by families as the key to unlocking a range of services and support that will help them and their families at what is the beginning of a lifelong journey.

And I think when families get no diagnosis, there’s a real concern on behalf of families, a, that they don’t understand how their child’s going to be affected by the condition. What we’re really careful to say to families is, “Just ‘cos you don’t have a diagnosis with a name, your child is still the same person they were before. They still have exactly the same bundle of needs as they had before, and you will still need to work with the NHS and with wider services to make sure that they can access speech and language therapy, and physiotherapy, and all of the services that they are going to need and you are going to need to help them live their lives to the full.” But I think that moment of not getting a diagnosis is when people feel I think real – the uncertainty continues, and uncertainty, we know, is a really hard thing to live with, and the lack of clarity about which services you’ll be able to access. So, I think psychologically it’s a massive impact on the family not to have the answers that they were looking for, or the key to the services that they were hoping would be there.

**Lisa: Thank you, Louise, yeah, I would definitely agree with that. We had a no primary findings result in I think it was 2019. It was a really bittersweet moment because my daughter’s list of various different conditions kind of – by this point, named parts of difficulties for her spans over sort of two pages of A4, and yet on the letter back from the genomics service, it just says that, you know, nothing causative has been found. And so part of you is left wondering, well, how can there be all these different conditions or difficulties, and yet there’s still nothing there? And I know personally, I had comments when she was much younger, every time a test came back, where people would say things like, “Oh well, that’s great news,” and to some extent it was great news that something hadn’t been found, but also if that hadn’t been found, what was still out there? And that fear of kind of the unknown was extremely difficult.**

**And also paradoxically, there was a sense of some very well meaning people saying things like, “Oh well, if they haven’t found anything then there can’t be too much wrong.” But yeah, I have a child who is tube fed and on multiple different medications, and cared for basically for 24 hours a day, so that doesn’t really fit in with the picture of there not being very much wrong from a personal perspective. And I think it can make you as a parent/carer feel perhaps there’s a tendency to downplay that there is an issue and that perhaps, you know, you’re making it up, for want of a better word, and that sense of isolation around that can certainly be problematic. Celine, if I can come to you, that diagnostic odyssey, what are the common experiences and expectations of parents and patients who undergo that genetic testing from your perspective?**

Celine: Well, I think sort of parents go into genetics testing for a whole range of reasons really, and Louise has already alluded to many of these. Ones that I’ve come across in my own work include wanting to know why their child has a particular health problem, so that that child can access the most suitable treatments or therapies, or even access clinical trials. Even relief from guilt for many parents, a validation that the parents hadn’t done anything wrong during their pregnancy to cause the child’s condition, and that’s hugely important really, to try and get that relief from guilt. Also to know whether future children might be affected by the same condition, and then more social reasons really, for example, making contact with other parents through support groups, or access to social and educational support.

And I think there’s also a drive from many parents to feel that they’re doing everything absolutely possible for their child. I mean, particularly with something like the 100,000 Genomes Project, it was really a sort of first of its kind project, where patients were on a significant scale able to access this new whole genome sequencing technology. So, many of the parents taking part in that project felt like pioneers, and there was really a lot of expectations around whole genome sequencing in delivering a diagnosis for those parents who’d previously not been able to get hold of one.

**Lisa: Yes, I strongly can resonate with a number of the points you made there, particularly the feelings of guilt. I must have asked myself a thousand times whether, you know, something I did do, something I didn’t do, something I thought of, something I hadn’t thought of [laughter], all those questions that swirl around, particularly in the small hours of the night when you feel particularly alone. And yes, I can completely relate to that. And also although SWAN UK is primarily for children and parent/carers whose children don’t have a diagnosis, actually a number of the parent/carers on there will have children with diagnoses that are so very rare that absolutely, you know, very, very little is known. They might be the only parent – the diagnosis, for want of a better word, they may have received may just be a series of kind of numbers and genetic dot-dashes, forgive my layman’s terms there, but it may not actually help them any further along in terms of feeling that they know anything further or the direction of, you know, where that will lead their children, and that can feel very, very isolating, I’m sure, probably just as much for those of us who don’t have that diagnosis.**

Louise: Yeah, just to add to that, I think that’s absolutely right, Lisa, and I just want to give a shoutout – at SWAN UK, we tend to support families who don’t have a diagnosis at all, or, as you say, a small number of families who do but have been part of the SWAN UK family for so long that we’re very happy to keep them because of the support they’re finding from other parents. We work really closely with another of our members, Unique, who are a charity that support parents in exactly the situation you’ve talked about, where people have finally got a diagnosis and it’s that kind of relief of having a name, but it’s a super long name, and you find out you’re one of only three families in the world with that diagnosis. And so although there’s a real I think comfort for people, perhaps if you have a five year old and you’re meeting a family who have a 13 year old and a family of a 19 year old, then you start to see a little bit about how your child might develop, but there’s not enough kids affected that you can be really certain about that.

So, it gives you a little bit more information, but not the kind of wealth of information you were hoping for about how your child’s going to be impacted by a particular condition, and what the future might hold for you and for them. So, SWAN UK and Unique very much work alongside each other to kind of support families on whichever part of that journey they’re on, because there’s still a huge amount of uncertainty for families with those super rare conditions, as you say.

**Lisa: Definitely, and I’m sure you’ll be familiar, Louise, yourself if you get time to go on the online communities and seeing the question that pops up quite regularly when somebody has received a diagnosis of, “Can we still remain part of the SWAN UK family?” And they very much use that word, family, because I think they do feel that, although all our children are different, there are children with physical, medical, cognitive, a combination of all the above syndromes, conditions, etc, they feel that kind of embrace of all being in a collective club of rare and unique and undiagnosed, and that’s very comforting to the members.**

Louise: Absolutely, yeah, I think that sense of belonging and being able to reach out to other families that you’ve been on that journey with for many, many years. You know, many of our families join when their children are like one or two, and they’re still with us when, you know, their children are 26, 27 [laughter], and that sense of having that community and that family and that belonging is really, really important to people, I agree. It makes a big difference psychologically to be part of a community you can reach out to and ask the questions that perhaps you can’t ask to other people.

**Lisa: Celine, can I ask you how many patients for the 100,000 Genome Project have had a no primary findings diagnosis back?**

Celine: Well, back in 2021, there was a paper published in the New England Journal of Medicine, which reported that, in the initial pilot for the 100K, a diagnosis was found for around 25 percent of rare disease participants, and other studies looking at the diagnostic yield of whole genome sequencing have put the number anywhere between 25 percent to 55 percent, depending on the clinical indication. And we know that even already from the 100,000 Genomes Project, this pioneering project has led to more than 6,000 diagnoses being identified, and that number will obviously continue to go up as they explore the data and gather new insights. However, that still obviously leaves a significant number that won’t get a result from whole genome sequencing, as many as half of those rare disease patients, and that was really the basis of the study that Jana and I worked on.

So, we felt that there had been so much research really looking at the experience of parents who do receive a genetic diagnosis, and that a lot of attention rightfully does focus on the amazing successes of the 100,000 Genomes Project and genomic medicine more broadly, but actually that there is a considerable number of patients and parents and families who don’t get a result, and we felt that it was important that we also focus on those parents and patients, and try and understand their experiences.

**Lisa: Yes, you can feel, if your child, for example, is under multiple different care specialists, that it can be quite hard, when you’ve just got this list of different names of things that are wrong, that you feel very much still out on the limb and forgotten about. But it’s clear that, from your work, you’re identifying that and pointing that back to the specialists, the consultants, to remind them that these parents and these children are still finding their ways through. Can I ask you, Jana, the study that was conducted, what would you say the main things from that study told us? Can you describe some of the emotions experienced by the parents, and what challenges that they have faced along that receiving the no primary findings diagnosis?**

Jana: Yes. So, many participants really felt very strong disappointment and sadness on receiving that no result, and for many, it kind of reflected the feelings they had had when they first realised they had a child and there was no diagnosis for their condition. And as Celine said, this was such a new technology that people had invested a lot of hope in, and so many felt that it had been their last chance of finding a reason for their child’s condition, and that they’d come to the end of the road with that no primary finding result. And, well, one person described it as another door shut. And people talked about the actual toll taken, the emotional and physical toll, and one person described feeling low for several weeks following the result. And some talked about the timing of the result. Somebody got it as a letter just before Christmas, and so their whole family holiday that they’d prepared was marred by getting that news just before Christmas.

And it often seemed to leave parents feeling isolated and unable to contribute to normal parental roles, such as going to parent groups, etc, because they felt that other mothers particularly - as it’s mothers we were speaking to, other mothers, their experience of motherhood was so incredibly different to their own, and they felt a lack of support. And one parent actually talked about wanting to lock everyone in the house just to escape the feeling of judgement and pity from outside the front door. And some parents talked about finding it hard when other people would post on support groups that they had got results from the 100,000 Genomes Project, which was very difficult. And some talked about hope as finding it hard to keep hopeful but needing to keep hopeful. So, they talked of hanging onto a little bit of hope, as though that was quite an intense thing, which I think, Celine, you’ll agree, that made us able to kind of identify that hope was really part of a coping mechanism for this whole process of going through this diagnostic odyssey.

Celine: Yeah, people sort of talked about not wanting to let go of hope and the importance of hope, and that without hope, there was no sense of wanting to continue this journey of trying to find a diagnosis, and that it was still very important to people. And I think that parents did understand that, even though a no primary findings result now, that doesn’t necessarily mean that they won’t get a diagnosis at some point in the future. So, there’s obviously the opportunity to do future reanalysis of the genome, particularly as we understand more about the function of different genes, and as new genes are added to many of the panels that we’re using in whole genome sequencing. So, I don’t think not finding a result means that there is no hope in these circumstances, but for many parents, they did talk about hope being too painful, and not wanting to be let down again, and really preferred to focus on the here and the now rather than necessarily focus on the future.

**Lisa: Yes, I can only speak from my own experience here, but I think I primed myself to actually forget about going on the 100,000 genomes sequencing because, having undergone genetic testing for certain conditions that they were quite convinced my daughter had from around the age of four months through to around the age of three years, I’d gone to so many appointments and thought, “Oh, this’ll be the time that I turn up and somebody will tell me this is what is the diagnosis.” And when I then joined the 100,000 Genomes Project in 2015 with my husband and my daughter, the genetic experience, the discussions that we had at the time were very helpful in that it was made quite clear to me that potentially we wouldn’t get a finding, and actually that any information that did come forward was perhaps unlikely to be hugely beneficial to our family at that point. So, I was quite clear what potential finding would mean to us.**

**But I think in the back of my mind, subconsciously, I had hoped that, when we eventually got a diagnosis, it would – I don’t know, bells, whistles, balloons going up, fireworks, etc. And then the experience of a letter thumping on the doormat, and I recognised the postmark quite quickly, and it was at that moment I suddenly thought, “Oh gosh, I haven’t buried all these feelings of hope.” Because I opened that letter with quite trembly hands, and then this diagnosis or lack of diagnosis, you know, nothing had been found, and it was a bit… I don’t know if it’s been described as like a nail in the coffin experience, because I really hadn’t realised I was still clinging to this hope all that time, and then again it was, you know, another, “No, nothing’s there.”**

**And I think because of the work I’ve undertaken with SWAN UK as a volunteer, and being quite involved in wanting to sort of educate myself and learn more, I did understand that, even though we had no primary findings, it didn’t mean that the study, everything was closed to us. It didn’t mean, you know, that things won’t still be looked for. But equally, at the same time, it just meant that we had nothing yet to pin anything on at that point. And I think it’s quite hard to pick yourself up and dust yourself off again, to be like, “Okay, we’re still here, we’re still circling that drain,” as it were.**

[Music]

**I think actually that takes us on quite nicely really, about what role hope has in the experiences of a child with rare and undiagnosed conditions. And again if I can just say that there’s hope and there’s realism, and somewhere along the way, if you’ve been on the journey for quite a long period of time like ourselves, you have to try and find a way of living with that hope and realism all at the same time. So, we’re still hopeful that one day we might get some answers, but we’re realistic that day to day we need to focus on the difficulties or the experiences that my daughter has, so that we can manage to give her the skills to live her life to the very best of her abilities. Certainly, that’s our experience. And also I think if I’d let myself dwell forever on not having a diagnosis or a pathway specifically for that, it would have been quite difficult to carry on, pick ourselves up every day. What would you think about the role of hope there, Louise? What would you say your experience is from chatting to fellow parent/carers?**

Louise: Yeah, I think you’ve described it really eloquently and better than I’ll be able to do, but when we talk to people, the phrase I always have in my head is kind of hope for tomorrow and help for today are the two things that people are looking for. So, making sure that that hope for tomorrow’s still there both in terms of, you know, the NHS being really clear that it will provide support for individuals without a diagnosis, and there may be opportunities for reanalysis in the future as science makes future progress. And, you know, there is progress being made so fast at the moment in genomics and that’s really welcome. So, making sure that people who’ve already had whole genome sequencing but not found anything continue to have access to that potential reanalysis I think is really important.

As you’ve rightly said, Lisa, as well, thinking through in terms of hope for tomorrow, the opportunity to take part in clinical trials and to make that as easy as possible where treatments are being delivered, to have the opportunities to take part in trials for non-condition specific treatments, whether that’s for epilepsy, which affects people across a whole range of conditions, or sleeplessness, which affects people across a whole range of genetic conditions. You know, there are both trials that only people who have a particular condition can take part in, and trials that are open more broadly, so making sure those opportunities are available as well, so that people have that kind of hope for the future.

But alongside that, I think it’s really important for the NHS to be clear with people about what help for today will continue to be available, and so we are working really hard with the NHS to emphasise the fact that when no diagnosis is possible, the NHS still needs to be clear to people about how they will be supported, whether that’s through the genetics team or a particular discipline, perhaps the one that is the closest fit for their child’s biggest need, whatever that may be, that they can still access more joined up care. So, you know, who is the person in the NHS, if you don’t have a diagnosis, who’s going to help you secure referrals to speech and language therapy, to physiotherapy, to learning disability nurses, and to the package of care that your child may need.

Who is the clinician, if you don’t have a clear diagnosis, who’s going to be the person with the authority and the confidence to lead the multidisciplinary team, maybe up to 30 healthcare professionals who are going to support your child. You know, who is going to be the lead clinician that’s going to pull that multidisciplinary team together and make sure that your child’s not being prescribed stuff that’s contraindicated, or that’s going to help one element of their condition but make another element worse. So, we are really trying to work with the NHS to make sure they’re thinking through, where will that support be for the family in terms of their healthcare.

And alongside that, you know, many wider services like schools or social care or employers welcome the chance to talk to a geneticist or a genetic counsellor or nurse to understand what adjustments they might need to make for someone who clearly has a genetic condition but doesn’t have a clear diagnosis. And so we’re trying to kind of make sure the NHS is both focused on the kind of science side and making sure that the hope for future findings is there, but also the help side, and making sure that the right package of care is still available for families who clearly have a genetic condition.

**Lisa: Actually Louise, yeah, you’ve really summed it up excellently there, and whilst I am hugely grateful to the NHS and the various services, I can say, hand on my heart, my daughter has a huge number of professionals involved, both from the health side of things and social care side of things, and actually the person that kind of holds all that together is myself. And because we’re under multiple different teams, every time a new medication, for example, is prescribed, I need to go back to our lead team, which in this case happens to be neuromuscular, and check that, for example, if gastroenterology have prescribed a medication, that it’s not contraindicated from a neuromuscular side of things and so forth.**

**It’s all a bit like having sort of interlocking parts of a jigsaw, but perhaps no picture to follow [laughter], and that can be quite an isolating experience. And certainly, having chatted to fellow parent/carers, I know that’s their experience as well. And I imagine, Celine and Jana, you found sort of similar experiences when conducting the research.**

Celine: Yeah, so my PhD actually was focusing on the sort of journey for parents as they go through the diagnostic process, and one of the things that came out really strongly from that body of work was how the parents were really carving their own care pathway, how they had to sort of push and fight to access services, but at the same time were the gatekeepers for their child’s health. Having to make sure all the various teams and clinicians were kept up to date with all the different tests that they had and all the results. And, you know, at times, this could be really frustrating for a lot of parents, ‘cos they had to keep repeating their story over and over again, particularly ‘cos they didn’t have a diagnosis. So, these parents really were having a very different parental experience to many of their friends and family, because their experience of being a parent to a child with an undiagnosed condition was really sort of as being a patient advocate, and as having to push and fight to access services.

**Lisa: Yeah, it’s quite a unique experience. You are the specialist for your own child in that sense, I think would be the way I’d describe it. And I suppose over the years, I’ve got so used to sort of trotting out different medical explanations in terms that you can almost sound like you know what you’re doing [laughter]. And a few times when I’ve been at medical appointments, and perhaps we’ve met a new specialist or consultant, they’ve said, “Oh, what’s your field? What’s your area of expertise?” And actually you just think, “No, I’m just a specialist in my own child” [laughter]. But that’s quite an empowering feeling actually, so I guess that plays back into the feelings around hope and expectation, even with having an undiagnosed child.**

**Lisa: When I was recruited to the 100,000 Genome Programme, we didn’t actually as a family receive genetic counselling specifically, and I know that this is something that is incredibly important to many families, and how that can support you sort of going forward. We were quite lucky in our experience in that we knew that our daughter was definitely going to be our last child, so we didn’t have the thoughts and insecurities around potentially what it might mean for any future children that we had. But certainly as my daughter has got older and she’s asking her own questions, and our older children are at a stage in life where they’re looking at potentially having families in the future, I know that those things have come up, and we’re just still exploring what that will mean in the bigger picture. But can you tell us, Jana, really what can genetic counsellors do to help parents feel less isolated and better to cope with the uncertainty surrounding their child’s condition?**

Jana: Yes, well, I’m sorry to hear you didn’t have any genetic counselling prior to going on the 100,000 Genomes Project, because that consent conversation right at the beginning, before the whole genome sequencing, is really important. It’s important to know what the range of outcomes may be, so that it may be that you might get a result, you might get a variant of uncertain significance, or you might get no result. And parents in our study did suggest that their sense of isolation when they got a no primary finding result would have been alleviated if they’d known how many were not getting results. So I think in the longer run, it’s 40 percent perhaps received a result, so that’s 60 percent that didn’t receive a result, so those parents were not alone, but they felt very alone. And some suggested if they’d just had a leaflet really explaining that, and explaining that they’d still contributed to research and that that had been, you know, a good outcome in a sense, then they would have felt better about it.

So, a lot of work can be done before the testing really, to explore how you might feel on that range of results, and then that way sort of prepare parents for how they’re going to feel, and perhaps that helps them to have things in place, to know that it might be a vulnerable time with that letter, although that was particular for the 100,000 Genomes Project, to get the result in a letter in that way, and as you described, after such a long time, that you’d been able to forget that you’d been on the project. But to actually be a little bit prepared that it make take its toll on you might actually help with preparing oneself. It also might be helpful to include ways of promoting ways to enhance health and wellbeing for parents in terms of practical support, such as those things that you’re already attempting to access, like the respite services, school support, support groups, and thinking about psychological wellbeing and ways of managing stress, psychological support for parents, and possibly spirituality based resources as well.

And focusing maybe on what is known about the child’s condition even without a diagnosis, so what’s likely to be beneficial, and support parents in actively coping, such as what research they might be able to access, and continued medical support. And also actually having a named person within the genetics service, so they have someone to go to for any follow-up that has a name, and so they don’t feel isolated from the genetic service. And signposting to those external resources, such as SWAN UK, can be very important as well, of course.

Celine: I think it’s also really important to add that hope isn’t necessarily lost when you don’t get a diagnostic result. And in a sense, what can be really helpful is for genetic counsellors to reframe that hope, if you like. So, one thing that we talk about in our paper is that it might be useful for health professionals to ask a question such as, “In light of the new information that we now have from the whole genome sequencing result, what are you hoping for now?” So in a way, it’s sort of reframing that hope, sort of giving it a different context.

**Lisa: Definitely, and I think one of the things as well is that, because potentially for when parents were first recruited to a study such as the 100,000 Genome specifically in this case, that it might be quite a length of time between that initial recruitment and when the actual result comes out. And of course, in that time, with the advances in genetics, it’s sort of somewhat of a Pandora’s box really, isn’t it, in that we’re almost kind of finding the information out quicker than we actually know how to process it and what it potentially means. So actually if there’s a genetic counsellor available to speak to those parents, or for those parents to be signposted to somebody who can say, “Well look, since you were recruited, actually this is happening, that’s happening,” or, “These research projects are happening,” personally, I can say that is going to be really helpful and handy, and would have been really useful. I just know that for myself anyway and my family, that if there was a leaflet or something that had given me a way of knowing how I could contact somebody in the future, that would be really helpful.**

[Music]

**What ways do genetic counsellors use in maintaining a delicate balance between not creating false hope but also providing meaningful support to parents? What would you say around that, Jana?**

Jana: I think as we’ve already touched on, it’s that managing expectations from the outset when the test is offered. So, not generating too much hype or excitement, but setting those expectations, giving that information about the diagnostic yield. Also, informing parents that what people do experience has been described as a rollercoaster of emotions. It’s normal. You might also want to explore people, not only what they’re hoping for, but also the outcomes that they might be fearing, and giving them a chance to voice those, because they can be very powerful things as well. A diagnosis might not be what you want to hear, so there can be a lot of ambivalence around wanting a diagnosis when it might actually be a life limiting condition, that you didn’t really want that certainty.

And also helping parents to explore how not receiving a result might feel, so that they’ve actually rehearsed it a little bit, and where they might go to when they need a bit of extra support. So, they already know, “I go and talk to my friends, that’s where I get my support from,” so that they’re kind of ready for it, and that might help them with that sense of isolation, but also validating these feelings. So, it’s okay, it’s okay to have that dip, it’s okay to feel, that it’s something that many people experience. And creating a safe space for people to feel that, so if they want to talk to a professional or a friend, that those feelings are validated.

And in that way, kind of with that pre-counselling really, helping parents to develop their own set of resources, so they’ve got those to draw on. And as you’ve mentioned, Lisa, it’s like having your own resources also helps generate that feeling of empowerment and control. And as Celine has said, it’s really facilitating parents through that passage of reframing what you’re hoping for, reframing what the future looks like, if you had one picture of a future. You need to become comfortable with the future you’re now looking at.

**Lisa: Thank you, Jana. Louise, if I can ask you really, we’ve already touched on the role that SWAN UK can play for parents dealing with undiagnosed rare conditions, but perhaps if you could home in on that and explain in more detail the main focus of SWAN UK, and what that can do for parent/carers.**

Louise: So, what SWAN UK primarily does is bring together parents who are in a similar situation. So, we have a team of amazing parent representatives, who Lisa is one, who help us shape the support that SWAN UK can provide, and really make sure that it’s based on a really strong understanding of what it’s like to be a parent of a child with an undiagnosed genetic condition, and an understanding of that kind of expertise that parents who have been on that journey themselves will bring. So, we have a series of Facebook groups. Some of them are for different regions, so people come into contact with other parents in their area who are going through similar circumstances. Some of them are more around age. So, you know, we have Facebook groups for parents who are waiting for a diagnosis or have got a new diagnosis, and then we have a group called SWAN Graduates, which is for children who are older and over 18, so their parents can come together and share their experiences.

So, it’s really to help parents be able to talk to one another, to share their experiences, to support one another, and often to ask for advice. They’re often kind of practical questions about, you know, “My child needs this kind of wheelchair, has anybody been able to source that from somewhere?” “My child’s having real difficulties eating at the moment, can anyone give some advice on this particular challenge?” “This thing someone else has faced, how did you approach it? Where did you reach out for support?” So, that peer to peer advice and support is really at the heart of SWAN UK.

And then what we try and provide around that is access sometimes to information events, where there’s particular issues that are affecting a lot of SWAN families. So, we hope over the coming year to have a series of information events targeted at families with children who don’t have a diagnosis, and some of it is just trying to have social events and bring people together again. We’ve had, for example, an active dads group in Wales, who’ve been bowling and wanted to go axe throwing, and really they just want to come together with other dads who are in the same situation, and being able to talk to one another and provide emotional support to one another.

So, that’s kind of the nub of SWAN UK and what we do, and then alongside that, that kind of fits in with Genetic Alliance’s wider goal, which is much more around campaigning for improved services. So for example, the Genetic Alliance UK team has worked really closely with commissioners in Wales, who actually commissioned the first SWAN clinic, which is in Cardiff. That was a two year pilot, to see what support could be provided both to help SWAN families get a diagnosis, but far beyond that, to make sure that the care for families who don’t have a diagnosis is better joined up. And that we feel has been a real success. Again, there hasn’t been a really high diagnostic yield, there have been very few new diagnoses, but the support provided to the families who are in contact with that clinic, in terms of helping them access better joined up care both from the NHS and from services more widely, has been brilliant. And we’re currently working with NHS England in the UK, who are exploring an opportunity to commission two SWAN clinics in England.

So, that trying to kind of improve services, and then the third aspect of that is just working generally with the new genomic medicine service alliances as they emerge across England, to try and make sure they are thinking through what support they will need to continue providing to families who’ve gone for whole genome sequencing in future, not through a research project like 100,000 Genomes, but just through routine clinical practice and routine clinical diagnostics, what support will they need to provide for families who go through that process and don’t get an answer. And that won’t change the support they will need from the NHS. It will just mean that perhaps that clinic needs to play a more active role in helping them access those services. So, all of that kind of campaigning to have better services for family who have an undiagnosed genetic condition continues as well.

**Lisa: So, I think one of the things really just to finish off today, is of course looking at the future. Considering advancements in technology, would you say that future reanalysis of the 100,000 Genome Project is going to yield additional insights? Celine, can I ask you to comment on that?**

Celine: Yes, absolutely. As we understand more about the role and function of different genes, and as new genes are added to the panels, we will definitely be able to provide a diagnosis for more parents and more families. But I think we don’t yet necessarily know exactly what that reanalysis will look like, and it’s not really clear yet how this will work in practice.

**Lisa: And Louise, would you have anything else to add to that at all really?**

Louise: No, I think it is just that hope for the future and kind of help for today. I think the NHS needs to be equally clear about, you know, there’s some amazing investment by the UK government in genomic research, and that’s brilliant and we want that to continue, but equally we want the investment to be taking place into routine clinical services and diagnostic services, so that we can talk to people both about the hope of potentially getting a diagnosis in future, but making sure that the help continues to be available for as long as they don’t have a diagnosis, and that help for families who don’t have a diagnosis is going to be just as important. And what we try to ask for is both real clarity around what the NHS can provide, and really clear signposting to organisations like SWAN for families that continue to not have a diagnosis. And again, just to give an equal shout out to Unique, who are able to support families who have an ultrarare diagnosis, where perhaps they’re the only person in the country with that particular diagnosis, or one of a handful of families around the world. Signposting to that peer to peer support will continue to be a really important part of the process as well, so that families can help one another, learn from one another, and just give each other support that they are kind of sharing that same journey and walking alongside one another on that journey as it continues.

**Lisa: And bringing this podcast to a close, can I just ask you really, any final thoughts, anything that you would sum up from your experience of researching the no primary findings and where we now are today?**

Celine: I think the main thing for me is just to sort of make it clear to parents that a diagnosis isn’t necessarily a magic wand, even though it is obviously very important to a lot of parents. But that even without a diagnosis, we still have the opportunity to manage patients’ symptoms, and often a diagnosis doesn’t make a substantial difference, because parents are sometimes left with a lot of uncertainties and a lot of unanswered questions. So I think, and as Louise and Jana have said before, it’s really sort of on focusing what we do know, and thinking about what we can offer and what support we can provide to parents and families even without a diagnosis.

[Music]

**Lisa: Thank you very much to our guests today, Jana Gurasashvili, Celine Lewis and Louise Fish, for joining me as we discussed the impact of a no primary findings result. If you’d like to hear more like this then please subscribe to the G Word on your favourite podcast app. Thank you for listening. I’ve been your host, Lisa Beaton. This podcast was edited by Mark Kendrick at Ventoux Digital, and produced by Naimah Callachand.**