Childhood cancer awareness

The G Word transcript

**Naimah:** Hello and welcome to the G Word. My name is Naimah Callachand, and I'm the Head of Product Engagement and Growth at Genomics England. On today's episode I'm joined by Dr. Jack Bartram, who's a consultant paediatric haematologist at Great Ormond Street Hospital.

Today we are going to be discussing how genomics has been integrated into care for childhood cancer, and the outcomes and impact this has had on children and their families. If you enjoy today's episode, we'd really love your support. Please like, share and rate us on wherever you listen to your podcasts.

First of all, let's start with giving me a little bit of introduction of yourself and a little bit about your background and your work in cancer so far.

**Jack:** Thank you for the invite to the podcast today. My name is Dr. Jack Bartram. I'm a consultant paediatric haematologist at Great Ormond Street Hospital for Children, where I work with children with cancer.

**Naimah:** And can you tell me specifically what you do at Great Ormond Street?

**Jack:** So I'm a paediatric haematologist, I look after children with blood disorders and primary blood cancers. The majority of my work is treating children with leukaemia. Leukaemia is the commonest childhood cancer, but equally one form of leukaemia is also one of the most treatable cancers we treat.

**Naimah:** I'm sure it's very difficult, but I'm sure you’re always trying to keep good spirits up?

**Jack:** The first question everyone asks me is; “it must be horrendous working in oncology”. And it's actually not. Yes, there is sad days, but we do cure the majority of children. And like I said, the hospital environment, certainly Great Ormond Street Hospital, there's something about it. It's just an amazing place to work. There's just an atmosphere, like a buzz there really, which most of that's obviously the patients, but also the staff and then the other research opportunities it brings there and all the kind of other people working around you. It's an amazing place.

**Naimah:** So, as you know, it's Childhood Cancer Awareness Month, and I wanted to speak to you about it and if you could kind of give me a bit of an overview of why we're recognising Childhood Cancer Awareness Month and if you'd give me a little bit of background as to how you got into working in cancer.

**Jack:** As you mentioned, it is Childhood Cancer Awareness Month this month, so it's really trying to highlight qll the work that we are doing and both here and across the world into to improve outcomes for children with cancer.

How did I get into haematology? So, I qualified back in 2003 and I made my way through paediatric training, and then I happened to land kind of almost by accident into a job at Great Ormond Street Hospital, working in the haematology oncology ward as a junior doctor then.

From day one, I found they were absolutely fascinating. People would expect it to be a sad place, but actually, what you what you see working on the ward there, it's an amazing place to work. You get an incredibly close relationship with families and generally the atmosphere in the hospital is really positive.

From that sprung my interest, and there's a heavy, heavy research background as well so it really allows you to align both interests of working both with people and doing the research on the side. From there, I never really looked back. My aim was to become a consultant there and I worked my way over the next 10 or so years to get into that position.

**Naimah:** It would be good to understand a bit about some of the statistics around cancer in children. Could you tell me a bit about some of the most common cancers that affect children in UK, for example?

**Jack:** There's roughly around 2000 cases of cancer diagnosed in children in the UK every year. If you take it on a daily base, that's about 5 children a day, which is a large amount of cases. And although the majority of cases survive, if you look overall. The number of deaths is still too high, and hence why we're all working hard to try and improve this.

**Jack:** The problem with childhood cancer is because even though those numbers sound large, if you look at cancer as a whole across the adults, it accounts still for less than 1% of all cancers diagnosed in the UK.

Therefore, because it's so rare, trying to understand the risk factors involved and exactly why these occur, it's not fully understood. And then obviously funding, because it accounts for a smaller proportion of cancer overall in the country, is often less.

We're all trying to work hard as a global community now to try and get larger cohorts of patients to look for reasons why cancer occurs and then more importantly, how we can provide better therapies, more targeted therapies, less toxic therapies, so we can cure more children.

**Naimah:** And that really segues into my next question, what role does genomics play in childhood cancer in relation to these things that you've mentioned, diagnosis, personalized treatment, screening?

**Jack:** Yeah, it plays a massive role. And even in my short career I’ve really seen the evolution of genomics. When I left medical school, these big advanced molecular diagnostics as we know it now, didn't really exist. We were doing going gene by gene, and although genetics was a fascinating topic at medical school for it, we didn't have the access to these mass sequencing machines and data that we do now.

We've seen full integration really from single gene testing, all the way up to these massive gene panels and now even whole genome sequencing, which is allowing us to really make diagnosis one more accurate, try and direct therapies better. And then on the, on the research front, look for new therapeutic targets.

And importantly, answer that question that family's always asking, why did this happen to my child? And then equally; “what about my other children? and what about the rest of the family?”. I think we've really gone from diagnostic diagnosis down the microscope to diagnosis from a sequencing machine and looking at the underlying DNA to really label what is the tumour and learn about how it would behave, so allow us to target that treatment more effectively.

**Naimah:** I guess some parents might be apprehensive of the children undergoing genetic screening, what's involved if the patient is going to undergo a whole genome sequencing, for example?

**Jack:** We have been, as I say, doing genetic diagnostic for many years, and the area I work in, leukaemia, has really led the way for advanced genetic diagnosis, and we've been doing it for a number of years.

But now, with more broad gene sequencing panels, there is the possibility that you'll find something that you weren't looking for. I mean, to reassure people in the tests that we use, we'd only be looking for cancer related genetic mutations, and not for risk of heart disease, et cetera.

Although you potentially have the ability to do that, certainly how we target our approach at the moment is information that's only relevant to the patient. What it involves is it's nothing extra additional to what we've done previously, we take the tumour, which in children I treat tends to be leukaemia, so that's cancer of the blood, we just take the blood cells or cells from the bone marrow, and we extract DNA from that.

Then that's sequenced on one of these large sequencing machines and the results are fed back to us and we interpret the data in line with the clinical information given from the patient.

**Naimah:** And I wonder as well, has genomics noted any difference between childhood and adult cancers?

**Jack:** There is a big difference between childhood and adult cancers and both in how they present, how they behave, and their response to therapies. And again, genomics is slowly unpicking this and in fact, we can use cancer in children really as a model of how cancer can develop in adults.

They work in synergy really, and a lot of the stuff we've learned from adult populations, we apply to our analysis in children, but equally we're using childhood cancer as a model of cancer so it can help us to treat and target therapies better in adults.

**Naimah:** Moving on, I wonder if you could potentially share any case studies as an example of where genomics has played a crucial role in either diagnosis or treatment within a child?

**Jack:** If we look back on the last two or three years when we've really, really ramped up how we've implemented this advanced genetic diagnosis, it's really changed how quickly one, we can, can make more accurate diagnosis and, really aided how we can risk stratify and apply therapies to children.

If I look back on and if I reflect on the last three years, we can probably accurately say for at least a quarter of patients it's given us additional information, which is either aided in diagnosis or like I'd say to help re-stratify a patient or potentially reveal a target for a therapy that we didn't know of before.

And what this has led to and what we've seen over the last three years or so is that we have actually changed management of patients based on this. So definitely we've got examples where you can clarify the diagnosis, we've changed the risk category, or we've identified, for example, an unexpected cancer predisposition in a family, which has then led on to screening for the family. Which can then give the family the knowledge that to try and do things to either modify the risk of cancer in the family or at least screen for it so they can detect things early, to prevent things presenting too late. I think overall, we've certainly seen a massive shift in the last three years and my colleagues would equally say the same that, this has revolutionized how we are treating patients.

**Naimah:** Yes, and I assume that you've seen a real difference in the outcomes and impact of these things on the patient's families and the patients themselves, the children themselves?

**Jack:** Yes. I mean, certainly obviously the biggest cases are the ones where you've changed a diagnosis, for example, based on, on genetics.

We've seen how that can have a massive impact on the family, going from potentially a diagnosis for which the outcome was poor, less than 50%, to then changing that to a diagnosis where with a targeted therapy, you've got an outcome of over 90%.

And certainly, along the question of the cancer predisposition, this is a question families always ask, on day one is, you know, why did this occur? Or what about my other children? Some of the testing we're doing now allows us to at least answer in part that question that, no, there is no predisposition.

There is nothing anyone could have done about this. This, even though it's a, it's a terrible terminology to use, that this is bad luck. But what our hope is, is that we're going to uncover what that bad luck is. Because as well as giving us clinical information, all this advanced diagnostics, if allowed to be used for research, can really start to answer those questions of, what actually caused this? What is this bad luck? There must be some explanation for this.

Working both locally across the UK and then globally, there's a massive drive now to try and pull our information, to try and improve the outcomes for children.

**Naimah:** I wondered as well, if you could illustrate maybe any scenarios or examples where genomics hasn't been integrated into the care of a child with cancer?

**Jack:** Yeah, it's hard to give specific examples, but I think now, and certainly it's been recognized, that if you're not using these more advanced diagnostics, that things potentially could be missed, which could then eventually lead to either the wrong treatment being allocated, which I'm sure has happened in the past, with everyone having had the best intentions, we just didn't have the technology, or opportunities potentially have been missed because of the speed of the diagnostics coming back.

I think now certainly in childhood and adult cancer now, the focus is on really on these advanced diagnostics and fully integrating them to give the best overall picture of what's going on with the patient to then be able to really target your therapy to be the most effective and importantly the least toxic therapy.

**Naimah:** I think a lot of people are aware of some disparities and challenges to access of genomic space care. And I wondered if we could touch on those a bit and the challenges that you see within this area.

**Jack:** Yeah, I think as we touched on the speed with which these technologies have come about is really, really fast, and trying to integrate that into a standard of care health practice is challenging. And certainly, we've seen that here and we've worked incredibly hard to try and do that. I think the first thing which I always say is education. One, people have to know it exists, both patients and healthcare providers.

But then also how you actually access that and the logistics around that, because it's not a straightforward you just tick a box and this happens. The logistics involved in all of this testing, it is massive.

And with that in mind, I think the education has to go all the way back to starting potentially at school, increasing awareness of genomics generally in the community, in the school curriculum, importantly, in medical school and, other allied health professionals training and then carried through medical education.

I mean, the first question I always ask medical students when they come to our institution is, tell me about how much teaching you've had in genomics. What do you know about genomics? Because as I see it, and I think everyone does as well this is really the future of medicine.

It has to take centre stage in education because it's not only in childhood cancer that this is important. This is important across the board in healthcare. So education, education, education, I guess. And we're certainly seeing that through NHS England, through Genomics England.

Then at a more local level, both within genomic laboratory hubs, and then even at the institutional basis, we're really trying to work hard to highlight genomics and there's so much you can access now online and other education tools that I think it really is starting to get together momentum.

Certainly I've seen that with the uptake of the cancer sequencing for childhood cancer over the last year, especially we've gone from a position where, [00:14:00] probably were sequencing less than half of children with cancer, to the point now where we get to sequence the majority, if not all, all of patients.

At Great Ormond Street, any patient who comes with either a new diagnosis of cancer or relapse of cancer will have advanced genomic sequencing done on the tumour, including whole genome sequencing.

**Naimah:** And is that a service that's offered across the UK?

**Jack:** The majority of institutions across the UK would offer advanced genomic diagnostics.

Not all places at the moment offer whole genome sequencing, and that's a slight disparity across the UK at the moment. In England, all children with suspected cancer have universal access to whole genome sequencing, which means every child has access. But in some of the devolved nations, this isn't the case at the moment. We're all trying to work hard to close that disparity and make it available for all patients.

**Naimah:** Just thinking on that as well, how does it compare to what's offered worldwide in treatment of childhood cancer? Can you give me an idea of that?

**Jack:** England is uniquely positioned now with the Genomic Medicine Service we have, and the fact that we offer whole genome sequencing universally to every child with cancer, that's integrated into our health system and makes us completely unique I think.

There's many other institutions in the world who are offering these large sequencing programs, but often they're institutional based. And there's only a few other countries who are offering this as a kind of rollout service to every patient diagnosed.

The advantage again we have in the UK, is that we have a really great health service, which comes down to essentially everyone carrying an NHS number and then all of your health information is related to that. It makes it a really powerful tool, both in terms of diagnostics and the potential for research.

So, I think, as I said, we're uniquely positioned to try and really make a difference.

**Naimah:** I wanted to ask you about as well, the ethical considerations that parents and healthcare providers should be aware of when they're considering genomics-based care. Could you talk me through some of those?

**Jack:** Yeah, I think this is a really important point, because there's many myths and many pitfalls here, because we are testing your underlying DNA, so the genetic code you carry.

When we are talking through this with patients, I think it's important that we explain exactly the process of what happens, which we've already touched on in terms of physically what happens, but then the information that can be potentially gleaned from that.

So, it's important that we discuss potential implications of finding a, for example, a cancer predisposition in a family, because of obviously immediate, physical impact that could have on a child potentially at risk of having cancer. But also, the massive psychological impact and potential financial, in terms of disclosing a cancer predisposition in a family, say to a health insurance company or mortgage company or something like that.

We do take a lot of time to discuss with families what we're doing, we run through a formal consent process, give patients time to think about, what they want tested and what they don't want tested, and then try and tailor it to each individual family.

But I think overall, my experience has been the uptake has been incredibly good because generally, patients and families want as much information as they can. I think traditionally, as healthcare professionals and physicians, we've been quite protective over our patients, and actually people want to be empowered with all of the information they can.

I think it's our duty to offer this, at least, not withhold the potential for whole genome sequencing and all these advanced genetic diagnostics. It's often a case of who are we protecting? Are we protecting ourselves because we don't know how [00:18:00] to deal with that data? Or are we protecting the patient?

And it's a constantly evolving ethical discussion, something that we have in our department, nationally, and internationally about the rollout of these various as the genetic sequencing programs get broader and broader, who and how those discussions happen.

And then, of course, you have to set in place something within your institution, if you were to find a cancer predisposition you have to have a clinic set up for that or someone who can deal with that information. It's not fair to offer these tests and then not be armed with the tools to then offer the rest of the family a screening program or what have you.

So certainly, we've worked hard to set up groups, we have a large what we call “tumour advisory board”, which contains a wide degree of lots of clinicians, the clinical scientists in the laboratory who do the majority of the work.

There's geneticists, there's genetics advisors, and many other people from this kind of multidisciplinary team who, once we've made a decision on a patient, we've already got the plan in place to offer the appropriate triage afterwards in terms of screening and rollout and, who's the best person to, to deliver the information to the family.

And again, this comes back to our point about education and why that's so important, not only for all the health professionals involved, but equally public and patients.

**Naimah:** I agree with what you said that people like to be armed with information, there is a lot of misinformation online as well. That can lead to a lot of mistrust around data storage, maybe lack of understanding, skepticism around commercial interests and companies offering these genetic testing services. So, we've spoken about education, but in what ways can healthcare professionals better communicate the risks and benefits of genomic testing to parents and the general public.

Are there any campaigns you've seen or anything that's been really effective, even childhood Cancer Awareness Month? Maybe this is an opportunity to really educate people and help them understand.

**Jack:** There's lots of charities and patient advocacy groups around, many of them take advice from, us, the physicians who are pioneering these technologies. I guess it's our responsibility really to ensure that the governance of these, and making sure that we have, educated families correctly before they embark on some of this sequencing.

And constantly reviewing, you're reviewing the process, we're in the midst of just reviewing our experience, for example, of our first experience of the whole genome sequencing, being used in anger as it were in the, in the clinical space, to make sure those things, what we're finding is valid, and there is benefit to the patients, of which we definitely find that is the case.

In terms of other spaces, there is lots of misinformation online, but equally there's lots of good information, I especially point people towards NHS England's resources and Genomics England's resources, which are really, really powerful as educational tools.

**Naimah:** And informed consent as well, that plays a role in education.

**Jack:** Yeah, I mean, certainly. We're trained since medical school, there's whole modules now on informed consent and that plays a massive part in counselling patients as part of their treatment. But equally now as we do more and more genomic testing, NHS England again has produced a really good guidance for us, really clear guidance for physicians called the Record of Discussion actually for whole genome sequencing, which really does form quite a nice template for how you go about discussing this with a patient or their family.

This information is freely available, and it's just a really good resource for clinicians like myself, to guide you through that conversation. And again, to ensure that you're not missing important bits and questions, and then giving families time to actually think about it, because as you can imagine, it's fairly emotive time when someone's just been diagnosed with cancer.

I think the knee jerk of all patients and families would be yes, just everything, everything. But you have to give the families time to be able to think about these things and then also go back to give them the right to say actually “I said yes at the time, but no, I've thought about it, we've had a good chat in the family, and although we understand the full implications of this, I don't want this kind of testing done”

Or, the question sometimes asked is about research, because research is important and having access to these unique data sets for us to try and make improvements is really important, but equally, you have to respect the fact that this data is as precious as a sample of it is part of the patient.

It has to be clear, clear guidelines around which data we can and can't use. And I think we're fairly good at communicating that to patients, and certainly then patients can also see the feedback of how their health data has helped in the form of publications and other research projects that were ongoing.

**Naimah:** What would you say to those who think, obviously parents and families of people who have been affected with childhood cancer, that the progress is a bit slow, and they're in the position where they're waiting for treatment and diagnosis?

**Jack:** I think we can use childhood acute lymphoblastic leukaemia as a model for how outcomes have massively improved for a single cancer. The hope is that we can get the outcomes for all other types of childhood cancer up to that cure of over 90% and the eventual aim of 100%. We're working hard to do that in our institution, both locally, nationally and internationally.

It's through a lot of this collaborative work on these big genetic sequencing programs that I think we will be able to unpick the cause as we already have of many cancers. Equally, working in collaboration with other research groups and technologies to try find more novel therapies where we've pinpointed a genetic cause for the cancer, we then need to find a novel therapy for that.

That will be the key over the coming years. And again, like I've mentioned previously, not only to cure, but we want to prevent the complications and the toxicity of therapy. So, I think I'd say to families, we're working incredibly hard on this.

We've already made massive improvements in many, many diseases, but equally we're continuing to work hard to try and improve those outcomes to a 100% and importantly reduce the toxicities that children suffer from these treatments.

**Naimah:** Finally, just to ask, how do you see this progression of the use of genomics integrated into childhood cancer, like treatment and diagnosis, in the next five years?

**Jack:** It's a really good question, and it’s hard to predict because how quickly things have gone in the last three years. We've quickly gone from single gene testing, to panels of gene testing, to now whole genome sequencing.

I guess the next step will be making the turnaround of that even quicker, which we can already see in action. The turnaround times have already come down around really quickly. There's many critics out there at the moment who don't like to engage in that process of whole genome sequencing because of the turnaround times.

With the hard work we've done here, we've seen those come down and as technology advances, we know it's going to get quicker and quicker and cheaper and cheaper. I do see a day when you’ll have the whole genome sequence back of the cancer within 24 hours, which you can imagine would really change the shape of how you’re guiding treatment.

Because as oncologists, there's always this balance between giving the right amount of treatment to cure a child, versus too much treatment where you cause toxicity. In the area I work in, leukaemia, we're really at tipping point for that at the moment, because our outcomes are actually very good, especially in acute lymphoblastic leukaemia.

We're now at the point where we need to reduce therapy because the toxicity is more of a problem. If we could better select those patients on day one, then we'd be able to have an even larger impact.

And the other things we touched on about, new therapeutic targets, which you'd only be able to find from a whole genome sequence, for example, or the cancer predisposition. The quicker these things can be done, always the better. And just as we have more and more whole genomes coming back from patients, it just gives us more and more data to work from. And that doesn't even touch on then the potential research aspect of this.

Because we're uniquely positioned in England with our health service and everything going back to this single NHS number, as it were, you start to be able to make some really, really powerful inferences about the causes of cancer, and then the outcomes and how people have responded to treatment.

I think there's going to be a big integration, trying to get the most out of all this data is going to be the key over the next few years.

**Naimah:** And it's certainly rapidly evolving. So we'll be interested to see what happens. So we'll wrap up the podcast there. Thank you to Dr. Jack Bartram for joining me today as we discussed the role of genomics in childhood cancer.

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