A Day of Discussion: The ELSI Conference 2025

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Introduction

Our research team forms one of the ‘nodes’ within Rare Disease Research UK (RDRUK) – our focus is on ethical, legal and social issues in rare condition research and practice (ELSI). The goal of the ELSI node is to improve research and clinical practice for people living with rare conditions. This article is a summary of the first ELSI Conference, which covers the key themes, priorities and challenges of rare condition clinical trials. We are proud that this was a patient-centred event, made up of interactive discussions where people involved with and living with rare conditions shared their experiences and opinions. We have included participants’ own words in text boxes.

Key Themes: click to be linked directly to the corresponding key theme section

Equity, equality, diversity, and inclusion (EEDI) and ethical issues in clinical trials

Equitable access to clinical trials is a key priority for people living with rare conditions. However, people sometimes miss opportunities to take part due to not knowing that a relevant clinical trial is happening. Parents/ carers of children with rare conditions do not always have time or energy to seek clinical trials on top of their caring responsibilities.

> *It is a full-time job having a child with a rare condition. We've often got full-time jobs on top of those full-time jobs and we would do whatever we can do to improve the health outcomes of our children [...] but it feels like it's another thing that we have to do to try and seek these opportunities.* (Parent)

Families also face practical and financial barriers to taking part in clinical trials. Travelling long distances, sometimes internationally, is not uncommon.

> *Where family life, the ability to work, or whatever, is going to be disrupted, or there's high travel costs and so on [we need to ensure] that all of that is properly recognised, funded and supported so that these things are open to people regardless of their financial situation.* (Patient group representative)

These barriers may reduce diversity in clinical trials, with fewer participants from disadvantaged and marginalised groups. Cultural and language barriers present further challenges.

> *Patient information leaflets are very long, and how would something like that be translated into a different language to make it more understandable and accessible to people from different ethnicities, who speak different [first] languages?* (Patient group representative)

Currently, researchers do not routinely collect demographic data (e.g. about people's ethnicity, where they live, or their socioeconomic status). Without this, it's difficult to begin to address EEDI issues in clinical trials. For ultra-rare conditions with very small numbers of participants, it's important to have inclusion criteria that maximise the likelihood that trials will be accessible.

We discussed the roles and responsibilities of healthcare professionals/ the NHS, patient organisations, researchers, and industry in improving EEDI in clinical trials. There was a strong feeling that the systems created for clinical trials for more common conditions do not work for rare conditions, and act as a barrier.

> *You're fitting the wrong shaped object into the wrong shaped hole.* (Healthcare professional)

While patient organisations have a pivotal role in advocating for change, they vary in size (particularly for ultra-rare conditions), resources, and funding, and can't always help as much as they want to. This can exacerbate inequities within the rare disease community. Alliances of patient groups can counter this by sharing resources. More partnership working to share these important responsibilities would also help.

Addressing EEDI is an important ethical issue. Another ethical issue discussed is how clinical trials are designed: specifically, the use of a placebo or non-treatment cohort for rare conditions that may be debilitating or degenerative.

> *In rare conditions because we have tiny populations and because it's really hard to do trials, I don't think there's the same acceptance that [placebo trials are] unethical.* (Patient group representative)

Patient and public involvement in research (PPI)

As experts by experience, the voices of people living with rare conditions are crucial. Patient and public involvement in research (PPI) treats people as partners rather than simply participants.

> *The answer is quite simple, ask rare condition patients!* (Patient group representative)

People living with rare conditions have been involved, for example, in the design of trials and patient-facing materials, and co-authoring research. To do quality PPI it is important to start as early as possible. Patient organisations are happy to hear PPI ideas. Whilst it's exciting that rare conditions research is happening, this should not mean that PPI contributors aren't paid properly for their time and effort.

> *I think it's really important that we change that narrative of being grateful that someone's looking at our condition and ensure that it's [PPI] properly funded and properly supported.* (Patient group representative)

This is a challenge, as budgets are limited and there can be issues with when in the research process the funding for PPI is available.

Decision making and motivations for taking part in clinical trials

People need to balance the potential costs and benefits of trial involvement. A key factor is quality of life.

> *There is always a risk with everything. But I know how much [trial drug] benefits me and I know how much I need it to function properly for the week. I think that outweighs everything anyway. And I don't really think about the risks for it because I just know that it's doing me good.* (Person living with a rare condition)

With rare conditions, there is often uncertainty – as a parent said, *“I just wanted a crystal ball”* - and factoring the future into decisions is challenging, especially because there aren’t a lot of real-life stories to relate to. Again, this highlights the importance of patient organisations.

> *You're kind of looking at risk versus rewards but not from like your current condition, but what your condition will be in 10 years’ time. So you're kind of trying to predict the future and decide for yourself whether the decision you're making right now is the right one.* (Person living with a rare condition)

An altruistic motivation for research involvement was to build those communities and evidence bases.

> *Not just potentially benefiting [my son], but benefiting other people who have the same condition, that's why we’ve taken part in so many research projects […] it might not benefit him. But if, you know, he can be part of a study that will benefit other people then that's a win as well.* (Parent)

The importance of clear, accessible, and open communication

One of the biggest factors in making decisions was the communication about the clinical trial. Every trial comes with written information, such as a leaflet, that should help people to decide whether to participate. These should be appropriate and accessible in language and design. There should be clear information about the potential practical impact, e.g. time commitment; what support will be available for travel etc. PPI and patient organisations can help with content and design. Unfortunately, leaflets can often be long and complex, which is a significant barrier.

> *Oh my gosh, I've never read a 35-page scientific document in my life. How can I start with this?*
> (Patient group representative)

Providing information in different formats can really help. In addition, *“an upfront open honest conversation, where the uncertainties are explored and made clear”* (patient group representative) is vital. Healthcare professionals’ role is not to just repeat information, it’s also to *“help frame a risk/ benefit discussion”* (healthcare professional).

> *Don’t feel you have to ask everything now, take the information leaflet and look through all the pages and, you know, it’s a hard thing to do and I remember flicking through it and picking bits out, I certainly didn’t sit there and look through it thoroughly […] but we were very lucky that everything that we felt we needed to be explained to us, was, and that we could go back and ask questions at any point.* (Parent)

Children, communication, and consent

A key issue for parents/carers is that they usually have to decide if their child will take part. However, children should be involved in the process as much as possible.

> *Obviously I was a child. So my parents had to make that decision for me but that did mean that I was always familiar with like, hospital settings, talking to consultants. And I do think that I was able to make those decisions and experience a maturity at an earlier age. So even though there's a lot of parental consent, I do think that if you are discussing clinical trials with a patient that has got a rare genetic disease, that you are kind of looking more towards the patient than the parents, because I think that the patient themselves needs to have that voice as well.* (Person living with a rare condition)

Healthcare professionals have a role in encouraging parents to speak to children about clinical trials, and in making information accessible and age-appropriate.

Parents/carers said they found consenting for their child *"really difficult"*. Again, this involved thinking not just about the immediate situation, but looking into the future.

> *You're aware that you're making such a massive decision for your child and that it is going to impact them. And you don't know whether there's going to be certain triggers left from that that are going to affect them for the rest of their lives.* (Parent)

There are also ethical challenges of consenting children for trials.

> *We don't consent children formally for trials for lots of very good reasons. And who would agree, if you're a five-year-old to just having a blood test? If you can't think about what how this might help me in 10 years' time, because that's not what you do when you're five, think about 10 years' time. So you can't understand everything, but, at the same time, you know, you are taking a risk with someone who's not able to make that decision for themselves. So I do always slightly worry about how these young people will view me in the future.* (Healthcare professional)

A parent panellist described their *"gut feeling",* and hope, as ultimate decisional factors.

> *If there's a slight chance that this is going to help her, then we can't not do that. We've got to give it a chance.* (Parent)

This was reflected by a young person talking about their decision-making process:

> *It's kind of weighing up those consequences of like, can you really live the rest of your life without going through with that clinical trial, or is it kind of best to kind of take that jump and just have faith in your clinicians that it'll go as expected.* (Person living with a rare condition)

The importance of trust: the relationship with healthcare professionals

Ultimately, it was that trusting relationship between healthcare professionals, people living with rare conditions, and families that encouraged participation in clinical trials.

> *I think that relationship that patients and their parents have with their care team, it's so important. And one of the probably biggest deciding factors of whether or not you decided to get involved in clinical trials or experimental procedures or other interventions.* (Patient group representative)

For one panellist, an experience of damaged trust led to them declining a procedure. This is a powerful learning opportunity about the importance and fragility of trust, and how it should be built and protected.

> *[The doctors were] not really asking permission or explaining what they were doing and it's just things like that. It's not necessarily the things that they said, it's the way that they behaved as well [...]. So it's just helping the medical team to be aware of it's not just your verbal language, it's your body language and how you behave around that patient, even when you think they can't see you as well.*
> (Patient group representative)

A highlight of the day was seeing a trusting relationship between a young person (and their parent), and the consultant who had known them for many years and been with them on their clinical trial journey. This was not only a factor in deciding to take part in the trial, but was intrinsic to their experience of the clinical trial itself.

> *Nothing was a silly question and I think it just boils down to, it's that relationship and as parents and as, um, patients feeling able to ask anything at any point.* (Parent)

Experience of taking part in clinical trials

The support of healthcare professionals and patient organisations is especially important considering the significance of a clinical trial for people living with rare conditions.

> *I think it's just like you [doctor] being there for me and being a kind face to see, to have and to see, you know, when I was so young. You were just so kind to me and stuff and um I think cos I was so young I can't remember everything that happened back then but [...] it's the ways everybody handled it, it was, it was a nicer experience than 'we're gonna jab you with a needle', you know, it's more down to all the nurses being nice to me and the play specialists and you being silly that kind of stuff.* (Person living with a rare condition)

There are logistical impacts and disruption to normal routines such as school. There is also the significant impact of the trial intervention itself, which can be invasive. Trial drugs carry the risk of side effects or reactions, which may need extra medication. These impacts may not be just for the trial – they can be lifelong.

> *A lot of clinical trials are there to better your quality of life and to sort of make your life easier. But what can come with those trials is a sort of commitment that you have to make that you didn't have before. So you obviously had your regular [treatments] that you never had to do before then, and you're kind of making a commitment that is, you know, you're putting your time and your energy into. Um, but you're - it's worthwhile.*
> (Person living with a rare condition)

In addition to the challenges of trial participation there are also some secondary benefits, such as forming friendships. This recognition and connection were important for people living with rare conditions.

> *I guess that's why I was so happy to go there because I would be like, well, I'm not seeing my friends in school today, but I'm gonna be seeing them, and that was even more exciting, cos they look like me, you know, there's that familiarity there.* (Person living with a rare condition)

Families benefited from the supportive atmosphere whilst enrolled. This could have an emotional impact when the trial ended.

> *I always felt coming into that hospital I was wrapped in a comfort blanket. I always felt like that and I really miss it now because I think it upset me to leave there.* (Parent)

There can be other challenges when a trial ends, for instance a difficult period after the trial drug stops but before it becomes available on the NHS. This is an ethical issue.

> *To see the improvement in [my daughter] and then think well that's great but you can't take it away from her now, that to me was very unethical, to give them this drug. Yes, we'll show that it works. And then to take it away.* (Parent)

This family's story had a positive conclusion thanks to tireless advocacy and support from patient organisations. Again this is an EEDI issue and something that more joined-up working could help with.

Patient reported outcome measures (PROMs)

Trial participants undergo various assessments to see if the intervention is having an effect. These can take time and energy.

> *I remember the walk test because it was on the sixth floor, it was boiling and you're always hot anyway. So if you were struggling I'd have to follow behind you with the wheelchair.* (Parent)

For these experiences to be acceptable, they should be at an appropriate level, and there needs to be a trusting relationship with healthcare professionals.

> *[I didn't mind it] because there was a cartoon on the screen and I just got to see a dinosaur or someone blowing bubbles [...] I didn't think of them being part of that clinical trial when I was younger [...] but I think knowing that it was helping me in some way, I don't know what I thought it was helping me with, but um knowing that it was helping me and knowing that I trusted everybody, that they wouldn't make me do this if it wasn't like... I think that just helps.* (Person living with a rare condition)

Some of the ELSI node's research is about patient reported outcome measures (PROMs) and the best way to measure outcomes in clinical trials. Especially in rare conditions, it can be difficult to do this appropriately and meaningfully.

> *Most doctors' view of your condition was that it was all about how big your bones were, yes? And yet, when I would speak to young people with your condition in clinics, they would tell me often how tired they were and how limited they were by how much energy they had and so um, the trials focused not so much on how tall you were but, um, what you could do. And while that's not a PROM, it might be a little bit closer to what you cared about.* (Healthcare professional)

Conclusion

The ELSI conference was an enjoyable and interesting patient-focused day. Everyone appreciated the open and honest conversations about how to improve the rare conditions research landscape.

> *We all know about the diagnostic odyssey for rare diseases and with an odyssey you don't know where you're going to end up and it's lots of twists and turns along the way. And I think what we don't want is for clinical trials and research to be another odyssey for families with rare conditions, and if we can make it more of a journey where there's a pathway, where there's support and where you have some idea of where you're going, and then I think that will serve families better.* (Patient group representative)