Transcript of the Webinar 2 questions and answers Topic: Ethics and values

Date of webinar: Monday 15th May

Introduction
Audio recordings were made of each of the webinars and transcripts were made of these. The following questions and answers are what was recorded in webinar 2 and are set out below. The only edits that have been made are to remove filler words (for example 'um') and repeat words. Some footnotes have been added which provide post webinar clarifications from the Spectrum 10K team.

Question: How much can the controversy on values be attributed to the changing definitions and criteria for autism? What is the current definition of autism on a behavioural or psychological level?

Answer: It's been really helpful that we've had this chance to pause the study, to really reflect on our values, and make them really explicit. Because a lot of the time in research, people just do research and they don't think about what the values are of the team, and what are the values that the community might expect to hear about? In a way, what the pause has done is create this opportunity to really make things explicit.

The values that we've articulated were that we oppose eugenics. That's to say we oppose using any data at all that could have the risk of preventing autism[1], we took this as clear. But actually, we've decided to be much more explicit about this on our website. And we oppose the development of a prenatal test and we oppose a cure for autism, although we do support treatments and interventions for co-occurring conditions that might be causing distress, or suffering, but not autism itself.

Question: Is this because of changing definitions and changing criteria for autism?

Answer: I've got the benefit of a long history in this in this area, and certainly, definitions of autism have changed over 20 or 30 years. If we think back to 1994, most of the criteria for autism and the definition of autism was about people who are autistic and who also had learning disabilities. The introduction of Asperger's syndrome in 1994 really opened the way for that changing definition where you could be autistic, but without learning disabilities. I think that

[1] Spectrum 10K clarification: We oppose the use of data and research that aims to prevent autism.

has made community participation much more accessible, because you need different types of engagement for people with or without learning disability. I think probably the changing definitions, the changing demographics of who gets a diagnosis of autism, has influenced why we're now having this debate about values.

The question is also what's the current definition of autism on a behavioural or psychological level? And just being really brief the current definition is really about, does the person have social and communication difficulties and difficulties with unexpected change? But the definition also includes sensory hypersensitivity, and we've also got the neurodiversity lens through which we view autism, which is not just about disability, it's about difference, that autistic people process information differently, and that some of those differences are strengths and even talents. Our definition is actually quite broad.

Question: This question links to the first question asked about the findings from Spectrum 10k and how they can be used. Could they be used for prenatal testing, whether the spectrum 10k Principal Investigators want to or not? Because the GWAS variants, and the polygenic scores will be the main results of the study that will be published. Will those be available for anyone to use without permission being sought?

Answer: Let’s try and give a several different answers to this. Because permission is needed, what we are hoping will come out of the consultation is the creation of this Data Access Committee or Data Sharing Committee. In a way, that committee will have to give permission. And if someone who is requesting data is intending to use the data to develop prenatal testing, then the data wouldn't be shared with that person - that's my understanding. That would contradict the values of the research team. It may well contradict the statements in the consent form. We may want, at the end of the consultation to revise the consent form, to make it really clear that the data can't be used for that purpose. Is it the case that our research team could ever prevent data being used to develop a prenatal test? All we can do is do our absolute best by using a Data Sharing Committee to vet any requests for our data. But, when data is published, and there's lots of data already published - not from our team - on the genetics of autism, I don't think this study is going to be able to control how that is used. Just to give a very concrete example, in the genetics of autism, if you look at the safari website, where they list all of the known genes associated with autism, there's well over 100 of them. These are called rare genetic variants, like mutations. There's probably nothing to stop a company who wanted to develop a prenatal test from using that published data already, but that would contravene our values. And we wouldn't allow our data to be used in that way.

Just so everyone is aware that we had built in a Data Access Committee or a data screening committee from the outset of this project, it was built into original ethics, you can't share data without some kind of oversight. That's just the way it is. In terms of concerns about prenatal

testing, I can understand why the community would worry about that. But I think it's important to remember that autism is not purely genetic. It's a combination of genetic and environmental factors, and that you can't diagnose purely on one aspect. So I think that's a very important consideration. Once the data is published, we can't control future researchers, but we can control who has access to the data. And that will be the case for any research project. And one of the things that we've realised is that in stopping to do the consultation, we also might be setting a new standard for how genetic research is done in autism, which means that might put pressure on other groups, other countries to follow what we've tried to do here.

I think it's a central point that what we're doing in this study, where we're saying let's develop a safe Data Sharing Committee, made up of autistic people, their carers, as well as the scientists and clinicians. So, we've got all of the kinds of stakeholders sitting around the table deciding who data should be shared with, and data sharing criteria should always be measured against the stated values, that relates this back to the previous question. If that becomes the gold standard for every project internationally, using data that could be contentious in this way. I think the field will have moved on considerably if that's the case. So this could become a model of how to do safe research internationally.

Question: It comes up in the last sentence in that question that GWAS variants, and polygenic scores will be the main results of the study that will be published and available for anyone to use. Will those results be published and available? Or will they be held in a database that people need to apply to access?

Answer: In terms of a data sharing platform, or how external researchers would apply to use the data, they would apply to a database, such as the European Genome Archive, which is an international platform where researchers apply, they would apply to us directly via that platform, and then to our Data Access Committee, we would then provide permission[2]. The nature of the data, it would depend obviously, on what was being requested. It's not a case of just everything that's been put out there. And anybody can just take it as, as they wish. There would be a request for specific sets of data and relation to their use and associated with ethics and so on. And this needs to go to the working group, particularly around the design of this Data Access Committee, because the way that this last sentence is worded at the moment, the GWAS variants and the polygenic scores will be published. The question is, how much could somebody do with that information that we might not want them to do? And as far as I understand, the GWAS variants refers to what are called SNPs, single nucleotide polymorphisms.

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[2] A clarification from the Spectrum 10K team: This has now changed, the EGA no longer applies. Applications must be made to the Data Access Committee directly and approved researchers would access via a University of Cambridge platform which would prevent users being able to download or copy the data.

The ones that get published are likely to be in combination with other datasets, not just Spectrum 10K, because Spectrum 10K, although it's large, it's 10,000 autistic people, GWAS, typically needs even bigger sample sizes than that. So these are the sorts of issues that the working group needs to sit down with the geneticists actually, to say, well, what can be published safely? And which data might need much more safeguarding through the Data Access Committee? I think these details need to be worked out with the geneticists.

Question: Could I just clarify, when you say the working group, are you referring to the co-production group that is working at the end of this consultation process?

Answer: Yes, as a result of the consultation, we are setting up a co-production group that will work with Spectrum 10K, to change and amend things in the documentation, and to advise on the Data Access Committee and how it works. And those details so that's what's being referred to there. And that will be working quite quickly in June, to make sure these things are changed in recognition of what the consultation has said.

Question: Will the changes to the grant application - although possibly not changing the application, but only the ethics, I don't know - resulting from this consultation, will they be published? If so, when, and where?

Answer: I very much hope that the changes that we make to the study design will be not just publicly available, but the subject of some publications, because it's all part of documenting what I think is quite a historic situation in autism research. Namely, we've paused a study, so we can show, what was the study design before we paused. Then we had the consultation through three phases. What was the outcome of that consultation? And what has changed in the standard design as a result of that consultation and co-design? So an answer to when and where I'm imagining that publications could arise between about October and Christmas of this year, we could start drafting those. But I think we've got quite a tight schedule for the consultation itself. And then we've got a bunch of hurdles, after the consultation to do with revising the ethics application and submitting that to the Ethics Committee and the Health Research Authority. And maybe redesigning the website where people are going to take a lot of the measures, and changing consent forms and information sheets, quite a lot of work all before October, when we hope that the study will relaunch. But I think once we've got to that point, we could start thinking about dissemination of you know, the outcomes of all of this. And in terms of where, I think it will probably be a mix of outlets. So some in the scientific journals, and some in the less technical outlets, for example New Scientist, which are available to the general public.

I just want to clarify, I don't think we're going to be making changes to the grant application because we've already applied and received the grant. While we would be making changes to the ethics application and the protocol, which would have to be reviewed by the Ethics Committee, and then try again, before we could ever relaunch the study. And I think there are different steps. So, the first step is that Hopkins Van Mil and Leneh would create a report for us. That is from phase three from the consultation, we will take that feedback into the co-production group, and we would be basing our changes on that feedback from phase three. Then we would eventually publish what changes we made based on the consultation feedback. So those are two things that we would publish. So HVM and Leneh would publish their feedback, we would then feedback what we were able to change or improve on. And finally the ethics application, and whatever we submit, can also be reported on so I think those are three different things that we would plan to share with the community. And I mean, this is not usually done when you're applying to ethics, you don't really share this. Not practically anyway, not many researchers do that. But because we're doing a consultation, we do want to track all the feedback and how we've been able to implement that into the study and whatever changes we made.

Question: Spectrum 10K plan to investigate which tissues, gene sets, cell types, and developmental periods are enriched for a genetic risk of autism. What does the study team see as a genetic risk?

Answer: I can say straight off that the use of the word risk is inappropriate. And we would not use that word. So sometimes language has crept in which now that we've had the opportunity to review it, because there's a lot of documents, we can acknowledge, that's not an appropriate word. So, we would use the word likelihood, rather than risk for the reasons that risk implies that autism is something negative, which we don't see autism is something negative. We see autism as a mix of disability and difference. But we don't want to use any language that could suggest that autism is negative. So, I think that's really just a typo, and it'll get corrected.

I mean, it's probably less of a typo than really just the language that is used in genetics, and in some sciences. And I think it's been used, words like risks have been used in the past, because when the field was developed, you were looking at diseases, so something like cancer where you would want to say you have a risk for cancer. But of course, when you're now looking at neurodiversity, for example, it doesn't make sense to say risk. But the language needs to catch on and that's really just something that we have reviewed. We've reviewed our protocol, and we've highlighted all the other bits that need to be changed so that we don't perpetuate stigma. But we've just highlighted the changes, and we still want to work with the co-production group, to see how do we change the language? How do we maintain it, and so on.

Answer from Hopkins Van Mil re. consultation findings: That's something important in the report we're writing about the consultation, about the use of language, and how it's developed and how those who've been involved in the consultation so far in each of its phases, have informed those discussions as well.

Question: You say you support treatments and interventions for co-occurring conditions. If Spectrum 10K reveals possible cures or prevention for co-occurring conditions which also have an impact on core autism, would you endorse that or not?

Answer: In terms of spectrum 10k, this study is not going to be looking at treatments or interventions for co-occurring conditions. What we've said is that this study can look at genetic and environmental factors that influence autism or co-occurring conditions but within the timeframe of the study, which after the consultation will only be two years, we won't be looking at specific treatments and interventions, but the findings may well have relevance for those. And then in terms of the Autism Research Centre at Cambridge, we do support research which evaluates treatments and interventions for co-occurring conditions. And we've got one ongoing at the moment, for example, into music therapy. And the co-occurring condition that is aimed to address is anxiety, and mental health or wellbeing as the outcome measure. So we're not looking at does music therapy change the person's autism? We don't think that's a legitimate question, but we do think it's okay to look at whether music therapy influences an autistic person's mental health or wellbeing. So that would be an example. And I think the specific question here is, if you find that an intervention not only impacts the co-occurring condition, but also impacts autism itself, would we endorse the finding? It says impact/ cure/ prevent. We've said very clearly, we're not interested in cure or prevent, prevention of autism. I think if the findings are about the co-occurring conditions, we would endorse those.

This is a very good philosophical question, because at the moment I'm not aware of any intervention, that could both for example, cure epilepsy, and that would prevent autism. But if in the future, there would be something like that, we would not endorse something that would prevent autism. That would be clear, and I don't know that there is a possibility that something would cure, or prevent two things. But if there were, I would say that we would always prioritise our values, which is the non-prevention of autism or curing of autism.

I think this also goes to the heart of transparency and being really clear about your aims for any study. If the ARC's, that's the Autism Research Centre here, but any research group, are evaluating an intervention, they need to be really clear what is it that they're evaluating? Why is the study being done? What are they measuring? What are the outcome measures? And that's what they should be reporting on at the end. If there was a study that was saying, can we have an intervention that would make somebody less autistic? We wouldn't want to be involved in a study like that and nor would we want to endorse it. But if it was, can an intervention make an

autistic person less anxious? We would be interested in a study like that. So it's about clarity about the aims and the measures, because that's what should be reported on.

Question: While curing autism is surely morally questionable, is there an ethical case for aiming to enable autistic people to have better relationships with other people, including their partners?

Answer: This is a really helpful question because it is getting us to focus on the ethics of different studies and what each study is intended to do. In this particular case, supposing there was an intervention that helped autistic people have better relationships, that's the example they've given, we could tell you about a study that we've done, which is relevant to this, we were one of the first groups to evaluate what's called Lego therapy, or Lego clubs, which now a lot of primary schools offer and even secondary schools. But this is where, autistic children or teenagers are invited to play with Lego with peers, to do something that they might enjoy, and that they might even feel confident in. And the process of doing that improves their self confidence in social situations, so that the outcome measure could well be something that's self-confidence, self-esteem, or even just being more comfortable. So that relates to the answer I gave to the earlier point about anxiety. So it may have a benefit for relationships. But it's studies like this, and I think we should really focus on you know, going forward, how would we like to co-design intervention studies with the autism community? With regards to the goals for the intervention, we should pick those outcome measures with autistic people and their parents and their carers.

Question: Spectrum 10K apologized for an email in which they told NHS Trust not to engage with “trolls.” Then they said, Oh, we didn't mean it. And then they use “trolls” again later. So why did the study team call autistic people with legitimate concerns “trolls”?

Answer: We certainly don't see the autism community as trolls and through this entire consultation process we can be very clear that the points that have been raised by the community and the work that we have done and we are doing and what we are learning through this process is incredibly valuable not just to, well it is incredibly valuable to Spectrum 10K but also to autism research more widely. And ultimately this this entire process is going to benefit the study, autism research, the ARC’s genetic research more broadly, and ultimately lead to better outcomes for lots of patient groups or not just autism, but other groups that are dealing with genetic research and ethical questions around genetics. So this has been a huge learning process for everyone involved, and part of this is having this conversation and learning and developing and improving based on hearing all sides of off of the discussion. But we certainly do not see concerns about autism, or concerns from the autism community as trolls.

Question: Do you know why they were referred to as trolls at the time?

Answer: I don't know why they were mentioned, the word came in. In the midst of some of the criticisms that were received, I think someone outside of the team or maybe on social media had introduced that term. It was definitely not part of my vocabulary. I didn't even know what a troll meant. I'm not on social media. So I didn't know. But I think once this was raised, we realised we should be more careful what type of words we use, not just in research, just being very aware of what type of language we pick up from others. It wasn't really something that we were using before the launch of the study, it wasn't in our vocabulary. It was just part of everything that was happening, and I also want to acknowledge that it is a shame that it was picked up within our communication, we shouldn't really use that language anyway. We never consciously thought that anyone voicing their concern would be an internet troll.

Question: Could pre-natal testing be a dangerous tool if it fell into the wrong hands? Or the wrong political setting? [And linked to this question] around what's wrong with prenatal testing, you can't do it without parent consent. Some parents might find it helpful to know if there's a genetic factor that may cause social communication problems. It may help with raising children from an early age. There's no need to cure autism, as many people have amazing skills unique to autism. But it may help to understand that your child sees the world around you differently.

In webinar comment from the Consultation Co-leads: I'm clumping those two questions together. Partly I'm not quite sure that there a specific question in there. It's an ethical point that is being raised across those two questions.

Answer: I think this person has put their finger on why it is that we've had to be, we want to be really explicit, that we oppose the development of a prenatal test. Just because there is that risk, and I'm now using the word risk deliberately, in a considered way, there is that risk that prenatal testing could be used dangerously. And we know this just because we know about everything that happened during the Second World War, it's probably the clearest example where, in a particular political climate, a dictatorship, the government created a list of everybody who had disabilities for prevention and eradication. One of the groups who were victims of the Nazis were people with disabilities. So that would be an extreme example of how prenatal testing could become a dangerous tool in a dangerous situation.

But the other question, what's wrong with prenatal testing? And particularly if there's parental consent? Well, that is the current situation on the NHS. And that some forms of prenatal testing already exist. And we know the clearest example is Down syndrome. We, as a research team have thought about this a lot and decided that our values are still to oppose the development of a prenatal test for autism because of basically the lesson that could be learned from what's happened with Down syndrome. In the case of Down syndrome in some countries,

90%, even higher, 99% of people with Down syndrome, who would have lived, were prevented from living, because of the manner in which prenatal testing is offered to parents. So it's had a massive impact, not only on the individual foetus, but on that that whole community. And that's why we're simply saying, if you want to use prenatal testing, just to get early identification so that parents can start to plan what their child might need, why not do it postnatally, developing some screening tests. Postnatally removes any risk that the test would be used for prevention, but it could be used for early intervention, for support for co-occurring conditions, like language development, for example, speech therapy. But it would all be postnatal; it just removes that one possibility of how a test could be misused.

Question: Can you use any data from outside study? [Example of a specific case where genetic testing had been done.]

Answer: If they've done some genetic testing outside of the Spectrum 10K study, we wouldn't be able to access that data. They would have to sign up for this study and I'm not really sure… they've done whole genome sequencing, so it would be different type of data analysis.

Question: How can you guarantee that ARC's amniocentesis study combined with learnings from Spectrum 10K will not pave the way towards prenatal testing for autism?

Answer: We've always been really clear that when we use amniotic fluid, which is what gets collected in amniocentesis, this is purely in the context of research where the mother has consented for the fluid to be used, just to understand, in the case of our studies, hormonal factors that might influence likelihood of autism. But we've been very explicit that we would not endorse the use of that for prenatal testing. This goes back to about 2009, when we first reported on amniotic fluid, and where the media reported on it, I think it was in The Guardian, saying that scientists were developing a prenatal test and we corrected them very quickly saying we are not developing a prenatal test and we wouldn't want to develop a prenatal test. So this question is about how can you guarantee it? And this is really tricky because it's not just about amniocentesis, we've already covered this in relation to genetics and any other data that any study collects. How is it that we can make any kind of guarantees or promises and, so far, the best we've come up with is about Data Access Committees, we think that's the mechanism for each study guaranteeing who they're going to share data with, and for what purposes, we can only do it for the studies we're involved in. But we're trying to set a new standard, that every research team internationally should be really clear. You should be using a Data Access Committee or a Data Sharing Committee to be really clear about and for what purposes, would they share data? And what purposes would they not share data?

I think I would agree with what can we do at our end, to safeguard our data, who gets access to it, and who can process it. It's not all we can do, because I think there's also the social

aspect of it the precedents that we're creating here. So those are two powerful ways in preventing prenatal testing. I mean, I don't think we've touched on this, but I know that prenatal testing has been compared to Down syndrome. But with Down syndrome, you can predict whether someone will have the syndrome when they're born. And I don't think that's the case with autism. I think it would be highly unethical to do prenatal testing for the, you know, for for the option of abortion, if we're not if we can predict with certainty anything. But you know, with autism, I think is so complex. And as you said, it's a behavioural, you know, we diagnose it based on behaviour, so I think that's also an it's an important part of the question.

I think what you're saying is, since it's not possible scientifically anyway, that would already make it unethical. But then even if it was possible, you know, we value autistic people as part of the world. We don't want prenatal testing because prenatal testing could open the doors to prevention. So we're just stating clearly our values. And we're not speaking on behalf of other scientists, but I think we're trying to encourage other scientists to be clear about that about their values too.

Question: How will you balance opposing interests in deciding what research to approve access to the data from Spectrum 10K?

Answer: It would be part of the discussion within the working group, there'll be kind of two levels. So first of all, in terms of redesigning aspects of the study, or making changes to the project, obviously, the working group will, we'll be working together to work it out. However, ultimately, our ethics committee and our sponsor, and our ethics committee will have the final say, on the decisions around what is the final parameter of what's acceptable. In terms of data access, and who we will be sharing data with, part of the work we will be doing as part of the redesign and submission to ethics would be the drafting of a data access committee terms of reference, which will be submitted to ethics. So that will be completed in partnership with the working group. And through that, we will be able to come to a decision around the types of researchers and the types of research that we want to share information.

What we'd be trying to achieve is consensus on this Data Sharing Committee. Because you're saying that, you know, not all autistic people are going to have the same views as you'd expect. And not all parents or carers are going to have the same views. But the aim would be can we achieve consensus about which data can be shared? And for what purpose? But I think, because we've stated our values, we’re against a cure for autism, that would become a bottom line for the study team. If somebody wanted the data in order to cure autism, we would say no, just being really clear.