

Workshop report: Participants not subjects – engaging patients and families in paediatric clinical research

Friday 27th March 2015: John Walton Muscular Dystrophy Research Centre at Newcastle University and Policy Ethics and Life Sciences (PEALS)

Summary

Because of the lack so far of effective treatments for rare inherited paediatric muscle disease and because of their severity, many parents report feeling that clinical trials offer their only hope of a therapy for their child. This puts the family and the patient in a vulnerable position as desperation to be included into a trial can lead to consent at almost any cost. For all clinical research but under these circumstances in particular, an environment which enables ongoing discussion and collaboration between the clinician, the trial staff and the families recruited is needed. This is important in order that a partnership is created where patients and families have a voice and are involved in decisions and planning rather than being subjects on whom research is carried out.

One aspect of this is the development of clear, engaging information about clinical trials in general and specific trials in particular in order to better enable families to make informed decisions.

This workshop aimed to bring together stakeholders with an interest in the involvement of children and families in clinical research in order to discuss the benefits of more meaningful involvement, the barriers to this and ways in which better patient engagement and involvement can be enabled.

This report summarises the discussions between the attendees of the workshop and lists the action points which have been suggested as a result in order that there is real and meaningful follow up and further discussion and collaboration in the future.

Agenda:

09.15 Welcome address, Dr Simon Woods, PEALS, Newcastle University

09.25 Benefits of better patient engagement with research, Professor Bridget Young, Institute of Psychology, Health and Society, University of Liverpool

09.45 Framework for interaction between the European Medicines Agency and patients and their organisations, Nathalie Bere, Patient Relations, EMA, London

10.05 The role of relational autonomy in children's decision-making, Dr Sarah Skyrme, PEALS, Newcastle University

10.25 Current practice – a clinician's experience of paediatric clinical trials, Dr Alexander Murphy, John Walton Muscular Dystrophy Research Centre, Newcastle University

10.40 The patient and family perspective on clinical trials, Alex Johnson, Joining Jack

10.50 Coffee break



11.10 Group discussions:

a) Benefits of increasing patient and family engagement

b) Creating new resources and changing practice to achieve improved levels of engagement

12.10 Feedback from discussion, Chair: Dr Simon Woods, PEALS, Newcastle University

12.40 Next steps and final questions, Dr Simon Woods, PEALS, Newcastle University

13.00 Close

The morning began with presentations from each speaker with time for questions afterwards. This was followed by group discussions. Notes from both are below.

Notes from presentations

Bridget Young:

Patient and public involvement (PPI) is now a 'must'. It increases quality and success of research. It makes the research more ethically valid.

Engagement needs to be defined and measured.

Engagement is important in shared-decision making - part of a process that helps patients participate.

Patients that feel engaged in decisions have greater sense of trust and satisfaction.

RECRUIT study looked at the process of recruitment in clinical trials.

Conclusions of RECRUIT –

Little vocal contribution from families in these discussions and they did not seem very engaged on the surface. But practitioners tended to ask yes/ no questions rather than seek opinions on the trial and often tried to pre-empt questions.

This is significant because misunderstandings were observed that make parents less inclined to join a trial but also *more* inclined – so it's really important that these misunderstandings are avoided.

Some young people felt it was very hard to say no, felt very pressured by parents to enter trials. They appreciated being offered a choice to speak with the doctors separately from their parents. They said it was important to have a friendly, fun atmosphere in that meeting, and wanted their doctors to get to know them as individuals.

So, engagement is not just observable interactivity – the qualitative views are important too. Although parents are sometimes seen as getting in the way of children’s engagement, they also came out as facilitators.

Asking ‘are there any questions?’ at the end typically signals the end of the session and does not encourage questions. Clinicians now do receive more training in communication skills, but this was not always the case and is not universal across the EU.

Nathalie Bere:

Patients are formally part of the governance structures of EMA.

Framework for EMA PPI relies on having network of EU patient orgs; having a form of exchange; having a pool of patients; facilitating capacity-building and training in order that patients can join the discussions.

The European Medicines Agency Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (more commonly known as the Patients' and Consumers' Working Party or PCWP) provides recommendations to the European Medicines Agency and its human scientific committees on all matters of interest to patients in relation to medicinal products. The PCWP meets four times a year.

Opportunities have been created to involve patients throughout the medicine lifecycle at EMA. So industry can come to them long before they have a drug, and work on the trial design, get scientific advice etc, all with the patient perspective.

You have to have a Paediatric Investigation Plan (PIP) by law now, for any medicine that may be used in children. Drug developers can come to EMA and they will help them with their PIP - patients are part of these meetings.

Patients are often nervous about coming to the meetings and ask what they can contribute. One of the key things is for them to share their day-to-day experiences. The EMA often find that patients are very willing to face large risks for relatively small benefits – that ratio is very interesting for regulators to see. If a drug could result, say, in a small extra movement, the regulators may not feel the risks are worth it so to hear that actually that small movement will allow you to do x,y,z and that this is important to the patient, is important.

The Paediatric Committee (PDCO) is the committee at the European Medicines Agency that is responsible for assessing the content of paediatric investigation plans (PIPs) and adopting opinions on them. This includes assessing applications for full or partial waivers and assessing applications for deferrals. The EMA is now at a stage where they involve adults quite well, but not children or young people. They need to explore how to engage them (and it will be in different ways). One way is through the PDCO.



Many paediatric trials do not start because of under-recruitment. The EMA would like to create a network of young people's advisory groups.

Anyone can come to EMA for advice in marketing a medicine. If it's an Orphan drug, you get free advice, you get reduced fees, 10 year market exclusivity, etc.

Web-radar (IMI project led by MHRA) are developing a phone App for reporting side effects. The plan is that they roll this out to include giving information to patients.

Sarah Skyrme:

There are many aspects of isolation for people living with muscular dystrophies, and some disabled children and young people may not be used to expressing themselves and their preferences, which can then impact how decisions are made.

Important that people can express their independence somehow and make decisions. Making your own mind-up about things, even, or particularly when one is physically less able can be a way of retaining a sense of self. The role of parents is crucial, in terms of providing emotional support and liaising with doctors, and providing more practical help.

The debt of care and parental bond can certainly influence decision-making on the part of the child. The ideal would be a balance, where the parents are there giving advice and support, but the child still feels the decision is theirs.

Alexander Murphy:

Children are unique and special and so paediatric trials are vital. You cannot just consider them small adults and half the dose. They are not the same anatomically, physiologically etc. And across different ages of children there are differences, e.g. in rate at which the body can excrete a particular medicinal product.

There is a difference between consenting and actually participating.

There is a major difference between assent and consent. You must be very careful to ensure you are not inadvertently taking advantage of desperate people. Importance of clinical trials to parents is clear – clinicians worry that they don't always fully appreciate that these drugs are not going to perform miracles.

What are the barriers to clinician involvement? People are nervous about the time-consuming aspects, about extra work; about the burden of being in a big multi-centre trial; may be worried about raising expectations if you are the main clinician; these are some of the barriers to clinician – esp. junior- engagement in research.

Alex Johnson:

Need for trials with endpoints other than 6MWT.

Desperation of parents to get their children included in trials is huge.

Sponsors should give clear information to participants on the possibility of extension studies after the current trial.

Parents and patients want to limit exposure to placebo.

There is a way to reduce the burden on families by for instance doing the infusions (for exon skipping) nearer to home and coming to the main trial site for the biopsies and MRIs etc (the endpoints).

Discussion Group Notes

What are the disadvantages of patient and family involvement/engagement?

- Financial burden and uncertainty of being in a trial - travelling takes much time, trial appointments being delayed or moved around is very inconvenient
- Informed parents are competitive in DMD now – can create an odd atmosphere
- Important to distinguish between being informed and being persuaded. How far do you entice a child to participate?
- Time and resource needs
- Can be unpredictable and diverse
- Too much data to share – risk of overloading patients
- Silent majority could be excluded
- May be an impact on scientific integrity – can you still do what you wanted, still have a placebo arm for example?
- Competing trials and competing parents
- May slow down the process further – patients definitely do not want this!

What are the advantages of patient and family involvement/engagement?

- It is ethically and morally right to do so
- Find out things you didn't know
- Increased recruitment and retention
- Improvement in clarity and usefulness of information provided
- Ability to testify to the benefit/risk ratio – patient perspective

- Ongoing communication with children in order to check that they are still willing to participate (e.g. enrolling them as infants, one should check at a later age they still wish to be involved).
- Create a better understanding of how and why research funding (which is raised in part by patient groups) is spent
- Use of outcome measures which are meaningful to patients
- Research is aligned with patients' priorities

Examples of good and bad practice

Good:

- Patient information days – using lab equipment, lab visits, meet the scientist
- Use of various media – video, story books, drama, gaming
- Taking account of children's personalities – treating them as individuals
- Use of play therapists
- Involving patient groups in research projects
- Consultation with patients on information materials, trial design and research planning
- INVOLVE initiative

Bad:

- Hierarchy in medicine
- Tokenism
- Having fixed ideas about what PPI is and not being flexible/open to new ideas
- Making patients/families feel that 'being difficult' will impact their care
- Ignoring the participant in research – talking over people, eg talking to just the parents.
- Not enough evidence on these things around engagement and how to make informed decisions – need more work on this. Very variable between these skills.
- Giving information in packages is helpful – so maybe practical things like feeding bits at a time, or using virtual Apps

How can the situation improve? Practical suggestions grouped into areas for potential future activity/working parties

Communication with patients and families

- Communication skills training and constant re-skilling
- Improvements in questioning techniques
- More research on what kind of communication works

- There is an ethical issue about people wanting to please their treating physician – should the trial be broached by an independent person?

Trial design

- Take into account Nuffield Council Research (<http://nuffieldbioethics.org/wp-content/uploads/Children-and-clinical-research-full-report.pdf>)
- Consider siblings in research
- Monitor inconvenience for patients and families – collect data on this from patients.
- Add cost of patient involvement into research proposals properly
- Identify best practice and promote/highlight

Information resource provision

- Drug companies compete for patients and parents have to pick between trials – really complex thought process. So fully informed consent on this is a major issue
- How do you get that independent information if you aren't so self-motivated? This is a possible role for patient organisations
- Use multi-media – must be of high quality eg apps, gaming, story-boarding, child talking to child (but don't be seduced by technology)
- Develop resources together with patients
- Avoid duplication – map current resources
- Share resources

Ethical review and authorisation

- Ethics reviews do not consider competing studies – they only look at what is on that proposal, don't consider the ethical issues for patients eligible for competing trials
- Have patients involved in the ethical side from the start, eg to judge what is a burden and what isn't. HRA could learn a lot from EMA on this, and HRA are looking at how to formalise the patient involvement in the ethics approval process
- Patients reviewing the consent forms could be mandatory
- Include training on consenting for each trial

Involving patients in research as a whole

- Create patient and family ambassadors
- Engage with young people's groups
- Engage with more patient organisations, regulators, industry and all stakeholders

Next steps

- Circulate report to attendees
- Draft a paper to report on the outcomes of this workshop for publication
- Establish working parties such as the above to develop ideas across the main themes identified
- Plan additional workshops to involve different stakeholder audiences – eg industry, (also for focussed groups from ethics, patient organisations, regulators, clinical trial staff)
- Identify and apply for additional funding sources for work identified by working parties

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