Research priorities for sickle cell and genomics

The G Word Transcript

**Marie:** Hi everyone. I'm Marie Nugent. I'm Community Manager for Diverse Data here at Genomics England, and I'm really pleased to have with me today two very special guests. I have John James, CEO of the Sickle Cell Society, and Suzannah Kinsella from the James Lind Alliance, and we are going to talk about the priority setting partnership that we are developing together as part of our Diverse Data initiative here at Genomics England, to focus on engaging patients and healthcare professionals so we can create a top 10 future research priority area for sickle cell and genomics.

So, John, I'd like to come to you first. If you could just introduce yourself and give me a bit of a recap of the first time you came and interviewed for the G Word. You came and spoke to our CEO, Chris Wigley. It would be lovely to hear from you what you covered in that conversation and some of the work that you've been doing at the Sickle Cell Society since. And then we'll come to you, Suzannah.

**John:** Thank you, Marie. I'm John James. As Marie said, I'm the Chief Executive of the Sickle Cell Society.

I remember it well because it was a few years ago when I met the Chief Executive of Genomics England, and we had the first podcast about sickle cell. Why I remember it well is because I was arguing that, why isn't there any action being taken by way of research and genomics for sickle cell. It was effectively a call to action to say, ‘come on Genomics England, you know this is an important area’, and in fairness to Chris, we are here today talking about the diverse data, which is specific work to help us prioritise what the research priorities for sickle cell should be.

So, it's taken a little longer than we would've liked as an organisation, but we are here now, and I thank Chris and Genomics England for responding to the call for action.

**Marie:** Yes, thank you, John. I had the pleasure of listening to that podcast myself, and I must admit there did feel like a bit of a call to action there, quite rightly, and it's wonderful to have you back with us now. I think three years after you got invited on. I think Chris said two, but there you go, we’ve made it.

So, Suzannah, it'd be lovely to come to you now. If you could introduce yourself and talk about the work that you do at the James Lind Alliance, as there might not be many people who have come across that organisation before. If you could just talk a little bit about the kind of work that that does, that'd be wonderful.

**Suzannah:** Great. So yes, I'm an advisor for the James Lind Alliance. The James Lind Alliance is really a methodology that is there to ensure that the voices of people with lived experience of health conditions and also health and care professionals really are brought to the fore when it comes to what matters and what are the really important questions for health and care research.

It was set up with that mantra to bring those voices to the forefront rather than all research being designed, delivered and dictated by pharmaceutical companies, researchers, universities, etc., who all have, I'm sure, brilliant intentions, but they perhaps don't know what are the priorities, what are the questions that really matter to people who live with the condition and those who work with them.

The James Lind Alliance has been going for just shy of about 20 years and has run about 110-120 priority setting partnerships over that time, but it's worth saying that this priority setting partnership will be a first for two reasons. It'll be the first to look at priorities for sickle cell disease, and it'll be the first that is completely focused to the area of genomics.

**Marie:** I didn't realise it was 20 years actually, that the James Lind has been around. I was very fortunate to come across the work of the organisation in my previous role, and I was just so excited to have the opportunity to bring that opportunity into the work that we're doing here, through Genomics England, to look at sickle cell.

120 as well. I mean, again, it is staggering really the body of work there. It's a real privilege to have you with us, to facilitate us through that process because at the end of the day, it's really focused on this sort of trust building methodology, and we recognise just how important it is that word trust and to take a sort of trust leading the way, I suppose, approach to this work.

So, on that note, John, I think there's a wonderful opportunity here for you to maybe lay out a lot of the work that has come about over the last two to three years since you last came and spoke to us here. It would be great to hear some of the work that the Sickle Cell Society has done, but maybe the work of the APPG and the report that was released.

There's a lot of work now coming about because of that really important work. So, if you could just tell us a little bit more about that, that'd be fantastic.

**John:** I'm happy to do so. We've been on this journey at the Sickle Cell Society and that journey is about addressing health inequalities that have affected the sickle cell population over many decades. What I mean, to be specific about health inequalities, is a lack of research and funding, poor experience of people living with sickle cell for hospital services, particularly accident and emergency, premature deaths of young people living with sickle cell.

That journey took us to a point where, we had a young man called Evan Nathan Smith, who died at North Middlesex Hospital in really challenging circumstances and that was a catalyst to say, we can't go on like this. Improvement needs to be made. Outcomes need to improve. More research for sickle, and all these things. So, what we've been able to achieve in that time is we have, for example, got NHS England to agree adult transplantations, which weren't available for adults with sickle cell, who other treatments didn't work for. I say other treatments because it's back to health inequalities. Those other treatments, you can count them on one thumb or finger. The standard treatment is hydroxycarbamide which has been around for 30 years. 18 months ago, we got a new disease modifying treatment called crizanlizumab.

So, the point about transplantation policy is that our position is that there needs to be a range of more options – curative options and disease modifying treatments. That was a success in terms of getting NHS England to fund adult transplants and the 'No one's listening' report, which was the catalyst of Evan's death.

Of course, people died before Evan, and people have died since Evan. But it was the catalyst to say, we can't go on like this and the 'No one's listening’ report highlighted this based on evidence. This is patients’ parents from across the country expressing their dissatisfaction with aspects of services, and that report has proved to be exceedingly helpful in getting NHS England, NHS Trust, the Department of Health to begin to listen.

So, there's no mistake in it, calling it no one's listening. But you know, the simple answer is people are beginning to listen. I'm not complacent and think that because they're listening that that will result in immediate changes. But I can today say that there are plans from NHS England to look at how people can bypass A&E. The evidence shows that if you get to your specialist in time, you'll get a better outcome. There are plans to have a digital care record. There are plans to improve take up of prescriptions through low-income schemes and prepayment schemes. And there is work on genomics that the NHS are doing now. These things, when I spoke to your Chief Executive, were not even on the agenda. So those are examples of the progress that we are making, and as I say, I don't want to be complacent.

We still have a long way to go but those things have started and hopefully will come to a positive conclusion, which at the end of the day links to what Suzannah said – is that we want better outcomes for patients and more equitable funding and care.

**Marie:** Absolutely. So, I just want to share a bit of a reflection, I suppose, because you know, here at Genomics England, this is the first time we are looking at sickle cell. This is a new area for me personally, and of course there's been a lot to learn and a lot to consider.

I think that it's fair to say that I've learned through looking at sickle cell almost how you can look at what's missing as an indicator of inequality, because it really is quite stark when you do start looking at these things and you start making comparisons. So, we've got this wonderful challenge here where you've quite rightly, John, said to us, have this extensive background, career and experience in working within the NHS, you've told us quite clearly that we have to do quite a bit of work to raise the awareness of genomics.

We also have to do quite a lot of work to build the relationships and connections in the area of sickle cell, not just with patients of that area, but actually specialists in this are sometimes few and far between. And then what we are trying to do with the James Lind Alliance, and with Suzannah's wonderful help, is almost bring these two very niches, potentially for a lot of people, together and almost look for where do these things really come together to bring benefit to patients. So yeah, that's definitely something that I'm appreciating. I didn't know if you, either of you wanted to say a little bit more about that.

**Suzannah:** I think this is where what comes in is the way in which we're going have to tweak the process, the JLA process. So let me just briefly explain, a standard JLA process kind of has three main parts. We go out to the community of the health condition and ask everyone, and by everyone, as I said, I mean people affected, directly affected by the condition, and the specialists who work with them. We ask them questions for research. Now we're talking about genomics and we're talking about sickle cell, and whilst people would probably be able to say, these are the questions I have about my treatment, about living with sickle cell, about caring for someone with sickle cell, if you put the word genomics in there they might have a big question mark in their head and saying, well, what's that got to do with my condition?

So, we're going change the process. Instead of doing just a cart blanche survey, we're going to do a more gradual kind of thoughtful information sharing process where we will show people and take people through what are the opportunities, what is the potential around genomics in sickle cell, and get them to think about, okay, this really could be something that could be amazing for me, or it could be amazing for my children, or other parts of my community. Then use that to take it into the second stage, which would be a prioritising shortlisting survey.

So, out of these conversations, focus groups, discussions, workshops with both healthcare professionals and with people with sickle cell disease, gather up their priorities and then take them into a survey, which we would again reach out to as wide a group as we can get from the sickle cell community and specialists, and ask them to say of these, which do you think are the 10 that matter most to you? Then the final piece in this public – the third part of the JLA process – would be to run a final workshop with about 30 people where we would come together, and through a process of consensus discussion is to then come together and agree what are the 10 most important questions. So, it's a tweak on the process, but it's one that's necessary so that people can really understand what is genomics when it comes to sickle cell.

**Marie:** Yeah, I think that's really helpful to break down, and so over to you, John.

**John:** What Suzannah has just described is really, really important because part of that process is about building up trust with the sickle cell community. We've seen scepticism during covid about new vaccines. There are new treatments coming out beyond transplantation for gene therapy for sickle cell, and therefore when you introduce the word genomics the question will be what’s that going to do? Which is why Suzannah's deliberative process is so important and that we spend time with the community answering questions and clarifying so that we get the best outcome of which of the areas we need to focus on.

So, I think that we are doing this differently and recognising that the community has faced disparities and other issues. We need to spend the time to work through the issues with them. Part of it, and I remember saying to your chief executive, part of it is, what can genomics do for sickle cell? So, you know, we're looking forward to doing the work with you and the James Lind Alliance.

**Marie:** Absolutely. I genuinely really look forward to getting all of this started because I think, again, a reflection if you like, of all the groundwork we've got to do in terms of being able to get people to the point where they can actually start making these decisions about priority areas. It really does just show the kind of gap in knowledge that would be needed across the board, whether they are people in communities, whether they are patients for different areas, whether they are healthcare professionals themselves. Again, there's this unique and exciting challenge of how we bring these two areas together to kind of really bring maximum benefit to patients.

So, taking this approach where we essentially have to think a lot about how we are training and informing healthcare professionals along the way as well. There's an interesting element to that, that I don't know, Suzannah, whether you've had to almost take that similar approach in other priority setting partnerships that you've been able to deliver, has there been almost an equivalent sort of skills or knowledge gap in a particular element that you've had to explore? And if so, is there anything that you could give us as tips along the way?

**Suzannah:** That's an interesting question, and I would say it's less of a knowledge gap than perhaps deep areas of expertise. So, I'll give you an example particularly where you might have surgical techniques where, of course, you and I would be asleep for. We have no idea whether the surgeon's using X technique or Y technique and why that would matter, if the surgeon says, we desperately need to do research on this particular technique, X or Y, that would be quite lost on the individual. So, in which case, we really need to express it in terms that they will understand, avoid using crazy, medical clinical terms that would completely blow your mind. But it's an important question that would really dramatically change patient outcomes if they knew actually, we don't just go and base it on what Dr X has said for the past 25 years. We need to base it on evidence.

So, I guess more around helping everyone understand particular possible interventions that need to be explored and understood. And so, we do that by making sure the language is accessible, getting rid of jargon wherever we possibly can and using any explanations, kind of examples that will help people navigate and understand the potential priority that's there.

**Marie:** Thank you. I just wanted to also come back to this word trust and we've talked about this a lot already in our conversations together, and it's something that we're all incredibly passionate about, and I think we recognise just how vital it absolutely is. And just again, sort of recognise that we've got layers of trust to build here because genomics is a new and sometimes quite quickly developing technology. There are a lot of things about it that still needs to be figured out in a way that we're sort of bringing people along on this almost social contract way of thinking about things.

So, what I mean by that is how are we going out and having dialogue with people in wider society about where are your red lines? What would be good for you, what would be bad in your opinion, in terms of say, your data, how it's applied, who you want to be able to see that under what conditions? We're trying to do that in a way that we're addressing this need to build trust in genomics. Within the healthcare system, we're also needing to build trust in genomics and genomics medicine or personalised medicine and where that can get to, the trajectory for this newly developing area.

We need to also, of course, do that for wider society and the public, but we are now kind of trying to bring this as we've said to the sickle cell population. And, I suppose, are there any sort of extra special considerations that we have to take, in your view, John, to do that well and really build that trust?

**John:** I think that's a really important question, and I don't see what I'm about to say as anything controversial whatsoever, but I think there are two important factors about this piece of work and building up that level of trust.

First, it's fair to say that many in the black community, I'm not talking about the sickle cell community, have known that over the years, through slavery, through other things that have happened over many years, that many black and brown people have been experimented on. You know that is a fact. So, there can be scepticism about these new, you know, developments and particularly genomics because not many people know what it means for the future.

So, I think trust is part of addressing myths and busting myths and allowing people to feel safe, to be able to share their opinions in a safe space whether they understand, agree, or have whatever views about it. We want to get rid of myths and concerns and the way to do that is to build up that body of trust and, as Suzannah says, explain things in a way that isn't academia or anything like that. I think that helps to build up the trust, which is why I'm very supportive of the process that the James Lind Alliance are proposing for sickle cell.

**Marie:** Suzannah , in your view, do you think that there are extra special considerations that do need to be taken into consideration when you are doing, say for example, priority setting partnerships, delivering these exercises in trust building that need to be taken into account for people who do have certain lived experiences or certain historical or social cultural context that they're coming from, that essentially, there are very good reasons as to why maybe people are not forthcoming when it comes to getting involved in research?

**Suzannah:** I think it all comes down to that word research, and it links back to what John said earlier, that actually if you hear the word research and you think, well, why should I be bothered about that because the history of it has excluded me. Not only that, it's actually exploited me.

So, we have to understand that for some people the word research is brilliant and exciting and offers potential, but for others it actually means something negative and oppressive and not so good. I think we need to start with that, and we need to think about the language that we use and talk about more in terms of what are the outcomes.

Research is a mechanism, but what are the outcomes? What could change in the way in which genomics could have an impact on sickle cell? And really make that clear all the way along. So it wouldn't surprise me if, actually, you know, we don't hang everything on the word research, but we talk about what's the potential for genomics in this area, for this condition, what's unique to this condition and how it can perhaps lead to the wider objective of creating a more diverse data set for the whole genomics field, and also being exemplar for that so that it doesn't start and stop with sickle cell, but looks across conditions that could lead to priority setting and other conditions that also have been perhaps underrepresented in this area.

**John:** Can I just quickly add to something, and again, Suzannah makes a really important point about the connotations of the word research to different groups. One of the contradictions in the work that we'll be doing as a collaborative is that, so first of all, there's not much choice of available treatments for sickle cell. What's important is that there is this feeling within the community of wanting to have more choice, wanting to have a better quality of life because of the lived experience. Genomics is one of those potential solutions. So, on the one hand, you have people who will be sceptical of research, but if it's presented in a research way we have to find ways of not making it, you know, this isn't about researching you, it's about trying to find the right solutions to enable you and your children with sickle cell to have a better quality of life in the future.

I just want to add that there is this appetite from many in the community to see improvement, to see change, but to enable that, you have to follow a process that builds that trust and isn't just labelled as research.

**Marie:** I just to say that I think what's abundantly clear is that it doesn't just happen, does it?

It won't just naturally happen because of doing research with good intentions. You must be really proactive and intentional about building that into how you are going to go about it, even thinking about the research you do and want to do and why, and what are you starting with. And I just want to pick up on some of the words that we've been using here, impact and outcomes and trust. These are words that, you know, we use really intentionally in this world of work.

I just want to bring us to the kind of impact we want to see, so something that I really am excited by with this opportunity to work so closely with you both and go out and spend all this time and effort bringing a load of different people who have various lived experience with sickle cell, whether they are people living with the condition, supporting those with their condition, whether they're healthcare professionals or provide care in some sort of way and just having the opportunity to have those interactions. I'm really looking forward to that and it's not only a privilege for me to be able to work with people that have just got such incredible resilience and generosity, when it comes to it. I'm learning so much along the way already and I just wanted to share with you an insight that I've noticed already, just from some of the very early conversations that I've had.

Sometimes there are words like ‘hard to reach’ that are used in the context of research engagement. And it's abundantly clear to me that, you know, people aren't hard to reach, they're quite easy to ignore, though. I've had the chance to speak to a small group of people with sickle cell, and quite rightly, Suzannah, when you were talking to John and I about whether we could do this work together, you said to me, well, have you spoken to patients, and what do they think about doing something on genomics? And I said that I’m really pleased to say that there is something about a new area that's being developed, a new technology, a new opportunity, that despite all the difficulty or the baggage that we are sort of referring to here, they are so pleased and so enthusiastic to see a new area focus on sickle cell. Again, the generosity that I'm talking about here really comes into play here where they absolutely acknowledge that I might not be the beneficiary of the kind of research that can happen as part of this process, but I am more than willing to contribute to this if it means that future generations do not have to deal with the kind of challenging experiences that I've had to face.

So, I just wondered if you wanted to comment on that as well, John?

**John:** Yes, that links in part to what I said before about this contradiction of the support community wanting to see change but why do they want to see change, because it has been ignored. Sickle has been completely ignored for decades and decades, and I think when you talk to individuals living with sickle cell, they want to see change. And some of them, I have to say, are very angry about, why is it taking so long for either people to listen or services to improve when, and this is no criticism of my colleagues in the Cystic Fibrosis Society, but if you compare the two, there are lots of hundreds. I'm talking about treatments for Cystic Fibrosis and there are two treatments for sickle cell, licensed treatments.

The sickle community know that, ask the question why? So, this is part of wanting to see change and the opportunities that Genomics England, the James Lind Alliance and the Sickle Cell Society, and of course healthcare professionals and people with lived experience, need to do this work.

I haven't been part of those conversations that you've had with individuals, but, I'm pleased that, you know, that's what you've picked up, which is consistent with what we know in the Sickle Cell Society.

The last thing that I would say is that your point about resilience, think about, you know, people of a particular age. The seventies weren't that long ago, but in the seventies, doctors and nurses, and indeed parents and individuals didn't understand what the condition was and there was no treatment. The seventies weren’t that long ago, the reason I mentioned that is a really big shout to the resilience that you mentioned of parents and individuals with sickle cell, to carry on decade after decade, trying to find a voice.

You'll have picked this up from some of the people that you have spoken to, as it's well known in the community, that individuals are known as warriors across the world. Whether it's in the UK, the United States, Africa, the Caribbean, India, Brazil, they call themselves, and we support them in calling themselves, warriors because it's part of the resilience that they've had to deal with over many, many years.

**Marie:** So, just coming back, as I say, about impact and the kind of impact that we want to see. I think for me it's about – I want people to be able to walk away from this process that we'll go through together to create this top 10 future research priorities, feeling that they have really contributed positively to rallying research around the areas that will bring the most benefit to patients in the future.

If I can support people to connect and share their stories and, you know, build their own knowledge and whatever it is else that they want to get from this process, then I know I can walk away from this happy, that we've set a national agenda and that we can do our job to support that to continue happening. What would you really like to see come about as a result of this, John?

**John:** Well, I agree with everything you say because what we would want to see at the end, as a national patient advocacy organisation, is that there is a clear agenda for change around genomics that is informed by people living with the condition. That’s what we want to see, that there is a forward agenda that is clear. But I'd also like to see that the processes that we've collectively used have gained the trust and the commitment and the interest and the insights of the people that we are working with. To get to that point of having an agenda of the things that we're going to focus on for genomics and sickle cell. It needs to be informed by a process where we have built up trust and understanding.

**Marie:** So, Suzannah, again, you are incredibly experienced in running these priority setting partnerships. In your view, what would real impact look like going through this process, particularly for sickle cell and genomics?

**Suzannah:** It has to be that it goes beyond just being nicely illustrated top 10 list of priorities. It becomes real when it gets funded. When it goes in and actually starts to change the way in which sickle cell is managed as a condition through genomics, managed, diagnosed, treated, etc.

I love the term warrior because the easy bit is doing and agreeing what the top 10 bit, the bit where the warrior mentality will really have to come in is saying, this isn't just a nice list that you can wave at people and go, look at this work we did. It's carrying it on. It's having the warrior mentality to say, who's going to fund this? When's it going to happen? Who's going to be involved? And also, really importantly, that the involvement of people in the community doesn't stop at the top 10. That they're involved in saying, what does this research priority area look like? How are we turning it into something so that the journey continues, that's the important bit.

**Marie:** I think that's such a wonderful point to make. And, just to say that I think something that's wonderful about developing partnerships is that you get held accountable by your partners and you become hopefully very good but critical when needed.

I completely agree that this will just be the starting point and again, something else that I think we've got a wonderful opportunity to start building and shaping as we go along this priority setting partnership work is about what do we need to do in terms of how we go about supporting further research. What do we need to do differently to make sure we continue to sustain the trust and involvement of those voices in the research that can continue and be spared from that point on?

**John:** I think if we do this well, and I'm very confident that we will do this well as a partnership, that this could be a template for use for other conditions in what were previously deemed hard to reach groups, because the Sickle Cell Committee is not hard to reach in any way whatsoever. So, I think that this could be a good template, and I think as a partnership we need to learn from it as well because there may be things that we will learn from the process and we need to kind of take that learning and not dismiss it because, I have to say, not everything might be easier.

So back to the warrior mentality, it might be, this isn't right. And we haven't got to be frightened of that, but we have to address it and listen carefully, so I think there's a lot of learning that comes from this process beyond what we are seeking to achieve in terms of a longer term agenda that is appropriately funded.

If I can say, because it's part of this call to action, I think when we come out with those priorities, the challenge will be, where do you stand, Genomics England? And where are you going to put your hand in your pocket in relation to whatever may be relevant in that menu of priorities?

**Marie:** I completely agree, and I think what we've got here is an opportunity for absolutely to be held accountable, as I said. We have a role to play. We are extending, you know, the kind of areas that we are looking at in Genomics England and I think that this is where we can start really developing really good partnerships to ensure that we are going about that in the best way possible. We are doing everything we can as part of this whole ecosystem, that we all need to do our bit to make sure that, you know, proper change does come and benefits to patients really do come because of that.

I just wanted to wrap up our podcast now because essentially, we've got World Sickle Day, which is the 19th of June, and I know that the theme for this year is progress. So, John, do you just want to give us a little insight into the kinds of things that are going on around World Sickle Day, what people can look out for, if there's anything that people can go and look for as a result of the colour events and things that are happening this year.

**John:** Thank you, Marie. I would encourage people listening to the podcast today to look on our website. We'll be doing a range of things under this banner of making progress, but those range of things will include podcasts like we are doing today, radio interviews and general information about areas of work and the very fact that not many people even knew that there was a World Sickle Day.

So, it's taken the time to amplify that there's a World Sickle Day and this will be for people not only in the UK, across the world. But it will be trying to show those snippets of progress that we have made and we plan to make, because all those things are good for people who live with sickle cell, but equally importantly, it's good for people who might not have heard about sickle cell or knew anything about it. So, the information will be on our website, but we'll also be using our social media platforms to promote lots of information around World Sickle Day.

**Marie:** Thank you, John, and it's certainly just the start of the conversation, which is really the important take home here. We're just getting started and I think that it would be wonderful as we may be reaching towards the end of our priority setting partnership work together, maybe we can come back and share how we've got on with that and what we can really do with what we've learned. And I think that's another wonderful word to use in this context when we're all learning together, so thank you so much both for your time today.

It's been an absolute pleasure to have you as always, I always learn so much from our conversations and I really look forward to working with you both.

That's all for this episode. Thank you for listening to this discussion about the G word and for joining us on this journey to highlight and debate the implications of genomics as it becomes more mainstream in healthcare and society. You can find out more about the work of the Sickle Cell society [here](https://www.sicklecellsociety.org/) and the James Lind Alliance [here.](https://www.jla.nihr.ac.uk/)

If you want to find out more about the work of diverse data and our sickle cell programme [here](https://www.genomicsengland.co.uk/initiatives/diverse-data). If you have any views on these topics or have a person in mind you would like us to interview, please write to us at podcast@genomicsengland.co.uk.

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